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Pandemic Profiles in Brazil

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CHAPTER 1

MAJOR EPIDEMICS IN WORLD AND BRAZILIAN HISTORY: HISTORICAL PERSPECTIVES ON COVID-19 AND RECURRING EPIDEMIOLOGICAL, SOCIAL, AND POLITICAL PATTERNS

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Abstract

Introduction: epidemics have recurrently shaped human history, influencing demographic processes, social organization, economic systems, and public health policies. The COVID-19 pandemic has renewed interest in understanding historical epidemic patterns and their implications for contemporary health systems. Objective: to analyze the most impactful epidemics in world and Brazilian history, contextualizing COVID-19 within a historical framework and identifying recurring epidemiological, social, and political patterns. Methods: this is a narrative historical-epidemiological review based on classical and contemporary literature, historical documents, epidemiological records, and scientific publications addressing major epidemics and pandemics from antiquity to the present, with emphasis on Brazil. Results: the analysis demonstrates that epidemics such as plague, cholera, influenza, smallpox, tuberculosis, and COVID-19 share common determinants, including population density, social inequality, urbanization, sanitation deficits, and delayed public health responses. Recurrent social reactions, misinformation, resistance to sanitary measures, and political tensions were observed across different historical periods. Conclusion: epidemics are not isolated events but recurring phenomena shaped by social, environmental, and political contexts. Historical knowledge is essential to strengthen public health preparedness, guide evidence-based policies, and reduce the impact of future pandemics. Keywords:

Keywords: Epidemics; Pandemics; Public Health History; COVID-19; Brazil.

Resumo

Introdução: as epidemias têm moldado recorrentemente a história da humanidade, influenciando processos demográficos, organização social, sistemas econômicos e políticas de saúde pública. A pandemia de COVID-19 renovou o interesse em compreender os padrões históricos de epidemias e suas implicações para os sistemas de saúde contemporâneos. Objetivo: analisar as epidemias de maior impacto na história mundial e brasileira, contextualizando a COVID-19 em um quadro histórico e identificando padrões epidemiológicos, sociais e políticos recorrentes. Métodos: trata-se de uma revisão histórico-epidemiológica narrativa baseada em literatura clássica e contemporânea, documentos históricos, registros epidemiológicos e publicações científicas que abordam as principais epidemias e pandemias da antiguidade aos dias atuais, com ênfase no Brasil. Resultados: a análise demonstra que epidemias como peste, cólera, influenza, varíola, tuberculose e COVID-19 compartilham determinantes comuns, incluindo densidade populacional, desigualdade social, urbanização, deficiências de saneamento e respostas tardias de saúde pública. Reações sociais recorrentes, desinformação, resistência a medidas sanitárias e tensões políticas foram observadas em diferentes períodos históricos.

Conclusão: as epidemias não são eventos isolados, mas fenômenos recorrentes moldados por contextos sociais, ambientais e políticos. O conhecimento histórico é essencial para fortalecer a preparação em saúde pública, orientar políticas baseadas em evidências e reduzir o impacto de futuras pandemias.

Palavras-chave: Epidemias; Pandemias; História da Saúde Pública; COVID-19; Brasil.

INTRODUCTION

In December 2019, cases of pneumonia of unknown origin emerged in Wuhan, China. Shortly after, Chinese authorities identified a new coronavirus as causing the disease[1]. The International Committee on Taxonomy of Viruses named the virus SARS-CoV-2[2], and the World Health Organization (WHO) designated the disease as COVID-19. After the steady increase in the number of confirmed cases, on January 30, 2020, the WHO declared the viral epidemic a public health emergency of international concern[3].

Called COVID-19, this viral disease is characterized by symptoms such as difficulty breathing, fever, cough, fatigue, and muscle pain, with the possibility of the condition getting worse to become the Severe Acute Respiratory Syndrome (SARS) and leading to death[4]. In addition, due to its high viral proliferation, it has high prevalence rate due to its rapid transmissibility and high mortality among those infected[5].

As of June 30, 2024, more than 776 million cases of COVID-19 were recorded worldwide, resulting in 7.1 million deaths. The Americas was the most affected continent in terms of number of deaths, totaling 3,023,053 deaths[6]. These figures highlight the severity of the pandemic and the continued need for surveillance and control measures. The high mortality rate in the Americas underscores the importance of implementing effective public health strategies and vaccination programs to reduce the impacts of the virus[7].

One of the main current challenges to fight the pandemic is the emergence of new variants of SARS- CoV-2 at the global level, since the accumulation of mutations resulting from subsequent viral replication is a natural phenomenon. While most mutations have no noticeable impact, some of them give rise to new, high-risk variants. The high mutability of SARS-CoV-2 demands the continuous update of treatments and vaccines, as mutations can affect the effectiveness of existing vaccines[8].

The development and updating of safe and efficacious vaccines are of immediate necessity to contain the damage of the pandemic in the areas of health, economy, and society in general. In recent years, several vaccines have been approved to reduce the negative impacts of COVID-19 and the rapid authorization of the vaccines can play a crucial role in the effective management of this serious disease[9].

Even after the implementation of vaccines and non-pharmacological strategies to combat COVID-19, such as the practice of hand washing and the maintenance of social distancing, the virus has caused high morbidity and mortality worldwide. In Brazil, from the beginning of the pandemic until mid-July 2024, 38,840,012 cases were registered by the Ministry of Health, more than 712 thousand of which resulted in death[10].

The mortality rate of 339.08 per 100 thousand inhabitants reveals the seriousness of the challenges faced by the health system, evidencing the seriousness of the complications caused by COVID-19. In addition, the incidence rate of 18,482.30 per 100 thousand inhabitants highlights the spread dissemination of the virus throughout the national territory, impacting urban and rural communities, large centers and more remote regions[5].

The southeastern region of Brazil had the significant number of 15,511,185 accumulated cases with 343,520 deaths, while in the State of São Paulo there were more than 6 million cases and more than 183 thousand deaths[10].

These numbers put into perspective the seriousness of the situation faced by the Southeast of the country. The state of São Paulo, the epicenter of the pandemic in the region, faced significant challenges in terms of hospital capacity, distribution of medical resources, and ongoing efforts to contain the spread of the virus.

The high incidence of cases and deaths reflects the population density and the complex public health management involved in facing a health emergency. There are many questions unanswered in the literature, because knowledge about COVID-19 is still uncertain about the long-term efficacy of vaccines, how long the immunity conferred by vaccines ism and how new variants affect the effectiveness of existing vaccines.

Furthermore, there are gaps in knowledge about public policies already implemented and those under implementation, as well as documentation of regional inequalities, interaction with other diseases, predictive modeling, data quality and interdisciplinarity methodological challenges.

Empirical basis of the literature

Knowledge of the past is essential for understanding the present, because in different contexts many phenomena are repeated. Mistakes made in similar situations, if known, can be prevented more effectively.

A notable example of this is found in the Code of Hammurabi in Babylon, dated 1750 B.C. In it, the governor shows concern for public health by establishing punishments for those who urinated or defecated in the canals that supplied water to the city. Even without an understanding of microorganisms or contamination, it was already perceived that such practices would compromise water quality and could cause diseases.

Although the great technological advances of the last decades may suggest the idea that the past should be set aside, it is essential to recognize that it is precisely on these historical foundations that modern science was built. The study of the past, therefore, not only helps us understand the present, but also provides the necessary foundations to build a more secure future.

In medicine, this relationship is even more evident, as the history of medicine reveals that epidemic diseases affecting humanity arise and return periodically. Understanding past outbreaks and their connections to current ones is crucial, not only from a scientific point of view, but also from a social and economic point of view. The devastating impact of an epidemic can affect various sectors of society.

Thus, it is relevant and necessary to revisit the most remarkable epidemics in history, both in the global context and in Brazil, to properly understand the damage caused by COVID-19. This study can also provide valuable subsidies for the development of strategies that mitigate the impacts of future pandemics.

In this context, we will explore the most impactful epidemics in world and Brazilian history, with a focus on COVID-19, to analyze the effects of epidemics over time.

Conceptualization of epidemics

Major epidemics have devastated nations in the past, decimating populations, limiting population growth, and often altering the course of history. These catastrophes, which affected entire populations or a large portion of them, were often referred to as the plague[11].

However, the terms “epidemic” and “endemic” have a long history in medicine. Hippocrates (fifth century B.C.) already used the term “epidemic”, and Galen (second century A.D.) used the term “endemic” with the same meaning attributed to them today[11].

The epidemic is characterized by the high number of new cases of disease and its rapid spread. Endemic, on the other hand, refers to a disease that is peculiar to a particular people, country, or region. The term “endemic” derives from the classical Greek “endemos”, which means “originating in a country”, “referring to a place” or “found among the inhabitants of the same place”[11]. In other words, “epidemos” was the term used by the Greeks to designate individuals who did not live in cities, while “endemos” referred to permanent inhabitants. Thus, these terms were associated with diseases: those of sudden onset, which affected a large part of the population, did not originate in the place and disappeared over time, were called epidemics[12].

The term “pandemic” also originates from Greek, from “pan” (whole, whole) and “demos” (people), that is, pandemic means something that affects the entire population. The word was first used by Plato (fifth century B.C.) in his book On the Laws, in the generic sense of any event involving an entire population. Aristotle (fourth century B.C.) also used the word in the same sense[13].

Galen (second century A.D.) used the adjective “pandemic” to describe epidemic diseases of great diffusion[14]. The definitive incorporation of the term “pandemic” into the medical vocabulary occurred in the eighteenth century, when it was recorded in the Dictionnaire Universel Français et Latin de Trévoux, in 1771. In Portuguese, the term was included in the dictionary as a medical term by Domingos Vieira in 1873[15].

The modern concept of a pandemic, as defined by the World Health Organization (WHO), is that of a large- scale epidemic that spreads across several countries and continents, with sustained person-to-person transmission[16].

Throughout history, changing human habits, such as the transition from hunter-gatherer societies to agrarian societies, contributed to the rise of infectious diseases among humans16. Factors such as the clustering of people in cities and their expansion, the rise of civilizations, and human interactions through travel, territorial conquests, and trade also played a significant role in the spread of infectious diseases[17].

The term “emerging infection” refers to infections that have recently emerged in a population or spread to new geographic regions[18]. Zoonotic transmission has been a key mechanism through which emerging infections affect humans[19].

Since humans began to domesticate animals, increasing contact with them, there was an increase in diseases transmitted by such animals. This phenomenon has been further intensified by the growth of interactions with wild animals, through hunting, breeding, and trade in animal foods, or exotic animal markets. The COVID-19 pandemic is a clear example of a disease transmitted from animals to humans, a result of these mentioned factors.

Causal agents

The microbiological agents responsible for epidemics are mainly viruses and bacteria. To fight them, the human body mobilizes its antibodies and triggers the immune process, known as immunity.

In medicine, the main tools to fight diseases are vaccines, in the case of viruses, and antibiotics for bacteria. Vaccines were discovered in 1796 by Edward Jenner, while antibiotics were identified by Alexander Fleming in 1929, with their use beginning on a large scale since 1941.

Although decades have passed since these discoveries, both vaccines and antibiotics remain the most effective ways to fight germs. In addition, prevention, with its various strategies, complements these weapons, is one of the most efficient methods to avoid diseases.

Since the invention of vaccines, many other immunizers have been developed, each specific to different viral diseases. However, some viruses can mutate, which can reduce the effectiveness of vaccines. Similarly, bacteria can acquire resistance to antibiotics, especially when they are used inappropriately or without appropriate medical advice. This problem led to a continuous effort by scientists to create new generations of antibiotics, capable of overcoming such resistance.

The most remarkable epidemics in history

Many diseases have devastated humanity since man has existed on Earth, but, in the form of epidemics, some of them, due to their largely deleterious effect and the exacerbated number of victims, were more impactful and, in addition, there are impressive reports about them from their contemporaries that made them better known[20].

In this sense, using this paradigm, we will discuss those that we have chosen as the most impactful in history.

The plague of Athens (V century B.C.)

It struck Athens in the fifth century before Christ. More specifically, in the summer of 430 BC, a mysterious disease arose and quickly spread among the inhabitants of Athens, which caused a great impact.

The disease was unknown, and by this time Athens was at war with Sparta, the Peloponnesian War, for dominance of Greece. The two city-states headed the major military alliances of the time, the Delian League, led by Athens, and the Peloponnesian League, led by Sparta.

The latter city-state eventually emerged victorious and gained supremacy from Greece, and probably the plague of Athens was an influential factor in the Peloponnesian War that favored Sparta. The Peloponnesian War was very well described by the Greek historian and general Thucydetes (Thukydides, 460-400 BC) who wrote “History of the Peloponnesian War”.

Concerned with impartiality he reports the facts concisely and seeks to explain the causes, he saw the Peloponnesian War as an event of great relevance to the history of Greece, more than any other previous war. Thucytes also became the most important author on the Plague of Athens, because it occurred in the city when he was weaving his accounts of the conflict.

The disease began in the port area and then spread to the rest of the city. The epidemic devastated the city between 430 and 429 BC, lost strength in 428 BC and intensified in 427 BC. It is believed that she may have been responsible for the deaths of 35% of the population of Athens[21] which may, in fact, have influenced the outcome of the long war between the two cities, even more so that, among the fatal victims of the epidemic, was Pericles, the great leader and military strategist who idealized the Delian League, who died of the plague in 429 BC.

Interestingly, years earlier, when Xerxes, the powerful Persian king, invaded Greece, an epidemic had helped the Greeks defeat the Persians and was described by Herodotus as the Plague of Xerxes, because the dysentery that spread among the Persian army weakened the soldiers causing Xerxes and his army to be defeated at Plataea, ridding Greece of the Persian threat[12].

Thucytes’ account of the plague of Athens is impressive: “people were first attacked by intense heat in the head, redness and inflammation in the eyes, and the inner parts of the mouth (both the throat and the tongue) immediately turned the color of blood and began to exhale an abnormal, foul-smelling breath. In the next stage, sneezing and hoarseness appeared, and shortly afterwards the illness descended into the chest, followed by a strong cough.

When the disease settled in the stomach, it was disturbed and vomiting of bile of all kinds mentioned by the doctors occurred, followed also by terrible malaise, in many cases there was a desire to vomit producing violent convulsions, which sometimes ceased quickly, sometimes a long time later”

... “The unknown disease punished with such violence that it disconcerted human nature. The birds and carnivorous animals did not touch the corpses, despite the multitude of them that remained unburied. If anyone touched them, he fell dead...”

... “No temperament, robust or weak, resisted the disease. Everyone got sick, whatever the regime adopted. The most serious thing was the despair that took hold of the person when he felt attacked: he immediately lost hope and, instead of resisting, he gave himself up entirely. They defiled each other and died like flocks” [21].

Thucytes also reports that the population, fearing death and judging it inevitable, surrendered to hedonism (*) to satisfy their desires without caring about the consequences of their actions, in addition, the large number of deaths caused unburied corpses to spread throughout houses, streets, and religious temples[21].

The situation described would be repeated in other epidemics, at other times in history. The disease certainly, as many historians believe, found virgin soil in Athens, that is, the population had never had contact with it and that is why it was so disastrous.

He also observed that birds that fed on the flesh of corpses also died and people who had been affected, but survived the disease, were not affected again or if they were, had mild symptoms, anticipating immunology[21].

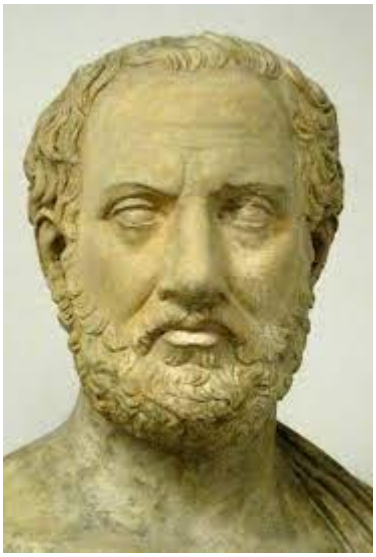

Figure 1: Thucytes (460-400 BC).

About what was the disease that caused the Plague of Athens, there are controversies among historians and scientists, however, studies in a mass grave in an ancient cemetery of Athens, allowed the Greek Manolis Papagrigorakis, in 2006, to raise the hypothesis of typhoid fever, because DNA samples found in the teeth of the victims of the Plague of Athens identified the presence of the bacterium that causes typhoid fever Salmonella enterica serovar typhi. The tests for the agents of plague, typhus, anthrax, tuberculosis, smallpox and bartonellosis were negative[22].

Here is an observation: the identification of the causative agent of past epidemics was done through techniques of identifying the DNA of the germ directly from the skeleton of the victims, however a great advance in paleomicrobiology techniques was the isolation of microbial DNA directly from the dental pulp of victims of past epidemics[23].

This new method became possible because the bacteria are trapped in the dental pulp of the victims at the beginning of the bacteremia and can be isolated from their preserved teeth. Therefore, the analysis of the dental pulp is more effective than that of the bones and is what has made it possible to discover the disease-causing agents of the past, as in the case of the Plague of Athens.

The way Greece was established and devastated in that period, the number of victims, as well as Thucydetes' accurate accounts make the Plague of Athens one of the most striking epidemics in history.

The Justinian Plague (XVIII century) VI A.D.)

A large-scale epidemic that began in Egypt and spread throughout the Eastern Roman Empire between 541 and 544 AD[24].

The Justinian Plague claimed the lives of an unprecedented number of people in the Eastern Roman Empire, making it one of the great pandemics in history. The capital, Constantinople, was the most affected and after the initial outbreak there was a resurgence every 8 to 12 years for two centuries. High mortality may have contributed to the decline of the Eastern Roman Empire.

The Justinianic plague was reported dramatically by Procopius of Caesarea (490/500 – 560/70) who was a historian, military chronicler and his reports constitute the main source on this pandemic episode[25].

He wrote "The History of Wars" which narrates the military campaigns undertaken by Emperor Justinian I aimed at the reincorporation of the Italian Peninsula and North Africa into Roman rule but ended up reporting the disease contemporary to the emperor's period that remained known as the Justinian plague.

Figure 2: "The Plague of Athens" (1652) Painting by Michael Sweertz (1624-1664).

The identification of the pathogen of this epidemic was made by DNA samples taken from the skeletons of the victims, with Yersinia pestis (formerly called Pasteurella pestis) being the etiological agent identified as the causative agent of the bubonic plague[26].

Yersinia pestis is a gram-negative, rod-shaped, facultative anaerobic bacterium transmitted by fleas associated mainly with rodents[27]. Fleas acquire the bacteria by sucking the blood of an infected rodent, inside them the bacteria multiply rapidly and block the fleas' alimentary canal[28]. The fleas then transmit the bacterium to new rodent hosts, regurgitating the clotted blood. Plague manifests itself in three forms: bubonic, septicemic, or pneumonic[29].

The pneumonic form is the deadliest, has a fulminant onset and is fatal if left untreated, the bubonic is fatal in 50 to 90% of cases, and the septicemic form is more deadly than the bubonic[30].

The earliest account, however, of the plague is found in the Bible referring to the plague that struck the Philistines. They took the ark of the Lord and were punished: "The hand of the Lord came against that city with great vexation, for it smote the men of that city from the small to the great, and they had hemorrhoids in the secret parts" (1 Samuel 6:9). "Make therefore images of your hemorrhoids and the images of your rats, which go about destroying the earth, and give glory to the God of Israel" (I Samuel 6:19, The Holy Bible, 1981, pp. 287- 289)[11].

It is noted that the peoples of that time already established a relationship between buboes (mistakenly translated as hemorrhoids in the Bible) and rats, otherwise the offering of atonement would not be constituted in this way[31].

The reference to hemorrhoids would have been a translation error because the term "Epholim" in the original Hebrew text has the meaning of swelling, swelling and could refer to the infarcted ganglia in the inguinal region (buboes) and not to hemorrhoids, so much so that in other more recent editions of the Bible its organizers changed the term hemorrhoid to tumors (The Holy Bible, 1993 pg. 302-303)[11]. In any case, this seems to be the oldest report on the disease.

The Black Death

Beginning in the Middle Ages, having emerged in East Asia, it swept through Central Asia and Europe through the land and sea trade routes of the Medieval Silk Road[32].

It was called the Black Death due to the bruises that appear on the victim's body and appeared in 1347 and remained until 1551. In this period it killed, according to historians, 30% of the European population, but others claim that this number may have been higher, reaching half the population of the Old Coninent[12].

One of the most interesting accounts of the plague is in the book Decameron by Giovanni Boccaccio, as he wrote the work between 1348 and 1353, therefore in the midst of the Black Death. Right at the beginning of the work he reports:

"... we had already reached the year 1348, when, in the very important city of Florence... the deadly pestilence has come... no prevention was worthwhile, all the measures of men were in vain... Neither doctor's advice nor virtue of any medicine seemed to bring cure or benefit to the treatment.

The plague in Florence did not behave in the same way as in the East. In this one, when the blood came out of the nose, whoever it was, it was an evident sign of inevitable death... At first, both in men and women, or in the groin or armpit, some swellings appeared... the one who called the people buboes... it began to reappear and appear everywhere. Then the appearance of the disease began to change; dark or pale spots appeared on the sick. In some they were large and scattered, in others, small and abundant"[33].

Boccaccio also reveals the behaviors of the population at that overwhelming moment, in two main types: lust, people began to drink and indulge in pleasures and the other recollection, people withdrew in groups, praying and practicing asceticism, that is, having disciplined and controlled behaviors.

A parallel is noted here with Thucytes' description of the hedonistic behavior of people in the plague of Athens, showing how people are reacting in similar conditions.

Another impressive account is that of the surgeon Guy de Chauliac who lived in Avignon, France and was the most famous surgeon of the time, including the physician of Pope Clement VI. Chauliac who survived the plague left the following account:

"... The great slaughter began in Avignon in January 1348. The epidemic presented itself in two ways. In the first two months it manifested itself with fever and bloody expectoration and the sick died within three days; After that time, he manifested himself with continuous fever and swelling in the armpits and groin, and the patients died within five days. It was so contagious that it spread quickly from one person to another; the father did not go to see his son, nor the son his father; charity had disappeared completely"[11].

Possibly based on experiences of ancient cultures dealing with contagious diseases, medieval societies observed the link between the passage of time and the eruption of symptoms.

Noting that after a period of observation, individuals who did not develop symptoms of the disease would likely no longer be affected and, more importantly, would not spread the disease upon entering the city. To this end, they began to institute mandatory isolation.

The first known quarantine was decreed in Ragusa (city-state of Dubrovnik) in 1377, where all arrivals had to spend 30 days on an island near Lokrum before entering the city. This 30-day period (Trentino) was later extended to forty days (forty giorni or quarantine)[34].

The institution of quarantine was one of the rarely effective measures that occurred during the Black Death, and its use spread rapidly throughout Europe. Quarantine remains in place today as a highly regulated public health measure, nationally and internationally, available to combat contagion[35].

The plague also inspired the creative imagination of famous painters. The most notable paintings are: The Plague in Athens, by the Belgian painter Michael Sweerts (1624-1664); The Plague in Naples, by Domenico Gargiulo (1612-1679); The Triumph of Death, by the Belgian painter Pieter Bruegel the Elder (1510-1569) and Saint Roch, by Bartolomeo Mantegna (1450-1523). He also inspired Albert Camus, Nobel Prize for Literature, to write one of his best-known works: The Plague11 (Figure 3 and 4).

Although this was the largest pandemic in history related to Y. pestis, the plague continued to reappear in Europe until the nineteenth century, having been the most damaging appearances

after the Black Death (1347-1351), the plague of Milan (1630), the great plague of London (1665-1666) and the plague of Marseille (1720-1722)[37].

It is believed that the bacterium may have persisted in rodent reservoirs in Europe and therefore periodically resurfaced in the human population[37]. Another hypothesis suggests that the new waves of plague in Europe in the seventeenth, eighteenth and nineteenth centuries were caused by Asian rodents and may have arisen due to maritime trade.

Figure 3: "The Plague of Naples" (1656) by Domenico Gargiulo (Micco Spadaro) (1609-1675)(National Museum of Naples – Italy).

Figure 4: "The Triumph of Death" (1562) by Pieter Bruegel the Elder (1525-1569)(Prado Museum – Madrid).

The last plague pandemic originated in the midnineteenth century in the Yunnan region of China and spread to Hong Kong[33] and ended up reaching Japan, Singapore, Taiwan and India through the ships. In the following years it became endemic in many countries[37].

In 1894, the Swiss Alexandre Emile Jean Yersin discovered the bacterium that causes the plague, studying cases in Hong Kong, where the third great plague epidemic was taking place. In his honor, the bacterium was renamed Yersínia pestis.

The plague has currently been classified by the World Health Organization (WHO) as a reemerging infectious disease since the 1990s. Between 2010 and 2015, the number of plague cases was estimated at 3,248 with 584 deaths worldwide, most occurring in the Democratic Republic of Congo, Madagascar, and Peru[38].

Cholera

It produced seven major global outbreaks and therefore deserves to be highlighted, remaining endemic in Asia until the beginning of the nineteenth century, more specifically until 1817, when a first pandemic spread from India to other regions of the world. It is an acute, often fatal, disease of the gastrointestinal tract caused by Vibrio cholerae. The pathogen is transmitted by water. Humans become infected through contaminated water used for drinking or preparing food[39].

The bacterium is gram-negative and is a facultative anaerobe that colonizes the small intestine and produces cholera toxin, which is responsible for the rapid and massive loss of body fluids, leading to dehydration, hypovolemic shock, and death[30].

V. cholerae can form a three-dimensional biofilm where organisms can survive for long inter-epidemic periods[40].

The main factor that made cholera go from being an endemic disease to the pandemic was the improvement of transportation, because with the advent of steamships and railways, travel time was significantly reduced, bringing people closer together, expanding trade and thus enabling contact with infected people[35].

Subsequently, five major cholera epidemics spread to other continents from India[39]. When the second cholera pandemic hit the British Isles in 1854 during the cholera outbreak in the city of London, Soho, Doctor John Snow did observational work using epidemiological methods to discover the origin of the outbreak that he identified as a public water pump in a well contaminated by feces that came from a nearby cesspool[40,41].

He then proposed removing the handle from the pump so that it would no longer be used and was able to stop the outbreak[42]. This is considered the first epidemiological study carried out and for this reason Snow is cited by many authors as the father of epidemiology.

Figure 5: “Cholera” (1848) Painting by Pavel Fedotov (1815-1852).

The cholera bacillus was discovered by Robert Koch in 1884, during the fifth pandemic that affected South America. Koch also stressed the importance of drinking water in preventing the transmission of the disease[42].

Cholera is still present today and it cannot be eradicated because it is a natural inhabitant of aquatic ecosystems. In 2019, 923,037 cases and 1,911 deaths were reported to WHO in 31 countries.

However, the global burden of cholera is estimated to be higher due to underreporting. Between 2008 and 2012, the number of cases ranged between 1.3 and 4 million per year, with 95,000 deaths[43].

The cholera pandemics that occurred in the nineteenth century show situations that are very similar to those that occurred with COVID-19, especially regarding information controversies and inappropriate and erroneous manifestations by a part of the media.

An interesting article published in the journal "História Ciências, Saúde-Manguinhos" in 2011, authored by Maria Antônia Pires de Almeida of the New Lisbon University of Portugal, shows how the press acted unfavorably in relation to the Cholera Epidemic in Portugal that occurred from 1853 to 1855, prioritizing the economic side to the detriment of the health of the population.

The newspapers countered the sanitary measures imposed by the authorities, which prohibited the concentration and circulation of people and goods, with the denial of contagion, which evidenced the uselessness of these measures:

"Now it seems to us that if cholera were contagious, like plague, scabies, or leprosy, at least it would have seized you. health delegate, who has had so much contact with and trade with people coming from the Douro..." (O Comércio, June 21, 1855, p.2;44).

The newspaper "O Comércio" of Portugal also transcribed an article published in the "Jornal do Commercio" of Rio de Janeiro on September 4, 1855 that sought to reassure the population:

"After vigorous observation, fatal experience, and serious discussion, all the most cultured peoples of Europe agreed to regard cholera as non-contagious. ... Let us see, then, some proofs, observations, and experiments. In truly contagious diseases, such as syphilis, bladders, hydrophobia, vaccinium, etc., there is always an organic substance secreted during the illness, which, when inoculated, will infallibly produce the same disease.

In cholera morbus none of this is observed. The symptoms are those of a veritable poisoning by an imponderable agent spread in the air, producing the annihilation of the vital forces, diminution or suppression of the main functions, and followed by a violent but healthy reaction when the toxic principle is repelled from the economy. "The rapidity of the spread of the epidemic should still dispel the idea of its contagion" ... "without it being possible to admit the transmission of miasmas emanating from the body of the sick"[44].

This discussion present in the newspapers reflected the trend of the time, which divided the defenders of the contagion theory and its opponents. The nineteenth century saw the emergence of a new generation of scientists who denied it, basing themselves on the ineffectiveness of quarantines and cordons sanitaires (especially at the time of the cholera epidemic of 1832), consigning it to the realm of the fantastic, absurd and childish[44].

Thus, a clear association between anti-contagion theories and commercial interests was verified. Porto, a liberal, mercantile city in full industrial and commercial development, reacted violently against the authority of the capital, which forced it to the cordon sanitaire[44].

All this shows how behaviors are repeated, how interests overlap with care in human societies regardless of the time of occurrence of an epidemic, and why it is so important to know the past.

The flu

Responsible for one of the most impactful pandemics in history, the Spanish Flu, it is considered a seasonal disease. Its causative agents, influenza viruses, are classified into four types: A, B, C and D. Among these, only type A has pandemic potential[45].

The influenza A virus is endemic in several species, including humans, birds, and swine. The possibility of genetic rearrangements between influenza A viruses of human and animal origin may give rise to new viral subtypes with pathogenic capacity for humans[46].

The origin of the term "influenza" is controversial. Some authors suggest that the name stems from the ancient belief that diseases were caused by the influence of the stars. Others claim that it comes from the Italian influenza del freddo, coined in the sixteenth century, alluding to the higher incidence of the disease during the winter[47].

Another hypothesis goes back to the miasmatic theory, according to which the cold wind would bring miasmas, odors or poisonous elements from swamps or decomposing matter, therefore, the disease caused by the "influence" of the winter winds[12].

The term "flu" would have French origin. The word grippe means "complaint", although there are records of the use of gripper, also from French, with the meaning of "to grab". The French used this term to describe the disease that "grabbed" a person and left them bedridden for a few days[12].

It is not known for sure when the flu virus began to infect humans, nor what its first pandemic was. However, many historians point to the sixteenth century as the probable period of the first influenza pandemic[48].

There are also those who argue that the term "flu" originally meant "passing disaffection" or "sudden fantasy", having been used by Voltaire in a letter of 174348. Of all the epidemics recorded, the flu stands out as one of the most deadly in history and has accompanied humanity since its beginnings. Historical records mention diseases with symptoms compatible with influenza.

Hippocrates, considered the father of Western medicine, would have described, around the fifth century B.C., a respiratory disease that killed many people in a few weeks and then disappeared, suggesting what today would be recognized as an influenza outbreak[49].

Although the identification of the virus was only possible with the invention of the electron microscope in the 1930s, it is believed that several previously documented diseases were, in fact, episodes of influenza, based on clinical and epidemiological descriptions[47]. Scientific publications have referred to influenza since 1650, and there are indications of pandemics since the sixteenth century[50].

Even in the face of scarce data and the absence of formal scientific reports, researchers have been dedicated to identifying possible influenza pandemics throughout history, analyzing the symptoms described in old records[50]. There are also reports of outbreaks in the fourteenth and fifteenth centuries[47]. One of the first more detailed medical descriptions was made by Molineux, between 1688 and 1693, in Ireland and England[47]. From the last decade of the nineteenth century, the records became more reliable and subject to revision. In the second half of the twentieth century, with viral analysis, it is possible to scientifically confirm the status of a pandemic[50]. With the advances in science in the twenty-first century, researchers have been able to access genetic material from the Spanish Flu virus.

In a first, a team led by John Kash of the University of Washington in Seattle traveled to Alaska to obtain lung tissue samples from an Eskimo woman preserved by frozen ground since 1918. The virus identified was H1N1, one of the strains of influenza[12].

The Influenza virus, belonging to the Orthomyxoviridae family, has a single-stranded RNA segmented genome. About 75% of emerging human pathogens are RNA viruses, many of which are transmitted through the respiratory tract or mucosa[51]. Types A, B, and C were isolated in 1933, 1940, and 1947, respectively[52].

Type A can infect humans and animals and is associated with epidemics and pandemics. Type B, which affects only humans, is linked to moderate outbreaks. Type C, on the other hand, is more stable, and affects humans and pigs, causing disease that is usually subclinical and without epidemic potential[47].

Due to their high transmissibility and ability to mutate, viruses A and B represent a constant concern for public health, especially due to their potential to cause high morbidity and mortality. Type B is subdivided into the Yamagata and Victoria lineages[52]. Influenza A viruses are classified based on the surface proteins hemagglutinin (HA) and neuraminidase (NA), which are responsible for the entry and release of the virus into host cells[53].

The first well-documented flu pandemic was the so-called Russian Flu, which occurred between 1889 and 1893[54]. Serological and epidemiological evidence suggests that it was caused by the A/H3N8 virus[54]. This virus spread rapidly, going around the world in just four months. For three years, it reappeared annually, causing about 1 million deaths. Despite this, its lethality was considered low, with rates between 0.10% and 0.28%[55].

The Spanish flu

The 1918-1919 pandemic, caused by the Influenza A/H1N1 virus, originated from the genetic adaptation of an avian influenza virus to a new human host56. This pandemic event developed in at least three distinct waves over a span of just nine months.

The first wave, which occurred during the spring and summer of 1918, was characterized by high morbidity and low mortality. In contrast, the second and third waves, between the summer and autumn of 1918 and the winter of 1918-1919, had high mortality rates. The pandemic, known as the Spanish Flu, is estimated to have caused approximately 500 million infections and about 50 million deaths worldwide[57].

The dangerousness of the influenza virus is largely due to its ability to infect several animal species, such as migratory and aquatic birds, swine, and domesticated birds. This wide range of hosts favors the emergence of hybrid viral strains with pandemic potential.

A virus originally present in waterfowl, for example, can acquire the ability to infect humans, for whom there is no prior immunity. In addition, there is a possibility of co-infection in pigs with avian and human viruses, resulting in genetic rearrangements that originate a new strain with fragments of avian, porcine and human RNA, endowed with high transmissibility and lethality[12].

This seems to have been the evolutionary dynamics of the Influenza A H1N1 virus responsible for the Spanish Flu. With contemporary scientific resources, it was possible to identify the virus through the analysis of RNA fragments taken from the lungs of victims of the pandemic, whose bodies were preserved in regions of frozen ground.

The most accepted geographic origin of the pandemic dates back to the city of Haskell, in the interior of the state of Kansas, in the United States, in 1918. At the time, Haskell was a rural community of approximately 1,700 inhabitants, dedicated to grain production and the raising of animals such as pigs, poultry, cattle and horses, ideal conditions for the emergence of a mutant influenza virus[12].

The local doctor, Dr. Loring Miner, trained in Ohio, noticed a sudden increase in the number of cases of flu with severe clinical condition, affecting even previously healthy young people.

Despite having alerted the authorities, the cases temporarily ceased, which reduced the perception of risk[58]. However, about 300 km from Haskell, there was a military camp with about 56,000 soldiers, gathered in tents in precarious conditions, waiting to be embarked on the European front of the First World War.

This agglomeration favored the spread of the virus. Infected soldiers, when receiving visits from family members or on leave, spread the disease to various regions of the United States[12].

Although some theories suggest that the disease originated in China, based on the presence of 140,000 Chinese workers recruited by the British in 1917[59]. Or even that it was already circulating in Europe before the arrival of the Americans[12], the hypothesis with the greatest scientific acceptance is that of American origin.

The name “Spanish Flu” arose from the fact that Spain, as a neutral country in the war, openly reported the epidemic, unlike the belligerent nations, which avoided disseminating information so as not to shake the morale of the troops.

The pandemic spread rapidly across the globe, with a mortality rate of between 0.5% and 2% of the world’s population. It is estimated that between 20 and 50 million people have died, although there are authors who point to even higher figures, close to 100 million deaths[50].

The mortality rate varied significantly between regions, being higher in places where influenza had not previously circulated. In the United States, for example, it reached about 1% of the population; in Samoa, 25%; in Alaska, it decimated entire communities of Eskimos; and in India, an estimated 12 million lives are lost[12].

From August 1918, the second wave began, significantly more lethal than the previous one. In the northern hemisphere, the death rate peaked: about 45,000 American soldiers were hospitalized, with mortality around 10%. Germany accounted for approximately 225,000 deaths; Italy, 375,000, with 400 deaths per day in the city of Turin alone. Paris recorded 5,000 weekly deaths and England reached 225,000 fatalities[12].

Faced with the overload of funeral services, coffins became scarce, being replaced by improvised coffins with wooden doors. Trams began to transport corpses and the use of masks was compulsorily adopted in several cities12. University gymnasiums, churches, theaters and public offices were converted into field hospitals (Figure 6).

In a few days, the cases multiplied and the deaths began. He notified the authorities, but shortly thereafter the cases decreased and not much importance was given to what happened[58].

Figure 6: Dr. Loring Miner (1860-1935).

However, about 300 km away there was a military camp, as the US had entered World War I since April 1917 and 56,000 soldiers housed in tents were waiting to embark for Europe.

The place became conducive to the virus, with such a large human agglomeration in close proximity since the camp did not have the proper conditions of a barracks. Soon many of the young soldiers fell ill and spread the disease to various corners of the USA, because, on leave or receiving visits from family members, the contamination advanced[12].

This was the trigger for the spread of the Spanish flu, although there are authors who raise the possibility that the disease originated in China, since at the end of 1917 there were 140,000 Chinese recruited by the British as war workers[59].

Others claim that the flu was already circulating in Europe before the arrival of the Americans[12]. However, the most accepted hypothesis is in fact the American origin. The name “Spanish Flu” came about because Spain, being neutral in the War, reported in its tabloids the emergence and advances of the flu and the belligerent countries naturally did not do so so as not to shake the morale of the troops.

The Spanish flu quickly spread around the world, with a high mortality rate. Around one fifth of the world’s population has been affected, with a mortality rate of about 0.5% to 2%. The statistics of the time and yet, due to the circumstances of war, are not precise, it is estimated that 20 to 50 million people died worldwide, although there are those who predict the possibility that this number is much higher, reaching up to 100 million. In any case, these are numbers that will never be known precisely, but 20 million is a very low estimate for the size of this pandemic[50].

Mortality varied from region to region and was much higher in places where influenza had never manifested itself, where the population therefore lacked immunity. The United States of America has reached the mark of 1% of its population, in Samoa, in Oceania, mortality has reached 25%, in Alaska several groups of Eskimos have disappeared and in India, the country with the record number of deaths, it is estimated that 12 million lives have been lost[12].

From August 1918 onwards, a second wave of the disease began, much more lethal than the first that occurred earlier that year. The death rate peaked in the Northern Hemisphere, Americans admitted 45,000 men to war hospitals, and about 10% died. The Germans lost 225,000 people, Italy 375,000, with 400 deaths per day in the city of Turin alone, Paris had 5,000 deaths per week and England reached the mark of 225,000 deaths[12].

The mortality was so overwhelming that there were not enough coffins to cover the demand, even wood from old doors was used to make coffins, and public transport, such as trams, had their seats removed and turned into hearses. The population started to wear masks on the face, which is mandatory in some cities (figure 2). University gymnasiums, churches, theaters, public offices, clubs, were transformed into field hospitals[60].

Figure 7: Professionals and passers-by wearing masks in the US, which in severalcities has become mandatory.

Octors at the time tried to contain the spread of the disease with available resources, recommending inhalations with eucalyptus oil, camphor and menthol substances, as well as oral hygiene with potassium permanganate, gargling with warm water and salt, alcohol intake and hygiene practices such as washing hands and isolating the sick[60].

The pandemic potential of influenza guarantees it a prominent place in the history of epidemics[53]. The most well-known and well-documented pandemics were those of 1889, 1918, 1957, 1968, 1977, 2003, and 2009 (50,52), with emphasis on the 1918 one, considered the most devastating. The viruses that caused these pandemic episodes were:

The influenza viruses that caused these pandemics were: 1889-1890 (research suggests the Influenza A virus subtypes H2 and H3); 1918 -1920 (Influenza A H1N1 Virus); 1957–1958 (Asian Flu, Influenza A H2N2 Virus); 1968–1969 (Hong Kong Flu, Influenza A H3N2 Virus); 1977–1978 (Russian Flu, Influenza A H1N1 Virus); 2003- 2004 (Avian Influenza, Influenza A H5N1 Virus) and 2009 (2009 Pandemic, Pdm 09, Influenza A Virus, H1N1)[47].

The most remarkable epidemics in the history of Brazil.

We can consider the most striking epidemics in the history of Brazil to be those that affected a large number of the population with a high mortality rate in a short time. Therefore, we will analyze some aspects of these epidemics.

Brazil's first major epidemic

Before the arrival of European colonizers, the indigenous population of the territory that today corresponds to Brazil had a good state of general health, with a low incidence of infectious diseases. Among the few diseases recorded among these peoples, yaws, also known as pian or piã, a skin infection prevalent in tropical regions, and goiter, observed especially among populations far from the coast, with low iodine intake[61].

The arrival of the Europeans, however, triggered a real epidemiological disaster among the native peoples. Diseases that had not existed on the American continent until then, such as influenza, measles, dysentery and smallpox, were introduced into the territory by the colonizers. The indigenous people, isolated for millennia from the centers of diffusion

of infectious agents in Eurasia and Africa, had not developed immunity against these exogenous pathogens. Thus, despite their low burden of pre-colonial diseases, which included, in addition to yaws, diseases such as cutaneous leishmaniasis, these people became extremely vulnerable to the new health reality[62].

Indigenous resistance to the European invasion proved ineffective in the face of the devastating impact of infectious diseases. The death of the native population occurred mostly as a direct or indirect consequence of these imported diseases, rather than as armed confrontations with the invaders.

In this context, the wars waged by the indigenous people against the colonizers were, in a way, already lost even before they began, given the absence of a minimum collective immunity against foreign pathogenic agents[62].

The same phenomenon occurred in other territories of the Americas invaded by Europeans, as in the case of the Spanish conquest of the Aztec Empire, led by Hernán Cortés, in which epidemics contributed decisively to the collapse of local civilizations.

It is estimated that, in the sixteenth century, the Brazilian indigenous population varied between two and four million individuals. Currently, this number is around 800 thousand, representing a population reduction of more than 80%[12].

In this sense, historian Warren Dean's observation is particularly blunt:

"Of all the weapons carried in the caravels of Europeans, none was as effective as their diseases in doubling the resistance of the peoples of the New World. In fact, the epidemic disease is the key to understanding the course of imperialism in the New World"[63].

In the seventeenth and eighteenth centuries, Brazil was still an essentially agrarian country, characterized by large farms, especially the mills in the Northeast. During this period, the absence of large urban centers and low population density were factors that hindered the occurrence of epidemics of great magnitude. Cities like São Paulo, for example, until the end of the eighteenth century, remained small villages, with a very rudimentary urban structure.

However, from the nineteenth century onwards, especially in its second half, with the advent of the Industrial Revolution in Europe, Brazil began a more accelerated urbanization process, following the patterns of the Old World. Rio de Janeiro, then the capital of the country, grew significantly after Independence, while São Paulo began to industrialize, attracting a significant contingent of European immigrants. At the same time, there was intense internal migration, from the countryside to the cities, which led to the formation of tenements and precarious housing in urban regions that were not prepared for the disorderly population growth. This scenario has created favorable conditions for the spread of infectious diseases in an epidemic way.

The sanitary conditions in the main Brazilian cities began to reflect, belatedly, the problems already experienced in industrialized Europe. In London, for example, women and children were subjected to working hours of more than 12 hours; in Manchester, there was one latrine for every 250 people; in Liverpool, 40,000 individuals lived in unsanitary basements, and it was common for three people to live together per bed[12].

In Brazil, the situation was also critical. In Rio de Janeiro in the nineteenth century, for example, the enslaved were responsible for transporting the population's waste in large vats, emptying it in the rivers or directly into the sea, due to the lack of an efficient sanitary sewage system. The lack of hygiene and adequate urban infrastructure, combined with the growing population agglomeration, has transformed the Brazilian urban environment into a fertile ground for the outbreak of epidemic outbreaks.

Thus, from the nineteenth century onwards, Brazil began to be more susceptible to the occurrence of epidemics, as a direct consequence of accelerated urbanization and precarious sanitary conditions. After the epidemics that decimated indigenous populations at the beginning of the colonial period, those caused by yellow fever, tuberculosis, cholera morbus, smallpox, bubonic plague, Spanish flu and, more recently, the COVID-19 pandemic stand out as the most impactful in the country's history.

Yellow Fever

The first reference to yellow fever in Brazil dates back to 1685 with the occurrence of an outbreak in 4 urban areas of the Captaincy of Pernambuco: Recife, Olinda, Ilha de Itamaracá and Goiana[64].

The yellow fever virus and the mosquito that transmits it Aedes aegypti, came together from Africa on slave ships. In 1686, its African origin was admitted, so much so that the French colonies received instructions to take sanitary measures to avoid the yellow fever infection coming from Africa[64].

Although the concept at the time was linked to the miasmatic origin of epidemic diseases, sanitary measures were taken at that time and it seems that they would have been the first of their kind. Among these measures were the burning of clothes and the lighting of fires to ward off miasmas, but, coincidentally, they were measures that had an effect, not for the reasons imagined, but because they drove away the causative mosquito, then unknown[64].

Sometime later, from 1686 to 1692, the disease reached the population of Salvador in Bahia where it caused about 25,000 sick people and 900 deaths during the 6 years it raged there[64].

Until 1849, however, yellow fever was not very active in the country, however, when the American ship "Brazil" arrived in Salvador that same year, coming from New Orleans and Havana, places where the disease existed in an overwhelming way, it spread through the ports and coast of Brazil[64].

An article published in the Gazette Medicale of 07/06/1850 gives an idea of what was happening in Rio de Janeiro at that time:

"The latest news from Rio de Janeiro, dated March 29, announces that the intensity of yellow fever had only decreased in Rio de Janeiro, with more than 200 deaths per day in the city"[65].

The yellow fever epidemic of 1850 had an excessive number of deaths in Rio de Janeiro of the 166,000 inhabitants the disease reached 90,658 causing 4,161 deaths, that is, 2.5% of the population[66].

An American newspaper of the time published that yellow fever was the most serious of the 3 most present infections in Rio de Janeiro, the other two were smallpox and bubonic plague, as it had killed around 60000 people in Rio de Janeiro between 1850 and 1908.

The then director of public health, Oswaldo Cruz, appointed by the President of the Republic, Rodrigues Alves, had carte blanche to fight yellow fever. He instituted a mosquito killing brigade that invaded houses even without the residents' knowledge to destroy possible foci of dissemination of the mosquito vector of yellow fever.

Oswaldo Cruz, despite being harshly fought and criticized by the press of the time, managed to beat yellow fever in Rio de Janeiro, having been internationally recognized.

In São Paulo it was much less intense, with the largest outbreak occurring in the city of Campinas, at the end of the nineteenth century.

Tuberculosis

Tuberculosis is an ancient disease, whose origin dates back to prehistoric times. Archaeological evidence indicates the presence of the disease since at least 5,000 B.C., with records of bone lesions compatible with tuberculosis identified in human skeletons dated by carbon-14, although, in these cases, the etiology cannot be stated with certainty[67].

The first more robust evidence of the disease was identified in 44 Egyptian mummies from Thebes, dated between 3,700 and 1,000 BC. Many of these mummies showed destruction and fusion of vertebrae, alterations compatible with what is currently called Pott's disease – the bony form of tuberculosis. In one of the mummies, the preserved lung had pleuropulmonary lesions and the presence of blood in the trachea, reinforcing the presumptive diagnosis of the disease. Several Egyptian pharaohs fell victim to tuberculosis and died at a young age, including Pharaoh Amenhotep IV and his wife Nefertiti, around 1,300 BC[67].

Despite its long existence in human history, tuberculosis gained significant epidemiological importance from the nineteenth century onwards. In large cities, workers began to live in extremely

precarious conditions, often crowded into basements, tenements, and unhealthy housing, a scenario that decisively favored the spread of Mycobacterium tuberculosis[12].

Close and constant contact between individuals in overcrowded environments allowed tuberculosis to take on epidemic characteristics. In the nineteenth century, disease became a true social scourge in various parts of the world. During the urban remodeling of Paris, promoted by Baron de Haussmann, for example, it is estimated that approximately 80% of deaths among the poorest population, expelled to the outskirts of the city, were caused by tuberculosis. In the rest of Europe, during the same period, the disease was responsible for about 30% of all deaths[67].

In Brazil, records indicate that, in 1855, approximately one in every 150 inhabitants had the disease68. However, it was only in 1882 that the German physician Robert Koch identified the etiological agent of human tuberculosis, Mycobacterium tuberculosis. The first effective antibiotic against the disease, streptomycin, was only developed in 1943.

Between 1851 and 1950, it is estimated that tuberculosis caused the death of about one billion people worldwide, which is equivalent to an annual average of 10 million deaths, or approximately 833 thousand per month and 27,766 per day. Even with the therapeutic advances achieved in the twentieth century, the disease continued to cause a high number of deaths. Between the 1990s and 2000s, between 30 and 35 million people died from tuberculosis, with 98% of these deaths concentrated in poor or developing countries[67].

In Brazil, the infection rate remains high. Data from the Epidemiological Bulletin of the Ministry of Health, dated March 26, 2018, indicate that, annually, between 70 and 100 thousand people are infected by Koch's bacillus and develop tuberculosis.

In 2016, the disease was responsible for the death of 4,426 Brazilians. More recent information from the Pan American Health Organization (PAHO) indicates that, globally, about 1.4 million people die annually as a result of tuberculosis, which represents a monthly average of 116,666 deaths, or approximately 3,888 per day. In Brazil, the March 2020 Epidemiological Bulletin counted 4,490 deaths from tuberculosis that year.

The severity of tuberculosis throughout history is also evidenced by the number of notable victims that the disease has caused in Brazil. Among the deceased are renowned names in the arts and politics, such as Glauco Velásquez (30 years old), Álvares de Azevedo (20 years old) and Castro Alves (24 years old), among many others[67].

Cholera morbus

Cholera remained restricted to Indian territory for millennia, without causing an epidemiological impact in other regions of the world until the beginning of the nineteenth century. This scenario began to change from 1817, when, with the Industrial Revolution, the conditions for international travel became more favorable, also facilitating the spread of infectious diseases.

Prior to this period, the progression of cholera was limited, as those infected often did not survive the long journey of sea voyages on sailing ships. However, with the advent of steamships, distances were shortened and crossing times shortened, which allowed infected individuals to arrive still alive, but contagious, in new territories[12].

The first cholera pandemic began in the Ganges River Valley, in India, between 1817 and 1823, spreading rapidly to several regions of Asia, Africa and Europe. In the context of the third global pandemic of the disease, cholera arrived in Brazil in 1855, and the first location affected was the then Province of Grão-Pará, current state of Pará.

The vector was the ship Defensor, from Portugal, which landed in Brazil with 12.8% of the crew dead as a result of symptoms compatible with cholera, such as intense diarrhea and dehydration. From the north of the country, the disease spread to other regions, reaching the states of the North, Northeast, Southeast and South regions (Figure 8).

Figure 8: "Cholera Morbus" (1858) by Constantino Chaves da Motta, portrays the arrival of cholera in Pará, in 1855, brought by the ship Defensor from Portugal.

In December 1855, cholera had already reached the province of Pernambuco. The impact was devastating, it is estimated that, in that province alone, there were 32,586 deaths, in a period when Recife, the capital of the province, had about 60 thousand inhabitants. In the city of Recife alone, until May 1856, 3,338 deaths were registered, which represented approximately 5.5% of the local population.

In the 12 years following the introduction of the disease in the country (1855 and 1867) it is estimated that cholera caused approximately 200 thousand deaths in Brazil. At the time, the national population was estimated at about 13 million inhabitants, which represents 1.5% of the total population. For comparison purposes, if mortality had been proportional to the current Brazilian population (211 million inhabitants), the number of deaths would be equivalent to approximately 3.165 million people.

The first effective antibiotic substance against Vibrio cholerae, the etiological agent of cholera, was doxycycline, discovered in 1955 and made commercially available from 1967 onwards. However, the main method of controlling the disease still lies in prevention, through basic sanitary measures, such as access to drinking water, sewage collection and treatment, and public sanitation policies[12].

Smallpox

Smallpox is among the diseases that have caused the most deaths throughout the history of humanity, being known since time immemorial. It is estimated that its lethality rate varied between 20% and 43% of cases, in addition to frequently leaving permanent sequelae, such as deep scars and blindness[69].

A key milestone in the fight against the disease occurred in 1796, when Edward Jenner, in England, developed the first smallpox vaccine. Their finding was based on the observation that women who milked cows rarely contracted smallpox, as they had already been exposed to Variola vaccinia, a mild form of the disease.

In Brazil, the first official record of smallpox dates back to 1563, on the Island of Itaparica, in Bahia, where the disease affected and killed numerous indigenous people. At the beginning of the twentieth century, a violent epidemic hit the city of Rio de Janeiro, then the federal capital, during the winter of 1904, resulting in a high number of deaths.

In contrast, the city of São Paulo, although it has a neighborhood called “Bexiga”, a direct reference to the disease, had a milder impact during the same epidemic. At the time with an estimated population of 239,820 inhabitants, the city recorded 328 deaths from smallpox, which corresponded to approximately 0.14% of the population.

In this context, the sanitary doctor Oswaldo Cruz, already consecrated for his work in the fight against yellow fever, sent the federal government a bill that aimed to ratify and regulate the mandatory vaccination against smallpox. Although this obligation had already been provided for since 1832, the rule had never been fully applied[70].

The proposal generated intense controversy. The National Congress and the press became the stage for heated debates, and opposition to the measure emerged from various sectors of society, including the military, monarchists, workers influenced by positivism, students, journalists and even medical professionals[70].

The peak of tensions was the outbreak of a popular revolt between November 10 and 16, 1904, in the city of Rio de Janeiro, known as the Vaccine Revolt. The trigger was the publication, in the newspaper “A Notícia”, on november 9 of that year of the project to regulate mandatory vaccination. Among the measures planned were the requirement of proof of vaccination for school enrollment, access to the labor market, and the work, travel, accommodation and weddings, in addition to the application of fines to those who refused to get vaccinated[70].

For a week, thousands of people took to the streets of the capital to protest. Businesses were closed in several neighborhoods, the public transport system collapsed and the urban order was deeply shaken. During the instability, there was an attempt at a military coup, with the aim of deposing President Rodrigues Alves, who refused to remove Oswaldo Cruz, the main target of popular dissatisfaction.

The government declared a state of siege on November 16 and, with the support of the Army, managed to quell the revolt. The mandatory vaccination campaign was temporarily suspended. The final toll of the Vaccine Revolt was severe: 30 dead, 110 injured, 945 arrested, sent to Ilha das Cobras, and 461 people deported to the then territory of Acre (Figure 9).

Figure 9: Cartoon from the magazine “O Malho” 29/10/1904 about the “vaccine revolt”.

In 1906 the number of deaths from smallpox in Rio had fallen almost to zero, to only 9, however 2 years later, in 1908 a new and violent epidemic raised the number of deaths to more than 6,500 cases, around 1,000/100,000 inhabitants, an unusually high rate, the revocation of the vaccine mandate took its toll[70].

In the sixties of the twentieth century, Brazil instituted a smallpox eradication program beginning in 1966. In August 1973, an international commission presented Brazil with the certificate of eradication of smallpox. Mandatory vaccination remained until 1975[70].

Bubonic Plague

The bubonic plague, caused by the bacterium Yersinia pestis, has manifested itself in several outbreaks throughout history, the most devastating being the one that occurred in the fourteenth century, known as the Black Death, which killed about a third of the European population, already addressed in a previous chapter[71].

In Brazil, the first officially recorded cases of bubonic plague occurred on October 18, 1899, in the port city of Santos, being diagnosed and confirmed by the physician and scientist Vital Brazil. It is believed that the disease arrived in the country from China, transported by merchant ships that docked in Brazilian ports[72].

The spread of the plague throughout the national territory was rapid. In 1900, the disease reached the city of Rio de Janeiro, then the federal capital, and, the following year, it reached the city of São Paulo. Faced with the growing threat, Brazilian health authorities have adopted emergency measures. In June 1901, the newly created Butantan Institute began the production of anti- plague serum, considered at the time the main therapeutic weapon against plague, according to the guidelines of the Pasteur Institute in Paris. The following year, the Butantan Institute also began to manufacture the anti-plague vaccine, based on the technique developed by the Italian physician Camillo Terni, in turn inspired by the vaccine created by the Russian physician Waldemar Haffkine[73].

It is important to note that the Butantan Institute was founded in 1901, under the name of Serum Therapy Institute, installed at the Butantan Farm, in the west of the city of São Paulo74. Its main objective, since its foundation, was the production of vaccines and serums against the bubonic plague, in line with similar efforts carried out in the federal capital, where the Federal Serum Therapy Institute had been created in May 1900, installed on the Manguinhos Farm, in the north of Rio de Janeiro[75].

The fact that the Butantan Institute was able to develop and start the production of an effective vaccine in just one year, as early as 1902, shows the institution's long scientific tradition and its ability to respond quickly to health emergencies76. Such a historic feat acquires special relevance when considering the scenario of the COVID-19 pandemic, during which the institute was once again the target of unfounded criticism by sectors of society that, due to ignorance of the history of medicine, claimed that it was unfeasible to produce a vaccine in the short term. However, historical experience shows that, since the beginning of the twentieth century, Brazil already had scientific institutions capable of developing immunizers with efficacy and agility in the face of epidemiological crises[77].

The bubonic plague caused significant mortality in Brazil. Between 1900 and 1901, in the city of Rio de Janeiro, approximately 500 people died as a result of the disease[78]. In São Paulo, the outbreak reached not only the capital, but also several cities in the interior of the state, later expanding to other regions of the country, such as São Luís (Maranhão), Porto Alegre (Rio Grande do Sul) and locations in the state of Rio de Janeiro.

The Spanish flu in Brazil

The first references to the presence of influenza in Brazilian territory date back to the initial period of colonization. Among the diseases brought by the European colonizers, who devastated the indigenous populations, the flu was already present as one of the infectious agents responsible for this high mortality[12].

However, the most expressive manifestation of the disease in Brazil, as well as in much of the world, occurred during the Spanish flu pandemic, which arrived in the country in September 1918. The main vector of the introduction of the virus on Brazilian soil would have been the Demerara ship, with an English flag, coming from Liverpool, with a stopover in Lisbon, which docked successively in the ports of Recife, Salvador and Rio de Janeiro[79].

The arrival of the virus in the country and its rapid spread have exposed the fragility of public health policies, evidenced by the initial hesitation of health authorities and the press itself to recognize the seriousness of the problem[47].

At first, the epidemic was treated with neglect by government authorities, media outlets and even the population. Many described the disease as a common flu, without major consequences, and even labeled it as a "flu to clean up the elderly", alluding to its selective lethality among the elderly and weakened. Popular concerns focused more on the possible restrictive measures to be adopted by the authorities than on the disease itself[12].

However, reality imposed itself in a forceful way. The first serious cases began to appear in the city of Rio de Janeiro, then the federal capital, and deaths quickly multiplied. Doctors and sanitarians warned that health services were on the verge of collapse, given the shortage of beds and the high demand for medical care. With the uninterrupted advance of cases, criticism of the ineffectiveness of government measures, considered slow and insufficient, has also increased[79].

Public opinion, the media and the political opposition began to put pressure on the government. In response to the crisis and the loss of legitimacy, several members of the administration were dismissed, including those directly responsible for combating the epidemic[12]. Contemporary reports at the time reveal the extreme severity of the clinical condition of the Spanish flu. Mota Rezende, in 1919, described in great detail the symptoms and the rapid evolution of the disease:

"The speed of contagion was extremely fast, the incubation period was short and the number of people affected by the disease was very high, as well as the degree of lethality. The symptoms were varied. From simple ringing in the ears, deafness, headaches and simple hyperthermia, the disease developed with symptoms such as chills, hemorrhages, urine and vomiting of blood, accompanied by disturbances in the heart nerves, infections in the intestines, lungs and meninges, leading the victim to suffocation, diarrhea, stabbing pain, lethargy, coma, uremia, syncope and finally death in a few hours or a few days"[11,80].

Faced with the health crisis, the federal government turned to one of the greatest medical authorities in the country: physician Carlos Chagas, then director of the Oswaldo Cruz Institute, since Oswaldo Cruz's death in 1917. Chagas was appointed to lead the national campaign against the Spanish flu. His performance was decisive80. He organized field hospitals in the main Brazilian cities, ordered the closure of schools and prohibited events with agglomerations of people. In Rio de Janeiro, 27 service stations were established at railway stations, aiming to expand the population's access to medical care[81].

In addition, he led a broad awareness campaign through newspapers, posters and pamphlets distributed to the population, with guidance on hygiene, food and isolation of the sick. He called on the medical community to collaborate in facing the crisis and, through the Oswaldo Cruz Institute, fostered scientific research on the new virus[81].

Thanks to these actions, by the end of 1918 the pandemic was relatively under control in Brazil. In recognition of his work, Carlos Chagas was appointed by President Epitácio Pessoa to take over the direction of the newly created National Department of Public Health in 1919, consolidating himself as a central figure in the history of Brazilian public health[82].

Figure 10: Improvised field hospitals.

The Spanish flu pandemic had profound and wide- ranging repercussions in Brazil, affecting not only the public health sphere, but also national politics. One of the most emblematic episodes of this tragedy was the death of the then re-elected president Rodrigues Alves, who died on January 16, 1919, victim of the disease, even before taking office for his second presidential term[83].

As the epidemic worsened, the number of deaths increased rapidly. The daily life of cities was drastically altered: commerce collapsed, with stores being closed due to the absence of employees in working conditions, and public services became insufficient to deal with the dimension of the health catastrophe[84].

Many citizens fell ill and died at home, without any kind of medical care. There are historical reports that point to desperate practices adopted by the population, such as the exposure of the feet of corpses in the windows of homes to signal to the health authorities the need to remove the bodies. In more extreme cases, the dead were left directly on the streets, evidencing the collapse of funeral services[84].

As expected, the regions with higher population density suffered a more severe impact. It is estimated that the city of São Paulo lost about 1% of its population, while Rio de Janeiro, then the federal capital, recorded an even higher mortality rate, close to 1.5%. Both cities were epicenters of viral dissemination in the country, concentrating on the highest number of severe cases and deaths[85].

The data regarding the number of victims of the Spanish flu in Brazil, however, are the subject of controversy among scholars. Official records point to about 35,000 deaths in the national territory. However, authors such as Bertolli Filho[73] estimate that in the cities of São Paulo and Rio de Janeiro alone, deaths totaled at least 35,240 people, a number considered underestimated in relation to the real magnitude of the tragedy. In Brazil, official data suggest that the death toll may have reached 300,000 deaths, which places the pandemic as one of the most lethal episodes in Brazilian health history.

The Spanish flu in São Paulo

In Brazil, the disease arrived in September 1918 and affected the State of São Paulo in October of the same year. The State of São Paulo was going through a condition that possibly increased the vulnerability of the population to diseases, since, in that year, coffee growing, the main source of dividends in the State, had suffered two hard negative impacts, a strong frost and a cloud of locusts had decimated a good part of the coffee plantations in São Paulo, causing an increase in prices and food prices[86,87].

The flu drastically affected the social organization of the State because it significantly altered routines, habits and customs, including making many of the determinations of the Sanitary Code of the time impractical.

São Paulo, however, was not yet the gigantic industrial center that it would become, but its population already had about 600,000 inhabitants, while in the federal capital, Rio de Janeiro, it reached 910,710[73].

In 1918, São Paulo had 204 municipalities. The Spanish flu devastated practically everyone; however, the most affected cities were naturally the most populous, with the capital being the most affected, including the highest number of deaths. Statistical data began to be carried out in São Paulo after the creation of the Sanitary Service in 1892, because among its multiple functions was to organize demographic-sanitary statistics with the objective of preventing and combating communicable diseases[88].

Although in 1919 some municipalities in São Paulo had an increase in the number of deaths from influenza, according to statistics, the impact of the Spanish flu in general in São Paulo was much greater in 1918 than in the second outbreak that occurred in 1919[88].

In a comparison with the total number of deaths in the state between 1917 and 1919, it is observed that, in 1917, of the total of 7,908 deaths, 74 were due to influenza, in 1918 of the total of 14,811 deaths, 5,372 were due to influenza and in 1919, of the total of 9,985 deaths, 354 were due to influenza[74].

Regarding the behavior of the Spanish flu, Bassanezi's study shows that in the various localities of the state of São Paulo, the population affected by the disease showed different traits in the different localities analyzed, although some of these traits were common to all of them and even to other countries, because, in these traits, the volume and characteristics of the population interfered, the natural conditions, the socioeconomic and sanitary context, the way the authorities and the population of the localities reacted to that calamity, etc[89].

The intense process of urbanization that the city of São Paulo was going through at that time, with the arrival of immigrants and migrants from other states and by the natives of the state themselves coming from the interior in search of better working conditions, significantly and quickly increased the population, making São Paulo the most populous municipality in the state and therefore the most affected, reaching the death rate from the Spanish flu between September and December 1918 of 1% of the population[90].

Another aspect is that the Spanish flu affected more men than women because at the time men occupied more public spaces more frequently and for longer than women and also, due to immigration in search of work, the population also had a larger contingent of men than women[84].

Another interesting condition concerns the population at risk. The elderly, in the beginning, were naturally considered the population at risk, however, what was observed was the opposite, they were not the biggest victims of the flu. In the state of São Paulo, they corresponded to between 2% and 4% of deaths from influenza, while children aged 0 to 2 years represented, in the city of São Paulo, 30.4% of deaths and in the other municipalities around 20% of deaths[91].

The Spanish flu also affected, on a larger scale, the young population with greater productive and reproductive capacity (20 to 23%) in the state of São Paulo and in the city of São Paulo the population between 15 and 49 years of age reached a mortality rate of 46.7%[92,19].

According to Bassanezi, in the first half of the twentieth century, in São Paulo, foreign mothers, in addition to the children they already brought with them from their places of origin, were responsible for more than half of the births that occurred in the state of São Paulo and, in addition, most of them were illiterate, unaware of prophylaxis care, which was possibly the reason they can't stop the high mortality rate of their children[20].

In the city of São Paulo, 85.9% of the deaths from the Spanish flu occurred in November 1918 and in December the number of deaths fell drastically. The new wave in 1919 lasted until May, but in the city of São Paulo, it was much weaker, although in some cities in the interior, very few, they claimed more victims than the outbreak of 1918.

The COVID-19 pandemic

On December 1, 2019, the world was about to experience another critical moment in its history, as in the city of Wuhan in Hubei province in China, a new coronavirus capable of infecting humans was identified. It was registered and reported, on December 31, 2019, to local health authorities as something new and capable of causing damage to public health.

The fact, initially, did not draw the attention of the rest of the world in a significant way, being interpreted as another seasonal disease to affect the Asian continent and that should be restricted to that country.

On January 1, 2020, China began to take steps to clarify and control the disease, such as isolating people who had had contact with sick people and in addition to carrying out tests that identified the virus that causes the disease. Studies began to be carried out to clarify more about the origin and transmission, aiming to guide authorities and health professionals[93].

With the first death, days later and the number of cases increasing, a market for exotic animals in Wuhan drew attention, which had been known since 2007, as publications had warned about the risk of consuming exotic animals because these are reservoirs of uncataloged viruses that could cause diseases still unknown[94].

The hypothesis was raised that a mutant virus originated from bats, animals consumed as delicacies by the local inhabitants, and similarities with the virus that causes SARS were then established. However, the contagion of people unrelated to the place and the consumption of these animals was surprising[95].

China closed the city of Wuham, establishing a strict quarantine from January 23, 2019, when the rest of the world began to turn its attention to the millennial country, but it was too late, the new coronavirus had already crossed borders starting a pandemic. The name of the virus has a Latin origin, corona means crown and refers to the spikes of the protein coating that covers it, a condition that increases its transmission capacity and its ability to adhere to cells. It is an enveloped RNA-positive virus, from the same subgenus as the virus that causes SARS (severe acute respiratory syndrome) in 2003, which is why it was named SARS-COV-2[95,96].

It was called the new coronavirus because it is a mutant virus with the potential to infect humans and cause a pandemic, since it has no natural defenses for them. Many hypotheses were then raised, as is common when something new emerges for which science has no evident explanation, such as that the virus would have been created in the laboratory[95].

The World Health Organization (WHO) declared on March 11, 2020 that the world was facing a new pandemic and named the disease caused by the new coronavirus COVID-19 (“CO” for coronavirus, “V” for virus, “D” for disease, and 19 because it began in 2019). The WHO started to issue alert bulletins to countries, passing a week after the 1st Bulletin, the risk from moderate to high[96].

The Old Continent collapsed, countries like Italy and Spain had a brutal increase in cases and also in the number of deaths, with the health system collapsing, with no ventilators and beds for all patients, health professionals had to choose who would live or die. The most affected age group was over 60 years of age. Soon after, it was the turn of the United Kingdom, which at the beginning had, like other countries, underestimated the disease, which was the reason for an apology, later, from its Prime Minister. Drastic measures such as the closure of shops, schools, curfews and even lockdown (confinement of people at home) were taken. North America, especially the United States, also saw cases multiply in a frightening progression and the country became the champion in the number of deaths[97].

In South America, Brazil was not far behind, although it took safety measures such as quarantine, even before the appearance of the first case in the country on February 26, a month after the first case already had almost 3,000 infected. Five months later, in July, the country already had 2 million infected and 85,000 deaths98. In March 2021, Brazil ranked 2nd in the total number of deaths from COVID-19, behind only the United States[99].

COVID-19, caused by the SARS-CoV-2 virus, emerged in December 2019 in the city of Wuhan, China, and quickly spread around the world, being declared a pandemic by the World Health Organization (WHO) in March 2020. The disease is transmitted mainly by respiratory droplets and aerosols, but it can also spread through contaminated surfaces. The most common symptoms include fever, dry cough, fatigue, and loss of taste or smell, while severe cases can progress to pneumonia, severe acute respiratory syndrome (SARS), and multiple organ failure. The pandemic has profoundly impacted health systems, economies, and societies around the world, with millions of cases and deaths recorded[100].

To control the spread of the virus, governments have adopted measures such as lockdowns, social distancing, wearing masks, and frequent hand hygiene. In addition, the development of vaccines in record time, using innovative technologies such as mRNA and viral vectors, was

crucial to reduce severe cases and deaths. However, uneven distribution of vaccines and vaccine hesitancy in some regions posed significant challenges. Variants of the virus, such as Delta and Omicron, have emerged over time, increasing transmissibility and, in some cases, partially escaping the immunity conferred by vaccines or previous infections[100].

By 2023, COVID-19 began to become endemic in many regions, with seasonal outbreaks and an adaptation of societies to living with the virus. Despite this, the pandemic has left a lasting legacy, highlighting the importance of science, global collaboration, and preparing for future health crises. Lessons learned include the need for robust health systems, strategic stockpiles of medical supplies, and rapid and effective response plans. Equity in access to vaccines and treatments has also proven essential for an effective global recovery.

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CHAPTER 2

INTEGRATED ACTIONS AND STRENGTHENING PUBLIC HEALTH SYSTEM IN BRAZIL IN A TIME OF PANDEMIC

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Abstract

The National Health System, being named unique in the Constitution because it refers to a set of elements, such as universalization, equity, integrality, decentralization and popular participation and which is in convergence with the Constitution of 1988 of the Federative Republic of Brazil, which states that health is a right of all and a duty of the State.Thus, with the creation of SUS, the entire Brazilian population now has the right to universal and free health care, financed with resources from the budgets of the Union, the States, the Federal District and the Municipalities, as regulated by article 195 of the Brazilian Constitution. It is noteworthy that SUS is one of the most powerful and important in the world and it serves about 220 million people. It is characterized by a foundation of three pillars: universality, integrality and equity.

Keywords: Public health; Unified Health System; Universalization of Health; Health Equity.

Resumo

O Sistema Único de Saúde (SUS) é a denominação do sistema público de saúde no Brasil, sendo nominada de único na Constituição por se referir a um conjunto de elementos, tais como a universalização, a equidade, a integralidade, a descentralização e da participação popular e que está em convergência com a Constituição da República Federativa do Brasil de 1988, em que nomina que a saúde é um direito de todos e dever do Estado. Assim, com a criação do SUS, toda a população brasileira passou a ter direito à saúde universal e gratuita, financiada com recursos provenientes dos orçamentos da União, dos Estados, do Distrito Federal e dos Municípios, conforme rege o artigo 195 da Constituição Brasileira. Destaca- se que o SUS é um dos mais pujantes e importantes do mundo e que atende cerca de 220 milhões de pessoas. É abrangente e se caracteriza por três pilares de sustentação: a universalidade, a integralidade e a equidade.

Palavras-chave: Saúde pública; Sistema Único de Saúde; Universalização da Saúde; Equidade em Saúde.

The National Health System (SUS - Sistema Único de Saúde), being named unique in the Constitution because it refers to a set of elements, such as universalization, equity, integrality, decentralization and popular participation and which is in convergence with the Constitution of 1988 of the Federative Republic of Brazil, which states that health is a right of all and a duty of the State[1].

Thus, with the creation of SUS, the entire Brazilian population now has the right to universal and free health care, financed with resources from the budgets of the Union, the States, the Federal District and the Municipalities, as regulated by article 195 of the Brazilian Constitution1. It is noteworthy that SUS is one of the most powerful and important in the world and it serves about 220 million people. It is characterized by a foundation of three pillars: universality, integrality and equity[2].

The SUS is comprised by the next components: care centers and basic health units, public hospitals - including university hospitals, laboratories and blood centers (blood banks), health surveillanceservices,epidemiologicalsurveillance,environmentalsurveillance,inadditiontofoundations and academic research institutions and scientific entities.

Universality is a principle that considered health as a right of all and a duty of the State, with the health of the citizen being a fundamental right and of stone cause1. Comprehensiveness gives the Brazilian State the duty of extensive care, with priority for preventive actions, without prejudice to assistance services in relation to the access that any and every citizen is entitled to. The principle of equity is related to the constitutional commandment that health is a right of all, and that all citizens must be treated in a way that their rights to health are guaranteed by the Brazilian State in an impartial manner, respecting the equality of rights[1].

Decentralization, on the other hand, refers to public health actions and services that are part of a regionalized and hierarchical network and constitute a single system, organized at all federal levels - Union, States, Federal District and Municipalities. The principle of social participation also called social control, acting in the formulation and control of the execution of public health actions and services[1]. Thus, SUS is constantly evolving and is characterized as the Duty of the State and of Brazilian society.

In this view, epidemiological surveillance, which aims to promote the detection and prevention of communicable diseases and their risk factors, as well as the preparation of studies and standards for epidemiological surveillance actions, are essential for an effective action of SUS, how to plan, monitor and standardize techniques for immunization in the State; institute, develop, implement, train, coordinate and evaluate actions of epidemiological surveillance and assistance, with the purpose of constant integration with Primary Care, aiming at the exchange of information and efficient execution of the proposed plan, having as a target the identification of risks factors, preventive activities with vaccination, focus on early diagnosis, containment of outbreaks and the provision of appropriate treatment.

During the time of pandemics where there is a high impact on public health due to the high number of cases in a short period of time with a greater number of infected people, the country is able to (re)organize health practices that can quickly provide assistance to the population, from prevention and promotion to actions aimed at treatment, control, cure and rehabilitation.

In this understanding, preparedness plans are needed to face pandemics, making it important to distribute the responsibilities of every sector of Brazilian society. It is up to the population, in the event of a pandemic, to follow the guidelines of health authorities, such as containment and mitigation. The Containment phase refers to early identification, treatment and isolation of cases and following up on close contacts. The Mitigation phase, on the other hand, consists of monitoring the epidemiological situation and prioritizing assistance to serious cases or those with potential for complications.

The SUS should seek guarantees for the best service to the Brazilian population and to all those in its territory. In this line, it seeks a strategy to develop actions that range from non-pharmacological practices aimed at empowering the population to research for new discoveries, such as medicines and vaccines.

At the presente time, Brazil is suffering a pandemic, and the SUS is facing it, however, it must be point out that investment in research in national science has decreased over the past recent years, as well as maintenance research granaries, in the laboratories of the various Brazilian Universities, especially those public ones. There was a restriction on the transfer of resources and no supplementation of funds, which caused losses for the completion of research and application of new protocols already outlined.

It is not possible, in the event of a pandemic, to bring new discoveries, since the research processes are totally dependent on the systematization and ordering of scientific processes.

In turn, in order to maintain the scientific debate, as well as the dissemination of science, the Journal of Human Growth and Development - JHGD, in the year of its thirtieth anniversary, continues to contribute to the scenario of disseminating research in the multidisciplinary field and Public health.

Their articles in issue one of volume 30 highlight several scientific contributions, such as Pimentel et al.[3] on the spread of COVID-19 outside China and its exponential growth in Europe and its spread to the American continent; Vieira et al.[4], on the nutritional profile of women served by the Family Health Strategy Maranhão, Brazil, with the conclusion that socioeconomic factors have a significant association with the Body Mass Index of women, being an important contribution to the full understanding of the role of the strategy of Family Health.

In the same line, the contribution of Diniz et al.[5] on the monitoring of adolescents from the program Health at School (Programa Saúde na Escola), brings out the fact that they are specific actions that do not meet the needs of teenagers. For Macêdo et al.[6], doing an assessment of growth and nutritional status of school-age children in Public Schools in Florianópolis, Santa Catarina, found overweight and obesity among those children.

In addition, aspects of guidelines and practices in the feeding of children with Cerebral Palsy[7], speech therapists are essential to provide protective measures to the lower respiratory tract[6].

In the motor control of movement, there is a contribution from Santos et al.[8], showing that girls who practice classical ballet have specific characteristics of plantar pressure and develop different strategies for postural control. Furthermore, in the body self-perception of school age children with Down Syndrome (DS), Silva et al.[9], found that there is a relationship between body and environmental stimuli on psychomotor and cognitive development, however, development does not occur in children simultaneity with growth, with chronological differences.

Education is another topic under discussion. Nowadays, the problems experienced at school are still latent. Thus, bullying in the school environment[10], from the understanding of educators, the solution of this problem should be sought between the association of educators and the family nucleus, from the detection of a situation of bulling in the school environment by educators. For Pacheco et al.[11] the reception room for socio-educational measures, as a long-term space for psychosocial and medical care, violates the basic rights of comprehensive care for adolescents.

For Moura et al.[12], the interactions of babies/ young children in a host institution (shelter), were uncommon, however when they occurred, children showed sensitivity and responsiveness to emotional- communicative expressions, contributing to a good emotional development.

In regards to perinatal health, there is an important contribution on the validation of a food consumption frequency questionnaire for pregnant women attended in basic health units, with the suggestion of a potential instrument to be used in the evaluation of food consumption in pregnant women[13]. About overweight/obesity and subjective food insecurity, Viera et al.[4] highlight the need for the State to provide effective strategies for the population to become aware that an adequate nutritional status is the best prevention against occurrences resulting from chronic diseases common among obese people, being the competence of the public power, to defend and protect the population in their human rights adequate food and health, meeting the demand for a democratic, fair and egalitarian society.

The diversity of contributions is added to the interesting article on cannabis: from a plant condemned by prejudice to one of the great therapeutic options of the century[14], due to the understanding of molecular signaling that modulates the different senses, being a potential revolution in the therapeutic area in which phytocannabinoids represent one of the great options of the century.

From the Amazon region, Martinelli et al.[15] highlight that the use of a low-cost instrument, such as the one that measures the beats in the RR intervals, is effective in the clinical management of adolescents with juvenile idiopathic arthritis. Câmara et al.[16], on the other hand, report the epidemiology of snakebites in the whole Western Amazon and stand out that they still behave as a public health problem of great importance due to their high incidence.

And finally, Silva et al.[17] report an interesting study on the engagement of medical students in practicing “Sexting”, highlighting that the lack of empathic skills can be worrisome among people who had already shared intimate images of their partners and creating more problems with the Brazilian criminal justice system.

Thus, the JHGD fulfills its role by disseminating scientific information in the field of public health, highlighting from COVID-19 to the daily routine of human behavior in its various settings.

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CHAPTER 3

A TIME-SERIES ECOLOGICAL STUDY PROTOCOL TO ANALYZE TRENDS OF INCIDENCE, MORTALITY, LETHALITY OF COVID-19 IN BRAZIL

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Abstract

Introduction: since the first case of COVID-19 was confirmed in February 2020, Brazil has reported more than 20 million cases and more than 600,000 deaths on October 31, 2021. The behavior of the pandemic was also different in the various states, from the less developed to the more developed, such as the state of São Paulo. **Objective:** to describe step-by-step time series for analyzing trends in mortality, lethality and incidence of COVID-19 in Brazil. **Methods:** a protocol for an ecological study of time series, covering the 26 states and the federal district (Brasilia). **Results:** the descriptions have the potential to provide information for the government and society in decision-making about knowledge and conduct, clinical, epidemiological and research investments in health care services for the Brazilian people. It is focused on fully understanding the spread of SARS-COV-2 infection in the Brazilian territory and developing a database for public and universal access for comparative studies between countries and continents. **Conclusion:** databases built from ecological studies are essential for a full understanding of the virus behavior, its transmissibility, lethality and mortality, and a repository for data collected and integrated from multiple sources. They are relevant tools for the search of information and decision-making in global health.

Keywords: COVID-19; Protocol; Time-Series; Epidemiology; Indicators.

Resumo

Introdução: a Introdução: Desde que o primeiro caso de COVID-19 foi confirmado em fevereiro de 2020, o Brasil notificou mais de 20 milhões de casos e mais de 600.000 mortes em 31 de outubro de 2021. O comportamento da pandemia também foi diferente nas várias regiões do país, desde aquelas de menor desenvolvimento econômico à de maior desenvolvimento econômico, tal qual o Estado de São Paulo. **Objetivo:** descrever o passo a passo de séries temporais para análise das tendências de mortalidade, letalidade e incidência de COVID-19 no Brasil. **Método:** etapas de um protocolo para um estudo ecológico de séries temporais e com cobertura dos 26 Estados e Distrito Federal (Brasilia). **Resultados:** as descrições possuem potencial de prover informações para o governo e sociedade nas tomadas de decisões acerca do conhecimento e conduta, clínica, epidemiológica e de investimentos em pesquisa cuidados à saude do povo brasileiro, com foco no pleno entendimento da disseminação da infecção pelo SARS-CoV-2 em território brasileiro, bem como desenvolver banco de dados para acesso público e universal para estudos comparativos entre países e continentes. **Conclusão:** banco de dados construídos a partir de estudos ecológicos são imprescindíveis ao pleno entendimento do comportamento do vírus, sua transmissibilidade, letalidade e mortalidade, bem como constitui-se em repositório para busca de informações e tomadas de decisão em saúde pública.

Palavras-chave: COVID-19; Protocolo; Séries Temporais; Epidemiologia; Indicadores.

INTRODUCTION

After the COVID-19 disease was declared a pandemic by the World Health Organization (WHO) in March 2020, governments and health authorities all over the world faced the difficult task of making decisions that seek to minimize the health, social and economic consequences of the pandemic. For example, closing borders, businesses, schools, non-essential establishments, and at the same time seeking strategies regarding when to reopen those activities and establishments[1].

Brazil is ranked second in fatalities after the United States. Since the first case of COVID 19 was confirmed in February 2020[2], cases reached more than 20 Million and there were more than 600.000 deaths as of October 31, 2021 (Coronavirus panel).

The country has a vast territory of more than 8,5Km2, Brazilian Institute of Geography and Statistics – IBGE[3] and shares borders with ten countries in South America. The pandemic has shown different trends in the various regions of the country and the less economically developed regions have been heavily affected[4].

The strategies to control the spread of the virus and consequently reduce mortality generally show a lack of coordination between the federal and state governments (University of Miami, COVID Observatory)[5]. Yet, decision-makers need estimates of the number of cases, fatalities, and lethality of the disease that may not be perfect but well-founded to allow them to make more accurate decisions. For this reason, it is essential to analyze the trends of COVID-19 incidence, mortality and lethality indicators, as well as examine the variability of these indicators over time and how they are modified according to age, sex, and place.

The analysis of those data in a given period supports estimates of disease transmission trends in the future. The conduct of ecological time-series studies may thus play an important role in forecasting those trends6 and support timely decision-making by health authorities. To conduct such analysis, we created an umbrella protocol to study future scenarios of COVID-19 incidence, mortality, and lethality for each of the 26 Brazilian states and a Federal District (Brasília).

The objective of this study is to present the protocol for the development of time series ecological studies to analyze the trend of indicators of mortality, lethality and incidence of COVID-19 in all Brazilian states.

METHODS

This is a population-based umbrella project, where each state of Brazil will be analyzed separately, following a standard protocol for ecological time-series studies. The country has 26 states and a Federal District, distributed into five well-delimitated regions (figure 1).

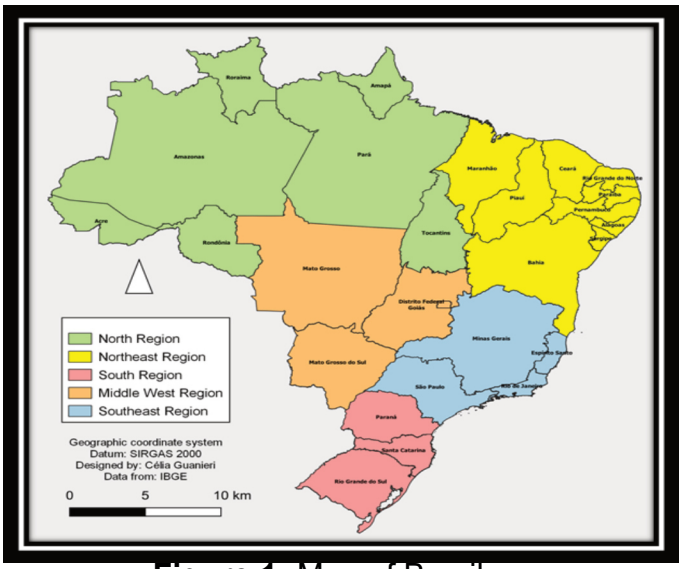

Figure 1: Map of Brazil.

Each study will be based on secondary data collected from the official database of the Ministry of Health. Figure 2 shows an overview of the main steps of the protocol that will be followed in each state.

All notifications of cases and deaths of COVID-19 reported during the selected study period will be included using the International Classification of Diseases 10th edition (ICD-10) of "U07.1 COVID-19, identified virus" or "U07.2 COVID-19, virus not identified"[7], according to clinical, laboratory or epidemiological confirmation. The cases will be classified according to symptoms and deaths data and organized by date of reporting.

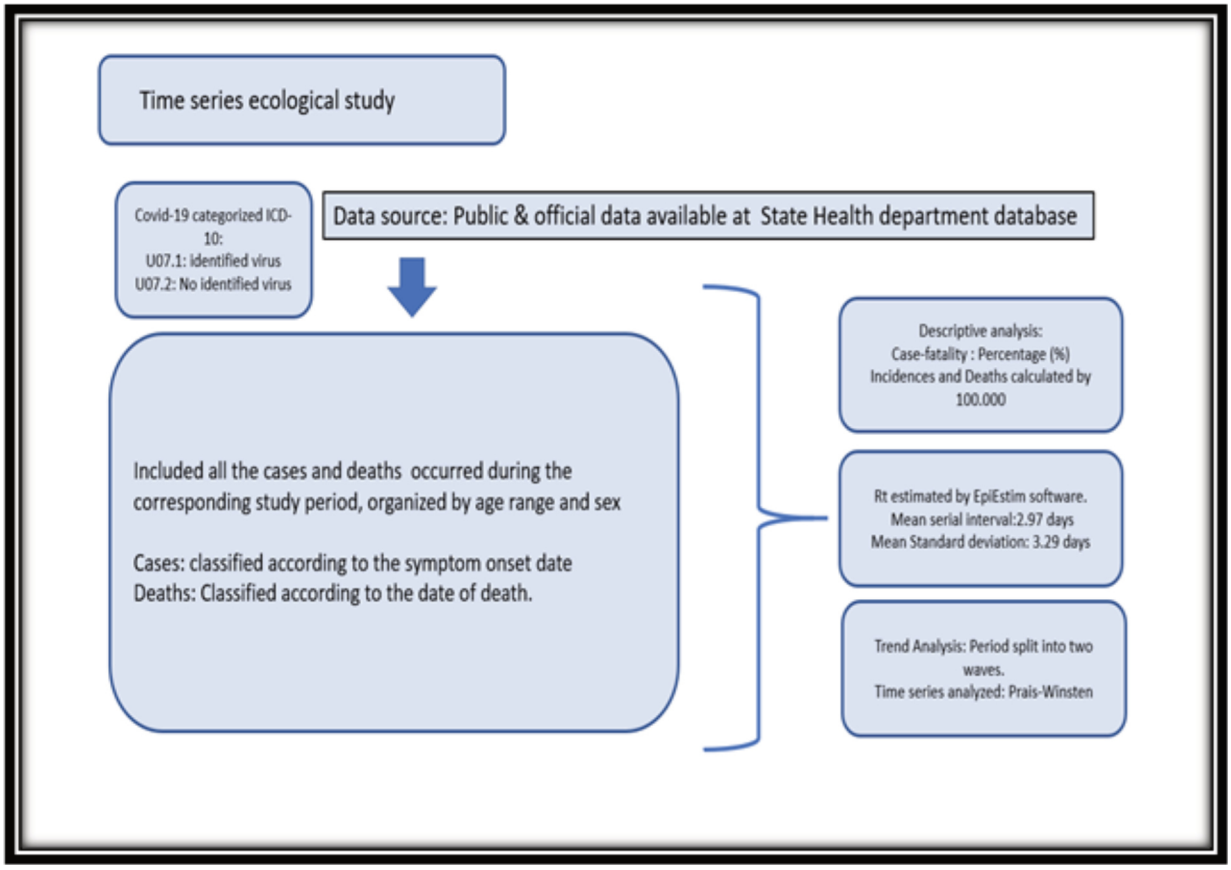

Figure 2: Overview of the main protocol stages to analyze incidence, mortality, and case-fatality by COVID-19 in Brazil.

Two researchers will extract the data independently to minimize collection bias and guarantee data quality and reliability. In case of disagreements, a third researcher will verify the data. The retrieved data will be organized in an Excel spreadsheet. The effective reproduction number (Rt) will be estimated using the R studio software EpiEstim package[8], version 2.2.4, a previously time-dependent reproduction number for epidemics guided by Thompson et al.[9]. We employed a mean serial interval of 2.97 days with a mean standard deviation of 3.29 days, as described in prior studies[10,11].

The incidence (A) and mortality rate (B) will be calculated per 100,000 inhabitants, and case-fatality (C) represented as a ratio. Those indicators will be calculated according to the formulas below:

(A) $\frac{\text{number of cases}}{\text{population}} \times 100.000$	(B) $\frac{\text{number of deaths}}{\text{population}} \times 100.000$	(C) $\frac{\text{number of deaths}}{\text{number of cases}} \times 100$

Legend: (A) - Incidence rate ; (B) - Mortality rate ; (C) - Case fatality

The mortality rates for the entire period will be stratified by sex and age. The population will be taken from state projections for the year 2020[12]. For the trend analysis, time periods will be split into two separate waves. The first wave will end in the month with the lowest mortality rate, which indicates the end of the wave. Time series analysis and calculation of the mortality and fatality trends will follow the method proposed by Antunes and Cardoso[13], based on the the Prais-Winsten regression model for population mortality rates.

The following values will be calculated: probability (p), and Daily Percent Change - DPC, considering a 95% level of significance, as illustrated in the following formula:

$$(D)\ DPC\ [-1+10^{\beta}]*100\%$$
$$(E)\ IC\ 95\% = [-1+10^{\beta min}]*100\%;\ [-1+10^{\beta max}]*100\%$$

Legend: (D) - Daily Percent Change ; (E) - level of significance

The STATA 14.0 software (College Station, TX, U.S. 2013) will be used for statistical analysis. The effective reproduction number (Rt) will be estimated using R studio software EpiEstim package[8], version 2.2.4, a time-varying reproduction number for epidemics developed by Thompson and colleagues[9]. As described in previous studies, there will be used a mean serial interval of 2.97 days with a mean standard deviation of 3.29 days[10,11].

DISCUSSION

To our knowledge, this is the first umbrella project aimed at analyzing trends in incidence, mortality, and case lethality of COVID-19 in all Brazilian states applying the method of time series ecological design. There is evidence[14] that the examination of the variability of incidence, mortality, and case-fatality in a defined period enables better understanding of the trends of the COVID-19 pandemic, which is essential to assess its severity and risks.

Conversely, the use of the traditional cumulative case-fatality rates may potentially underestimate the real mortality and morbidity[15], since each state and/or region in Brazil has experienced different trends.

This protocol uses official, public secondary data from the Ministry of Health, which is the best source of information about the COVID pandemic in Brazil. The time series regression method suggested in this protocol will allow the calculation of Daily Percent Change (DPC) in mortality rates, which is useful to assess the trend variability of the pandemic in each state.

On the other hand, the studies developed with this protocol will provide partial information because the pandemic is still ongoing.

CONCLUSION

The evidence available in Brazil does not meet the demands of the pandemic of COVID-19. Population studies showing the reality of each state and/or region are relevant to support public health initiatives to prevent and control the spread of this disease.

Results of these studies will provide guidance for decision-makers and are valuable for future research analyzing the trends of incidence, mortality, and case fatality of COVID-19.

The database built from ecological studies are essential for a full understanding of the virus behavior, its transmissibility, lethality and mortality, and a repository for data that's been collected and integrated from multiple sources. It is a relevant tool for the search of information and decision-making in global health.

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Conflict of interest

The authors declare no conflicts of interest.

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CHAPTER 4

THE DISSEMINATION OF COVID-19: AN EXPECTANT AND PREVENTIVE ROLE IN GLOBAL HEALTH

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Abstract

Coronaviruses (CoV) make up a large family of viruses, known since the mid-1960s, which received this name due to the spikes on its surface, which resemble a crown (from the Latin corona). CoV infections can cause everything from a common cold to severe respiratory syndromes, such as severe acute respiratory syndrome (SARS-CoV) and Middle Eastern respiratory syndrome (MERS-CoV).COVID-19 (SARS- CoV2) is a new variant of the coronavirus, and its isolation occurred in China on January 7th, 2020. COVID-19 has stood out with a high impact on public health due to the high number of cases with infection in a short period of time. However, it is possible to observe that 17% of patients confirmed with COVID-19 have severe infections and about 2.5% of these patients die. Current studies have shown that the number of mild and asymptomatic cases may be even greater. Thus, the challenges for controlling unreported cases of patients with mild symptoms that are spreading the virus and interfering with the magnitude and real data of the cases stand out. The transmission of the coronavirus occurs between humans, and it can occur from person to person through the air, through coughing or sneezing, by touching or shaking hands or by contact with contaminated objects or surfaces, followed by contact with the mouth, nose or eyes. Given the fluctuation in the incidence and the lethality rate, it is essential to stand out the precepts of health promotion in search of reorienting hygiene practices, considering that there is validity in health care models, still with a curative approach and the current situation experienced by the world population requires a preventive stance.

Keywords: SARS-CoV-2; 2019 Novel Coronavirus; COVID-19, Health Promotion; Public Health; Epidemy.

Resumo

Os coronavírus (CoV) compõem uma grande família de vírus, conhecidos desde meados da década de 1960, que receberam esse nome devido às espículas na sua superfície, que lembram uma coroa (do latim corona). As infecções pelo CoV podem causar desde um resfriado comum até síndromes respiratórias graves, como a síndrome respiratória aguda grave (SARS-CoV) e a síndrome respiratória do Oriente Médio (MERS-CoV). O COVID-19 (SARS-CoV2) é nova variante do coronavírus, sendo que o seu isolamento ocorreu na China em 07/01/2020. O COVID-19 tem se destacado com alto impacto na saúde pública devido ao elevado número de casos com a infecção em um curto período de tempo. Entretanto, é possível observar que apenas 17% dos pacientes confirmados com COVID-19 apresentam infecções graves e cerca de 2,5% destes pacientes morrerem. No entanto, os estudos atuais tem evidenciado que o número de casos leves e assintomáticos podem ser ainda maiores. Dessa forma, destacam-se os desafios para o controle dos casos não notificados de pacientes com sintomas leves que estão espalhando o vírus e interferindo na magnitude e nos dados reais dos casos. A transmissão do coronavírus acontece entre humanos, podendo ocorrer de pessoa a pessoa pelo ar, por meio de tosse ou espirro, pelo toque ou aperto de mão ou pelo contato com objetos ou superfícies contaminadas, seguido pelo contato com a boca, nariz ou olhos. Dada a oscilação da incidência e da taxa de letalidade reforça-se a importância dos preceitos da promoção da saúde em busca da reorientação de práticas de higiene, considerando que há vigência nos modelos assistenciais em saúde, sendo hegemônico o curativismo e a atual situação vivenciada pela população mundial exige postura preventiva.

Palavras-chave: SARS-CoV-2; 2019 Novel Coronavírus; COVID-19; Promoção da Saúde; Saúde Pública; Epidemia.

INTRODUCTION

SARS-CoV2:

The new Coronavirus Coronavirus is a family of viruses that cause respiratory infections, being SARS-CoV2 the seventh coronavirus in this family. The new coronavirus agent was reported on December 31th, 2019 with cases registered in China. Most people are infected with common coronaviruses throughout their lives, but only four of them cause common cold symptoms: alpha coronavirus 229E and NL63 and beta coronavirus OC43, HKU1 (V)[1]. There are still two more serious ones, with a high mortality rate[1].

Currently, there is a widespread of this pandemic, called COVID-19, across all continents. Thus, we aim to describe key topics of COVID-19: The new Coronavirus(SARS-CoV2) and its advances in the world population.

First reports

On January 7th with COVID-19 being the seventh coronavirus in this family. Chinese researchers isolated the virus and three days later shared data from the viral genome internationally, calling it a new Coronavirus[2].

The genomic sequences from nine patients who were among the first cases of this serious infection (COVID-19) are almost genetically identical, which suggests the very recent appearance of this Coronavirus in humans[3]. Current data from this virus genome sequencing has demonstrated the existence of small mutations, but the rate of them is apparently low.

"Pneumonia of unknown etiology" (COVID-19)

Na Zhu et al.[4] conducted a study with the first 4 reported cases from December 31th, 2019 identified by local hospitals in Wuhan, China, the complete analysis of the genomes revealed a new coronavirus – SARS- CoV2 a highly pathogenic Sarbecovirus of the subgenus Betacoronavirus[3,5,6.]

COVID-19 is closely related to betacoronaviruses of bat origin, indicating that these animals are the probable reservoir hosts for this emerging viral pathogen, in addition to the association between the pneumonia outbreak and exposures in the Huanan wholesale market suggest a possible zoonosis[3,5]. Many hope that genetic testing of animals or environmental sources, such as cages and containers, from the Wuhan market will reveal clues as to the ultimate origin of the virus[7,8]. In addition, it is not yet clear whether a currently unknown animal species acted as an intermediate host between bats and humans[3].

Coronaviruses (CoV) make up a large family of viruses, known since the mid-1960s, which received this name due to the spikes on its surface, which resemble a crown (from the Latin corona). Coronaviruses are enveloped RNA viruses that are widely distributed among humans, other mammals and birds, which cause respiratory, enteric, liver and neurological diseases[4].

Other six species of coronavirus are known to cause human disease, four of them cause common cold symptoms. The other two, of zoonotic origin, more serious, were associated with the emergence of infections with a high impact on public health due to their lethality[7], they are: coronavirus of severe acute respiratory syndrome (SARS-CoV) the causal agent of the outbreaks in 2002 and 2003 in Guangdong province, China, and the other coronavirus of the Middle East respiratory syndrome (MERS-CoV) responsible for the severe outbreaks of respiratory diseases in 2012 in the Middle East[4].

COVID-19, SARS and MERS

The emergence of coronavirus infections with a high impact on public health began between 2002-2003 with the SARS-CoV outbreak and then in 2012 with the MERS-CoV.

Thus, the COVID-19 virus was isolated and is genetically similar to SARS-CoV (about 79.0% nucleotide identity) and MERS-CoV (51.8%)[3,7,9] and thus called SARS-CoV2. In both SARS-CoV and MERS-CoV, bats acted as a natural reservoir, with another host animal (Himalayan Palm Civet) for SARS-CoV and dromedary camels for MERS-CoV, but the origin of SARS-CoV2 needs further investigation for the discovery of a possible intermediate host[10].

Similar to the 2002/2003 SARS outbreak in Guangzhou, China, Wuhan City is also a rapidly expanding capital of Hubei province and a hub for central China. In addition, both outbreaks were initially linked to “wet markets”, where game animals and meat were sold[7,10].

High lethality was one of the main characteristics that differentiated the SARS and MERS coronavirus outbreaks from the other four species known to cause common cold symptoms. In particular, COVID-19 has stood out with a high number of reported cases in just three months since its first notification.

The case fatality rate reported is close to 3%. Thus, COVID-19 does not appear to be as lethal as SARS[11] and MERS[12]. However, it is reiterated that the total nnumber of cases of COVID-19, as well as the absolute number of deaths13 is already greater than the two previous infections - SARS[11] and MERS[12] (Table 1).

Table 1: Comparison between COVID-19, SARS and MERS coronaviruses.

	COVID-19	**SARS**	**MERS**
	New Coronavirus- 2019	Severe Acute Respiratory Syndrome Coronavirus[10]	Middle East Respiratory Syndrome Coronavirus[11]
Local	Wuhan, China	Guangzhou, China[10]	Middle East[11]
Host/Source	Bat?[9]	Cats 'palm civets'	Dromedary Camels
Year	2019-2020	2002-2003	2012
	Rising mainly in China	No more reports	There are still reports of intermittent sporadic cases[26]
	87.137 human cases and 2977 deaths[27]	8.422 human cases and 774 deaths.	2499 cases and 861 deaths.
Coutries	More than 100	29	27[26]
Incubation period (days)	2-14 mean of 6,4[28]	2-7	5
Frequent signs and symptoms	Fever , cough, dyspnoea[8,9,12,14]	Fever, cough and chills[11]	Fever, cough, dyspnoea, chills[11]
Laboratory Tests	high lactate, dehydrogenase, lymphopenia and leukopenia[15,16]	high lactate, dehydrogenase, lymphopenia, thrombocytopenia and leukopenia[16]	high lactate, dehydrogenase, thrombocytopenia, lymphopenia and leukopenia[16]
Imaging Exams	Presence of bilateral hilar infiltrates, lobar opacity, ground-glass imaging and possible pleural effusions, with lower lobe involvement generally more affected than the upper lobes[9]	Typical findings of unilateral/bilateral ground glass, opacities or focal unilateral/ bilateral consolidation. Abnormalities tend to progress towards bilateral consolidation in hospitalized patients[9]	Irregular or infiltrated densities, bilateral hilar infiltration, segmented/lobar, opacities, ground-glass opacities and possible small pleural effusions. Lower lobes generally more affected than the upper lobes[9]
Lethality	+/- 3%	10%	34.4%[26]
Nucleotide similarities with COVID-19	0	79%[2,6,8]	51.80%[2,6,8]

Clinical presentation

In China, the reported cases indicate that the majority of infected patients were male and average age of 55 years, with no cases in individuals under 15 years old[13,14]. In cases detected outside of China the average age is 45 years old, ranging from 2 to 74 years old and 71% of the cases were male.

The incubation period is between 2 and14 days, with potential asymptomatic transmission[2,7,11,] the duration of the onset of the disease until the first medical consultation was estimated at approximately 5 days, the average duration from the beginning until hospitalization was estimated at 12.5 days among cases with onset of the disease before January 1st, after this period the average decreased to 9 days[14].

Common symptoms of this disease has shown that the virus's confirmations varied in asymptomatic people or with mild symptoms to seriously ill people.

The symptoms ranged from a common cold to the presence of fever, dry cough, dyspnoea, myalgia or fatigue, followed by less common symptoms, such as sputum production, headache, hemoptysis and diarrhea[9,10,13,15,16], in addition to lymphocytes, platelets and hemoglobin below the reference standard for normality[10,16]. Lymphocyte labeling and quantification is a reference marker in the diagnosis of coronavirus infections[10]. Intensive care patients have high levels of lymphocytes[13].

In addition, of the confirmed, suspected and asymptomatic cases of COVID-19 in China, about 80.9% of infections are mild (with flu-like symptoms), 13.8% are serious[17]. The clinical evolution of these patients includes acute respiratory distress syndrome, acute cardiac involvement and secondary infection[10,13].

In the epidemiological analysis, it is observed that male individuals (4.7%), elderly people over 80 years old (21.9%) and those patients with associated comorbidities, such as cardiovascular diseases, are more likely to die (13.2%), diabetes (9.2%) and chronic respiratory diseases (8.0%)[16].

Diagnostic

Clinical evaluation is essential in the diagnosis of COVID-19. The most frequent symptoms associated with the infection are those elucidated in the clinical presentation. However, the clinical characteristics are not specific and may be similar to those caused by other respiratory viruses.

The most frequent symptoms associated with COVID-19 infection are: fever, cough and difficulty breathing. Sore throat, runny nose, headaches and/or muscle and tiredness can also occur. In more severe cases, it can lead to severe pneumonia with acute respiratory failure, kidney and other organ failure, and eventual death.

On imaging examination, there are foci of bilateral pneumonia, multiple spots and glass opacity and, in some cases, the evolution to pneumothorax[10,16,17]. Based on the clinical evaluation, laboratory tests and PCR Polymerase Chain Reaction and Genetic finger print are performed[18].

Magnitude

The first cases (66%) were exposed to the wholesale seafood market in Huanan, but there was an increase in the number of unrelated cases as of the end of December[13,14,19].

The spread of COVID-19 disease by asymptomatic individuals seems to be the major challenge for controlling this pandemic[20]. Evidence of the presence of this virus in asymptomatic people has raised doubts about the onset of this disease and also about the real numbers of existing cases[20].

Data on initial outbreaks continues to grow. It is estimated that each individual can spread their viral load to about 2 to 7 people, with the magnitude of the disease reaching exponential levels in the notification rate[1,14,21].

There are three parameters to be understood to assess the magnitude of the risk posed by this new coronavirus, which are the transmission rate, lethality and asymptomatic transmission.

In COVID-19 there is a rate of attack or transmissibility (the speed with which the disease spreads) of 1.5 and 3.5[17]. Confirmed cases demonstrate that possibly asymptomatic transmission has been possible, which directly interferes with confirmed case numbers and lethality rates. We can highlight that even if it is not possible to determine the real mortality rate of this new coronavirus, global health care stands out due to its attack rate and the possibility of asymptomatic transmission.

Thus, the World Health Organization declared the coronavirus outbreak as a Global Public Health Emergency[17].

The probability of risks related to the disease propagation trip was suggested[7,22-24] and indicated the potential for regional and global propagation. Numerous countries confirmed cases associated with travel, however, in addition to a tourist and economic route, we can highlight initially a mapping of cases in developed countries that had colder climates[25].

The cases notified by the World Health Organization (WHO) exceed the 100,000 confirmed cases worldwide and spread over more than 100 countries. These data reinforce that COVID-19 has shown a high prevalence, with the majority of them presenting mild symptoms (approximately 82% of the cases) and with a lower lethality to the MERS and SARS coronavirus.

Treatment

So far, there are no known useful treatments for the disease caused by this new coronavirus[26], so contact and respiratory precautions are the only effective measures to prevent infection of this emerging virus[18].

Control measures

During previous outbreaks of MERS and SARS coronaviruses, human-to-human transmission occurred through droplets, contact and fomites, suggesting that the mode of transmission of COVID-19 may be similar. Thus, limiting human to human transmission, including the reduction of secondary infections between close contacts and healthcare professionals, preventing transmission amplification events has been a principle to reduce the overall risk of transmission including measures such as: avoiding close contact with people who suffer from acute respiratory infections; frequent hand washing, especially after direct contact with sick people or the environment[27].

Also, when coughing or sneezing, cover mouth and wash hands immediately, and in the health units provide the improvement of infection prevention and control practices[28].

As measures to contain the transmissibility of the virus, an active search for symptoms suggestive of respiratory insufficiency is carried out during or after travel, especially air travel, encouraging travelers to seek medical attention and share their travel history.

In turn, the global health authority (WHO) has provided the strategy to identify, isolate and care for patients early, including providing optimized care to infected patients, as well as identifying and reducing the transmission of animal source.In turn, the global health authority (WHO) has provided the strategy to identify, isolate and care for patients early, including providing optimized care to infected patients, as well as identifying and reducing the transmission of animal source.In turn, the global health authority (WHO) has provided the strategy to identify, isolate and care for patients early, including providing optimized care to infected patients, as well as identifying and reducing the transmission of animal source.

There are incentives for the development of diagnostic tests and therapeutic approaches, including the development of vaccines[28 ,29].

Finally, it is highlighted that the concept of health has been transformed from the historical moments experienced, reflecting on the appearance of new formulations on thinking and doing health and new proposals for changes in health care models[30]. Given the fluctuation in the incidence and the lethality rate, the importance of hygiene care is reinforced, which are, at this moment, the most effective measure to prevent new infections from happening, followed by a reduction of places with crowded people.

These are non-pharmacological and health promotion measures, which are fundamental for reducing direct contagions in the population, especially those most vulnerable. This is a real global public health problem.

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CHAPTER 5

STATE OF THE ART OF NURSING EDUCATION AND THE CHALLENGES TO USE REMOTE TECHNOLOGIES IN THE TIME OF CORONA VÍRUS PANDEMIC

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Abstract

Introoduction: The Corona virus (COVID-19) pandemic caused, among others, the need for colleges and universities managers around the world to reinvent new ways of providing education preserving its good quality at the same time. With the new ordinances of the Ministry of Education and Health, all courses can use remote methodologies for the continuity on the current school year. With new challenges and paradigms emerging from this methodological proposal: provide for the user the feeling of immersion, of being in the class room, from the navigation and interaction in this virtual environment, at the same time that the educator, respecting the educational principles and the pedagogical approach that he believes, does not transform this moment into a simple distance education. **Objective:** To describe the state of the art on nursing education and the challenges of using remote technologies in the time of Corona virus pandemic. **Methods:** This is a reflective study based on secondary sources of literature relevant to the theme, considering articles from national and international journals and recent productions on education, health training, remote technologies, COVId-19 and public health. **Results:** It is evident that experiencing the effects of the corona virus pandemic (COVID-19) in the health educational sector, especially in the field of nursing, goes beyond a structural reorganization of courses. It implies change attitude of managers, teachers and students to reformulate educational practices (sometimes with traditional tools), with innovative practices preserving a methodology that provides to the student criticality reflection, dialogue, bonding and interaction; elements that are part of a training aimed at transformation, empowerment and not just the transmission of knowledge. In this context, the COVID-19 pandemic caused paradigm shifts perhaps not yet overcome by health science institutions, because when they perceived themselves within a reality that generated changes in the political, economic, cultural and social aspects at a global level, they had to reinvent and insert new ways of teaching in their work process; they had to discuss different educational approaches and, given the needs to readjust health teaching methods, they inserted remote technologies as essential tools to meet the real need for continuity of classes in non-face-to-face model. For many, it is a challenge, as it currently permeates a reflection on the attention of distance learning in the field of nursing and other courses in the health area. However, as it opened up to discussions about new ways of teaching mediated by innovation, it can be said that this will be one of the greatest impact of the pandemic in benefit the education: the contribution of new information and communication technologies in the teaching-learning process for training in health, as well as the reflection on distance education and its concepts, differentiating it from the concepts of remote methodology and the use of technologies. **Conclusion:** In nursing education, the discussion related to the use of remote technologies in the classroom has always been a point of debate. However, with the need to include these tools for the continuity of classes in the non-face-to-face model resulting from the social isolation strategy motivated by the pandemic of COVID-19, it can provide an opportunity to have a new look on the subject and perhaps there is an opportunity to expand the debate on the use of remote methodologies in health education, seeking a reflection on their interaction with the other teaching methods already implemented.

Keywords: COVID-19; Changes; Education; Health Training; Nursing; Technologies; Innovations.

Resumo

Introdução: A pandemia do Corona vírus (COVID-19) provocou em caráter emergencial a necessidade dos gestores das faculdades e universidades de todo mundo de reinventar novas formas de prover o ensino preservando a qualidade dele. Com as novas portarias do Ministério da Educação e Saúde, houve uma abertura para que todos os cursos utilizassem de metodologias remotas para continuidade do ano letivo, surgindo novos desafios e paradigmas com essa proposta metodológica: prover para o usuário, a sensação de imersão, de estar dentro do ambiente, a partir da navegação e interação nesse meio virtual, ao mesmo tempo que o educador, respeitando os princípios educacionais e a abordagem pedagógica que acredita, não transformar esse momento em uma simples educação à distância. **Objetivo:** Descrever o estado da arte sobre o ensino de enfermagem e os desafios do uso de tecnologias remotas em época de pandemia do Corona vírus. **Método:** Trata-se de estudo reflexivo consubstanciado por fontes secundárias da literatura pertinente à temática, considerando artigos de periódicos nacionais e internacionais e produções recentes sobre educação, formação em saúde, tecnologias remotas, o COVId-19 e saúde pública. **Resultados:** Evidencia-se que vivenciar os efeitos da pandemia de corona vírus (COVID-19) no setor educacional na formação em saúde, em especial no campo da enfermagem, vai além de uma reorganização estrutural dos cursos, pois implica em mudança atitudinal dos gestores, docentes e discentes para que reformulem as práticas de ensino (por vezes com ferramentas tradicionais), em práticas inovadoras preservando um ensino que propicie ao estudante a criticidade, reflexão, diálogo, vínculo e interação; elementos que fazem parte de uma formação que visa a transformação, o empoderamento e não apenas a transmissão do conhecimento. Nesse contexto, a pandemia do COVID-19 provocou mudanças de paradigmas talvez ainda não superados pelas instituições na área da saúde, pois ao se perceberem dentro de uma realidade em que gerou mudanças nos aspectos políticos, econômicos, culturais e sociais em nível mundial, estas tiveram que se reinventar e inserir no seu processo de trabalho as novas formas de ensinar; tiveram que discutir sobre as diferentes abordagens educacionais e diante das necessidades do readequar os métodos de ensino em saúde, inseriram as tecnologias remotas como ferramentas essenciais para atender a real necessidade da continuidade das aulas no formato não presencial. Para muitos um desafio, pois permeia atualmente uma reflexão sobre o cuidado do ensino à distância no campo da enfermagem e demais cursos da área da saúde. Entretanto, à medida que se abriu para discussões sobre novas formas de ensinar mediadas pela inovação, pode-se dizer que esse será o maior impacto da pandemia para o ensino: a contribuição das novas tecnologias de informação e comunicação no processo ensino aprendizagem para formação em saúde, assim como a reflexão sobre a educação à distância e seus conceitos, diferenciando-a dos conceitos de metodologia remota e o uso das tecnologias. **Conclusão:** No ensino da enfermagem, a discussão relacionada ao uso de tecnologias remotas em sala de aula sempre foi um ponto de debate. Entretanto, com a necessidade da inclusão dessas ferramentas para a continuidade de aulas no formato não presencial decorrente da estratégia do isolamento social motivada pela pandemia do COVID-19, pode oportunizar a se ter um novo olhar sobre o assunto e que talvez com esse momento vivido se haja oportunidade de ampliar o debate sobre uso dessas metodologias remotas no ensino em saúde, buscando uma reflexão sobre a interação destas com os demais métodos de ensino já implementados.

Palavras-chave: COVID-19; Mudanças; Educação; Formação em Saúde; Enfermagem; Tecnologias; Inovações.

INTRODUCTION

What to do in the face of a pandemic that transforms everyone's lives in political, economic, cultural and social aspects around the world, and that in the face of urgent needs for change, new ways of thinking/doing must be put into practice in a frightening way?

The challenges exposed in education through new ordinances allow courses, be they basic, technical and higher, to make use of remote technologies, never utilized before, as a teaching methodology. Thus, the institutions and their managers have had to reinvent and adapt to this new form of teaching, arising new needs for inclusion, management, of the faculty and students to work with new technologies; new for those who were not immersed in the virtual world, but for many and since some time ago, is a present reality seen as tools that promote the change of educational paradigm.

Within the current context much is discussed about the importance and quality of teaching with the advancement of new information and communication technologies (ICTs).Considering higher instruction, this advance determines an increasing demand for continuing education, both in the modality of face-to-face and Distance Education (EAD, in Portuguese), but the inclusion of ICTs in curricula has been a way to stimulate, enhance and improve their use, and, in turn, provide an innovative teaching process[1].

In the health field, it still seems challenging, but necessary, as it is imperative to have a closer look at the speed of technological innovations which drive social transformations; therefore, it is revealed a greater need for reflection on the part of educators and that these reflections permeate in the new way of teaching: educating with a humanistic approach in contrast to a rationalist and objective aspect still present today.

Thus, it is argued that at this conjecture, more than the immersion of technologies in teaching, it is to reflect on the pedagogical approach that the teacher prints and not just the technology itself. It must be understood that technology is not a self-sufficient tool; its pure and simple application will not solve all the problems inherent to teaching[2,3].

New parameters for teaching/learning are emerging, transforming the way of building knowledge, as well as the instruction methodology and the role of the teacher and his relationship with students[4]. In this context of health education in nursing field, the use of new teaching methodologies has enabled the understanding of different scenarios through technologies that reproduce educational experiences promoted through virtual environments[5,6].

Thus, in nursing, it is already evident the use of various technologies incorporated into existing teaching methodologies, implementedby teachers at different times, both by operating equipment and software in laboratories, and by differentiated teaching techniques[7], but only being complementary tools and not as the only method used.

With the need to incorporate remote technologies at this time of the COVID-19 pandemic, not only nursing courses, but other health courses, started to include new tools in their disciplines, considering the moment and the need for continuity of classes. However, despite having courses in Brazil with hybrid characteristics (use of technologies in teaching and traditional methods), the inclusion of virtual tools in teaching still seems challenging.

In an emergency caused by the pandemic of COVID-19, the managers of colleges and universities around the world had to reinvent new ways of providing education while preserving its quality. Particularly in Brazil, with the new ordinances of the Ministry of Education and Health allowing to all courses to make use of remote methodologies for the continuity of the academic year, a new challenge arises: to provide the users with the feeling of immersion, of finding themselves within the environment, from the navigation and interaction in this virtual environment. At the same time that the educator, respecting the educational principles and the pedagogical approach that he believes, does not transform this moment into a simple distance learning.

Thus, this study aims to describe the state of the art on nursing education and the challenges of using remote technologies in time of COVID-19 pandemic.

METHODS

This is a reflective paper on the effects of the pandemic caused by the corona virus COVID-19 in the education field, specifically in nursing, at the undergrad- uate level. This study is based on secondary sources of literature relevant to the theme, considering articles from national and international journals and recent productions on COVID-19, public health, health education and remote technologies.

RESULTS AND DISCUSSION

In early December 2019, a new corona virus appeared in the city of Wuhan, Hubei, China; the 2019 corona virus (COVID-19) caused by SARS-CoV-2 (corona virus 2). Since then, local and national governments have been adopting measures, in the social and economic fields, in response to the outbreak of the disease[8,9].

Non-pharmaceutical physical interventions, such as social distancing, prolonged school closings and closure of workplace premises, were among others measures to reduce the impact of the COVID-19 outbreak, initially adopted in Wuhan[10], but

governments around the world endorsed them. These measures have greatly influenced the life of the population, causing changes in the countries' economies as well as in social aspects of everyone's daily life.

Measures like these are necessary and are strengthened by evidence such as the one presented in the study on the effect of control strategies to reduce social mix on the results of the COVID-19 epidemic in Wuhan, China, indicating that non-pharmaceutical interventions based on sustained physical distance have a strong potential to reduce the magnitude of the COVID-19 epidemic peak and lead to fewer general cases. The reduction and flattening of the epidemic peak is particularly important, as this reduces acute pressure on the health system. Thus, the premature and sudden lifting of interventions can lead to an anterior secondary peak, which can be flattened by relaxing interventions gradually[11].

In this context, the closing of schools stands out as one of the most impactful but necessary interventions to reduce the epidemic peak; measure that has been promoting a reformulation of teaching practices and, consequently, in the restructuring of institutions so that, in this way, they meet the new rules of an exceptional nature.

In the health area, this movement around higher education schools emerges as a paradigm shift, especially for those who did not use methodologies with remote technologies in their curricula. In courses such as nursing, although the Ministry of Education Ordinances No. 2,253 / 2001, No. 4,059 / 2004 and No. 1,134 / 2016 formalize the possibility of offering distance learning courses in 20% of fullhour load of courses of higher education institutions in Brazil12-14, many do not implement them because they believe in having losses in the teaching- learning process.

However, it is argued that talking about remote technologies is beyond the use of technology itself, but how to use and make this instrument a mediating tool in the teaching-learning process, not necessarily used as a distance learning method, but to complement other pedagogical methods.

Thus, with the pandemic and the need to continue the classes, but through remote technologies, which implies online classes, the moment arises to rethink pedagogical and academic strategies so that it can adapt to the use of new teaching approaches and, in turn, reevaluate traditional practices and develop new skills and forms of teaching, preserving the principles of education, its guidelines and laws, however, involving, those who have not yet used ICTs.

In this context, the World Declaration on Higher Education, since 1998, has discussed information and communication technologies in higher education, considering the ability to generate changes in the methods of teaching and learning[15]. This discussion has been going on all over the world; the insertion of technological information and communication tools in higher education, currently, has been the subject of reflection on its importance and the quality of teaching, pointing to the advancement of ICTs in the context of higher education systems[1].

However, it is important to highlight that the use of technologies that can be applied both in the face-to- face and Distance Education modality, determines an increasing demand for continuing education, in the transformation of the conception about teacher-student interaction; in the adequate preparation of teachers, in addition to structural changes in educational institutions, both in the organizational domain and in the field of teaching and research. It is believed that the inclusion of ICTs in the curricula is a form to stimulate, enhance and improve their use and open up new teaching methods[3].

With regard to health training, specifically, of the nursing professional, it is known that over time, the discussion about the best path for training, considering the tripod comprised by teaching, research and extension, accompanies the historical and social changes, mainly by the representativeness of the profession in the health history of Brazil and worldwide. As a milestone for consolidation and as another step forward in nursing education, in 2001, the National Curriculum Guidelines for the Undergraduate Nursing Course were established, dealing with the pedagogical principles established, integrating the pedagogy of competences, learning to learn, the general instruction, humanistic, critical and reflective, and education centered on the student and the teacher as a facilitator[16].

Thus, through the development of skills, health training in the field of nursing seeks to provide a professional who acts in a multidisciplinary sphere, according to the needs of the National Health System (SUS- Sistema Unico de Saúde).To this end, this learning must transcend that teaching that aims at a mere pedagogical and didactic scientific update and promote the creation of spaces for participation, reflection and dialogo, thus developing the stimulus to clinical reasoning, the valorization of the articulation between theory and practice, the use of active teaching / learning methodologies and curriculum flexibility; active and differentiated teaching is advocated, elucidating new roles for the teacher and the student[15].

From this curricular restructuring mediated by discussions of the Curriculum Guidelines, Laws and Ordinances of the Ministry of Education, it has long been perceived the need to broaden the teacher's perspective for a learning that incorporate technological tools that, although they translate into advances and challenges for nursing education, in this context, the broad view of innovations and technologies is consolidated[17,18].

And suddenly, with the pandemic COVID-19 this discussion returns to be focus on higher education institutions in the health sector, because of the need of social isolation, schools stopped working on the classroom mode and starts to think in new strategies for its continuity.

In the meantime, innovation in teaching became the center of attention and with the constant technological evolution, decisions began to be guided by the use of remote technologies, according to Ordinance 343/2020, of the Brazilian Ministry of Education, published on March 18, 2020, which, exceptionally, instituted the execution of non-face-to-face classes mediated by these technologies, including courses of health sciences, as well as medicine[19].

Then the managers of colleges and universities started to reorganize their classes and think about cautious strategies, mainly, so as not to transform health education into a distance format. Such strategies that range from the structural organization of the school to teacher and student training, aiming above all to preserve the quality of education.

Therefore, how to think of the use of remote technologies suddenly, in face of educational institutions that did not include in their curricula methods with the use of virtual tools and, even in their organizational structure, did not have platforms for this purpose? How to think about providing education with these tools within an instruction that has disciplines which work with motor skills and complex technical knowledge? How to break with this traditional pedagogical scenario and incorporate a pedagogical approach that guides the teacher to incorporate technologies in educational environments?

There, we have the effect of the COVID-19 pandemic on education and its impact on health teaching, an effect that, as from Ordinance 343/2020, institutions had to enter virtual reality, get in the world where ICTs promote a innovative instruction environment capable of modifying a traditional pedagogical scenario.

In this context, the nurse educator, will have two major responsibilities: to create an atmosphere for learning that offers encouraging experiences for each individual to reach their full potential, for it he must accept the diversity of styles and the incorporation of technological tools in the process of work, then from a critical analysis of the fundamentals of educational approaches, understand other routes of access, since a nursing curriculum based on only one approach can restrict students' educational development[20].

Thus, considering the current moment of the pandemic and the race against time to resume classes of a non-face-to-face nature, managers and teachers started to dialogue and study the different strategies using remote technologies in health education, even not having visualized the benefits of these tools before.

I started to corroborate with the idea that the use of new remote technologies can enable motivating, reflective, multisensory, dynamic, flexible teaching in terms of time and geographical spaces, collaborative and still promoter the socialization of knowledge. Barbosa and Viana[15] already pointed out these results when analyzing the use of these tools in nursing education, which on the other hand they also revealed

that the use of technologies for teaching must integrate a broader pedagogical process, resulting from theoretical reflections and dialogical competences of the nurse as an educator.

However, even if in the short term and due to the needs to address the issues related to the pandemic caused by COVID-19, the institutions, represented by their managers, needed to promote ways to effectively implement Ordinance 343/20. However, it is worth reflecting that this is not only a matter of adhering to the rules to manage content and end the academic period, but that even in the face of this chaos caused by the pandemic, the quality of teaching should be preserved.

Within this frame of reference, it is important to understand that although in this current context, technologies are being used essentially to implement non-presential classes, its importance in the educational context is perceived, but that the use of remote methodology is a complement to face to face teaching practices, including it as a tool that will broaden the view of the student and teacher, contributing to a new way of producing knowledge, through the mastering of different forms of teaching, promoting the problematization and technological professional training in health[21].

It is also necessary to understand that the students also suffered an impact with this insertion, mainly due to the concern that they used to be part of a course face-to- face. For them, in addition to access difficulties, possibly remedied by the institutions, due to cultural reasons, they see this remote modality as a weakness for the teaching-learning process.

Thus, according to Markham[22], the development of didactic methodologies that use the new ICTs to aid in the teaching process, it requires managers to know the profile of access to these resources by the target population, as well as understanding of variables implicit in the use of the Internet, as a mean of communication and selection of information for students and continuing education, revealing limitations and addressing the social inequalities that are sometimes present, in public or private institutions.

For these reasons when the Ministry of Education, proposed these strategies for educational institutions, once the managers evaluated the students' profile, many of them chose to suspend classes, as they would not be able to attend their all students due to access issues, since that the use of these technologies is directly linked to the internet. This reality has mainly affected public educational institutions, which is one of the negative impacts in this moment of pandemic by COVID-19, the total paralysis of classes. Others opted for suspension because they believed that remote methodologies would not meet what was proposed by the institution.

On the other hand, despite studies pointing out that the introduction of new teaching techniques, using technologies in specific nursing contents, allows moments of reflection and problematization, ensuring learning for the school group[23]; at this time of the pandemic by COVID- 19, due to the fact that exceptions were made in the education with the insertion of these technologies in health courses, caution is necessary, because despite the benefits of using new remote technologies in teaching, the impact on the teaching-learning process must be considered.

To this end, the school must provide instruments that enable students to develop skills throughout their training and life, which are of a conceptual, procedural and attitudinal nature[24].

In this context, it is necessary to understand that in addition to this focus that the nursing graduation has to develop technical skills based on the retention of information, especially of a technical and procedural nature, to promote the formation of this autonomous, critical and reflective professional, capable of providing a humanized and health-promoting assistance[25] it is also necessary to develop content of an attitudinal nature, which are competencies that undergo corrections during the student-teacher interaction, which can be lost and become superficial and fleeting when using these remote technologies. It is believed that learning can be sustained and consolidated when teacher / student and student / teacher relationships occur effectively throughout the training process; so teaches the art of caring.

It should also be considered that as nursing skills that are taught to students, the strengthening of interpersonal relationships, bonding and welcoming are highlighted, skills that are related to the process of humanization in health. So, will it be that when using information and communication technologies as a tool for non-face-to-face classes, it will not strengthen the distance in the practice of the future professional and patient? The practice of teaching, in eye-to-eye contact, touch and experiences exchanged at the learning site is a sine qua non issue for cognitive assimilation; that remote technologies do not allow.

From this perspective, it is worth mentioning that the principles that govern nursing teaching must be fully respected and that it is necessary to think about the use of these technologies as tools that add value to traditional teaching methods, constituting a complement and not the only one way of providing health education. Due to the exceptional circunstance, the use of these tools was chosen for several disciplines, however respecting their peculiarities and within the percentile limit that would not weaken the student's teaching-learning process and, above all, mantaining the quality level of teaching.

Finally, it is evident that talking about the impact of the corona virus (COVID-19) in the health educational sector specifically in the field of nursing, goes beyond a structural reorganization of courses, as it implies a change attitude of managers, teachers and students to reformulate teaching practices (sometimes using traditional methods), in innovative practices preserving a teaching that provides the student with criticality, reflection, dialogue, bonding and interaction; elements that are part of a training aimed at transformation, empowerment and not just the transmission of knowledge.

It is learned, that the COVID-19 pandemic caused paradigm shifts, perhaps not yet overcome by institutions in the health field, as they perceived themselves within a reality in which they generated changes in the political, economic, cultural and social aspects worldwide, they had to reinvent and insert new ways of teaching in their work process; had to discuss the different educational approaches and, given the needs to readjust health teaching methods, they inserted remote technologies as tools to meet the real need for continuity of classes in a non-face-to-face format.

For many, it is a challenge, as it currently permeates a reflection on the care of distance learning in the field of nursing and other courses in the health area. However, as it opened up to discussions about new ways of teaching mediated by innovation, it can be said that this will be the greatest impact of the pandemic for teaching: the contribution of new information and communication technologies in the teaching-learning process in health field as well as the reflection on distance education and its concepts, differentiating it from the concepts of remote methodology and the use of technologies.

CONCLUSION

In nursing education, the discussion related to the use of remote technologies in the classroom has always been a point of debate. However, with the need to include these tools for the continuity of classes in the non-face- to-face model resulting from the social isolation strategy motivated by the pandemic of COVID-19, it can provide an opportunity to have a new look on the subject. Perhaps, with this moment lived, there is an opportunity to expand the debate on the use of these remote methodologies in health education, seeking a reflection on their interaction with other teaching methods already implemented.

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CHAPTER 6

EVIDENCE-BASED PHYSIOTHERAPY AND FUNCTIONALITY IN ADULT AND PEDIATRIC PATIENTS WITH COVID-19

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Abstract

Introduction: The corona virus (2019-nCoV OR HCOV-19 or CoV2), has emerged in China as the main cause of viral pneumonia (COVID-19, Coronavirus Disease-19). **Aim:** To provide evidence-based Physiotherapy and functionality in patients with adult and pediatric COVID-19. **Methods:** This is an integrative literature review using the MedLine / PubMed databases, library of Latin American and Caribbean Literature in Health Sciences (LILACS) and Physiotherapy Evidence Database (PEDRo). **Results:** Part of the patients with covid 19 show signs of respiratory deficiency with hypoxemia, with low severity in children. Impaired functionality is also expected. **Conclusion:** COVID-19 causes low pulmonary compliance and important changes in lung function with hypoxemia and cardiovascular repercussions. These changes lead to the need for Physiotherapy and the management of oxygen therapy and ventilatory support (invasive and non-invasive) for these patients.

Keywords: Physiotherapy, International Classification of Functionality, Disability and Health, hypoxia.

Resumo

Introdução: O corona vírus (2019-nCoV OU HCOV-19 ou CoV2), emergiu na China como a principal causa de pneumonia viral (COVID-19, Doença do Coronavírus 19). **Objetivo:** Avaliar evidências científicas sobre Fisioterapia e Funcionalidade em pacientes com COVID-19 adulto e pediátrico. **Métodos:** Trata-se de uma revisão de literatura do tipo integrativa utilizando a bases de dados do MedLine/PubMed, bioblioteca da Literatura Latino-Americana e do Caribe em Ciências da Saúde (LILACS) e Physiotherapy Evidence Database (PEDRo). **Resultados:** Os pacientes com COVID-19 apresentam sinais de deficiência respiratória com hipoxemia, com baixo impacto em crianças estas evoluem sem sintomas ou com quadro de baixa gravidade. além de observar impacto na restrição da participação. a fisioterapia atua na oxigenioterapia e ventilação dos pacientes. **Conclusão:** A COVID-19 causa alterações na função pulmonar com formação de deficiência respiratória hipoxêmica e de complacência, com repercussões cardiovasculares que leva a necessidade da fisioterapia no desfecho desta pandemia, seja por meio da oxigenioterapia e/ou do suporte ventilatório (invasivo e não-invasivo).

Palavras-chave: Fisioterapia, Classificação Internacional de Funcionalidade, Incapacidade e Saúde, hipóxia.

INTRODUCTION

The coronavirus infection pneumonia epidemic broke out in late December 2019 in the city of Wuhan in China, and spread rapidly across the country and all the continents of the world. Discovered through entire genome sequencing, the pathogen was considered a new beta coronavirus genus, and the pathology was called a new coronavirus pneumonia, defined by the World Health Organization[1-4].

Clinical conditions such as hypertension, respiratory, cardiovascular, and metabolic diseases seem to be important risk factors for the severity of covid-19[5]. Age is also an important unmodifiable risk factor. Patients with a mean age of 47 years had a mortality rate of 3 to 5%, oxygen therapy was necessary in 42% of these patients, 5% were admitted to the ICU, 2.3% underwent invasive mechanical ventilation (IMV), and of these, 1.4% died[6,7].

The coronavirus responsible for COVID-19, may have repercussions that go beyond the involvement of the respiratory system, harming several systems, including the cardiovascular system8. COVID-19 can trigger decompensation of the cardiovascular system, especially in people with previous disorders, such as heart failure and coronary artery disease. In addition, studies indicate the occurrence of acute myocarditis and severe acute respiratory syndrome (SARS), which favors systolic dysfunction and myocardial infarction[8,9].

Among the various professionals involved in the physical recovery of the patient with COVID-19, the physiotherapist stands out not for treating the disease but for preventing and rehabilitating respiratory deficiencies and the functional limitations of the daily life activity[10].

COVID-19 is a disease that causes deficiency of respiratory tract structures, leading to impaired breathing functions[11]. Not only, depending on the clinical severity presented, there may be impaired respiratory muscle function and exercise tolerance. Limitations, which make it difficult to carry out basic activities that involve the ability to move, affecting even routine tasks such as walking and performing self transfers[12].

As the Physiotherapist is in charge of the care process for these patients, there is a need to better understand the functional repercussions of COVID-19 in order to think about the best approach to the patient, thus, the objective of this work is to evaluate scientific evidence about Physiotherapy and functionality in patients with adult and pediatric COVID-19.

METHODS

It is an integrative literature review using the MedLine/PubMed database, library of Latin American and Caribbean Literature in Health Sciences (LILACS) and Physiotherapy Evidence Database (PEDRo). The approach was through a methodology that provides the synthesis of knowledge and the incorporation of the applicability of results of significant studies in practice on the scientific evidence for the performance of Physiotherapy at COVID-19. The literature review was carried out in March and April of 2020.

Thus, this study investigates and presents the scientific evidence in Physiotherapy and functionality in COVID-19 that can guide Physiotherapists in their daily conduct with these respective patients with recommendations.

Search strategy

The electronic search was performed by well- trained researchers with experience in the subject of the articles. The search was performed in March 2020 with the combination of the following terms: First combination: Covid 19 and coronavirus and coronavirus (COVID-19) infection. Second Combination: Physiotherapy and Covid 19 and coronavirus and coronavirus (COVID-19) infection. Third combination: Cardiac Involvement and coronavirus (COVID-19) infection. Fourth combination: Diagnosis and treatment and prevention and Covid 19 and coronavirus. From this search, articles were selected for full reading that met the inclusion criteria for this review.

Eligibility criteria

Published studies in English or Portuguese about COVID-19 and aspects related to Physiotherapy, mechanical ventilation, oxygen therapy and cardiac alterations were included. Reviews, meta-analyzes, editorials, original articles and Consensus were also included.

Summary of data

The summary included the extraction of the following data: authors and year of publication of the evidence, instruments and/or assessment equipment, and effects of the Physiotherapeutic performance in patients with COVID-19, with a focus on functionality. Finally, the outcomes pertinent to the therapeutic intervention in COVID-19 in respiratory function were evaluated for the production of evidence.

RESULTS

Despite the scarcity of studies, Table 1 shows the evidence found on the Deficiency of Respiratory Function in COVID-1913-25. The recommendations in Physiotherapy for patients with Respiratory and Cardiac Disability by COVID-19 follow in an appendix to this study. (Attachment 1)

Table 1: Evidence on Deficiency in Respiratory Function at COVID-19.

Author	Type of study	AIM	Evidence
Bouadma et al. 2020[13]	Review	Review practical considerations and management strategy for intensivists.	COVID-19 may have several cardiovascular repercussions, making continuous monitoring and a multidisciplinary approach necessary in the care of this patient becoming necessary.
Xu et al. 2020[14]	Case report	To investigate the pathological characteristics of a coronavirus 2 (SARS-CoV-2) patient by post-mortem biopsies.	The presence of myocardial infiltration by interstitial mononuclear inflammatory cells at autopsy, demonstrating the direct impact of the coronavirus on the myocardium.
Cai et al. 2020[15]	Case series	To describe 2019 coronavirus infection in 10 children from Wuhan.	Most children develop mild or symptom-free illnesses. In children with COVID-19, symptoms are generally less severe than adults and are mainly with cough, fever, pharyngeal erythema and more rare, diarrhea, fatigue, rhinorrhea, vomiting and nasal congestion.
Xia et al. 2020[11]	Review	To discuss the different characteristics of clinical, laboratory and chest computed tomography in adult pediatric patients with new coronavirus infection 2019 (COVID-19).	COVID-19 is a disease that causes deficiency of respiratory tract structures, leading to impaired breathing functions.
Guanghai et al. 2020[12]	Review	To evaluate the effects of confinement at home on children during the COVID-19 outbreak.	The control of the infection spread leads to the restriction of participation, interfering in tasks, such as recreation and leisure activities.
Shen et al. 2020[16]	Consensus	Summarize current strategies for diagnosis, treatment and prevention of infection by 2019-nCoV in children.	The critical presentation of the children's COVID-19 which is characterized by respiratory failure requiring ventilatory support. Children with COVID-19 class 4 are suffering from Respiratory Deficiency due to severe pneumonia, presenting: tachypnea and dyspnea, in addition to the presence of hypoxemia. The critical presentation of children's COVID-19 is characterized by respiratory failure requiring ventilatory support.
Respiratory care committee of Chinse Thoracic Society. 2020[17]	Consensus	To recommend high-risk treatments, based on current evidence and limited resources in some areas.	To prevent the spread of the virus, the use of a closed suction system is recommended.
van den Boom et al. 2020[18]	Retrospective analysis	To determine the ideal range using real-world data.	About 41% of all patients hospitalized with COVID-19 use oxygen therapy in the course of their treatment, and this number rises to 70% among cases with very severe evolution.

Continuation - Table 1: Evidence on Deficiency in Respiratory Function at COVID-19.

Author	Type of study	Aim	Evidence
Alhazzani et al. 2020[19]	Practical clinical guide	Guide the management of patients with Corona Virus and emergency unit. Recommend the practical action of Physiotherapy in the management of patients with COVID-19	Hypoxemia in acute conditions, SpO2 ≤ 92%, may favor dysfunction of organs and systems. The use of a high-flow nasal cannula should preferably be used with patients in beds with a negative pressure room using individual protective equipment.
Thomas et al. 2020[20]	Guide clinical practice	Recommend the practical action of Physiotherapy in the management of patients with COVID-19.	Patients with increased need for oxygen are referred to Physiotherapy for airway clearance, especially in those with cough deficiency and use of protective equipment, and early optimization of care and ICU involvement is recommended.
Cheung et al. 2020[21]	Practical clinical guide	Guide personnel safety during emergency airway management.	Procedures with Non-Invasive Ventilation (NIV) should be performed with personal protective equipment, such as professional mask PFF2 (N95), goggles for protecting the eye mucosa, long-sleeved, fluid-resistant apron, clean gloves for protection and if possible in negative pressure room.
Meng. et al. 2020[22]	Experience report	To report the experience during intubation and artificial ventilation in COVID-19.	COVID-19 shows that 14% of patients developed dyspnea, tachypnea, peripheral oxygen desaturation (Spo2) less than or equal to 93%, deficient oxygenation index with a Pao2 / Fio2 ratio <300 mmHg in 48 hours. Intubation and invasive mechanical ventilation may have been delayed in some patients, and this may have had a negative impact on mortality.
Murthy et al. 2020[23]	Review	To discuss issues related to regions where intensive care units are able to provide mechanical ventilation.	NIV can be used in places where access to invasive mechanical ventilation is limited or before patients have severe hypoxemic respiratory failure.
Wax & Christian 2020[24]	Practical clinical guide	Summarize important considerations about patient screening, environmental controls, personal protective equipment, resuscitation measures, and planning for intensive care unit operations.	It is important to be aware of the physiological signs of asymptomatic hypoxemic patients - referred to as silent hypoxemia.
Brewster et al. 2020[25]	Consensus	Review airway management and tracheal intubation.	An occlusive face mask (well adjusted to the patient's face) must be used, coupled to a mask valve bag (AMBÚ, or similar brand), connected to an oxygen source.

Caption: SARS-CoV-2: COVID 19 respiratory distress syndrome; nCoV: New COVID 19; SpO2: Peripheral oxygen saturation; Pao2 / Fio2: Ratio of arterial oxygen pressure and the inspired fraction of oxygen.

DISCUSSION

COVID-19 may have cardiovascular and myocardial repercussions[13,14], retrospective multicenter study using a database from Jin Yin-tan Hospital and Tongji Hospital in China, showed that 33% of deaths were caused by the association of heart and respiratory failure, with 7% of deaths caused exclusively by myocardial injury[25].

There is an indication for a closed suction system to perform bronchial hygiene therapy, as well as an occlusive face mask and in the pre-oxygenation of these hypoxemic patients[19], as these protocols protect health professionals from contamination.

Exhaled air is known to increase virus dispersion and subsequently the risk of nosocomial infection[26] and spread of the virus[12,16]. Procedures that enhance the aerosolization and contamination of health professionals are not indicated, associated with the absence of a proven benefit in the treatment of refractory hypoxemic respiratory failure[27].

Opportunistic airborne transmission generally occurs during aerosol-generating health procedures such as patient coughing and contact with surfaces[27], why 1716 healthcare workers were infected with SARS-CoV-2 in a hospital in China[28].

About 41% of all patients hospitalized with COVID-19 used oxygen therapy[18]. In the study performed during the SARS-COVID pandemic in 2002, administrative factors were identified for greater risk of an outbreak, including the O2 flow rate> 6L / min, considered as “high flow”. In this study, the adoption of high O2 rates increased the chances of providing a viral outbreak by 2.42 times than the adoption of low flow. Thus, the adoption of high oxygen flows should be discouraged in the absence of the respiratory isolation bed[29,30].

NIV procedures[23] should be performed with personal protective equipment and in those patients who develop dyspnea, tachypnea and peripheral oxygen desaturation. NIV can be used in those places where access to invasive mechanical ventilation is possible. Studies recommend only the use of a helmet with a double limb circuit, as they can reduce the risk of airborne transmission[21].

In children with COVID-19, symptoms[12,15] are usually less severe. COVID-19 is a disease that causes deficiency of respiratory tract structures[11], in addition to thinking that the control of the spread of infection leads to the restriction of children’s participation.

Infant COVID-19 is characterized by respiratory failure requiring ventilatory support. Neonatal and pediatric physiotherapy plays a fundamental role in multidisciplinary care, acting in order to identify, elaborate and develop kinetic-functional diagnosis in cardiorespiratory disorders caused by viral infection, through anamnesis, physical evaluation and complementary exams. In addition to developing promotion, prevention, rehabilitation and recovery strategies for children with risk factors for the development of problems and determinants of the health- disease process, at different levels of health care.

It is worth noting that patients who fail oxygen therapy, NIV, or have a direct indication for invasive mechanical ventilation, should be intubated quickly, as the need for intubation and IMV is common during this outbreak[31]. The need for intubation vary from 2,3% 4%[7,32,33], to 42% e 47%[30,32], considering the studies available in the literature. With differing rates regarding the need for intubation, attention to the patient’s characteristics, specific care and a careful evaluation are essential at this time. Additionally, patients using invasive ventilation should be isolated in a single room[12] and it is important to pay close attention to their handling with professional protection[21].

Scientific studies from professional experiences in other places that struggle to treat patients with COVID-1934, it appears that due to the unsatisfactory results, high failure rate, higher risk of spreading the virus, and unavailability of the appropriate interface (helmet), in In most Brazilian intensive care units, NIV should be rethought and indicated with greater evaluative and diagnostic precision, and should not be a first-line ventilatory strategy, intended for patients with SARS / COVID-19 and that can be extrapolated to the nasal cannula of high flow.

Patients with tachypnea (respiratory rate > 30 ipm), hypoxemia, Spo2 less than 93% at room air and a Ratio of arterial oxygen pressure and the inspired fraction of oxygen <300 mmHg[33], with progressive worsening of the clinical picture and with the prospect of continuing to worsen, and undergoing no clinical improvement at conventional oxygen therapy (face mask up to 5 liters or mask with reservoir, non-reinaline, up to 10 L/min)[21,33,35,36], orotracheal intubation[22] should be performed which must be performed with an occlusive face mask (well adjusted to the patient's face) coupled to a mask valve bag[24].

The need to carefully assess the physiological signs for indication of orotracheal intubation in asymptomatic hypoxic patients, referred to as silent hypoxemia[24], is emphasized, since the emergency intubation procedure poses a risk of cross infection[37].

CNAF[21] can be used in respiratory deficiency due to severe hypoxemia as long as it presents a potential response in oxygenation in the first 30 minutes of therapy. The use of CNAF should preferably be used with patients in beds with a negative pressure room, in order to reduce the potential for contamination with the formation of aerosol. It is worth mentioning the need for the health care team to use individual protective equipment during the application of this therapy. To date, the literature does not provide a basis to support the routine use of CNAF for the treatment of patients with COVID-19[20,38].

Patients evaluated and prescribed for Physiotherapy[21], must always promote Physiotherapeutic adaptations with the guidelines of the "Crisis Unit" and approved by the Directors of the Institutes that manage patients with COVID-19, in the specific professional environment of each hospital.

CONCLUISION

COVID-19 causes low pulmonary compliance and important changes in lung function with hypoxemia and cardiovascular repercussions. These changes lead to the need for Physiotherapy and the management of oxygen therapy and ventilatory support (invasive and non- invasive) for these patients. The need for further updates to this document is anticipated as changes in functionality for Physiotherapy are better known.

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Brazilian Society of Physiotherapy - BSP

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CHAPTER 7

SOCIAL DISTANCING MEASURES COULD HAVE REDUCED ESTIMATED DEATHS RELATED TO COVID-19 IN BRAZIL

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Abstract

Social distancing was planned as a preventive measure to control the extensive spread of COVID-19. COVID-19-related deaths in Brazil were analyzed during the period of social distancing measures. Mortality data for COVID-19 was obtained from the Worldometer website (www.worldometer.info). Deaths were estimated up to the 31st day after the occurrence of the 5th COVID-19-related death in Brazil. Social distance was measured using Google's community mobility reports (https:// www.google.com/covid19/mobility/). The Brazilian epidemic curves were interconnected, and mathematical models were evaluated to fit the mortality estimation curves. The optimistic model was defined in the opening period of social distancing and, therefore, in the lower mobility (40-60%). The realistic model was calculated according to relaxed social distance measures (<40%) and the pessimistic model was calculated based on the transmission rate between 2-3. Thus, the equations of the mathematical models provided the outcomes for the date of June 9, 2020, as follows: realistic model with 40,623 deaths, pessimistic model with 64,310 deaths and the optimistic model with a projection of 31,384 deaths. As a result of these analyzes, on May 24, 2020, there were a total of 22,965 deaths related to COVID-19, and those deaths included within the proposed mathematical models were 17,452 for the optimistic model, 22,623 for the realistic model and 32,825 for the pessimistic model. Thus, it is concluded that social distancing measures promoted by the Brazilian public managers contributes to the reduction in approximately ten thousand deaths related to COVID-19 in the current pandemic scenario.

Keywords: Beta-Coronavirus; Centers for Disease Control and Prevention (U.S.A.); Coronavirus; Coronavirus Infections; Death; SARS Virus.

Resumo

Introdução: O distanciamento social foi planejado como uma medida preventiva para controlar a disseminação extensiva da COVID-19. Nós analisamos as mortes relacionadas à COVID-19 no Brasil durante o período de medidas de distanciamento social. Os dados de mortalidade do COVID-19 foram obtidos no site da Worldometer (www.worldometer.info). As mortes foram estimadas até o 31º dia após a 5ª morte. O distanciamento social foi medido por meio dos relatórios de mobilidade comunitária COVID-19; Google (https://www.google.com/covid19/mobility/). As curvas epidêmicas brasileiras foram interligadas e os modelos matemáticos foram avaliados para se ajustarem às curvas de estimativa de mortalidade. O modelo otimista foi fundado no período de abertura da distância social e, portanto, na menor mobilidade (40-60%). O modelo realista foi calculado de acordo com medidas de distanciamento social relaxado (<40%) e o modelo pessimista foi calculado com base em R0 entre 2-3. Sob essa situação, o modelo matemático realista estimou 40.623 mortes em 9 de junho de 2020, enquanto o modelo pessimista antecipou 64.310 mortes e o modelo otimista projetou 31.384. Até hoje (24 de maio de 2020), um total de 22.965 foram relatadas, enquanto nosso modelo projetou 17.452 para o modelo otimista, 22.623 para o modelo realista e 32.825 para o modelo pessimista.

Observamos movimento reduzido ao longo deste período. Em resumo, o modelo matemático sugere que a mobilidade reduzida da comunidade diminuiu o total estimado de mortes relacionadas à COVID-19 no Brasil. Enfatizamos que mais procedimentos metodológicos serão necessários para confirmar esta teoria.

Palavras-chave: Beta-Coronavírus; Centros de Controle e Prevenção de Doenças (EUA); Coronavírus; Infecções por Coronavírus; Morte; Vírus SARS.

INTRODUCTION

Coronavirus Disease 2019 (COVID-19) has caused a global recession in the economic and health systems[1-3]. It is characterized as a pandemic in Brazil and worldwide. In reports released by The Imperial College (England)[4] emphasized the importance of non- pharmacological interventions to control the current pandemic. In addition, findings by Dehning et al[5] (in Germany) and Garcia and Duarte[6] (in Brazil) corroborate the hypothesis that social isolation is fundamental for disease control, being a non-pharmacological and effective measure for reducing the hypothetical epidemic curve for COVID-19.

Such measures have important impacts on daily activities, both on people's lives and on society in general, as reported by Garcia and Duarte[6]. There are several effects of this measure of social isolation, such as the increase in domestic violence for women and children, as these populations are more vulnerable in their homes and there are economic losses for people, families, companies and countries[6].

It is noteworthy that Brazil adopted the pandemic control scenario using social distance as one of the sanitary measures. Thus, studies with mathematical models are important to assist public managers in making decisions. Therefore, the objective of this study is to analyze the outcomes of deaths by COVID-19.

METHODS

This is a study of mathematical projection and secondary data. COVID-19 mortality data, which occurred in Brazil, were obtained from the Worldometer website (www.worldometer.info)[7].

Worldometer[7] is managed by an international team of developers, researchers, and volunteers, who provide global statistical health data, available in a timely manner to a global audience. It is published by a digital media company based in the United States of America, being recognized as independent from state influence and other agents of global society, having no political, governmental or corporate affiliations.

Deaths were estimated from the 5th death until the 31st day after the 5th death record. This data collection occurred between March 9th and April 17th.

Social distancing was defined as a reduction in the mobility of people and was assessed via COVID-19 Community Mobility Reports – Google (https://www.google.com/covid19/mobility/), which makes available Community mobility reports founded on charts with trends and inclinations over time by region and in different categories of locations.

Initially, a link was achieved for Brazilian COVID-19 mortality. Temporal adjustments were finalized, enabling the comparison of data on the Cartesian x-axis, and the adjustment of number of deaths per each 10,000,000 inhabitants, that permitted the procurement of data on the Cartesian y-axis.

Historically, there have been some regressions to determine the best mathematical model that would permit the representation of the mortality estimation curve for Brazilian COVID-19. Whilst searching for the correct mathematical model that best fits the mortality estimation curves, the subsequent models were evaluated: Linear, Logarithmic, Inverse, Quadratic, Cubic, Composite, S, Growth, Exponential and Logistic (Figure 1).

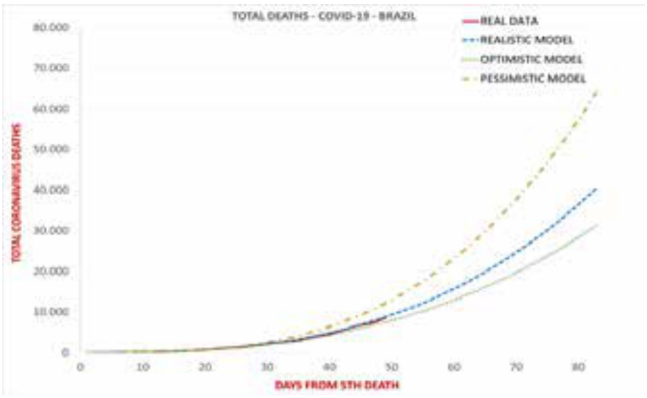

Figure 1: Optimistic, realistic, pessimistic projections and real data concerning deaths related to COVID-19 in Brazil.
Edited by Menezes et al. https://doi. org/10.1101/2020.04.28.20083675

The key model, from all available points, was termed a realistic model. Two other models were computed using parts of the data. One that has a greater vertical tendency (Pessimistic model) and another that was further compressed or flattened (Optimistic model).

The realistic model was computed according to extra relaxed social distancing measures (<40%) and the pessimistic model was calculated founded on a R0 ≈ 2-3. For this estimate, a significance of alpha, (α) less than 0.01 (p <0.01, <1%) and R2 > 0.95 was implemented.

The datasets were manipulated using Microsoft Excel version 16.36, for MacOS Catalina version 10.15.4. Statistical calculations were computed via IBM SPSS Statistic Subscription application 1.0.0.1347 64-Bits for MacOS. These values were considered statistically significant for (p<0.05, <5%) and the recognized beta, (β) value was 0.1.

Finally, data from the continuous PNAD10 was used, which promotes data collection for the Brazilian territory, by large regions, Federation units and Metropolitan regions containing Municipalities of Capitals, Integrated Development Region (RIDE) of Greater Teresina and Municipalities of Capitals for the collection of mobile data by cell phone[10].

RESULTS

It was found that the mathematical models that came closest were the cubic and quadratic models. However, the cubic model was better adjusted R2 = 0.998 (table 1).

In figure 2 there are optimistic, realistic and pessimistic models compared to the real data. It was observed that the cubic model approached the mortality growth curve, and algebraically approached as follows:

$$x(t)=11,422+0,269*t+0,265*t^2+0,069*t^3$$

t is the number of days after the fifth COVID-19 related death.

Table 1: Summary and parameter estimates.

Dependent variable: Deaths									
Equation	Model summary					Parameter estimates			
	R2	Z	df1	df2	Sig.	Constant	b1	b2	b3
Linear	.859	170.682	1	28	.000	-450.108	67.532		
Logarithmic	.545	33.587	1	28	.000	-789.488	556.986		
Invers	.188	6.495	1	28	.017	788.676	-1442.125		
Quadratic	.995	2654.798	2	27	.000	124.413	-40.191	3.475	
Cubic	**.998**	**4350.630**	**3**	**26**	**.000**	**11.422**	**.269**	**.265**	**.069**
Composed	.963	732.622	1	28	.000	13.567	1.204		
Potency	.947	497.163	1	28	.000	2.110	1.902		
S	.565	36.326	1	28	.000	6.343	-6.475		
Growth	.963	732.622	1	28	.000	2.608	.185		
Exponenctial	.963	732.622	1	28	.000	13.567	.185		
Logistic	.963	732.622	1	28	.000	.074	.831		

The independent variable is Days from the 5th Death.

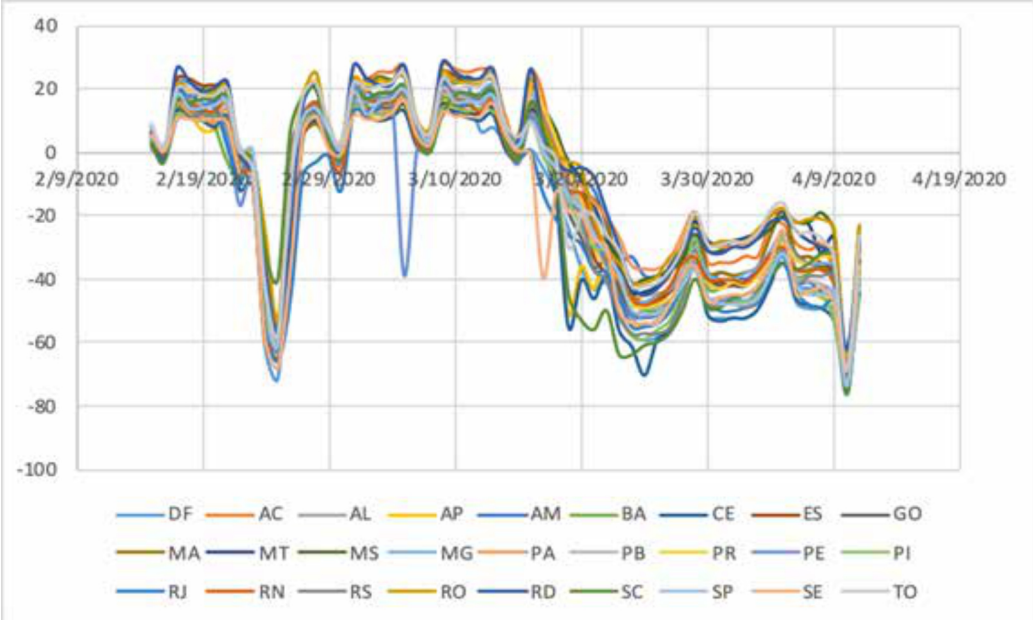

Figure 2: Comparison between total deaths related to COVID-19 in Brazil and projected via mathematical model.

For this situation, the mathematical model predicted 40,623 deaths on June 9, 202011. The maximum pessimistic model predicts 64,310 deaths and the maximum optimistic model predicts 31,384 deaths. In this date (May 24, 2020), 22,965 deaths have been reported, while our model projected 17,45211 for the optimistic model, 22,623 for the realistic model and 32,82511 for the pessimistic model (table 2).

Figure 3 illustrates data from community mobility reports in Brazilian states. There is a mathematical indication of a reduction in social mobility from the end of March 2020.

Table 2: Estimates of accumulated deaths related to COVID-19 in Brazil.

Day	Optimistic	Realistic	Pessimitic
May/20	14.760	18.091	27.028
May/21	15.405	18.944	28.407
May/22	16.069	19.823	29.832
May/23	16.751	20.729	31.305
May/24	17.452	21.662	32.825
May/25	18.172	22.623	34.394
May/26	18.910	23.612	36.013
May/27	19.668	24.630	37.682
May/28	20.446	25.676	39.402
May/29	21.243	26.751	41.174
May/30	22.060	27.856	42.999
May/31	22.897	28.991	44.877
Jun/1	23.755	30.156	46.809
Jun/2	24.634	31.353	48.796
Jun/3	25.533	32.580	50.839
Jun/4	26.454	33.839	52.938
Jun/5	27.396	35.130	55.095
Jun/6	28.360	36.453	57.309
Jun/7	29.346	37.810	59.583
Jun/8	30.354	39.199	61.916
Jun/9	31.384	40.623	64.310

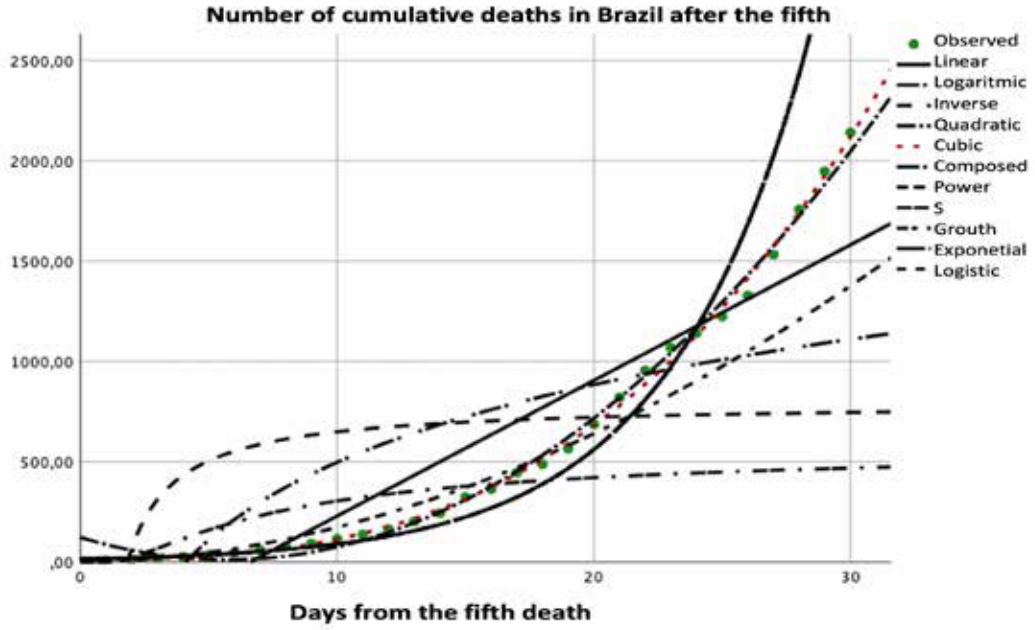

Figure 3: Community Mobility Reports in all Brazilian States. DF: Federal District; AC: Acre; AL: Alagoas; AP: Amapa; AM: Amazonas; BA: Bahia; CE: Ceara; ES: Espirito Santo; GO: Goias; MA: Maranhao; MT: Mato Grosso; MS: Mato Grosso do Sul; MG: Minas Gerais; PA: Para; PB: Paraiba; PR: Parana; PE: Pernambuco; PI: Piaui; RJ: Rio de Janeiro; RN: Rio Grande do Norte; RS: Rio Grande do Sul; RO: Roraima; RD: Rondonia; SC: Santa Catarina; SP: Sao Paulo; SE: Sergipe; TO: Tocantins.

DISCUSSION

This study was initiated to assess deaths related to COVID-19 in Brazil between March 9, 2020 to April 17, 2020. Thus, it was possible to design possible scenarios based on the non-pharmacological measure of mobility in the Brazilian community. It was found that the real data are closer to the realistic model. However, it is worth noting that the mathematical model presented was adequate, however, if the growth of deaths by COVID-19 continues to increase. In stabilizing the pandemic epidemiological curve or decreasing it, it will be necessary to revise the mathematical model.

In the mathematical model, considering the non- implementation of the non-pharmacological intervention mechanism of social detachment, it was predicted that on May 24, 2020 there would be a total number of deaths related to COVID-19 of 32,825. The findings in tables 1 and 2 and figures 1, 2 and 3 confirm the mathematical projections made. However, the number of actual deaths were 22,965.

In view of the initial mathematical projection, published in pre-print[10], in a specific projection for the date of June 9, 2020, it is estimated that there were approximately ten thousand lives saved by the exclusive action of Brazilian social distance.

However, in some research scenarios, such as the State of São Paulo, only a small number of cases of COVID-19 were reported (the State of São Paulo only communicates critical cases of COVID-19 and reports that it is a measure of full orientation Ministry of Health of Brazil). This situation promotes the event of underreporting of the disease. Thus, the regression model between total deaths and social mobility was not performed, since the number of COVID-19 cases increases exponentially. The dependent variable was social mobility, and this variable was registered via mobile cellular telephony.

Also, Garcia and Duarte[6] reported that the actions of the Unified Health System (SUS) and other areas of the social protection system are essential in an articulated way, in order to favor people's adherence to non- pharmacological interventions and minimize the impacts harmful effects of Community measures. The protection of public health should guide the decisions to be taken by managers. It is essential that these decisions are based on the best available evidence and communicated in a transparent manner, in order to promote the population's trust and that the guidelines of the authorities and people's adherence to the INF will be decisive for the course of the COVID-19 epidemic in Brazil[6].

It is salutary to highlight that mathematical estimates have limitations. One of them refers to the point of analysis of the variable social mobility, which was collected from mobile telephony. According to PNAD 201810, about a quarter of the Brazilian population does not have access to mobile telephony, therefore this population was excluded from the analysis of the raw data of this research, as the model does not include those Brazilians who do not have or do not use mobile cellular telephony[10].

Finally, it is concluded that the mathematical model demonstrated that the reduced mobility of the community, in the form of social distance, was able to decrease the total number of deaths expected and related to COVID-19 in Brazil, in approximately ten thousand lives.

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Author contributions

Pedro de Lemos Menezes draft the manuscript, wrote introduction and discussion section gave final approval for the version submitted for publication. Gustavo Nakamura Alves Vieira draft the manuscript, reviewed interpretation analysis and gave final approval of the manuscript. David M. Garner draft the manuscript, performed statistical analysis and improved interpretation analysis, reviewed English Grammar and Spelling. Vitor E. Valenti draft the manuscript, wrote introduction and discussion section and gave final approval for the version submitted for publication.

Competing interests

The authors declare absence of financial and non- financial interests.

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CHAPTER 8

OVERVIEW ON THE RECOMMENDATIONS FOR REASTFEEDING AND COVID-19

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Abstract

Introduction: Human infection caused by the new Coronavirus is a public health emergency of international importance, whose clinical spectrum ranges from mild symptoms to severe acute respiratory syndrome. However, there is weak information about the clinical presentations of Coronavirus in newborns and children. **Objective:** To describe the recommendations about breastfeeding during SARS-CoV-2 infection. **Methods:** Scope review study. **Results:** The discussion on viral transmission through breastfeeding is controversial and the recommendations vary according to experts of different countries. **Conclusion:** The scientific knowledge currently available does not allow to accurately inform the best conduct in the breastfeeding process, making each country decide the strategy that best adapts to its reality. Implications for the practice: It is important that the health team has a close eye to identify atypical signs and symptoms during this process to act preventively in the face of possible complications.

Keywords: Breastfeeding; Coronavirus Infections; Coronavirus; SARS Virus; Maternal-Child Nursing.

Resumo

Introdução: A infecção humana causada pelo novo Coronavírus é uma emergência de saúde pública de importância internacional, cujo espectro clínico varia de sintomas leves à síndrome respiratória aguda grave. Destaca-se que há informações fragilizadas sobre as apresentações clínicas do Coronavírus em recém-nascidos e crianças. **Objetivo:** Descrever as recomendações acerca da amamentação durante a infecção por SARS-CoV-2. **Método:** Estudo de revisão de escopo. **Resultados:** A discussão sobre a transmissão viral via amamentação é controversa e as recomendações variam de acordo com especialistas em diferentes países do mundo. **Conclusão:** O conhecimento científico atualmente disponível não permite informar com precisão a melhor conduta no processo de amamentação, fazendo com que cada país decida a estratégia que melhor se adapta a sua realidade. Implicações para a prática: É importante que a equipe de saúde tenha um olhar atento para identificação de sinais e sintomas atípicos durante esse processo para agir preventivamente frente às possíveis intercorrências.

Palavras-chave: Aleitamento Materno; Infecções por Coronavirus, Coronavirus; Vírus da SARS; Enfermagem Materno-Infantil.

INTRODUCTION

Human infection caused by the new Coronavirus (SARS-CoV-2), or COVID-19, is a public health emergency of international importance, whose clinical spectrum is diverse, ranging from mild symptoms to severe acute respiratory syndrome. Lethality varies according to each country, but it is clear that elderly and people with chronic comorbidities are the ones with the most complications. At the moment, no vaccines or drugs have been developed with proven scientific evidence for their definitive treatment and, currently, clinical management is aimed at supporting and controlling symptoms[1].

The number of people infected with SARS- CoV-2 in the world is impressive. As of August 30, 2020, approximately 25 million cases and 800,000 deaths have been reported since the outbreak began2. The mortality rate is between 0.2% and 0.4% for the age groups between 10 and 49 years, 1% for the elderly between 50 and 59 years, 3.6% for people between 60 and 69 years and 8% for over 70[3].

In view of the novelty of the disease and even with scientific advances to better understand the natural course of the disease, there is little information on the clinical presentations of Coronavirus in newborns and children. According to some studies, the condition of children infected with Coronavirus is mild or moderate[4-6], although newborns have recognized immaturity of the immune system, which suggests that they may be more susceptible to infection by the virus[7].

Currently, there is no consolidated evidence on the vertical transmission of SARS-CoV-2, since the virus was not found in samples of amniotic fluid, umbilical cord, swab in the throat of neonates and in human milk[4,8]. A study carried out in China found that, specifically, with respect to Coronavirus, children under one year old have higher rates of serious complications than older ones[5].

Since March 18th of 2020, the World Health Organization (WHO) indicates that women with COVID-19 are able to breastfeed, based on the idea that through breast milk, babies obtain antibodies and anti-infectious factors that help to protect them from various infections[9].

In this sense, breastfeeding is vital for health and can save the lives of more than 820,000 children under the age of five each year. In the first hours of the baby's life, breastfeeding, which has a multitude of protective properties, including immunological ones, decreasing the risk of infections by viruses or bacteria and reducing neonatal mortality, should be initiated. Likewise, it provides adequate nutrients for the healthy development of the child. For the mother, it reduces the risk of postpartum depression, anemia and different pathologies[10].

As it is a recent pathology, the transmission of Coronavirus via breastfeeding is still a limited and quite controversial subject, since the recommendations vary in different countries. It is worth mentioning that, during the pandemic, decisions regarding breastfeeding are constantly reassessed by the scientific community, which may adopt different guidelines as new data becomes available and experience is accumulated. In this sense, this study aims to describe the recommendations about breastfeeding during SARS-CoV-2 infection.

METHODS

Scope review study, which, according to Peterson and collaborators11, allows the identification of knowledge gaps, mapping the available evidence in a specific area of interest, defining the scope of a body of literature, clarifying concepts and investigating research conducts, gathering several drawings of search.

The following steps were taken to develop this review: (1) identify the research question; (2) identify the relevant studies; (3) selection of studies; (4) data mapping; (5) compile, summarize and report the data[11]. From the research question "What are the recommendations for breastfeeding during the COVID-19 pandemic?", the following elements were defined according to the mnemonic P - Population, C - Concept and C - Context P (women and newborns); C (breastfeeding) and C (COVID-19/SARS-CoV-2).

We sought to review the strategies and recommendations adopted by different countries in relation to breastfeeding during the Coronavirus pandemic in protocols, guidelines, government websites and search for scientific articles published in the databases: National Library of Medicine (MEDLINE/PubMed) and Literature Latin American and Caribbean Health Sciences (LILACS). Then, to ensure a thorough search, the controlled descriptors [Health Science Descriptors (DeCS), Medical Subject Headings (MeSH)] were defined: "Breastfeeding" and "Coronavirus" in English and Portuguese, combined two by two, using the Boolean operator AND. As an inclusion criterion, the selection included scientific articles available in full, in Portuguese, English, Spanish and Italian, which addressed the issue of breastfeeding in the context of SARS-CoV-2. The following were excluded: opinion and duplicated articles. There was no time frame for searching publications.

The articles were mapped using data collection indicators designated by title, type of study, country of origin and recommendations on breastfeeding. The results were submitted to a descriptive analysis of the content, using analytical tables that synthesized the key information of the studies, interpreting and comparing the productions, to describe the available evidence that answered the guiding question.

RESULTS

Board 1, below, describes and summarizes the results found on recommendations related to breastfeeding during the COVID-19 pandemic, in different countries. It is noteworthy that, of the publications found, 11 are scientific articles and 11 are documents such as protocols, guidelines and government websites.

Board 1: Characterization and synthesis of selected articles/documents. Brazil, 2020.

n.	Entity/author	Title	Summary
1	Wang L, Shi Y, Xiao T, et al.[12]	Chinese expert consensus on the perinatal and neonatal management for the prevention and control of the 2019 novel coronavirus infection.	The possibility of vertical transmission of Coronavirus cannot be ruled out. Thus, among other issues, babies of mothers with confirmed Covid-19 should not be fed breast milk.
2	Liang Huan, Acharya G[13]	Novel coronavirus disease (COVID-19) in pregnancy: What clinical recommendations to follow?	Temporary separation of the newborn, for at least 2 weeks, is recommended to minimize the risk of viral transmission, avoiding close and prolonged contact with the infected mother. The newborn should be cared for in an isolation ward and carefully monitored for any signs of infection. During this period, direct breastfeeding is not recommended.
3	Favre G, Pomar L, Musso D, Baud D[14]	2019-nCoV epidemic: what about pregnancies?	Chinese experts discourage breastfeeding and do not rule out the possibility of vertical transmission of the virus and, therefore, contraindicate breastfeeding, even in only suspect cases.
4	Comissão Nacional de Saúde da República Popular da China[15]	Press conference on February 7, 2020.	Two cases of neonatal Coronavirus infections where reported and it is suspected that both were infected in the postnatal period from contact with the infected mother. Researchers advise against breastfeeding even in infected mothers without symptoms.
5	Guan-jing Lang, Hong Zhao[16]	Can SARS-CoV-2 infected women breastfeed after viral clearance?	It reports the clinical course of a pregnant woman with COVID-19. The results suggest that breastfeeding can be practiced after a period of isolation.

n.	Entity/author	Title	Summary
6	Colégio de Ginecologia e Obstetrícia da Ordem dos Médicos de Portugal[17]	Covid-19: performance in pregnant women.	Researchers advise against breastfeeding even in infected mothers without symptoms.
7	World Health Organization[18]	Questions and answers about COVID-19, pregnancy, childbirth and lactation.	Encourages breastfeeding, even in women infected with Coronavirus, as long as some respiratory hygiene practices are practiced in order to prevent contamination of the newborn.
8	Centro de Controle e Prevenção de Doenças[19]	Considerations for hospital obstetric healthcare settings.	Encourages breastfeeding, even in women infected with Coronavirus, as long as some respiratory hygiene practices are practiced in order to prevent contamination of the newborn and adds that the decision to initiate or continue breastfeeding must be made by the mother together with the mother, family and the team of professionals who care for her.
9	Royal College of Obstetricians & Ginecologists[20]	Coronavirus infection and pregnancy.	It suggests a discussion between the risks and benefits of breastfeeding among pregnant women, family and the maternity team. Guides breastfeeding, even in women infected with Coronavirus, as long as respiratory hygiene is practiced in order to prevent contamination of the newborn.
10	Sociedade Italiana de Neonatologia[21]	Breastfeeding and SARS-CoV-2 infection (Coronavirus Disease 2019 - COVID-19).	Recommends breastfeeding in mothers with confirmed asymptomatic infection or with mild symptoms. Considers it necessary to separate the binomial in cases of symptomatic mothers, with confirmed infection, or suspicions, until obtaining the results of the samples.
11	Davanzo, Riccardo; Moro, Guido; Sandri, Fabrizio; Agosti, Massimo; Moretti, Corrado; Mosca, Fabio[22]	Breastfeeding and coronavirus disease-2019: Ad interim indications of the Italian Society of Neonatology endorsed by the Union of European Neonatal & Perinatal Societies.	Review of published literature, developed a consensus statement, endorsed by the Union of Neonatal and European Perinatal Societies (UENPS). The Italian Society of Neonatology (SIN), after reviewing the limited scientific knowledge on the compatibility of breastfeeding in the mother with COVID-19 and the statements available from Health Organizations, issued the following indications that were endorsed by the European Union of Neonatology and Perinatal Societies (UENPS). If a mother previously identified as positive or under investigation for COVID-19 is asymptomatic or paucysymptomatic at delivery, joint accommodation is feasible and direct breastfeeding is advisable, under strict infection control measures. On the contrary, when a mother with COVID-19 is too ill to care for the newborn, the newborn will be treated separately and fed with fresh breast milk, without the need to pasteurize it, as human milk is not considered a vehicle of COVID-19.

Continuation - Board 1: Characterization and synthesis of selected articles/documents. Brazil, 2020.

n.	Entity/author	Title	Summary
12	Ministério da Saúde. Fundação Oswaldo Cruz. Rede Brasileira de Bancos de Leite Humano[23]	Recommendations for Reception and Clinical Management in breastfeeding pregnant women, mothers and women who are asymptomatic or symptomatic of COVID-19 by the Human Milk Bank.	Provides guidance on breastfeeding and breast milk supply in times of COVID-19.
13	Sociedade Espanhola de Neonatologia[24]	Recommendations for the management of the newborn in relation to SARS-CoV-2 infection.	It recognizes that there is still insufficient data to make safe recommendations and initially did not support the indication to allow breastfeeding. However, in its most recent protocols, and considering the benefits for the binomial, it advises to maintain breastfeeding from birth, if the clinical conditions of the newborn and mother allow.
14	La Leche League Internacional França[25]	Breastfeeding information from A to Z. Coronavirus (COVID-19).	Encourages families to recognize the importance of human milk in providing immunological protection for the child and adds that it is important not to interrupt breastfeeding, even if the lactating mother becomes ill.
15	Centers of Disease Control and Prevention[26]	Information about Coronavirus Disease 2019.	Addresses that the benefits of breastfeeding outweigh any potential risks of transmission of the virus through human milk.
16	Royal College of Obstetricians and Gynaecologists[27]	Coronavirus (COVID-19) infection in pregnancy: information for healthcare professionals.	Review addresses the benefits of breastfeeding outweigh any potential risks of transmission of the virus through human milk.
17	Fernández-Carrasco, Francisco Javier; Vázquez-Lara, Juana María; González-Mey, Urbano; Gómez-Salgado, Juan; Parrón-Carreño, Tesifón; Rodríguez-Díaz, Luciano[28]	COVID-19 Coronavirus Infection and Breastfeeding: An Exploratory Review.	Bibliographic research was carried out through the databases. Breastfeeding in postpartum women with SARS-CoV-2 is highly recommended for the newborn, if the health of the mother and newborn allows.
18	Lowe, Belinda; Bopp, Benjamin[29]	COVID-19 vaginal delivery - A case report.	Case report of an uncomplicated vaginal delivery in a mother with COVID-19. Encouraging breastfeeding seems possible and safe when viral precautions are observed.
19	Salvatori, Guglielmo; De Rose, Domenico Umberto; Concato, Carlo; Alario, Dario; Olivini, Nicole; Dotta, Andrea; Campana, Andrea[30]	Managing COVID-19-Positive Maternal-Infant Dyads: An Italian Experience.	Experience report in a hospital in Italy. The authors argue that when SARS-CoV-2 is identified in the mother and child, there is no reason to stop breastfeeding and separate them. Whenever direct breastfeeding is not possible, the use of expressed breast milk should be considered and promoted to take advantage of its indisputable benefits.

Continuation - Board 1: Characterization and synthesis of selected articles/documents. Brazil, 2020.

n.	Entity/author	Title	Summary
20	Calil, Valdenise Martins Laurindo Tuma; Krebs, Vera Lucia Jornada; Carvalho, Werther Brunow de[31]	Guidance on breastfeeding during the COVID-19 pandemic.	Review of the medical literature that provides guidance on breastfeeding for mothers with suspected or confirmed COVID-19. We analyzed 20 recent publications on breastfeeding, COVID-19, and its transmission through breast milk. We present the possible options for breastfeeding and its consequences for the mother and child.
21	Davanzo, Riccardo32	Breast feeding at the time of COVID-19: do not forget expressed mother's milk, please.	The study cites that Chinese colleagues who recently dealt with COVID-19 simply do not consider the option of breastfeeding, nor the use of breast milk for newborns. Instead, from Switzerland, Favre et al. suggest avoiding direct breastfeeding. The study concludes that the protocols applied in maternity hospitals for the prevention of COVID-19 should consider, as far as possible, the promotion of breastfeeding, without disregarding the possibility of expressing breast milk.
22	Martins-Filho, Paulo Ricardo; Santos, Victor Santana; Santos Jr., Hudson P[33]	To breastfeed or not to breastfeed? Lack of evidence on the presence of SARS-CoV-2 in breastmilk of pregnant women with COVID-19	Rapid systematic review to assess current evidence related to the presence of SARS-CoV-2 in the breast milk of pregnant women with COVID-19. No breast milk sample was positive for SARS-CoV-2 and, to date, there is no evidence for the presence of SARS-CoV-2 in the breast milk of pregnant women with COVID-19. However, data are still limited and breastfeeding for women with COVID-19 remains a controversial issue.

DISCUSSION

Based on the synthesis of the results, the authors point out that the recommendations on breastfeeding in times of COVID-19 are controversial, given that the countries adopt different protocols based on the experiences of previous outbreaks and on the economic, socio-political-cultural issues.

Chinese experts discourage breastfeeding[12-14] and do not rule out the possibility of vertical transmission of the virus and, therefore, contraindicate breastfeeding, even in only suspect cases[12]. They say that the virus should be researched in the milk of suspected or diagnosed mothers and, only with the negative result, babies can be breastfed or fed with human milk. Still, they describe that human milk from healthy donors should also be screened for viral presence, as they claim that the virus can be excreted in milk during the disease's incubation period[12]. In addition, they report 2 cases of neonatal infection by Coronavirus and it is suspected that both were infected in the postnatal period from contact with the infected mother[15]. Another Chinese study suggests practices different from the practices mentioned above and declare that breastfeeding can be practiced, provided that a period of isolation is fulfilled[16].

Similarly, Portugal, through the College of Gynecology and Obstetrics of the "Ordem dos Médicos", advises against breastfeeding in mothers infected or suspected of COVID-19 and, when possible, stimulate the extraction of human milk with a pump[17]. Thus, it is noted that China and Portugal have adopted more preventive measures and advise against breastfeeding even in infected mothers without symptoms[15-17].

On the other hand, the World Health Organization (WHO) issued guidelines encouraging breastfeeding[18], even in women infected with Coronavirus, if some respiratory hygiene care is practiced, in order to prevent contamination of the newborn. Thus, it is necessary to wash hands before breastfeeding or before expressing human milk, use a face mask (completely covering your nose and mouth) during feedings, avoid talking or coughing during this process, in addition to strictly following the recommendations for cleaning the breast pump after use. If the mother does not feel comfortable to breastfeed the child directly, WHO advises that human milk should be milked, using hygiene measures and offered to the newborn by a healthy caregiver[18].

The Center for Disease Control and Prevention (CDC), in the United States, is in line with the WHO recommendations and adds that the decision to initiate or continue breastfeeding must be made by the mother together with the family and the team of professionals who take care[13]. The Royal College of Obstetricians & Gynecologists (RCOG) in the United Kingdom also shares the information provided by WHO[20].

In Italy, the Italian Society of Neonatology recommends breastfeeding in mothers with confirmed asymptomatic infection or with mild symptoms. It considers to be necessary to separate the binomial in cases of symptomatic mothers, with confirmed or suspected infection, until obtaining the sample results. In cases of separation, the Italian Society recommends that an asymptomatic person offers human milk to the newborn[21,22].

In clinical situations in which the mother is unable to breastfeed, it is recommended to express her milk and offer it to the newborn by means of a cup or spoon. If the mother uses accessories for the extraction of milk, the surfaces of the equipment must be disinfected with 70% alcohol, and the accessories must be washed and boiled for 15 min from the moment the water boils[18,23].

On the other hand, the Spanish Society of Neonatology recognizes that there is still insufficient data to make safe recommendations and, initially, did not support the indication to allow breastfeeding. However, in its most recent protocols, and considering the benefits for the binomial, it advises to maintain breastfeeding from birth, if the clinical conditions of the newborn and mother allow[24].

In the same direction, France, through the La Leche League International, encourages families to recognize the importance of human milk in providing immunological protection for the child and adds that it is important not to interrupt breastfeeding, even if the breastfeeding woman becomes ill. The League explains that the baby has already been exposed to the virus by the mother and/ or family and will benefit more from direct and continuous breastfeeding[25].

In Brazil, the Ministry of Health is in favor of maintaining breastfeeding in women with or suspected COVID-19, as long as the woman and the child are in satisfactory clinical conditions and follow the WHO hygiene recommendations in order to avoid viral spread for the newborn[18,23].

It should be noted that two published international reviews addressed this issue and emphasize that the benefits of breastfeeding outweigh any potential risks of transmission of the virus through human milk[26,27]. Furthermore, other studies argue that breastfeeding in postpartum women with SARS-CoV-2 is highly recommended for the newborn, if the health of the mother and newborn allows[28,29,30].

Given this scenario, it is noted that the scientific knowledge currently available does not allow to accurately inform the best conduct in the breastfeeding process[31,32,33]. These uncertainties make each country decide, by analogy, through limited experiences of previous outbreaks and the interpretation of the benefits of breastfeeding already consolidated in the literature and the possible complications that the infection can cause, the strategy that best adapts to its reality.

With the course of the disease, care guidelines are being standardized, but for this, complete data on Coronavirus infections during the pregnancy, puerperal and breastfeeding cycle must be collected and made available to the public. The approaches will evolve as more data becomes available, thus serving as a basis for describing the experience of the current epidemic instead of being based on previous circumstances of different types of corona viruses, as their epidemiology, clinical course and response to treatment may differ.

The limitations of this review are related to observational studies, with small and limited samples, the short observation period and research that is still incipient in relation to the theme. We opted to include gray literature to ensure greater possibility of discussion and knowledge, contemplating guidelines from the Ministry of Health and other health institutions in Brazil and the world.

In view of the epidemiological scenario, this review is essential for mapping, together with the literature, recommendations on breastfeeding during the COVID-19 pandemic, which can guide the care provided by health professionals and support future research. The strategies and recommendations found in this review are aimed at assisting women and children from the delivery room, until the return to their home, either during hospitalization or during the follow-up by Primary Health Care. Among the main guidelines found, the use of masks, hand hygiene before and after each feeding and the cleaning of the tools used for breast milking are pointed out. All these precautions are essential and must be carried out in partnership with the families.

Considering the different recommendations on the breastfeeding process during the COVID-19 pandemic around the world, it is important that the health team, regardless of the guidelines in each country, closely monitor the mother-child and their family in this process. It is up to the professional who assists these women, to provide appropriate guidance in face of the ideological, cultural, social and economic factors of the environment in which they live, in addition to listening to them in order to detect and correct possible difficulties and/or complications early, such as mastitis and breast engorgement that may favor early weaning.

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CHAPTER 9

TRENDS IN CASE-FATALITY RATES OF COVID-19 IN THE WORLD, BETWEEN DECEMBER, 2019 AND AUGUST, 2020

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Abstract

Introduction: CoV infections can potentially cause from a simple cold to a severe respiratory syndrome, such as the Severe Acute Respiratory Syndrome and the Middle East Respiratory Syndrome (MERS-CoV). The COVID-19 created a new reality for global healthcare delivery models. **Objective:** To evaluate trends in case-fatality rates of COVID-19 in the world. **Methods:** We conducted a population-based time-series study using public and official data of cases and deaths from COVID-19 in Argentina, Australia, Brazil, Chile, China, Colombia, France, Germany, India, Iran, Italy, Japan, Mexico, Morocco, New Zealand, Nigeria, Peru, Saudi Arabia, South Africa, South Korea, Spain, Switzerland, United Kingdom, United States and Russia, between December, 2019 and August, 2020. Data were based on reports from the European Centre for Disease Prevention and Control. COVID-19 was defined according to the International Classification of Diseases, 10th revision (U07.1). A Prais-Winsten regression model was performed and the Daily Percentage Change (DPC) determined rates as increasing, decreasing or flat. **Results:** During the study period, trends in case-fatality rates in the world were flat (DPC = 0.3; CI 95% [-0.2: 0.7]; p = 0.225). In Africa, Morocco had decreasing trends (DPC = -1.1; CI 95% [-1.5: -0.7]; p < 0.001), whereas there were increasing trends in South Africa (p < 0.05) and flat trends in Nigeria (p > 0.05). In the Americas, Argentina showed a decreasing trend in case-fatality rates (DPC = -0.6; CI 95% [-1.1: -0.2]; p = 0.005), the U.S. had flat trends (p > 0.05) and all other countries in the Americas had increasing trends (p < 0.05). In Asia, Iran had decreasing trends (DPC = -1.5; CI 95% [-2.6 : -0.2]; p = 0.019); China and Saudi Arabia showed increasing trends (p < 0.05), while in India, Japan and South Korea they were flat (p > 0.05). European countries had mostly increasing trends (p < 0.05): Germany, Italy, Spain, the UK and Russia; France and Switzerland had flat trends (p > 0.05). Finally, in Oceania, trends in case-fatality rates were flat in Australia (p > 0.05) and increasing in New Zealand (p < 0.05). **Conclusion:** World trends in case-fatality rates of COVID-19 were flat between December 31, 2019 and August 31, 2020. Argentina, Iran and Morocco were the only countries with decreasing trends. On the other hand, South Africa, Brazil, Canada, Chile, Colombia, Mexico, Peru, China, Saudi Arabia, Germany, Spain, United Kingdom, Russian and New Zealand had increasing trends in case-fatality rates. All the other countries analyzed had flat trends. Based on case- fatality rate data, our study supports that COVID-19 pandemic is still in progress worldwide.

Keywords: COVID-19; Trends; Case-Fatality; Epidemiology.

Resumo

Introdução: As infecções por CoV podem causar desde um simples resfriado até uma síndrome respiratória grave, como a Síndrome Respiratória Aguda Grave e a Síndrome Respiratória do Oriente Médio (MERS-CoV). O COVID-19 impôs uma nova realidade em termos de modelos globais de saúde. **Objetivo:** Avaliar as tendências das taxas de letalidade do COVID-19 no mundo. **Método:** Estudo de séries temporais de base populacional usando dados públicos e oficiais de casos e mortes por COVID-19 na Argentina, Austrália, Brasil, Chile, China, Colômbia, França, Alemanha, Índia, Irã, Itália, Japão, México, Marrocos, Nova Zelândia, Nigéria, Peru, Arábia Saudita, África do Sul, Coreia do Sul, Espanha, Suíça, Reino Unido, Estados Unidos (EUA) e Rússia, entre dezembro de 2019 e agosto de 2020. Os dados foram baseados nos relatórios do Centro Europeu de Prevenção e Controle de Doenças. COVID-19 foi definido pela Classificação Internacional de Doenças, 10ª revisão (U07.1). Para análise estatística, foi realizada a regressão linear de Prais-Winsten, a partir da qual foi possível calcular a variação percentual de mudança diária (DPC) das taxas, classificadas como crescentes, decrescentes ou estacionárias. **Resultados:** Durante o período do estudo, as taxas de letalidade no mundo permaneceram estacionárias (DPC = 0,3; IC 95% [-0,2: 0,7]; p = 0,225). Na África, Marrocos teve tendência decrescente (DPC = -1,1; IC 95% [-1,5: -0,7]; p <0,001), enquanto na África do Sul houve tendência crescente (p < 0,05) e estável na Nigéria (p> 0,05). Em relação às Américas, a Argentina revelou tendência decrescente nas taxas de letalidade (DPC = -0,6; IC 95% [-1,1: -0,2]; p = 0,005), os EUA demonstraram tendência estável (p > 0,05) e todos os outros americanos os países demonstraram tendências crescentes (p < 0,05). Na Ásia, o Irã apresentou tendência decrescente (DPC = -1,5; IC 95% [-2,6: -0,2]; p = 0,019); China e Arábia Saudita apresentaram tendências crescentes (p <0,05), enquanto Índia, Japão e Coreia do Sul mantiveram tendência estacionária (p > 0,05). A maioria dos países europeus apresentaram tendências crescentes (p <0,05): Alemanha, Itália, Espanha, Reino Unido e Rússia; França e Suíça demonstraram tendências estacionárias (p> 0,05). Por fim, na Oceania, a tendência nas taxas de letalidade na Austrália foi estável (p > 0,05) e aumentou na Nova Zelândia (p <0,05). **Conclusão:** A tendência nas taxas de letalidade por COVID-19 no mundo permaneceu estável entre 31 de dezembro e 31 de agosto. Argentina, Irã e Marrocos foram os únicos países com tendências decrescentes. Por outro lado, África do Sul, Brasil, Canadá, Chile, Colômbia, México, Peru, China, Arábia Saudita, Alemanha, Espanha, Reino Unido, Rússia e Nova Zelândia apresentaram tendências crescentes de letalidade. Todos os outros países analisados demonstraram tendências estacionárias. De acordo com dados de letalidade, nosso estudo confirma que a pandemia de COVID-19 ainda está em fase de progressão em todo o mundo.

Palavras-chave: COVID-19; Tendência; Letalidade; Epidemiologia.

INTRODUCTION

The coronaviruses (CoV) are a large family of viruses, so named because of surface spikes that resemble a crown (corona, Latim)[1]. The CoV infections can potentially cause from a simple cold to a severe respiratory syndrome, such as the Severe Acute Respiratory Syndrome (SARS-CoV) and the Middle East Respiratory Syndrome (MERS-CoV)[1,2]. The COVID-19 is a new variant of the coronaviruses, first isolated in China. The novel coronavirus differs from the others because of its high impact in public health and the huge number of new cases reported in a short time-period[2,3].

The COVID-19 created a new reality for global healthcare delivery models[1,2]. The scientific evidence so far available are not enough to meet the demands to face the pandemic, since data about specific treatment and vaccines are insufficient (WHO)[4], which forces governments to recommend social distancing as the principal effective strategy to contain the spread of the disease.

Pandemic scenarios require information in order to promptly (re)organize health practices and to provide health care, such as prevention and treatment, control and rehabilitation, since they are essential for health care managers and providers5. To address this demand, epidemiological studies are relevant to trigger public health strategies to control the spread of the virus.

Furthermore, this global scenario suggests that nobody can now be protected from an emerging and poorly known infectious disease. It would be unwise to make specific predictions about the natural history of the disease or efforts to contain SARS-CoV-2 outbreaks, but it is possible to make some incipient conclusions and to protect the most vulnerable from the virus[6].

Health research[7] is designed to develop reliable data on problems and needs that are important to the individual/community, with a particular focus on guiding practitioners. In line with that, findings about social distancing are probably effective to reduce case-fatality, since they are suitable to prevent and control the extensive spread of COVID-19[8].

There is a lack of population-based studies assessing the trends in case-fatality rates in different countries in the world, which is crucial information to understand the pandemic dynamic, the severity of the disease and to elaborate global public health policies[5]. The traditional cumulative case-fatality rates may possibly underestimate the real case-fatality, since each region of the world is experiencing a different stage of the pandemic[9]. Case-fatality rates are not static. Rather, they tend to be dynamic and change over time. Thus, we aimed to evaluate trends in case-fatality rates of COVID-19 around the world.

METHODS

This a population-based time-series study of public and official data available on the website of the European Centre for Disease Prevention and Control (https://www.ecdc.europa.eu/en).

Data were collected on August 31, 2020, by household address for COVID-19 reported cases. Population data were extracted from the Country Meters website (https://countrymeters.info/en), and included the following countries: Argentina (45,757,489 inhabitants), Australia (2,5949,452 inhabitants), Brazil (217,040,683 inhabitants), Chile (18,944,479 inhabitants), China (1,410,334,120 inhabitants), Colombia (50,697,280 inhabitants), France (65,790,781 inhabitants), Germany (81,466,451 inhabitants), India (2,195,755,104 inhabitants), Iran (84,341,761 inhabitants), Italy (60,016,386 inhabitants), Japan (125,901,152 inhabitants), Mexico (136,136,481 inhabitants), Morocco (36,833,644 inhabitants), New Zealand (4,695,515 inhabitants), Nigeria (208,242,721), Peru (33,538,625 inhabitants), Saudi Arabia (35,457,606 inhabitants), South Africa (57,581,898), South Korea (51,472,090 inhabitants), Spain (45,690,902 inhabitants), Switzerland (8,770,577inhabitants), United Kingdom (66,679,096 inhabitants), United States (333,487,241 inhabitants), and Russia (146,590,156 inhabitants).

The study analyzed cases and deaths reported between December 31, 2019 and August 31, 2020. New cases and deaths were collected according to day of reporting.

Study population, inclusion and exclusion criteria

The World Health Organization assigned the emergency ICD-10 code of “U07.1 COVID-19, virus identified” to a disease diagnosis of COVID-19 confirmed by laboratory testing.

Data collection started in different dates in each country according to the reporting of new cases. In Argentina, it started on March 03; in Australia, on January 25; in Brazil, on January 26; in Canada, on January 26; in China, on January 21; in Chile, on March 03; in Colombia, on March 07; in France, on January 25; in Germany, on January, 28; in India, on January 30; in Iran, on February 20; in Italy, on January 31; in Japan, on January 21; in Mexico, on February 29; in Morocco, on March 03; in New Zealand, on February 28; in Nigeria, on February 28; in Peru, on March 07; in Saudi Arabia, on March 03; in South Africa, on March 06; in South Korea, on January 21; in Spain, on February 02; in Switzerland, on February 26; in the United Kingdom, on January 31; in the United States, on January 21; and in Russia, on February 01.

All confirmed cases and deaths of COVID-19 were included. They were registered according to the 10th Revision of the International Classification of Diseases (ICD-10) as COVID-19, virus identified (U07.1).

Data Collection Procedures

Data were extracted from the public and official data system of the European Centre for Disease Prevention and Control (ECDC), section “Latest situation update, epidemiological curve and global distribution.” The ECDC is closely monitoring the outbreak, providing risk assessments and public health guidance.

Confirmed cases and deaths were collected from national health information systems responsible for registering, analyzing and publishing official country health data. The data were transferred to the European Centre for Disease Prevention and Control, which updated it daily.

Data about the resident population of each country was obtained from the Country Meters website and we projected population from January to August, 2020. The population data account for the total country population as of January 01, 2020.

In order to minimize possible discrepancies, the data were extracted by two different researchers independently.

Statistical analysis

The COVID-19 incidence (new cases / population) and mortality (deaths / population) rates were calculated, per 1,000,000 inhabitants, and case-fatality (total deaths / total cases) rates, as daily percentage, between January and May 2020.

For trend analyses, we used methods proposed by Antunes and Cardoso (2015)[10]. Time-series rates were calculated using a Prais-Winsten regression model, which allowed first-order autocorrelation corrections on values by time. Thus, the following values were estimated: angular coefficient (β) and respective probability (p), considering a significance level of 95% confidence interval (CI 95%).

The data modeling process included transforming rates (dependent variable = Y value) into a base 10 logarithmic function. The independent variable (X value) was days of historical series. We also used the Durbin– Watson test to measure the existence of a first–order autocorrelation of the time series of the daily coefficients, and to verify if the correlation was compatible with the random regression residuals hypothesis[11].

The logarithm rates results (β) of Prais-Winsten regression allowed to estimate the Daily Percent Chance (DPC) in each country, with the respective confidence intervals (95% CI)[10]:

$$\textbf{DPC} = [-1+10^{\beta}]*100\%$$
$$\text{IC 95\%} = [-1+10^{\beta min}]*100\%;\ [-1+10^{\beta max}]*100\%$$

This procedure made it possible to determine rates as increasing, decreasing or flat, and to quantify percent change in daily[12] incidence, mortality and case- fatality rates. The trend was considered to be flat when the coefficient was not significantly different from zero ($p > 0.05$).

To facilitate the visualization of the trends in case- fatality rates, we reduced the random variation in the graph using the five-order moving average technique[11].

We used the Stata 15.1 statistical software to conduct statistical analyses (College Station, TX, U.S. 2018).

Table 1: Cases, deaths and case-fatality of COVID-19, according to countries, between January and August, 2020.

	World			**AFRICA**				
Countries			Morocco	Nigeria	South Africa			
Cases	25.251.334		61.399	53.865	625.056			
Deaths	846.841		1.111	1.013	14.028			
Case-Fatality	3,4%		1,8%	1,9%	2,2%			
				AMERICAS				
Countries	Argentina	Brazil	Canada	Chile	Colombia	Mexico	Peru	United States
Cases	401.226	3.862.311	127.940	409.974	607.938	595.841	647.166	5.997.163
Deaths	8.401	120.828	9.117	1.965	19.364	64.158	28.788	183.069
Case-Fatality	2,1%	3,1%	7,1%	0,5%	3,2%	10,8%	4,4%	3,1%
				ASIA				
Countries		China	India	Iran	Japan	Saudi Arabia	South Korea	
Cases		89.895	3.621.245	373.570	67.865	314.821	19.947	
Deaths		4.722	64.469	21.462	1.279	3.870	324	
Case-Fatality		5,3%	1,8%	5,7%	1,9%	1,2%	1,6%	
				EUROPE				
Countries		France	Germany	Italy	Spain	Switzerland	United Kingdom	Russia
Cases		277.943	242.381	268.218	439.286	41.906	334.467	990.326
Deaths		30.606	9.298	35.477	29.011	1.724	41.499	17.093
Case-Fatality		11,0%	3,8%	13,2%	6,6%	4,1%	12,4%	1,7%
				OCEANIA				
Countries				Australia	New Zealand			
Cases				25.670	1.387			
Deaths				611	22			
Case-Fatality				2,4%	1,6%			

Source: Cases and Deaths data from the European Centre for Disease Prevention and Control (ECDC). Population data from the Country Meters.

Continent / Countries	DPC (CI 95%) Case-Fatality	p Value	Case-Fatality Trend	DPC (CI 95%) Incidence	p Value	Incidence Trend	DPC (CI 95%) Mortality	p Value
World	0.3 (-0.2 : 0.7)	0.225	Flat	4.9 (2.0 : 7.8)	0.001	Increasing	3.9 (1.5 : 6.5)	0.002
Africa								
Morocco	-1.1 (-1.5 : -0.7)	< 0.001	Decreasing	3.1 (2.4 : 3.9)	< 0.001	Increasing	1.3 (0.6 : 2.1)	0.001
Nigeria	-0.2 (-0.5 : 0.2)	0.371	Flat	3.4 (2.0 :4.8)	< 0.001	Increasing	0.6 (0.1 : 1.1)	0.031
South Africa	1.5 (0.4 : 2.6)	0.007	Increasing	4.9 (3.2 : 6.5)	< 0.001	Increasing	3.4 (3.0 : 3.9)	< 0.001
Americas								
Argentina	-0.6 (-1.1 : -0.2)	0.005	Decreasing	4.5 (3.9 : 5.0)	< 0.001	Increasing	2.8 (2.7 : 3.0)	< 0.001
Brazil	1.3 (0.1 : 2.6)	0.036	Increasing	5.8 (2.1 : 9.6)	0.002	Increasing	3.0 (1.0 : 5.1)	0.003
Canada	1.0 (0.2 : 1.9)	0.015	Increasing	3.5 (1.4: 5.6)	0.001	Increasing	-0.02 (-1.6 : 1.6)	0.985
Chile	1.8 (0.9 : 2.7)	< 0.001	Increasing	3.8 (0.9 : 6.8)	0.010	Increasing	2.5 (1.7 : 3.2)	< 0.001
Colombia	1.2 (0.1 : 2.2)	0.028	Increasing	5.4 (4.3 : 6.6)	< 0.001	Increasing	3.5 (3.2 : 3.8)	< 0.001
Mexico	1.5 (0.5 : 2.5)	0.004	Increasing	4.1 (1.1 : 7.2)	0.008	Increasing	3.6 (2.3 : 4.8)	< 0.001
Peru	0.8 (0.4 : 1.1)	< 0.001	Increasing	4.3 (2.7 : 5.9)	< 0.001	Increasing	2.6 (1.8 : 3.3)	< 0.001
United States	0.3 (-0.4 : 1.0)	0.367	Flat	6.0 (2.8 : 9.3)	< 0.001	Increasing	2.2 (-0.01 : 4.5)	0.051

DPC – Daily Percent Change (%); CI 95% – Confidence Interval 95%; p Value – probability of statistics significance

Source: Cases and Deaths data from the European Centre for Disease Prevention and Control (ECDC). Population data from the countrymeters.info.

Table 3: Prais-Winsten regression estimates and Daily Percent Change (DPC) of case-fatality, incidence and mortality rates due to COVID-19. according to countries of Asia, Europe and Oceania. Jan-Aug. 2020.

Continent / Countries	DPC (CI 95%) Case-Fatality	p Value	Case-Fatality Trend	DPC (CI 95%) Incidence	p Value	Incidence Trend	DPC (CI 95%) Mortality	p Value	
Asia									
China	0.4 (0.3 : 0.6)	< 0.001	Increasing	-0.2 (-1.5 : 1.1)	0.753	Flat	-0.5 (-1.5 : 0.4)	0.281	Flat
India	0.01 (-0.3 : 0.4)	0.060	Flat	6.2 (5.0 : 7.4)	< 0.001	Increasing	4.5 (3.5 : 5.5)		
Iran	-1.5 (-2.6 : -0.2)	0.019	Decreasing	1.7 (0.5 : 3.0)	0.007	Increasing	1.5 (0.8 : 2.1)		
Japan	-0.1 (-0.8 : 0.6)	0.727	Flat	2.7 (2.0 : 3.4)	< 0.001	Increasing	0.3 (-0.4 : 0.9)	0.432	Flat
Saudi Arabia	1.4 (0.3 : 2.4)	0.013	Increasing	3.0 (1.0 : 5.1)	0.004	Increasing	1.9 (1.3 : 2.4)		
South Korea	0.5 (-0.1 : 1.0)	0.08	Flat	2.2 (1.0 : 3.4)	< 0.001	Increasing			
Europe									
France	0.2 (-0.7 : 1.1)	0.627	Flat	3.6 (2.0 : 5.2)	< 0.001	Increasing	0.9 (-0.9: 2.8)	0.319	Flat
Germany	1.8 (0.7 : 2.9)	0.001	Increasing	3.5 (0.7 : 6.5)	0.015	Increasing	-0.4 (-1.8 : 1.0)	0.530	Flat
Italy	0.8 (0.1 : 1.6)	0.022	Increasing	2.6 (-0.3 : 5.6)	0.077	Flat	-0.6 (-2.4 : 1.1)	0.465	Flat
Spain	1.8 (0.05 : 3.5)	0.044	Increasing	4.0 (2.0 : 6.0)	< 0.001	Increasing	-1.4 (-3.1 : 0.2)	0.090	Flat
Switzerland	0.7 (-0.1 : 1.6)	0.071	Flat	1.0 (-0.6 : 2.7)	0.227	Flat	-1.0 (-1.8 : -0.1)	0.026	
United Kingdom	2.0 (0.6 : 3.4)	0.005	Increasing	3.5 (0.1 : 6.9)	0.045	Increasing	0.5 (-2.0 : 3.0)	0.707	Flat
Russia	1.2 (0.5 : 2.0)	0.001	Increasing	4.4 (1.9 : 7.0)	0.001	Increasing	1.7 (0.6 : 2.8)	0.004	
Oceania									
Australia	-0.2 (-1.2 : 0.7)	0.629	Flat	2.6 (1.4 : 3.8)	< 0.001	Increasing	0.6 (0.6 : 1.6)		
New Zealand	1.3 (0.1 : 2.5)	0.04	Increasing	-0.3 (-1.4 : 0.7)	0.533	Flat	-0.7 (-2.6 : 1.3)	0.462	Flat

DPC – Daily Percent Change (%); CI 95% – Confidence Interval 95%; p Value – probability of statistics significance

Source: Cases and Deaths data from the European Centre for Disease Prevention and Control (ECDC). Population data from the countrymeters.info.

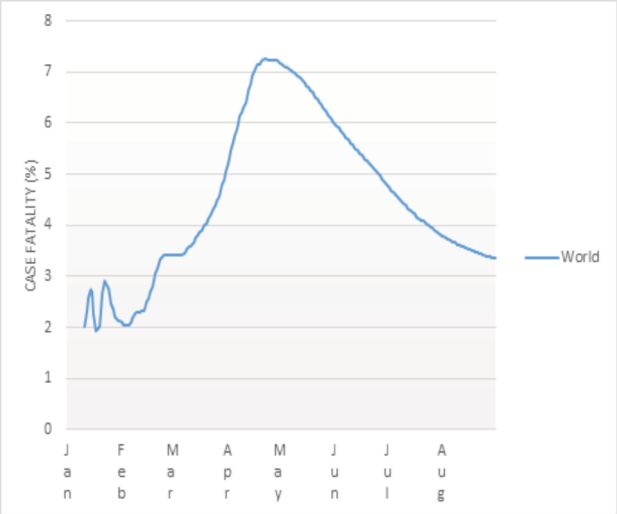

Figure 1: Temporal trend of case-fatality rates (%) of COVID-19 in the World. December, 2019 - August 2020.

Source: Cases and Deaths data from the European Centre for Disease Prevention and Control (ECDC). Population data from the Country Meters.

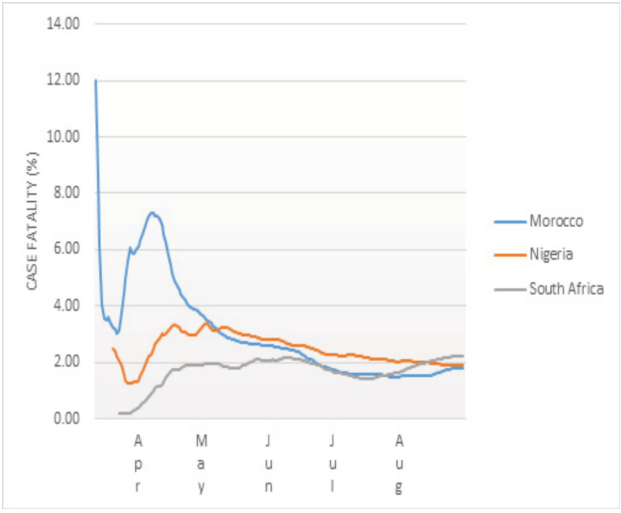

Figure 2: Temporal trend of case-fatality (%) of COVID-19, according to countries of Africa, December, 2019 - August 2020.

Source: Cases and Deaths data from the European Centre for Disease Prevention and Control (ECDC). Population data from the Country Meters.

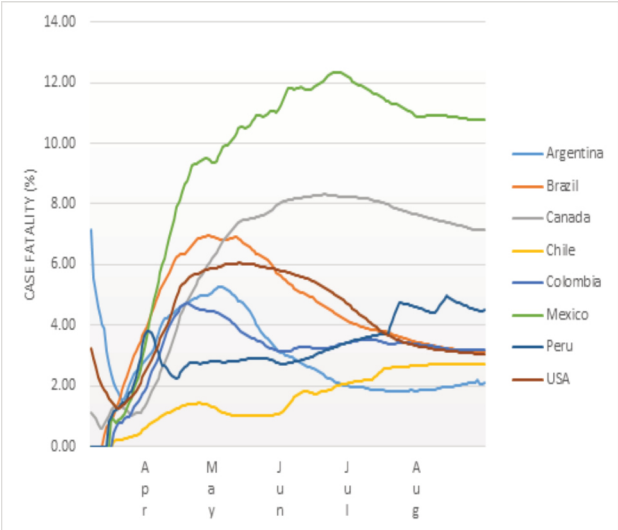

Figure 3: Temporal trend of case-fatality (%) of COVID-19, according to countries of Americas, December, 2019 - August 2020.

Source: Cases and Deaths data from the European Centre for Disease Prevention and Control (ECDC). Population data from the Country Meters.

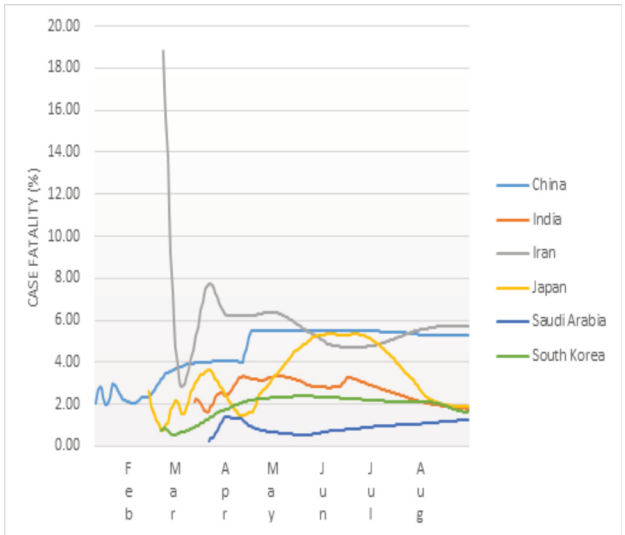

Figure 4: Temporal trend of case-fatality (%) of COVID-19, according to countries of Asia, December, 2019 - August 2020.

Source: Cases and Deaths data from the European Centre for Disease Prevention and Control (ECDC). Population data from the Country Meters.

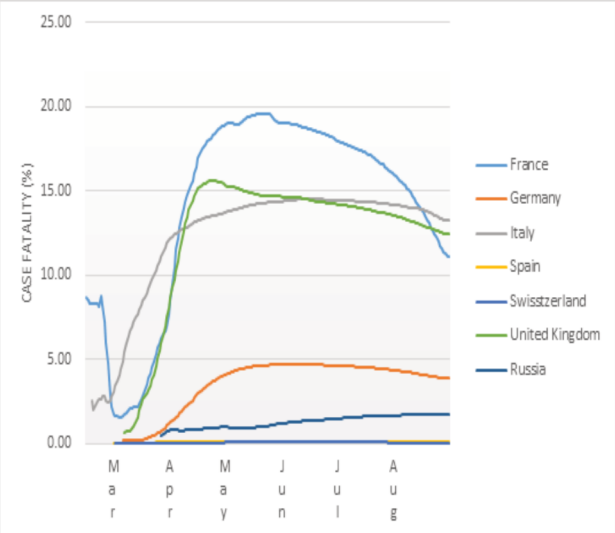

Figure 5: Temporal trend of case-fatality (%) of COVID-19, according to countries of Europe, December, 2019 - August 2020.

Source: Cases and Deaths data from the European Centre for Disease Prevention and Control (ECDC). Population data from the Country Meters.

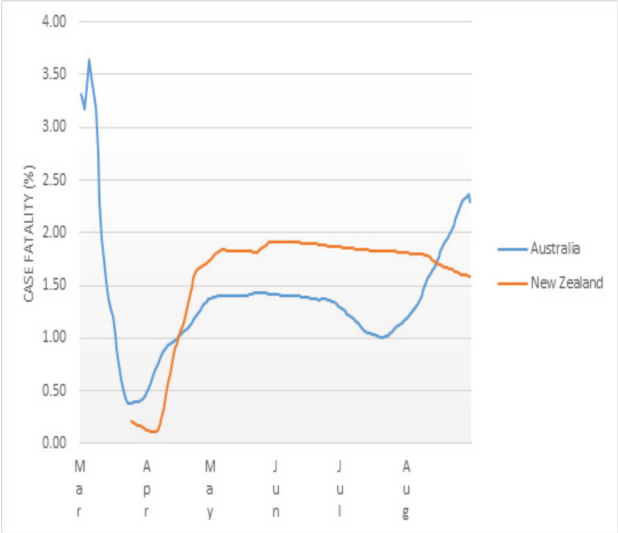

Figure 6: Temporal trend of case-fatality (%) of COVID-19, according to countries of Oceania, December, 2019 - August 2020.

Source: Cases and Deaths data from the European Centre for Disease Prevention and Control (ECDC). Population data from the Country Meters.

Case-fatality Rates

Between December 31, 2019, and August 3, 2020, the case-fatality rate due to COVID-19 in the world was 3.4%.

In Africa, among countries analyzed, the highest case-fatality rates was found in South Africa (2.2%), followed by Nigeria (1.9%) and Morocco (1.8%). Similar results were found in Oceania: Australia (2.4%) and New Zealand (1.6%) (Table 1).

In the Americas, Mexico had the greatest case- fatality rate: 10.8%, which represents the fourth country with the highest percentage. Canada also showed high case-fatality rate: 7.1%. In countries in America, we found similar percentages in case-fatality rates, except Chile, where it was 0.5%, the lowest rate between all countries (Table 1).

Asia had two different profile of groups: China and Iran had case-fatality rates above 5.0%, while the rest of Asian countries showed rates below 2.0% (Table 1).

Europe had the most heterogeneous results compared with other continents. Italy, France and United Kingdom had case-fatality rates above 10.0%. Spain and Switzerland show intermediary rates among European countries, while German and Russia were the countries with the lowest rates in case-fatality in the continent. (Table 1).

Trends in case-fatality rates

Trends in case-fatality rates in the world were flat (DPC = 0.3; CI 95% [-0.2 : 0.7]; p = 0.225) in the study period (Table 2, Fig. 1).

Morocco was one of the three countries in which the case-fatality rate was decreasing (DPC = -1.1; CI 95% [-1.5 : -0.7]; p < 0.001). In Nigeria, the case-fatality rate was flat, while in South Africa it was increasing (Table 2, Fig. 2).

In the Americas, Argentina had decreasing trends in case-fatality rates (DPC = -0.6; CI 95% [-1.1: -0.2]; p = 0.005), while all other countries had increasing trends. The United States, on the other hand, had flat rate trends. (Table 2, Fig. 3).

With regard to Asian countries, Iran showed decreasing trends in case-fatality rates (DPC = -1.5; CI 95% [-2.6: -0.2]; p = 0.019). China and Saudi Arabia had increasing trends, while India and South Korea showed flat tendency (Table 3, Fig. 4).

In Europe, France and Switzerland had flat trends in case-fatality rates, but all the other countries had increasing tendency (Table 3, Fig. 5).

Finally, in Oceania, Australia had flat tendency, while New Zealand had increasing trends in case-fatality rates due to COVID-19 (Table 3, Fig 6).

DISCUSSION

We estimated trends in case-fatality rates by calculating the Daily Percent Change in case-fatality rates, which allows the understanding of the dynamic of the pandemic better than simply analyzing rates[9]. Between December 31, 2019 and August 31, 2020, trends in case-fatality rates due to COVID-19 in the world remained flat. Argentina, Iran and Morocco were the only countries that had decreasing trends in case-fatality rates. Nigeria, United States, India, Japan, South Korea, France, Germany, Switzerland and Australia had flat tendency. All other countries showed increasing trends, which can indicate progressive severity of the disease around the five continents.

Our findings showed case-fatality rates in the world similar to Zhao et al. study, who found a rate of 3.1% after analyzing 30 studies with 53.000 patients[12]. Another study estimating case-fatality rates showed expected rates for this pandemic ranging from 2.9% to 3.0%[9]. As we already pointed out, case-fatality rates are not static, but rather dynamic. Our statistical analyses of world trends suggest a flat tendency ($p > 0.05$).

Increasing Case-Fatality Rate Trends

South Africa, Brazil, Canada, Chile, Colombia, Mexico, Peru, China, Saudi Arabia, Germany, Italy, Spain, United Kingdom, Russia and New Zealand had increasing trends in case-fatality rates due to COVID-19. Among all of them, Canada, Mexico, Peru, Germany, Italy, Spain and United Kingdom had case-fatality rates above the world's rate, which can possibly indicate an highest severity of the disease in those nations. Germany, Spain and United Kingdom showed the greatest Daily Percent Change, indicating that Europe still is the continent most affected by COVID.

With regard to Canada, our results contrasts with Abdollahi et al. findings, who found a case-fatality rate of 1.6% (CI 95% 0.7%–3.1%) on April 22, which is significantly lower than ours[13]. It demonstrates that COVID-19 has substantially increased over the past 4 months. Therefore, it is noteworthy that Canada had a high severity of the disease, which is still in progress.

Regarding Europe, we found the same behavior for case-fatality rates pointed by Pachetti et al., who described a significant lower rate for Germany (0.31% CI 95% [0.29; 0.33]) compared to the other nations, on April 30[14]. Although the estimation of case-fatality rates are not high in Germany, this country had the second increasing Daily Percent Change in case-fatality rates among all 26 countries analyzed. Aside from Germany, Russia had low case-fatality rates, but it had also increasing trends. The United Kingdom had the highest case-fatality rate and upward trend among the nations analyzed in our study.

Flat Case-Fatality Rate Trends

Nigeria, United States, India, Japan, South Korea, France, Switzerland, Australia had flat tendency in case- fatality rates due to COVID-19. France and Switzerland were the only nations with rates above the world's, which suggests the hypothesis that Europe is not in a regression phase of the pandemic.

With respect to Australia, Chin et al. already noted signs that pandemic was under control. They identified case-fatality rates raging 0.4% to 3.0%, tending to decrease after March 29[15]. This decrease may be attributed to timely implementation and strict enforcement of bans on travel and social gatherings, as well as concerted diagnostic and management strategies.

The United States also showed signs of controlling the spread of COVID-19. On April 22, Abodollahi et al. reported a case-fatality rate of 6.1% (CI 95% 5.4%– 6.9%)[13], which corresponds to approximately twice our results. This finding suggests that case-fatality rates might have decreased in the previous 4 months and a new flat trend emerged.

Decreasing Case-Fatality Rate Trends

Morocco, Argentina and Iran showed decreasing trends ins case-fatality rates of COVID-19. In spite of that, Iran was the only country in which case-fatality rates were above the estimate of the world's rate.

As of May 13, 2020, Ouchetto et al. reported a case-fatality rate of 5.26% in Morocco[16], almost 3 times greatest than our findings, supporting the hypothesis that the pandemic is tending toward control in this nation.

Regarding Iran, we have to interpret the results with parsimony, since according to studies, cases reported in official statistics at the beginning of the epidemics were likely to grossly underestimate the total of actual cases. Thus estimating the actual case-fatality rates due to COVID-19 is currently impossible[17].

It is important to highlight that our analysis was based on public and official secondary data from the European Centre for Disease Prevention and Control. Even considering unknown underreporting, these are the best available data to formulate public health policies. The analysis of incidence, mortality, case-fatality rates and their respective trends allowed for measurement of risk, severity, and magnitude, which are defining indicators to understand the dynamics of pandemics[6].

The time-series regression model used in this study allowed to estimate the existence the Daily Percent Change (DPC) in case-fatality rates, which made it possible to measure the dynamic variation of the pandemic among 26 countries around the five continents worldwide.

CONCLUSIONS

Trends in case-fatality rates of COVID-19 in the world were flat between December, 31 and August, 31. Argentina, Iran and Morocco were the only countries with decreasing trends. On the other hand, South Africa, Brazil, Canada, Chile, Colombia, Mexico, Peru, China, Saudi Arabia, Germany, Spain, United Kingdom, Russian and New Zealand had increasing trends in case-fatality rates. All other countries analyzed had flat trends. Based on case-fatality rates data, our study provides evidence that the COVID-19 pandemic is still in progress worldwide.

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CHAPTER 10

VACCINE COVERAGE AND MEASLES INCIDENCE IN NORTHERN BRAZIL

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Abstract

Introduction: measles is an immunopreventable viral disease, acute exanthematous and extremely transmissible. Infection occurs directly, from person to person, through respiratory secretions. The measles vaccine is low-cost and effective, but measles still affects around 40 million people worldwide and is responsible for at least 800,000 deaths, mainly in developing countries. **Objective:** to analyze vaccination coverage and measles incidence in Northern Brazil. **Methods:** this is an ecological study. Secondary data were used regarding vaccination coverage of the viral double, viral triple and viral tetra and incidence of measles in residents in the States of the Northern Region, Brazil, from 2010 to 2018. **Results:** confirmed measles cases in 2010 to 2018 in the Northern region of Brazil it registered 10,249, were reported in Amazonas (95.65%), Roraima (3.53%), Pará (0.80%) and Rondônia (0.02%). Outbreaks of measles cases in the Northern Region were reported in 2018, the highest incidence rate was in Amazonas with 237.7. Vaccination coverage in the North Region varied between the lowest rate in 2013 with 56.88% and the highest vaccination coverage achieved in 2010, with 104.02%. **Conclusion:** it was possible to observe a reduction in vaccination coverage during the study period, not reaching the percentage recommended by the Ministry of Health and increasing the incidence of measles in the Northern Region of Brazil and these indicators are important to determine the strategies to be carried out by the National Program for Immunization and Epidemiological Surveillance.

Keywords: Vaccination coverage; Measles; Incidence.

Resumo

Introdução: O sarampo é uma doença viral imunoprevenível, exantematosa aguda e extremamente transmissível. A infecção ocorre de forma direta, de pessoa a pessoa, por meio das secreções respiratórias. A vacina contra o sarampo é de baixo custo e efetiva, porém o sarampo ainda acomete cerca de 40 milhões de pessoas no mundo e é responsável por pelo menos 800 mil mortes, principalmente em países em desenvolvimento. **Objetivo:** Analisar a cobertura vacinal e incidência de sarampo na Região Norte do Brasil. **Método:** Trata-se de um estudo ecológico. Utilizou-se dados secundários referente a cobertura vacinal da dupla viral, tríplice viral e tetra viral e incidência de sarampo em residentes nos Estados da Região Norte, Brasil, no período de 2010 a 2018. **Resultados:** Os casos confirmados de sarampo em 2010 a 2018 na região Norte do Brasil registrou 10.249, foram notificados no Amazonas (95,65%), Roraima (3,53%), Pará (0,80%) e Rondônia (0,02%). Os surtos de casos de sarampo na Região Norte foram notificados no ano de 2018, a maior taxa de incidência foi no Amazonas com 237,7. A cobertura vacinal da Região Norte variou entre o menor índice em 2013 com 56,88% e a maior cobertura vacinal alcançada em 2010, com 104,02%. **Conclusão:** Foi possível observar uma redução da cobertura vacinal no período de estudo, não atingindo o percentual preconizado pelo Ministério da Saúde e aumentando a incidência de sarampo na Região Norte do Brasil e estes indicadores são importantes para determinar as estratégias a serem realizadas pelo Programa de Imunização e Vigilância Epidemiológica.

Palavras-chave: Cobertura Vacinal; Sarampo; Incidência.

INTRODUCTION

Measles is an immunopreventable, acute exanthematous viral disease, extremely transmissible, caused by viruses of the Paramyxoviridae family of the genus Morbillivirus[1]. The infection occurs directly, from person to person, through respiratory secretions, and the virus can remain active for up to two hours in the air or on surfaces[2].

The incubation period can last up to eleven days and the disease can last from three to four days, presenting a clinical picture of high fever, coryza, serumucosa, conjunctivitis with photophobia, dry cough. In addition, Koplik patches may appear, which are white dots located on the oral mucosa. Around the fourth day of the disease onset, the reddish maculopapular rash begins, starting with the face, retroauricular and cervical regions[1,3].

Most measles deaths occur from complications associated with the disease. They are more common in children under the age of five or in adults over the age of 30. These complications include blindness, severe diarrhea, severe respiratory and auditory system infections, even encephalitis3. Measles has an important cause of hospitalization, morbidity and mortality in childhood, and may be related to the degree of socioeconomic development of those infected[4].

Measles is still common in many developing countries. About 95% of deaths from measles occur in low-income countries and where there is a weak health infrastructure3. According to the World Health Organization (WHO), an estimated 36.5 million cases and 1.5 million deaths from measles occur worldwide each year[1].

Comprised of live attenuated virus (with low pathogenicity), the measles vaccine was introduced in Brazil during the years 1967 and 1968, becoming a nationally mandatory notification disease[5,6], however, it was used in a discontinuous way until 1973[7].

In 1973, the National Immunization Program (PNI) was created, which aimed to implement immunization actions across the country. In 1980, a vaccination campaign was carried out in places with low vaccination coverage. Until 1990, measles was considered an endemic disease, with some peaks every 2, 3 years, having its biggest epidemic in 1986. In 1992, Brazil instituted the National Measles Elimination Plan (1992), with the goal of eliminating measles by the year 2000, reaching 96.7% of vaccination coverage[7].

Brazil received the measles eradication certificate from the Pan American Health Organization in 2016. However, the outbreak that occurred in the north of the country in 2018 highlighted the need for continuous surveillance to control this pathology[1].

In 2018, Brazil faced the reintroduction of the measles virus and outbreaks were detected in at least 11 Brazilian states. According to the Ministry of Health, this outbreak is related to imports, because in a viral characterization, the D8 genotype was identified, identical to that circulating in Venezuela in an outbreak that the country suffered in 2017[8]. The North region was the most affected due to low vaccination coverage.

Thus, the objective of this work is to analyze the vaccination coverage and the incidence of measles in the Northern Region of Brazil in the period from 2010 to 2018, therefore, this study is justified by the importance of evaluating the epidemiological profile and vaccination status of measles in North region, since this region has the largest number of measles cases in Brazil.

METHODS

Study Design

This is an ecological study. Secondary data referring to vaccination coverage of the double, triple and tetra viral measles incidence in residents in the states of the Northern Region, Brazil, from 2010 to 2018.

Study Location and Period

Data were collected according to place of residence. The collection took place through the data available at the Department of Informatics of the Unified Health System (DATASUS - http://datasus.saude.gov.br/), National Immunization Program (PNI), Hospital Information System (SIH) and through the Ministry's portal of Health through epidemiological measles bulletin(http://www.saude.gov.br/saude-de-az/sarampo-situacao-epidemiologica). Secondary data corresponded to the period from January 1, 2010 to December 31, 2018. Data were collected from the seven states in the Northern region of Brazil: Amazonas (AM); Roraima (RR); Amapá; Pará (PA); Tocantins (TO); Rondônia (RO); Acre (AC).

Study Population and Eligibility Criteria

New measles cases were counted from the confirmed ones caused by Measles, occurred and notified Hospital Information System (SIH) and epidemiological bulletins according to the age group established by the World Health Organization (WHO).

Data from the Notifiable Diseases Information System (SINAN) were not used, since the last update of measles information was in 2014 and for this reason, it was decided to use confirmed measles cases by epidemiological bulletins. Knowing that these data can be changed, the study used the last bulletin with the number 37, of 03/19/2019.

For the construction of the incidence rate, data were collected from the population residing in the states of the Northern Region, Brazil from the 2010 and 2018 censuses and from inter-census projections for the other years (from 2010, to 2018), according to information provided by DATASUS.

All new measles cases from 2010 to 2018 were included, considering Chapter I (Some infectious and parasitic diseases), according to the 10th Review of the International Classification of Diseases (ICD-10) at: B05.0 - Measles complicated by encephalitis, B05.1 - Measles complicated by meningitis, B05.2 - Measles complicated by pneumonia, B05.3 - Measles complicated by otitis media, B05.4 - Measles with intestinal complications, B05.8 - Measles with other complications and B05.9 - Measles without complications.

Data Collection

The data were extracted from the file transfer service provided by the Department of Informatics of the Unified Health System (DATASUS) (website: http://datasus.saude.gov.br/), which started with the systematic registration of data from Vital Statistics - Mortality and Live Births and Epidemiological and Morbidity - Hospital Morbidity of SUS (SIH/SUS) and Diseases and Notifiable Diseases (from 2007 onwards (SINAN)), Health Care - Immunization (since 1994) of the National Health Program Immunization (PNI) and measles epidemiological bulletins. With the advances in the control of infectious diseases, the analysis of the sanitary situation started to incorporate other dimensions of the health status, including epidemiological and morbidity information, which were obtained through measles hospitalizations.

To consult the data, the TABNET and TABWIN programs were used. These tabulators were developed to perform quick tabs on files. Data were collected by two independent researchers to identify possible discrepancies.

Data Analysis

Descriptive statistics was used to characterize and summarize the data set. The frequencies were expressed by absolute and relative measures. For analytical statistical analysis, linear regression was performed using the GRAPH PRISMA 6.0 program, estimating the slope (β) and the respective probability (p), the determination coefficient (r2), considering a significance level of 5%.

To build the incidence rate, data were collected from the population residing in the states of the Northern Region, Brazil, from the 2010 and 2018 censuses and from inter-census projections for the remaining years (from 2010, to 2018), according to information provided by DATASUS.

Ethical and Legal Aspects of the Research

The present study involved only the description and analysis of secondary data: population-obtained by the general population census and deaths-collected from the Information System. All of these information sources are in the public domain. Information that is not freely accessible was not collected. In particular, no personally identifiable information was obtained for this study.

According to Resolution nº 510/2016, of April 7, 2016, of the National Health Council, it was not registered or evaluated by the CEP/CONEP system, as publicly available information was used.

RESULTS

Of the total of confirmed measles cases in 2010 to 2018, the northern region of Brazil registered 10,249. The following states were notified: Amazonas (95.65%), Roraima (3.53%), Pará (0.80%) and Rondônia (0.02). Of the outbreaks of measles cases in the North Region reported in 2018, the highest incidence rate was in Amazonas with 237.7 (Table 1).

Table 1: Number and percentage of confirmed measles cases according to the states of the Northern Region, Brazil, from 2010 to 2018.

Northern Region States	No. of confirmed cases	%	Incidence rate*
Rondônia	2	0.02	0.11
Acre	0	0.00	0
Amazonas	9.803	95.65	237.7
Roraima	362	3.53	68
Pará	82	0.80	0.93
Amapá	0	0.00	0
Tocantins	0	0.00	0
Total	10.249	100.00	

Source: Epidemiological bulletin No. 36, 03/19/2019. Incidence rate (No. of confirmed cases/number of residents *100,000 inhabitants).

Of the total of 10,249 confirmed measles cases from 2010 to 2018, only 03 cases were reported in 2010 in the state of Pará and 01 cases in Roraima in 2015 and the rest were exclusively in 2018. In 2018, cases measles were higher in the State of Amazonas (9.803), followed by Roraima (361). In the States of Acre, Amapá and Tocantins, measles cases from 2010 to 2018 were not confirmed, as shown in Table 2.

The largest number of people affected was male (53.4%) and 46.6% female. The greatest number of people affected by age group was from 0 to 4 years (60.42%).

Table 2: Number of measles cases confirmed according to the states of the North Region, Brazil, from 2010 to 2018.

State	2010	2011	2012	2013	2014	2015	2016	2017	2018	Total
Rondônia	0	0	0	0	0	0	0	0	2	2
Acre	0	0	0	0	0	0	0	0	0	0
Amazonas	0	0	0	0	0	0	0	0	9,803	9,803
Roraima	0	0	0	0	0	1	0	0	361	362
Pará	3	0	0	0	0	0	0	0	79	82
Amapá	0	0	0	0	0	0	0	0	0	0
Tocantins	0	0	0	0	0	0	0	0	0	0
Total	3	0	0	0	0	1	0	0	10,245	10,249

Source: Epidemiological bulletin nº. 36, 19/03/2019.

In Table 3, it can be seen that the largest number of people affected was male (53.4%) and 46.6% female. The greatest number of people affected by age group was from 0 to 4 years (60.42%).

Table 3: Incidence rate per hospitalization of confirmed measles cases, distributed by sex and age group in the states of the Northern Region, Brazil, from 2010 to 2018.

Variable	N*	%	Hospitalization Rate **
Sex			
Male	448	53.40	0.44
Female	391	46.60	0.50
Age group			
0 to 4	507	60.42	31.27
5 to 9	78	9.29	4.30
10 to 14	49	5.84	2.76
15 to 19	55	6.55	3.06
20 to 29	95	11.32	2.84
30 to 39	36	4.29	1.12
40 to 49	25	2.97	0.55
≥ 50 years	6	0.71	0.14
Hospitalization year			
2010	2	0.23	0.01
2011	5	0.59	0.03
2012	2	0.23	0.01
2013	3	0.35	0.02
2014	3	0.35	0.02
2015	2	0.23	0.01
2016	3	0.35	0.02
2017	0	0	0
2018	819	97.61	4.51
Total	839	100	-

Source: Hospitalization System (SIH/DATASUS). N* Number of hospitalization for measles. Hospitalization Rate (No. of hospitalizations/ number of residents *100,000 inhabitants).

As for vaccination coverage, the North Region had the lowest rate in 2013, with 56.88%, and the highest vaccination coverage achieved in 2010, with 104.02%. In 2017 and 2018, vaccination coverage of 64.78% and 68.84% was obtained, respectively. The state that obtained the highest vaccination coverage, between the years 2010 to 2018, was Rondônia, with around 94.71%. The one that reached the lowest vaccination coverage was in the states of Acre and Pará (Table 4). In 2013, the lowest vaccination coverage recorded in the period from 2010 to 2018 was obtained (56.88%).

Table 4: Vaccination coverage per unit of the Federation of the Northern Region, Brazil, from 2010 to 2018.

UF*/ANO	2010	2011	2012	2013	2014	2015	2016	2017	2018	Total
Region North	104.02	102.40	100.32	56.88	89.09	68.79	75.28	64.78	68.84	75.04
Rondônia	100.41	102.72	105.40	73.12	124.13	99.42	99.69	86.91	77.95	94.71
Acre	96.87	105.29	90.28	44.98	73.37	61.74	68.12	61.36	71.20	68.08
Amazonas	100.11	94.67	103.39	61.77	94.57	83.67	78.32	66.55	75.34	79.85
Roraima	94.49	97.98	87.83	43.46	96.55	97.80	85.97	85.33	86.13	84.44
Pará	110.95	109.25	102.20	51.13	79.60	51.82	64.78	57.31	60.74	67.59
Amapá	92.10	93.00	91.55	58.08	93.01	78.27	89.80	62.78	63.99	76.67
Tocantins	95.33	91.41	91.60	69.74	92.40	69.40	89.49	71.93	78.07	80.57

Source: Ministry of Health - SUS Immunization Information System (SII/SUS). UF* (Federative Unit).

In Amazonas, there was a reduction in vaccination coverage in 2017, but in 2018 the number of confirmed measles cases increased with the notification of 9.803 together with an increase in vaccination coverage, with coverage always being below what is recommended by the Ministry Health (Figure 1).

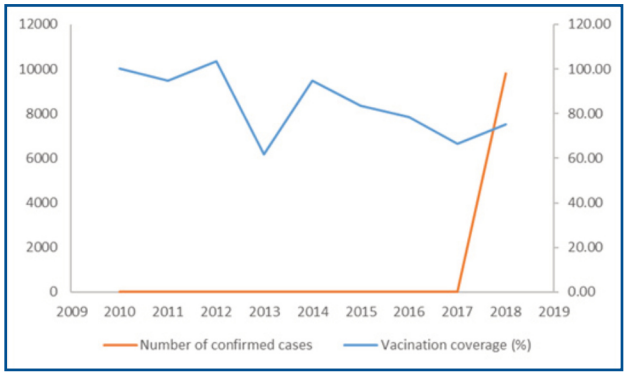

Figure 1: Number of confirmed measles cases and vaccination coverage in the state of Amazonas in the period from 2010 to 2018. Vaccination coverage is the Number of children with complete basic scheme at the target age for a given type of vaccine/Number of children at the target age* x 100 Source: Ministry of Health - SUS Immunization Information System (SII/SUS).

In figure 2, vaccination coverage dropped sharply in 2013 in the state of Roraima, but in the year 2016 to 2018 it remains stable and, in the period of 2018, there was a measles outbreak with 361 reported cases.

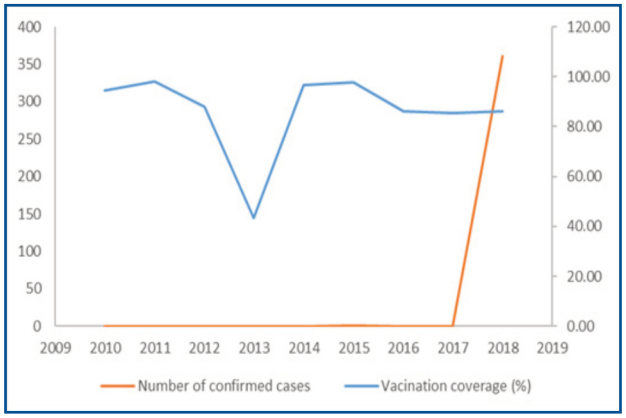

Figure 2: Number of confirmed measles cases and vaccination coverage in the state of Roraima from 2010 to 2018.

The average vaccination coverage in the years analyzed in the states of the Northern Region was 75.04%. In figure 3, it is shown that all states in the North region did not reach the goal recommended by the Ministry of Health and there is also a tendency to reduce vaccination coverage. The state of Pará (p-value <0.001) and the North Region (p-value <0.023) were statistically significant.

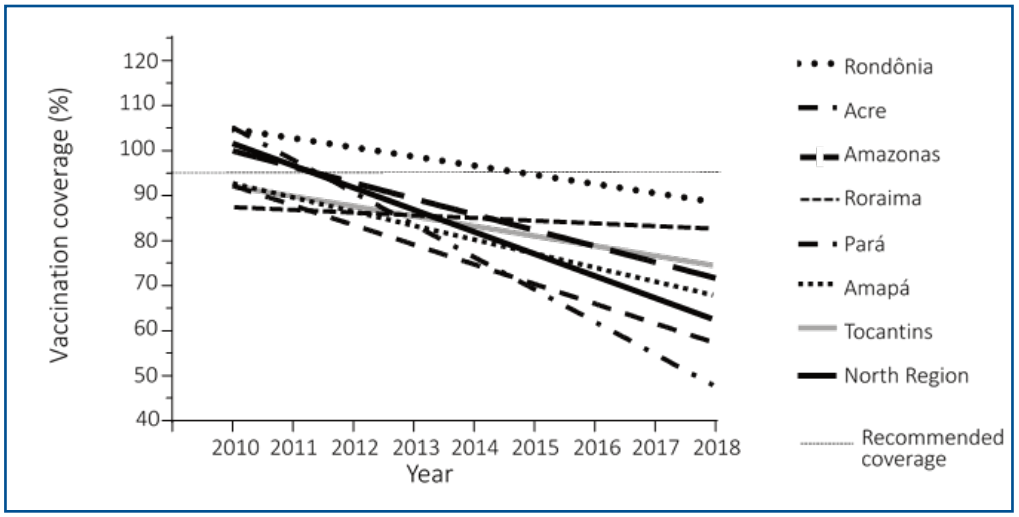

Figure 3: Trend in vaccination coverage by state and in the Northern Region from 2010 to 2018.

DISCUSSION

Over the years analyzed in this study (from 2010 to 2017), only 4 cases of measles were recorded for the North region, however, in 2018 there were 10.245 cases. In 2018, measles cases were highest in the State of Amazonas with 9.803 cases followed by Roraima with 361 reported cases. With regard to the average vaccination coverage in the years analyzed in the states of the Northern Region was 75.04% and in the years 2017 and 2018, vaccination coverage of 64.78% and 68.84% was obtained, respectively.

Brazil has been suffering from the increase in measles cases. 2018 was considered the period with measles outbreak, mainly in the North region. It is noted that this outbreak happened years after Brazil received the certificate of measles-free area. Some factors may be associated with the low vaccination coverage found in some years, such as, for example, anti-vaccination movements, the availability of vaccines in extreme regions and the lack of awareness among the population about the importance of vaccination in children. Another factor that may be influencing is the difficulty encountered by health technicians in the immunization data platform[9].

In outbreaks reported before 2013, both sexes were affected, with a predominance of males[10,11] corroborating this work, which also registered the highest occurrence of confirmed cases in males. Similar was also found in Ceará (northeast region) in 2013, which registered an epidemic with 1.052 confirmed measles cases, 13 years after having its last confirmed case. The high incidence of measles in males has also been demonstrated[12].

Report nº. 37 of the Ministry of Health in 2016 informs that Brazil received the certificate of elimination of the circulation of the measles virus by the World Health Organization (WHO)8. According to Report nº. 28 of the Ministry of Health 2018 before certification, the last measles cases in Brazil were recorded in 2015, in outbreaks in the States of Ceará (211 cases), São Paulo (2 cases) and Roraima (1 case) and associated with the Ceará outbreak[13].

The outbreak of the disease may be associated with anti-vaccination movements. These are old, but offer danger to populations around the world[14]. In 1998, an article was published in the The Lancet journal that related the mercury present in the triple viral vaccine with autism, but later that article was retracted and the author responded criminally. Anti-vaccines are still supported by this article and researcher. This movement was mentioned in the report of the World Health Organization, that talks about the ten biggest risks to global health. However, this movement has been growing and gaining strength worldwide, including in Brazil[15]. These movements question the effectiveness of vaccination, the benefit of the pharmaceutical industry. They also talk about the possible problems or reactions that can result after the vaccine, for religious reasons, among other reasons[14].

The northern region of Brazil shows measles growth, having one of the highest records in relation to the last four years. Of the 7 states in the region, three are in a state of alert and emergency in Public Health, contributing to the loss of the certification of eradication due to confirmed cases[16], and such data corroborates with the present study.

According to the Ministry of Health, the northern region is the location of the highest concentration of the virus with the same viral characteristic, the D8 genotype, circulating in Venezuela[8]. The states with the highest percentage of measles occurrence in the Northern region border and serve as refuges for immigrants, such as Venezuelans, Bolivians, Haitians, among others, thus possibly interfering in the spread of measles.

According to the Epidemiological Bulletin nº. 37, the state of Roraima received many immigrants from Venezuela, who were housed in shelters, homes, rented houses and public squares. In view of this, greater vigilance is needed in places bordering countries that are not rigorous in vaccinating the population[8].

The states of the North region with the highest incidence of measles was Amazonas, Roraima and Pará, and the least number of cases is Rondônia, whereas the states of Acre, Amapá and Tocantins had no records of the disease in 2018, maintaining vaccine control without the risk outbreak[16].

According to Leite et al. (2019), the State of the Northern Region that showed the lowest rate of vaccination coverage was Roraima[17].

There was a decrease in vaccination coverage in 2013 in all states in the Northern region in this study. This fact may be associated with the expansion of the Basic Child Vaccination Calendar with the introduction of the tetra viral vaccine to replace the triple viral vaccine for children aged 15 months[18]. According to Chaves et al. (2020)19, in 2013 the vaccination of the triple viral (D1) in 12-month-old children remained with good vaccine coverage, however, there was a drop in the North region in the vaccination of D2 and tetra viral (recently introduced)[20]. Even if D1 is performed, D2 or viral tetra is extremely important, since by failing to complete the doses for complete immunization, individuals remain susceptible, thus, they can maintain the circulation of the virus[19].

The data obtained in this study corroborate the study carried out by Chaves (2020)[19], in which the vaccination coverage trend has dropped sharply between the years 2013 to 2015, remaining so until February 2020[19]. Still according to the work by Chaves (2020)[19], the data obtained are predominant in both children and adults, which shows that vaccination at all ages is important for reducing the spread of the virus.

According to the Ministry of Health, some reasons may explain the reduction in vaccination coverage over the years in all regions of Brazil and especially in the North, reasons that stand out: diseases that are not common or that have disappeared, parents who have the perception that there is no need to vaccinate; ignorance of the vaccination schedule and mandatory vaccines; fear of the vaccine causing some side effect in the child; the fear that the number of immunizers will overload the immune system; socioeconomic conditions; the availability to go to the vaccination posts and even the family's link to the posts[9].

Herrera-Benavente et al. (2018)[20] demonstrated the evolution of measles incidence in Latin America from 1980 to September 21, 2018, and that from 2011, the number of cases increased each year, as well as highlighted countries with greater numbers of measles cases, comprising Canada, the United States of North America, Brazil and the Bolivarian Republic of Venezuela[20].

According to the Special Bulletin published by the Ministry of Health, with regard to immunization, in recent years, the coverage of the triple viral vaccine in Brazil has shown a decrease[21], similar to this study.

The age group of children aged 0 to 4 years was the most affected by the outbreak in 2018, thus, the Ministry of Health intensified vaccination campaigns with an emphasis mainly on children under five[22], as it is more frequent in this age group[3]. In this way, they launched the "D Day" of national mobilization against measles, where the goal was to vaccinate all children regardless of vaccination status, with the aim of increasing the recommended vaccination coverage and reducing measles cases.

Some actions in 2018 were carried out by the Ministry of Health with the objective of interrupting the transmission of the measles virus, such as: a) Acquisition of approximately 49.8 million doses of triple viral vaccine; b) Carrying out a "vaccination block" in suspected cases and in strategic locations; c) Intensive vaccination campaigns in places where the highest number of cases occurred; d) Rapid monitoring of post-campaign coverage[9].

According to Epidemiological Bulletin Special No. 2019, in all vaccination actions carried out in 2018, approximately 22 million doses of measles vaccine were administered[21].

In order to interrupt the circulation of the virus, the Ministry of Health develops some recommendations: a) Maintain high and homogeneous vaccine coverage of the triple and viral tetra; b) In positive measles areas, carry out sweeping and vaccination intensification; c) Systemic evaluation of vaccination coverage; d) Conduct the vaccination of groups considered at risk; e) Perform retrospective searches for patients with measles triad in silent municipalities; f) Reinforce the field investigation teams; g) Perform blocking within 72 hours of suspected cases; h) Produce a wide media campaign; i) Establish strategies for implementing rapid response actions in the face of new imported cases; j) Plan vaccination strategies in environments where crowds occur (airports, churches, schools).

Thus, it is evident the need for health strategies and campaigns so that vaccination coverage reaches what is recommended by the Ministry of Health, and should be carried out frequently and with emphasis so that new cases of measles do not arise and, mainly, the non-occurrence of death by an immunopreventable disease.

CONCLUSION

It was found that, during the study period, the reduction in vaccination coverage in all the years analyzed did not reach the percentage recommended by the Ministry of Health, as well as an increase in the incidence of measles in the Northern Region of Brazil in 2018 was evidenced. Hospitalization rate was higher in 2018, the year that the last measles outbreak occurred. These indicators are important to determine the strategies to be carried out by the National Program for Immunization and Epidemiological Surveillance.

Authors' Contributions

Conceptualization, C.M.P.; M.A.L.R., L.C.A.; methodology, C.M.P.; M.A.L.R., L.C.A.; data collection, C.M.P.; M.A.L.R.; data analysis, C.M.P.; M.A.L.R., L.C.A.; formal analysis, C.M.P.; M.A.L.R., L.C.A.; investigation, C.M.P.; M.A.L.R., L.C.A.; writing - preparing the original draft, C.M.P.; M.A.L.R., L.C.A.; writing - proofreading and editing, C.M.P.; M.A.L.R., L.C.A.; financing acquisition, L.C.A. All authors read and agreed with the published version of the manuscript.

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Conflicts of Interest

Nothing to declare.

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CHAPTER 11

COVID-19 FEAR SCALE - VALIDATION AND ADAPTATION FOR THE PERINATAL PERIOD

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Abstract

Introduction: The comprehensive effects on the mental health of the population due to the rapid global spread of COVID-19 are even more harmful to specific groups of individuals, including pregnant women. **Objective:** To analyze the psychometric properties of the COVID-19 Fear Scale for Perinatal Period (EMC19-9). **Methods:** This is a cross-sectional study with 204 pregnant women. Participants were recruited online through social networks. The criteria for participation in the research were: pregnant and aged 18 years or older. An electronic form was filled out, which included the preliminary Portuguese version of the COVID-19 Fear Scale (EMC19), containing the seven items in the original version and the two additional items related to pregnancy and baby, socio-demographic, psychosocial and related to pregnancy, as well as the validated Brazilian versions of the Perinatal Depression Screening Scale and the Perinatal Anxiety Screening Scale. The SPSS version 26 statistical package was used. For parametric measures, Pearson's coefficient and Student's T and non-parametric - Mann Whitney's U. And the magnitude of the correlation coefficients with perinatal anxiety and depression symptoms, Cohen's criteria. AMOS 26.0 was used for confirmatory factor analysis. For internal consistency, Cronbach's alpha. **Results:** The results indicate that EMC-19-9 is a one- dimensional construct, has robust psychometric qualities, very good internal consistency of the questionnaire and shows convergent validity, has a moderate and significant correlation with perinatal anxiety and a significant, albeit slight, correlation with perinatal depression. **Conclusion:** the Covid-19 Fear Scale for the Perinatal Period (EMC-19-9) has robust psychometric qualities and convergent validity. EMC-19-9 is a reliable and valid tool to assess the severity of fear of COVID-19 among women in the perinatal period in Brazil.

Keywords: Fear; Covid-19; Scale; Validation; Adaptation.

Resumo

Introdução: Os efeitos abrangentes sobre a saúde mental da população em razão da rápida disseminação global da COVID-19 são ainda mais perniciosos para grupos específicos de indivíduos, incluindo as gestantes. **Objetivo**: Analisar as propriedades psicométricas da Escala de Medo da COVID-19 no Período Perinatal (EMC19-9). **Método:** Trata-se de estudo transversal com de 204 gestantes. As participantes foram recrutadas online por meio das redes sociais. Os critérios para participação na pesquisa foram: grávidas e com idade de 18 anos ou superior. Houve o preenchimento de formulário eletrônico, que incluía a versão portuguesa preliminar da Escala de Medo da COVID-19 (EMC-19), contendo os sete itens da versão original e os dois adicionais relacionados com a gravidez e bebé, variáveis socio-demográficas, psicossociais e relacionadas com a gravidez, bem como as versões brasileiras validadas da Escala de Rastreio da Depressão Perinatal e da Escala de Rastreio da Ansiedade Perinatal. Utilizou-se pacote estatístico do SPSS versão 26. Para medidas paramétricas, o coeficiente de Pearson e o T de Student e não- paramétrica – U de Mann Whitney. E a magnitude dos coeficientes de correlação com sintomatologia ansiosa e depressiva perinatais, os critérios de Cohen. Usou-se o AMOS 26.0, para a análise fatorial confirmatória. Para consistência interna, o alfa de

Cronbach. **Resultados:** Os resultados indicam que a EMC-19-9 é um construto unidimensional, possui qualidades psicométricas robustas, consistência interna do questionário muito boa e mostra ter validade convergente, apresenta correlação moderada e significativa com a ansiedade perinatal e correlação significativa, apesar de ligeira, com a depressão perinatal. **Conclusão:** A Escala do Medo do Covid-19 para o Período Perinatal (EMC-19-9) possui qualidades psicométricas robustas e validade convergente. A EMC-19-9 é uma ferramenta confiável e válida para avaliar a gravidade do medo de COVID-19 entre mulheres em período perinatal no Brasil.

Palavras-chave: Medo; Covid-19; Escala; Validação; Adaptação.

INTRODUCTION

The comprehensive effects on the mental health of the population due to the rapid global spread of COVID-19 are even more harmful to specific groups of individuals[1], including pregnant women. In addition, the World Health Organization (WHO) classifies as a risk group for complications in the event of an infection by SARS-CoV-2, pregnant women at any gestational age, postpartum women up to two weeks after delivery and women who presented abortion or fetal loss.

The American Association of Gynecology and Obstetrics (ACOG) understands that many pregnant women are experiencing increased stress due to COVID-19[2]. ACOG encourages local facilities and systems, with the contribution of its obstetric care professionals, to develop innovative protocols that meet the health care needs of its patients, considering the emotional dimension of pregnant women in times of pandemic.

On July 18, 2020, the Brazilian Federation of Gynecology and Obstetrics (FEBRASGO) issues an Alert note on maternal deaths associated with COVID-19 which reinforces “the need to consider prenatal and childbirth care services as essential services and uninterrupted in the Brazilian territory at all levels of health care, and that pregnant women and puerperal women, being groups at risk of death by COVID-19, should have easy access to intensive care and hospitalization in ICU beds”[3].

A recent study[4] shows that, until now, there have been more maternal deaths due to COVID-19 in Brazil than anywhere else in the world, according to available international reports. Even considering the different testing and notification strategies adopted in each country, Brazil may have a high incidence of adverse maternal outcomes during the COVID-19 pandemic compared to current data available from other countries4. Part of the data collection of the aforementioned study took place through conventional media, which shows how the cases have been disseminated to the general public reaching all people, including pregnant women. The result may be an increase in fear linked to anxiety and perinatal depression.

Another recent Brazilian study shed light on the disproportionate impact of COVID-19 on pregnant women and black mothers in Brazil[5]. The findings by Santos et al.5 show that maternal mortality in black women due to COVID-19 was almost twice as high as that observed for white women in Brazil. The authors claim that this disparity should “draw our attention to the urgent need for containment measures focused on maternal health, which will require accurate and detailed analysis of all cases to support clinical decisions in the health system on a daily basis”. The racial / ethnic profile needed to be present in this study given the disparity in the development and outcome of illness by COVID-19 in the country among black women.

It is known that fear is a central emotional response to imminent threats, such as COVID-196. Fear is defined as an unpleasant emotional state that is triggered by the perception of threatening stimuli[7]. According to Pakpour and Griffiti[8], assessing fear is important when knowing the levels of fear about certain things between different groups due to specific sociodemographic variables (for example, sex, age, education, ethnicity, religiosity, etc.) to be able to know if education and prevention programs are needed and if they are needed which groups to target and where.

In an article written by anthropologist Catarina Barata, in the Portuguese newspaper "O Público", on August 2, 2020, it can be read that "in the face of the COVID-19 pandemic, many individual rights were suspended[9] advocated WHO recommendations[10], maternity hospitals were quick to impose restrictions on parturient preferences. The right to follow-up in most hospitals was suspended". On the matter, the anthropologist also mentions the increase in the number of inductions to labor performed without precise indication of births in the country.

Psychological factors play a vital role in the success of public health strategies used to manage epidemics and pandemics, says an editorial in the Journal of Anxiety Disorders[11].

These new tools can be useful to public health to better understand the correlations of fear of COVID-19 in the perinatal period, or to help identify people and groups at greatest risk. Psychologists could use the scale to see if the fear of COVID-19 is associated with specific personality traits. The grouping and application of this data can be used to plan education and / or prevention aimed at programs to help overcome the fear of COVID-19 and to mobilize these people to engage in preventive behavior.

METHODS

The participants were recruited online, through social networks. An invitation was presented to participate in the study, stating the objective and inclusion criteria - being pregnant, being over 18 years of age and being fluent in Portuguese. Participants who agreed to participate voluntarily gave their informed consent and then filled out a form in Google Forms, which included the preliminary Portuguese version of the COVID-19 Fear Scale (EMC19), containing the seven items from the original version and the two additional related to pregnancy and baby, some socio-demographic, psychosocial and pregnancy-related variables, as well as the validated Brazilian versions of the Perinatal Depression Screening Scale[12] and the Perinatal Anxiety Screening Scale[13].

These basically correspond to the validated Portuguese versions, by Pereira and collaborators[14,15], but the wording of the items was adapted to Brazilian Portuguese by two Brazilian researchers and confirmed as to their equivalence of meaning by two of the authors of the Portuguese versions[12,13].

Fear of Covid-19 Scale/ COVID-19 Fear Scale for Perinatal Period

The Fear of Covid-19 Scale (FC19S)[16] is a self- completed questionnaire consisting of seven items to be answered on a 5-point Likert scale, from "Strongly disagree" to "Strongly agree". In the original psychometric study, a one-dimensional scale was considered, with factor loads ranging from .66 to .74.

As for internal consistency, Cronbach's alpha, of α = .82, was favorable, as well as the correlation coefficients between the items and the corrected total, from .47 to .74. The test-retest stability of .72 was also acceptable. The scores in the FC19S correlated significantly and positively with the perceived vulnerability, anxiety and depression, assessed using the Likert scale[16].

The Brazilian version of this scale[17] has already been demonstrated recently, resulting in a one-dimensional model with satisfactory adjustment indexes (X 2 /g.l.=2.135; RMSEA = .061; CFI, TLI, GFI & lt; .095). Cronbach's alpha coefficient was .876, demonstrating construct validity, as well as good internal consistency.

The process of translating the FC19S into Brazilian Portuguese was as follows: first, the original scale in English (v1) was translated into Portuguese by Brazilian researchers (v2). Then, the translated Portuguese version (v2) was translated back into English by a translation software (v3). Finally, Brazilian researchers compared the English version (v3) with the original version (v1), item per item, to determine whether they were equivalent in meaning.

Subsequently, a Portuguese researcher revised it so that the proposed version could be used in Brazil and Portugal, a process after which the final version in Portuguese, called the COVID-19 Fear Scale (EMC- 19)[17], was obtained. Then two additional items were included, with content specifically related to pregnancy and the baby: 8. “I am afraid that something will happen in my pregnancy, childbirth or postpartum due to coronavirus-19” and 9. “I am afraid that my son is infected with coronavirus-19”. The specific items of the perinatal period follow the previous seven with the same possible scale of answers.

Perinatal Anxiety Screening Scale (PASS)[15]

To assess perinatal anxiety, the Perinatal Anxiety Screening Scale (ERAP) was used. This consists of 31 items developed based on the diagnostic criteria of the official international classifications [International Statistical Classification of Diseases and Related Health Problems - ICD 10 (1992)]; Diagnostic and Statistical Manual of Mental Disorders - DSM-5 (2013) for the various anxiety disorders. The frequency response range varies from “Never” (0) to “Almost Always” (3), so the total score can vary from 0 to 87, the more severe the symptoms, the higher the score is. In this sample, the Cronbach’s alpha coefficient, of internal consistency, was .936.

Perinatal Depression Screening Scale (PDSS-24)[14]

The 24 items of the ERDP correspond to symptoms that describe how the woman may be feeling during this pregnancy (last month) and to which she responds using a Likert scale, which ranges from “I strongly disagree” (1 point) to “I agree a lot” (5 points). The wording of the items refers to specific contents of the perinatal period, focusing on cognitive-emotional rather than somatic aspects. The higher the score, the greater the severity of the symptoms. In this sample, the Cronbach’s alpha coefficient, of internal consistency, was .953.

Statistical analysis

The statistical treatment was carried out with the program IBM SPSS Statistics, version 26 for Windows. Data processing was started by determining descriptive statistics, measures of central tendency and dispersion.

Given that the sample size is sufficient, taking into account the central limit theorem, parametric measurements and tests were used, such as Pearson’s correlation coefficient and Student’s T to compare average scores. When at least one of the groups in comparison was smaller than 30 and even if the t distribution with v degrees of freedom approached the normal distribution[18], the Mann Whitney U-equivalent test was applied.

The magnitude of the correlation coefficients was classified according to Cohen’s criteria: low if less than .19; moderate if between .20 and .49 and high if greater than .50.

The AMOS 26.0 software was used for confirmatory factor analysis (AFC). The violation of the normal distribution was verified with the coefficients of asymmetry and kurtosis. The adjustment of the models was made based on modification indexes greater than 11, $p < .001$, produced by AMOS and based on theoretical considerations[18]. To assess the adequacy of the model, the following adjustment indices were used: X2 / gl, Comparative Fit Index (CFI), Goodness of Fit Index (GFI), Tucker-Lewis Index (TLI), Root Mean Square Error of Approximation (RMSEA).

For the analysis of internal consistency, we used Cronbach’s alpha coefficient. In order to determine the particular contribution of each item to the internal consistency of the dimension, Cronbach’s alpha coefficients were determined, excluding the respective items, and then compared with the overall alpha of the dimension. To ascertain the discriminatory power or internal validity of each item, the correlation coefficients were analyzed between each item and the total (excluding the item).

Ethical and legal aspects

For the analysis of internal consistency, we used Cronbach's alpha coefficient. In order to determine the particular contribution of each item to the internal consistency of the dimension, Cronbach's alpha coefficients were determined, excluding the respective items, and then compared with the overall alpha of the dimension. To ascertain the discriminatory power or internal validity of each item, the correlation coefficients were analyzed between each item and the total (excluding the item).

The study was approved by the National Research Ethics Commission of Brazil - CONEP, according to the attributions defined in CNS Resolution No. 510 of 2016, in CNS Resolution No. 466 of 2012 and in CNS Operational Standard No. 001 of 2013, which was expressed by the approval of the proposed research project with the number of the CAAE: 32934720.3.0000.5556, under the title: Perinatal Psychological Disorder in times of COVID. The data was treated with conditionality, equality and fairness. All procedures followed were in accordance with ethical standards. Informed consent was obtained from all participants included in the study.

RESULTS

Participants

Between 19 June and 10 July 2020, 204 valid responses were obtained. The average age of the participants was 30.12 years (± 5.45), ranging from 19 to 42 years. The average number of weeks of pregnancy at the time of completion was 25.17 (± 6,553). The majority had an undergraduate degree or more (n = 153; 76.5%). Regarding marital status, most were married or in a stable relationship (n = 128, 64.0%), with 57 (28.5%) single.

Regarding the race with which they identified themselves, the distribution was the following: white, n = 92 (46.0%); brown, n = 70 (35.0%); black, n = 30 (15.0%); indigenous, n = 1 (.5%) and yellow, n = 7 (3.5%).

In terms of their situation at work, 98 (49.0%) women were working, 69 (34.5%) were unemployed, five (2.5%) had a certificate and 28 (14.0%) said they were "in another situation", of which 19 (9.5%) stated explicitly that they were out of work due to the pandemic.

Close to 1/5 of the women (n = 34, 26.1%) were health professionals, and of these, 15 (7.5% of the total sample), are "top professionals", that is, with direct contact with patients. Only three (1.5%) participants did not live in Brazil (they lived in Portugal) and three others were not born in this country. If they had a choice, 191 women (95.5%) preferred normal birth and nine (4.5%), cesarean.

When asked if, in the last year, there was any life event that caused a lot of stress (Examples: Separation / divorce; Domestic violence; Death of a loved one; Serious illness; Unemployment), almost half of the sample, n = 95 (47.5%) replied affirmatively. As for the relationship with the partner, 170 women (85.1%) reported being good; 21 (10.5%) reasonable; one (.5%) participant characterized it as bad and eight indicated that they had no partner (4.0%).

Regarding their perception on receiving the help and emotional support they need from their partner, 6 (3.0%) and 16 (8.0%) answered "nothing" and "little" respectively. But in relation to other family members or friends, these proportions were 2 (1.0%) and 17 (8.5%), respectively.

Construct validity

The initial AFC model of the perinatal version with nine items, as a one-dimensional measure, resulted in some unsatisfactory adjustment indexes (table 1). After correlating the five pairs of item errors (3 and 6, 3 and 7, 3 and 8, 6 and 7 and 8 and 9) with modification

rates greater than 1117, I obtained a very good adjustment (table 1, figure 1). Cronbach's alpha coefficient in this version was α = .890.

Table 1: Adjustment indexes of the tested models – EMC-19-9.

Models	Index	$\chi^{2/g.l}$	RMSEA	CFI	TLI	GFI
Inicial Model	Adjustment indices	6.866	.162	.825	.766	.808
	Interpretation of values[23]	Bad	Unacceptable	Poor	Poor	Poor
Final Mod-el*	Adjustment indices	2.480	.076	.964	.941	.947
	Interpretation of values[23]	Good	Acceptable	Very good	Very good	Very good

* With four pairs of correlated errors

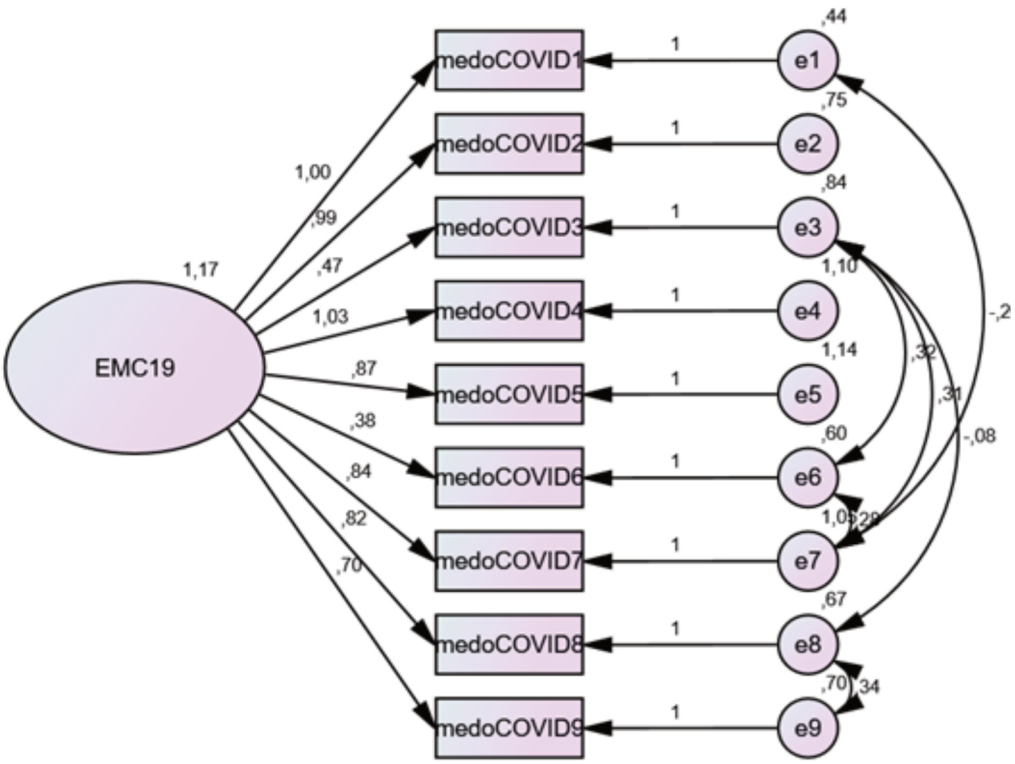

Figure 1: Confirmatory factor analysis of the final model of EMC-19-9, with 3 pairs of correlated items.

FIDELITY

Internal consistency

Table 2 shows, other than the average score and standard deviation of each item, Cronbach's alpha with each item excluded and the item-total correlation corrected, for the 9-item version. It was found that all items on the scale contribute to internal consistency, as they showed corrected item-total correlations greater than .40, ranging from .525 (item 6) to .738 (items 1) in the adapted version of nine items; the exclusion of each item would cause the Cronbach's alpha of the total scale to decrease.

Table 2: Mean score and standard deviation for each item, Cronbach's alpha coefficients excluding the item and corrected item-total correlations in EMC-19-7 and 9 (N = 200).

Items	Average	Standard deviation	Corrected item-total correlation		Cronbach's alpha excluding the item	
			EMC19-7	EMC19-9	EMC19-7	EMC19-9
1. I am very afraid of coronavirus-19.	3.80	1.272	.687	.738	.835	.868
2. I am uncomfortable just thinking about the coronavirus-19.	3.45	1.381	.686	.714	.834	.870
3. My hands get wet when I think of coronavirus-19.	1.60	1.052	.579	.530	.850	.885
4. I am afraid of losing my life because of the coronavirus-19.	3.32	1.535	.651	.689	.841	.873
5. When watching news and stories about coronavirus-19 in the media, I get nervous or anxious.	3.35	1.430	.614	.631	.846	.878
6. I can't sleep because I'm concerned about getting the coronavirus-19.	1.52	.879	.564	.525	.854	.886
7. My heart is racing when I think I can get coronavirus-19.	2.13	1.384	.686	.656	.834	.875
8. I am afraid that something will happen in my pregnancy, delivery or postpartum due to coronavirus-19.	4.20	1.207	-	.687	-	.873
9. I am afraid that my baby will be infected with coronavirus-19.	4.31	1.126	-	.644	-	.877

Table 2: Mean score and standard deviation for each item, Cronbach's alpha coefficients excluding the item and corrected item-total correlations in EMC-19-7 and 9 (N = 200).

Convergent validity

To analyze this parameter, Pearson's correlation coefficients between the versions of EMC-19 and the scales of depressive and anxious perinatal symptoms were calculated. Table 3 shows that the versions of nine items have a moderate and significant correlation with perinatal anxiety; on the other hand, perinatal depression is significantly correlated, although the magnitude of the association is slight.

Table 3: Pearson's correlation coefficients between EMC-19-7, EMC-19-9, ERAP and ERDP.

Scale	EMC-19-9	ERAP
EMC-19-9	1	
ERAP	.334**	1
ERDP	.160*	.770**

*p<.05; **p<.001

Average scores (per groups)

The average total scores on the EMC19-9 were 27.66 (± 8.29; range: 9-44). Table 4 shows the values corresponding to the percentiles (and quartiles) for the two versions.

Table 4: Values corresponding to Percentiles 5, 10, 15, 25, 50, 75, 85, 90 and 95.

Percentiles	EMC 19-9
5	12.0000
10	16.0000
15	19.0000
25	22.0000
50	28.0000
75	35.0000
85	37.0000
90	38.0000
95	41.0000

The race, categorized as white (n = 92, 46%) versus black / brown (n = 100, 50%), did not result in significantly different scores on the EMC-19-9 [t = -. 783 (190), p = .434)]. Also, the fact that the pregnancy was desired, at least by one of the parents (n = 154) or not (by both), (n = 56), does not seem to influence the fear associated with COVID-19 [Z = -. 741, (p = .460)], as well as the preference regarding the type of delivery EMC-19- 9: [Z = -1.321, (p = .188)].

Psychosocial variables, such as having had a stressful event in the last year, the quality of the relationship with the partner and the perception of support also did not generate significant differences in the average scores of the two fear scales of COVID-19.

Among employed women, compared to unemployed, there were no significant differences in the EMC-19-9 scores [t = 1,116 (165), (p = .266)], not even considering the 12 participants who explicitly stated that they were out of work due to the pandemic [Z = -1.722, (p = .085)].

In relation to other professionals, health professionals did not present higher scores in the totals of EMC19-9 [t = -1.077 (198), (p = .283)]. However, if you consider only the "top professionals", you can see that they have significantly lower scores of fear of COVID-19, on the scale of nine items (22.00 ± 7.03) than the rest of the sample, which obtained averages of 28.19 ± 8.22 [Z = -2,992, (p = .003)]; even in comparison with other health professionals, those who work in the front line have lower scores than those [30.52 ± 7.33; Z = -2.947, (p = .003)].

Thus, pregnant health workers who work on the edge are subject to repeated and prolonged exposure to the risk of contamination by COVID-19, which leads to a reduction in anxiety. This would be the result of desensitization or habituation and they will respond with less fear to stimuli related to anxiety by COVID-19. Studies about the desensitization phenomenon start from the habituation model, which states that three conditions are necessary for the ideal benefit of exposures: 1) activation of fear, 2) minimization of anxiety-reducing behaviors and 3) habituation[19-22].

According to the habituation model, exposure is effective because it provides structured contact with a feared stimulus, while minimizing the opportunity for avoidance, escape or ritualization[23]. It can be assumed that health professionals who work on the edge are exposed daily to the stress of COVID-19 and the risk of contamination, generating a reaction of habituation or desensitization. Habituation is related to decreased fear and cognitive changes[23].

Lang[24] suggests that fear reactions are composed of three response symptoms: verbal (i.e., self-reported quantification of the level of anxiety), behavioral (for example, observable avoidance and avoidance behaviors that work to reduce anxiety and fear, as compulsive rituals) and physiological (for example, heart rate and skin conductance. This data is important for more studies to be carried out in order to deepen this supportive effect of exposure to COVID-19 and the consequences in increasing personal vulnerability, as well as the adoption of preventive behaviors by health workers, especially pregnant women, in which case the process of desensitization or habituation could have negative consequences.

DISCUSSION

The threat of COVID-19 is particularly mysterious and unknown, which can trigger even more intense reactions in pregnant women. When she feels threatened, she reacts by activating defense mechanisms triggered by the activity of the survival circuits and fear is the most immediately triggered conscious emotion.

Fear and anxiety can be enhanced or minimized both by knowing or having more or less information, and by fear of the unknown related to expecting a baby.

Perceiving the threat of COVID-19 as serious was positively associated with preventive behaviors, suggesting that the perceived threat can be a motivational factor to smooth the progress of prevention, being a normal, functional response in the context of a pandemic[25]. However, further studies are needed to define the cutoff point, when through this value, you can consider fear above the functional. Lesser fear can also increase vulnerability.

Mental health interventions, with the increase in the psychological burden of the pandemic, are fundamental and understand as well as differentiate the normal fluctuation in suffering related to COVID-19, and how this is all enhanced when carrying another being in your body.

Functional limitations possibly due to extreme fear or even increased vulnerability due to the absence of fear are proposed challenges. Adherence to health measures is directly linked to the success of containing transmissibility[26]. One has to ask: What is the role of fear in the perinatal period in adhering to the behaviors followed by health services? The emotional cost of the pandemic among pregnant women remains to be understood and measured.

In this context, it is recommended to have an instrument to assess the fear of COVID-19 which affects the future mother. An attempt can be made to take the first step by adapting and validating the COVID-19 Fear Scale for the Perinatal Period, EMC-19-9. The results indicate that this first version has robust psychometric qualities, the internal consistency of the questionnaire is very good and shows signs of convergent validity, has a moderate and significant correlation with perinatal anxiety and a significant, although slight, correlation with perinatal depression. In addition, the results seem to show the unidimensionality of the construct.

It points out the need for a study parallel to obstetrics that is dedicated to understanding everything that involves association between fear, health promotion and habituation. It is a process of great complexity, which, when evaluated, requires multiple constructs, but that can be inserted in a macro-construct that allows to encompass the interrelations that can be felt and experienced during pregnancy, however, this can only be made explicit in its entirety.

It needs a better understanding of how these impacts on mental health are linked to the pandemic phenomenon in conjunction with pregnancy and link the direction of public health campaigns that can help to alleviate suffering. “It is vitally important for everyone to concentrate efforts to understand the consequences of the COVID-19 pandemic on mental health and to find evidence-based ways of addressing these issues”[10].

The findings of the present study should be considered in the light of some limitations. The sample consisted of pregnant women basically from Brazilians. A formal diagnosis of mood disorders has not been made. In addition, the form of data collection through social networks limits access to those Brazilians with better socio-economic conditions, it cannot be excluded that social problems and convenience factors may have influenced the participants’ responses to the questionnaire. Temporal stability has not been analyzed since we are under time pressure to have a valid instrument; that is, we considered that, given its urgency, there was no reason to wait two months for the re-test.

An investigation of larger and more representative samples of Brazilian participants is necessary to confirm the preliminary results provided by the present study. However, the total scores on the EMC-19-9 were comparable across all ages, which suggests that the EMC- 19-9 is a good psychometric instrument to be used in assessing COVID-19 fears among Portuguese-speaking pregnant women.

More research is needed to find out where the vulnerability factors for emotional distress fit, especially in the perinatal period. Health services must proactively respond to pre-pregnancy psychosocial risk factors. This study presents a scale that can measure the fear of COVID-19 in the perinatal period so that its results can plan actions to reduce the burden on health services and prevent long-term adverse effects for mothers and children.

CONCLUSION

The Covid-19 Fear Scale for the Perinatal Period (EMC-19-9) has robust psychometric qualities, the internal consistency of the questionnaire is very good and shows signs of convergent validity. EMC-19-9 is a reliable and valid tool for assessing the severity of fear of COVID-19 among women in the perinatal period in Brazil.EMC-19-9 allows planning education and / or prevention aimed at programs to help overcome the fear of COVID-19 and mobilize these people to engage in preventive behaviors and allow assessment of the effectiveness of strategies to prevent future emotional disorders arising of this very unusual period.

Author Contributions:

All authors contributed to the conception and design of the study. Material preparation, data collection and analysis were carried out by Monalisa N S Barros, Ana Telma Pereira, Marcella Aguiar, Frederica Carvalho and António Macedo. The first draft of the manuscript was written by Monalisa N S Barros and Ana Telma Pereira. All authors commented on previous versions of the manuscript. All authors read and approved the manuscript.

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Conflicts of Interest:

There is no conflict of interest.

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CHAPTER 12

COLLISION OF FUNDAMENTAL HUMAN RIGHTS AND THE RIGHT TO HEALTH ACCESS DURING THE NOVEL CORONAVIRUS PANDEMIC

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Abstract

Introduction: COVID-19 requires governmental measures to protect healthcare system access for people. In this process, the collision of fundamental rights emerges as a crucial challenge for decision-making. **Policy Options and Implications:** This policy review analyzes selected articles by the PubMed searcher about extreme measures taken in several countries during precedent pandemics and the current pandemic, and selects hard decisions relating to the exceptional measures taken by judicial departments in Brazil, connecting them to the "collision of fundamental rights and law principles." The collision of rights and principles imposed on decision makers a duty to provide balanced rights, and to adopt the enforcement of some rights prioritization. Ethical concerns were also verified in this field involving rights limitations. During a pandemic, the importance of extreme measures to protect health rights and healthcare systems is instrumental for focused, fast, and correct decision making to avoid loss of life and the collapse of healthcare systems. The main goals of this research are to discuss the implications and guidelines for public health decision making, the indispensable ethical and legal aspects for safeguarding health systems and the lives of people, and the respect of the Justice principle and of fundamental health and dignity rights. We conclude that COVID-19 justifies the prioritization of collective and individual health access rights. Acceptable standards of fundamental rights restrictions are established at the constitutional and international levels and must be enforced by rules and governmental action, to ensure fast and accurate decision making during a pandemic. Freedom rights exercises must be linked to solidarity for the realization of social welfare, for the health rights of all individuals and for health systems to function well during a pandemic. **Actionable Recommendations:** All individuals are free and equal, therefore social exclusion is prohibited. Institutions must consider social inequalities when discussing public health measures and be guided by ethical standards, by law principles, and rules recognized by constitutional and international law for the benefit of all during a health pandemic. Conclusions: Collective and individual health rights prevail over the collision of rights when facing pandemic occurrences, case by case, in health systems protection, based on the literature, on precedent pandemics and on legitimate Public Health efforts.

Keywords: Coronavirus Infections; Human Rights Abuses; Right to Health; Court Decisions; Jurisprudence.

Resumo

Introdução: A COVID-19 exige a adoção de medidas governamentais para proteger o acesso das pessoas aos sistemas de saúde. Nesse processo, o choque (colisão) de direitos fundamentais emerge como um desafio crucial para a tomada de decisões. **Opções de políticas e implicações:** Esta revisão de políticas

analisa artigos selecionados por meio de busca no PubMed sobre medidas extremas adotadas em diversos países durante pandemias precedentes e a pandemia atual, bem como seleciona decisões difíceis relacionadas às medidas excepcionais adotadas por órgãos do Judiciário no Brasil, conectando-as ao conceito de "colisão de direitos fundamentais e princípios do direito". A colisão de direitos e princípios impõe aos tomadores de decisão o dever de assegurar o equilíbrio entre direitos e de adotar a priorização da efetivação de determinados direitos. Questões éticas também foram identificadas nesse campo, envolvendo limitações de direitos. Durante uma pandemia, a importância de medidas extremas para a proteção do direito à saúde e dos sistemas de saúde é instrumental para uma tomada de decisão focada, rápida e correta, a fim de evitar a perda de vidas e o colapso dos sistemas de saúde. Os principais objetivos desta pesquisa são discutir as implicações e diretrizes para a tomada de decisão em saúde pública, os aspectos éticos e jurídicos indispensáveis para a salvaguarda dos sistemas de saúde e da vida das pessoas, bem como o respeito ao princípio da Justiça e aos direitos fundamentais à saúde e à dignidade. Concluímos que a COVID-19 justifica a priorização dos direitos de acesso à saúde coletiva e individual. Padrões aceitáveis de restrição de direitos fundamentais são estabelecidos nos âmbitos constitucional e internacional e devem ser aplicados por meio de normas e ações governamentais, a fim de assegurar decisões rápidas e precisas durante uma pandemia. O exercício das liberdades deve estar vinculado à solidariedade para a concretização do bem-estar social, para a garantia do direito à saúde de todos os indivíduos e para o adequado funcionamento dos sistemas de saúde durante uma pandemia. **Recomendações acionáveis:** Todos os indivíduos são livres e iguais; portanto, a exclusão social é proibida. As instituições devem considerar as desigualdades sociais ao discutir medidas de saúde pública e devem ser orientadas por padrões éticos, por princípios jurídicos e por normas reconhecidas pelo direito constitucional e internacional, em benefício de todos durante uma pandemia de saúde. **Conclusões:** Os direitos à saúde coletiva e individual prevalecem diante da colisão de direitos no enfrentamento de ocorrências pandêmicas, caso a caso, na proteção dos sistemas de saúde, com base na literatura, em pandemias precedentes e em esforços legítimos de Saúde Pública.

Palavras-chave: Infecções por Coronavírus; Violações de Direitos Humanos; Direito à Saúde; Decisões Judiciais; Jurisprudência.

INTRODUCTION

> *"Our rightsculturecannot constituteusunlessall rightscount, and all rightscannot count if all rightsareabsolute."**

COVID-19 (the new coronavirus disease) requires judicial decision-making and public policies for countries to protect public and private health systems and consequently the well-being, and in a prior way, the health rights of their citizens.

Both at legal and ethical levels, it is desirable that decision-making in public health, which is even more important in a pandemic context, respects the non-derogable guidelines of fundamental human rights, also constitutional rights, and respects law-guided ethical standards, in a way to better protect the health rights of people, and to also provide the secure maintenance of healthcare systems.

Extreme measures taken by countries and governments are justified in the context of the novel coronavirus infection pandemic by the fact that the disease has a high transmissibility rate and the methods o transmissibility are not completely understood by scientists.

However, there is scientific evidence that asymptomatic transmissions, for example, are possible at the same rate as symptomatic cases transmissibility. On the other hand, some studies suggest that asymptomatic cases could be less infectious and mainly contribute to the generation of new asymptomatic cases, also having an inferior rate of transmissibility if compared to symptomatic patients[1].

This way, it is not completely defined in what frequency and intensity asymptomatic cases contribute to the pandemic dissemination. In addition, COVID-19 has a critically high rate of contagion that can lead to the potential collapse of healthcare systems, especially as there is no effective treatment or vaccine available for the illness.

It is also quite normal for the hospitalization of critically ill patients to last several weeks (Table 1). A prolonged stay in an ICU facility creates legal, socio-economic, and political consequences that must be considered by governments in regard to healthcare system management in order to keep healthcare systems functioning during the pandemic, and also to avoid, as much as possible, the occurrence of new infections, in the case of shortage of beds in health institutions.

*Foreword GJ. Rights as trumps?(2018) 132 Harvard Law Review. 28, 96–117.

TABLE 1 | Median time of admission and hospitalization in ICU of critically ill patients with COVID-19 infections.

Articles	Median time for admission in ICU after symptoms	Median time of hospitalization after admission in ICU
Article (2)	10.5 days	11.5 days or more (survivals)
Article (3)	9 days (survivals) 11 days (non-survivals)	More than 17 days (survivals—at least 3 patients or 5,76% of admitted in ICU)

Source: Table developed by the authors by interpreting articles indicated.
Articles cited: full description on items (2) and (3) of the references section.

In this narrated scenario, the collision of fundamental rights emerges as a significant problem for government and healthcare management due to decision making regarding the need to delimit the extension of the acceptable exercise of freedom rights in times of a pandemic. They also need to consider the urgent need for fundamental human rights protection and the implications of pandemic measures on restricting people's rights related to liberty of movement, liberty of travel, liberty of work and to reopen schools.

In addition, more dense social issues demonstrate the illegal conditions of prison facilities and of confinement camps for migrants during the COVID-19 pandemic, that must be considered by authorities to guarantee the right of health for all and to cope with the spread of the virus.

This complex search for better solutions depends on the factual component of the reality of countries and societies. Besides that, communities and states need to attend to important rights for life, health, and human dignity, which are all surrounded by the urgency of public health prioritization.

There are no absolute rights. There are prima facie fundamental rightsand thereare thedefinitiveexercisestandards of each fundamental right, in each situation, that are defined beneath the facts and the legal norms of each situation under the law. All of the fundamental rights must be balanced to achieve the maximum protection for all fundamental rights in the reality of social life conflicts and in constitutional principles collision[4].

Post Second World War, European and Western countries, under directives from the United Nations (UN), built legal systems to face the barbarities committed by modern societies. The rights of life and human ignity were elevated to the top of the hierarchy of fundamental rights in constitutions, followed by the rights of freedom, which are also of extreme importance[5].

POLICY OPTIONS AND IMPLICATIONS

The Discussion of Balancing Rights to Freedom and the Necessary Decision to Prioritize the Fundamental Human Right to Health in the Context of the COVID-19 Pandemic

The Data Selection: Scientific Articles From PubMed Searches and Other Materials From Web-Based Public Data

Articles were selected from the PubMed database due to its large index and collection of world-leading research including scientific journals in health sciences detailing studies on before and after the SARSand MERS outbreaks.

Subsequently, filtering the database was accomplished by searching using the advanced search option in the PubMed website, with no restriction on language, and with the "date- completion" option set between 2003 and May 21, 2020. We used three sets of descriptors, one set for each search, with a total number of three searches, always within the same date range and only substituting the set of descriptors for each search.

The sets of descriptors used were MESH terms: "coronavirus infections and human rights abuses;" "coronavirus infections and right to health;" and "coronavirus infections and court decisions." The three searches returned, respectively, 2, 26, and 167 articles, totaling 195 articles for consideration. We conducted a search using allthe descriptors together but this failed as no results were returned.

The method of analysis we applied was to read the titles and abstract of the articles found within the search described and, subsequently, make a choice as to whether the article should be included in the research. We chose articles that were strongly related to the theme of the present manuscript from the authors' point of view and that matched the designed structure of our research.

For that intent, focusing on specific descriptors that could return important articles related to the theme of this research, we established the three sets of descriptors because we found it important within MESH terms to select coronavirus infections and human rights abuses, imagining possible violation aspects in restrictingrights within the pandemic. Next, we selected coronavirus infections and rights to health, health rights are the main rights to be balanced with priority in the face of other fundamental rights in the context of a pandemic.

For the last descriptor,we decided to include coronavirus infections and court decisions aiming to find different approaches to guide decision-making during a pandemic considering fundamental human rights and the rights concerning health prioritization.

Other scientific, journalistic, and opinion articles were included in the bibliography and used to develop the discussion within the research, in addition to the selected scientific articles from the searches performed as described above.

The PubMed material was complemented with data scraping carried out by Boolean operators performed in the Google free database before June 30, 2020. We used the Portuguese terms for coronavirus, COVID-19, court decisions, lockdown, quarantine, social distancing, prison, rules, legal acts, and jurisprudence. The selection criteria was based on the relevance of findings in regard to the focus of the present article.

These searches found references to Brazilian judicial court decisions in the scope of the COVID-19 pandemic, which were selected, read, and prepared for inclusion in the text. The authors utilized specific searches for judicial court decision numbers on the sites of the courts, as cited in Table 3.

The Points of View of Scientific Articles on Collision of Rights, Decision-Making, and Priority of the Right to Health During a Pandemic

The articles using the PubMed search engine can be seen in Table 2 to provide a better understanding of the findings. The main findings of the articles found on the theme of pandemic measures are set in this chapter. For example, a research paper on the scope of the Ebola pandemic only recommended quarantine in cases supported by scientific evidence justifying the balance between public security and human rights[6].

Another research paper on the span of the COVID-19 pandemic attributed the closure of the city of Wuhan as an effective epidemic control measure at that location. The authors of that study also noted that cases of the virus would have increased over time if individuals who were infected had not been contained by public efforts[7]. In the same sense, another research paper concluded that the lockdown measures were responsible for containing the epidemic in the city of Huangshi[8].

There was a critical article on street and road-blocking measures, as well as lockdown decrees, indicating that they were totally ineffective in containing COVID-19. Travel restriction measures imposed on Chinese citizens by other countries were contrary to in- ternational rules established by the WHO, according to this cited research[9].

However, the WHO (World Health Organization) International Health Regulations (IHR) from 2005[10], in article 43, does not preclude state parties to establish restrictive measures to prevent people's entry based on health risk demonstrated with scientific foundations, and respecting its internal law and international agreements, being more restrictive than international measures adopted by the WHO. However, this needs to be communicated to the WHO and a procedure of verification of its maintenance must be adopted after 3 months of the implemented measure.

On the other hand, the previous research indicates that it is common knowledge that it is necessary to contain person-to-person contagion in the scope of the COVID-19 pandemic in a way to reduce the infected number of people, and that this is possible if people maintain social distancing. Additionally, it is especially important to achieve the development of therapies and vaccines based on science to face the pandemic[9].

From an economic perspective, one article finds that it is questionable that there was justice in the restrictive air traffic measures related to Toronto during the SARS epidemic in 2003, which would have imposed a local loss for the Toronto travel industry of approximately 1.1 billion dollars[11]. This research considered that the restrictions would not have been ethical because the WHO did not listen to local authorities before the restrictions were imposed and the burden would not have been distributed equally[11].

TABLE 2 | PubMed articles selected and its findings.

PubMed articles Selected		Collision of rights	Governments and institutions decisions	Defense of health rights prioritization or not
6	USA	Public security and human rights	Quarantines and isolation	Only in cases supported by science. Quarantine if individuals are asymptomatic and the disease is transmissible before the symptoms appear, but only when benefits outweigh risks. Isolation only when individuals exposed are symptomatic.
7	China	Right to movement and public health efforts	Lockdown	Necessity to effective epidemic control at the location.
8	China	Right to movement and public health efforts	Lockdown	Containing the epidemic in the city.
9	China/UK	Public health efforts and human rights	Lockdown, street closures and travel restrictions	Defends that measures are ineffective to health and are against international human rights rules.
11	Canada	Travel economic rights and public health restrictions	Air trafficking restrictions	Defends that measures were unjust, didn't listen to economic sector and didn't distribute Fairly the burdens.
12	Canada	International right to health and public health efforts	Measures to avoid virus spread	China varies from complying (SARS) to not complying (HIV/AIDS) international right to health determinations.
13	Canada	Travel and tourism sector rights and public health surveillance	Travel restrictions	Arguments that surveillance on health care systems entry would be more effective than travel restrictions (suggest pandemic would be less widespread, end sooner and easily contained).
14	Singapore	Public health efforts, social rights and privacy rights	City closure, quarantines, contact tracing and temperature checks	Defends that besides effectiveness of draconian measures to contain the viruses, it is necessary to consider social impacts on privacy and people's rights, also considering legislative history and biomedical science.
15	Singapore	Public health efforts and rights to movement	City closure, quarantines, contact tracing, temperature checks	SARS is controllable and government measures were effective to control virus spread.
16	Canada	Freedom/Objection of Conscience	Health professionals refuse to attend to infectious diseases	There is a threshold that permits health professionals not to take personal risks and always will be volunteers to do the work.
17	United Kingdom	Collective health rights and individual health rights (Pandemics Scope)	Dehospitalization of long term internment with low health injury	Judicial decision defined that the patient should be dehospitalized to make hospital room for COVID-19 injured patients.
18	Tunisia	Freedom rights and government health based rights restrictions	Restrictions measures by government due to the pandemic	Government has the right and duty to take restrictive measures on freedom rights exercise in a pandemic context, based on the human rights order, the Constitution, the civil and administrative law.
19	China	Right to liberty (against arbitrary/illegal penal punishment) and rights to health	Penal law elaboration and punishment of acts during COVID-19 pandemics	Defends penal enforcements prevailing over liberty rights exercise during pandemics to punish health measures Infringements.
22	Switzerland	Liberty to work as a liberal health professional and rights to health	Determination to closure of health professionals clinics, permitted only emergency care	Measure unique for all health professions, difficulty to define emergency cases, the measure doesn't attend the need of health materials economy, and the measure can increase healthcare crisis by letting patients without necessary attendance.
23	Portugal	Right to liberty and public health	Restrictive, exceptional internment and isolation Measures	Restrictions in these cases, in a pandemic scenario, is intended to contribute to the liberty and health of all. Refusing isolation threatens liberty and health of other citizens.
24	Spain	Liberty and freedom rights, public health and right of access to information	Lockdown, quarantines, exceptional restrictive measures	Scientists claimed to be protected the healthcare system with restrictive measures to liberty rights exercise, and with conceding access to COVID-19 data for better formulating scenarios and possibly interventions in the benefit of public health.
25	USA	Right to liberty, right to social care, protection of the right to migrate and right to free health care	Liberty restriction measures	Liberty restriction measures should be mandatory. Besides, governments should do more specially for the vulnerable, guaranteeing healthcare to migrants, also vaccine and effective treatments, once it exists, free of charge to the population.

(Continued)

TABLE 2 | Continued

PubMed articles Selected		Collision of rights	Governments and institutions decisions	Defense of health rights prioritization or not
26	USA/Canada	Liberty to travel and right to health	Restrictions on air trafficking	Authors argue that air travel restrictions are contrary to the norms of international law. (The article 43 of IHR (International Health Regulations) of the WHO (World Health Organization) does not forbid the air travel restriction, "but such measures shall not be more restrictive of international traffic and not more invasive or intrusive to persons than reasonably available alternatives that would achieve the appropriate level of health protection"). Travel restrictions in past outbreaks were of limited Public Health effectiveness. The necessity of travel bans must be weighed against less restrictive alternatives. Social distancing and contact tracing would be more effective in banning the virus spread. Travel restrictions slowed the spread but not halted it. Governments are always seeking to restrict people's rights. Preventions on the diseases depends on international cooperation and rights protection. Instead of restricting rights States should follow WHO recommendations and practice transparent governance, expand testing capacity, and implement social distancing to protect Public Health. Travel bans unnecessarily provokes economic isolation and rights violation. Freedom rights were infringed with travel restrictions. Instead of travel restrictions States should have isolated people. The world is more secure when countries comply with Public Health necessities and Global Health law.
27	UK/Greece	Migrants rights (fundamental human rights) such as liberty and health rights	Policies of migrants confinement	Such policies of migrants confinement in Europe, and confinement camps, are inhumane. These policies deny migrants human rights such as liberty, health, dignity, work, and so on. This situation makes relevant the urgent need for countries to include universal access to health systems as a right of every human being.
28	USA	Individual freedoms and public health	Exceptional measures based on "Emergency Health Powers"	Due to public health protection the possible measures include compulsory treatments, isolation quarantines, limited liability protections, crisis standards of care for hospitals, powers to test, screen and restrict travel, real time requirements of health materials and products, medications, vaccines, person apprehensions if suspected of infection for treatment and tests for up to 72hours, confinement of infected persons with clear and convincing evidences. Compulsory Health Power should consider evaluating legal and ethical standards, that should include: 1. significant risk of individuals pose an infectious and dangerous disease; 2. interventions must be likely to ameliorate risks; 3. required least-restrictive necessary means to achieve public health objectives; 4. coercion proportionate to the risk; 5. assessments must be based on the best available scientific evidence, but in emerging crises when science is uncertain it is worth base restrictions on the "precautionary principle". But emergencies in Public Health do not permit coercion that is indiscriminate, overbroad, excessive or without evidentiary support. Home quarantines when correctly taken are much more protective of individual rights liberty and privacy than off-site restrictive measures.

On the theme of human rights, an essay indicated that China varied between complying with international determinations of the right to health (in the SARS case) and total non-compliance (in the HIV/AIDS case). In the case of SARS, China complied with measuresto prevent thespread of thevirus; in contrast it did not guarantee that Chinese patients suffering from HIV/AIDS had a right to access possible treatments[12].

According to the authors from the above article[12], rights in China do not have the same nature as the human rights in the international arena and in most Western democratic countries, where rights are considered inherent to every person. In China, there are only concessions of rights made by the government depending on a person's commitment to duties imposed by the government.

The prospects of rights in China, in comparison to other countriesruled by international human rights, arefundamentally diverse, because the rule of international human rights imposes the recognition of rights to every person, without conditions, such as liberty, political rights, dignity, life, health rights, social rights, and cultural and economic rights. Its intensity, extension, and depth vary according to the development stage and richness of a country.

Some dared to predict that if a new epidemic such as SARS appeared, and the local government instead of implementing airport passenger surveillance, affecting the economic travel and tourism sector, had only invested in surveillance at the entrance of health systems, the epidemic would end sooner. The pandemic would be less widespread and more easily contained[13].

Health surveillance and precise restrictionmeasures to avoid public movement in Singapore during the last pandemic demonstrated that fewer people traveling contributed to lower rates of infection. This happened during the SARSepidemic and now has happened during the COVID-19 epidemic[14].

Relating science data to social issues, the research paper demonstrated that measures to restrict and contain an epidemic must follow biomedical criteria and must also consider the social implications ofrestrictions on rights to movement that affect many people's privacy, liberty, and social rights. The island of Singapore is described to be generally closed during pandemic occurrences with a ring of protection, in conjunction with quarantine, contact tracing, and temperature checking measures in public places[14].

Besides, it was verified through a mathematical model that the interventions of Singapore's government i containing the SARS virus were able to stifle the outbreak of the disease[15]. This study did not focus on people's rights collision during the SARS pandemic but tried to answer two questions: was SARS controllable with restriction measures taken by the government and would these measures be effective?

This cited research[15] was successful in proving a positive answer to both questions above. This corroborates the defense of prioritization of collective health rights guaranteed by the measures taken in the SARS pandemic in Singapore. However, the limitation of the study, due to a focus on a mathematical model to prove efficiency of the restriction measures, did not demonstrate a broad view of people's rights in Singapore, which would have been desirable.

Among the possible measures of rights restrictions enacted by governments during a pandemic, there may be attempts to compel health professionals to assist patients with COVID-19 against of their own will (of health professionals). Would that be feasible? This question was raised during the SARS epidemic, where fatality rates were significantly higher than for COVID- 19 rates.

The fatality rates of health professionals during both the SARS and COVID-19 outbreak were very high and ethically some health professionals refused to treat infected patients. Could this choice be considered reasonable? In this specific case, because of the rule that permits health professionals to safeguard their own health, the option of not treating infectious patients is justified at least in the context of SARS since there will always be volunteers to do the work, this was the conclusion of other research paper (16).

Judicial decisions on healthcare have social repercussions in the United Kingdom due to the common law system, and the system of precedents[17]. An important case mentioned is the case of MB (patient name as initials, not publicized in full in the article for confidentiality reasons) admitted a few years ago to a London hospital.

The hospital sought an injunction to remove the patient from its facility in order to make room for COVID-19 patients. The hospital had already tried to move the patient to a communal home that would meet his needs; however, the patient refused. The judge decided on his removal and prevented him from returning to the hospital without express permission, except if brought by an ambulance [case: University college London Hospitals NHSFoundation Trust v MB [2020] EWHC 882][17].

In the context of Tunisia[18], the government's right to restrict freedom rights during the exceptional context of a pandemic stems from the international human rights order, the Constitution, and the administrative and civil law normative acts. The same is true in Brazil, and for most statepartiesin the WHO, and in the same exact order of importance[10].

One research article set in China suggests that local governments must urgently make adaptations to their legal systems with a focus on the penal system, like China has been doing, in order to be able to punish people who fail to comply with restrictive measures aimed at containing the advance of the COVID-19 pandemic[19].

The penalties for these crimes vary from several months of detention to more than 10 years of reclusion. In the article cited (19) the problem discussed is that after the beginning of the COVID-19 pandemic, authorities in China supposedly made some alterations in the penal law so that they could punish people for infringement of measures during the pandemic.

In the Brazilian case, the penal code has a prevision for the so called danger crimesthat can beapplied to actsthat do not adhere with governmental and health measures taken to avoid infections during pandemics, such as articles 131 and 132. The Brazilian penal code also prescribes the epidemic crime (article 267), the crime of infringement of sanitary measures (article 268), and the crime of disobedience (article 330)[20].

Caution is recommended because the main principle of the penal law is the legality principle, according to which the crime and the penalty for its commitment must be prescribed in law before the conduct that will be punished occurs (from the Latin sentence "nullum crimen nulla poena sine praevia lege")[20, 21].

Two additional issues: the criminal approach is different in the Chinese context, for reasons already discussed in this study, and human rights seem not to be fully respected in China compared to the international sphere. Therefore, considering that in criminal facts coercion measures applied to previous facts under the principle of criminal legality cited above, it is not acceptable that the advance of the pandemic can be contained, an intention necessarily directed toward the future, by law enforcement to punish the authors of crimes.

The penal approach to stop the virus spread is only acceptable if it respects the penal principles, the due process of law, fundamental human rights guarantees, and if it is extremely necessary, as the last choice of the authorities to contain individuals conducting imminent and dangerously deliberate spread of the virus. It is the ultima ratio legitimate intervention.

In Revue Médicale Suisse (RMS)[22], medical doctors argue that it is not possible to follow the determination of public authorities for non-urgent cases, the so called fermeture obligatoire des cabinet medicaux per le Ordonnance 2 COVID 19, with only permission for emergency medical care being maintained.

State restrictions have even created a definition for an urgent situation, such as one that cannot be postponed to another date. However, the authors claim that there are situations in which it is not possible to clearly determine if it is urgent or not, and that even patients whose conditions are originally not urgent can quickly evolve into an emergency that requires immediate intervention[22].

In Portugal there is context for the application of restrictive, exceptional, internment, and isolation measures indicated for reasons of public health, as detailed by constitutional interpretation and jurisprudence. There are no explicit provisions allowing restriction of liberty in the CRP (Constitution of the Portuguese Republic) in the case of a pandemic, but, as these authors explain, in these exceptional circumstances, restrictions are intended to contribute to the liberty and health of all, since the patient that refuses isolation threatens the liberty and health of the other citizens[23].

In the Spanish context of the pandemic, experts asked the authorities to decree a lockdown and to grant access to pandemic data to researchers, because it is indispensable to guarantee the right to information. This can also contribute to the formulation of exceptional measures to face the pandemic based on facts and scientific evidence[24].

Scientists also claimed, in addition, for the authorities to take more restrictive measures on freedom rights for the purpose of containing the advancement of COVID-19[24]. According to these authors, the Spanish government's timid measures were not enough to contain the pandemic's progress, and it eroded the foundations of the Spanish health system[24].

A finding in an article included in this study stated that people should follow the mandatory recommendations and restrictions, and comply with orders of social distancing. Moreover, governments should do their part, especially for the most vulnerable. For example, guaranteeing social and health care to immigrants, who fear deportation and would hide even if they were sick, causing individual and social damage. Governments must guarantee treatment, and, once a vaccine and effective treatments exist, they must be assured free of charge to the population, to avoid inequalities[25].

As a counterpoint to the idea that restrictions on the right to freedom should prevail to contain the advance of the pandemic, and consequently to safeguard the right to health, some authors advocate that restrictions on air travel are contrary to the norms of international law[26]. But as we saw above in article 43 of the IHR, measures that restrict people's entry into state parties of the WHO to face health risk are not forbidden but have to be founded on scientific evidence and have to adhere to a procedure of communication and verification.

According to another study[27], policies of confinement of migrants in Europe, mainly in countries with low to medium income, threaten theeffortsto contain theprogressof COVID-19 in major European centers. Thousands of migrants do not have access to water, soap, medicines, toilets, and electricity, and they are confined to detainment facilities, such as confinement camps, without basic health conditions[27]. These in humane

conditions are perfect for COVID-19 transmission, which can increase the rates of contagion in European centers going forward.

Several authorities in countries like Greece have already been informed of the need to eliminate such confinement camps in the scope of the pandemic, but no such measures were taken. Measures to cope with COVID-19, like those policies of the 2030 Agenda, should include universal access to health care systems for all people as an emergent need[27].

Restrictiveand social distancing measuresdo not work and are not possiblefor confined migrants, in thisinhumanescenario. All the efforts to contain COVID-19 could be in vain if there remain migrant confinement camps in the Mediterranean.

In the light of the declaration on January 31 2020 that the COVID-19 pandemic in the United States of America was an emergency and a clear exceptional situation o f crisis, the government had a special responsibility to carefully balance the protection of public health and individual freedom[28].

The present article is about unveiling pandemic extreme measures that can be taken by governments and health authorities and that make it possible to better protect rights to freedom and health, guaranteeing human rights protection and promotion in a solidarity and collective way during a pandemic.

Collision of Rights to Freedom in the Face of the Rights to Life and Health During the Novel Coronavirus Pandemic

Brazilian State Policies to Face the Pandemic and the Judicialization of Collisions of Fundamental Rights in Brazil in the Scope of the COVID-19 Pandemic

Fundamental rightsin Brazil are based on itsConstitution. There is a claim that fundamental freedoms and their exercise by individualsand groupsof peoplecollidewith theright to health in thescopeof thecurrent pandemic of COVID-19, which issimilar to what happens in different parts of the world, as described in Table 2.

In theCOVID-19 context wemust admit, by thedatacollected (Table 3), that the head of the Federal State of Brazil has adopted contradictory measures during the pandemic. It is also possible to detect that he does not deliberately implement global health recommendations, and rejects any coordination with local governmentsto copewith thepandemic effectsand containment.

TABLE 3 | Examples of Lawsuits in Brazil in the collision of fundamental human rights during the Coronavirus pandemic.

Lawsuit proposer	Action requests	Court	Decision
1. Democratic Work Party (by Brazilian Federal Deputy).	Unconstitutionality of a federal provisional law that removed the competence to impose restrictive measures from Brazilian States and Municipalities.	Brazilian Supreme Federal Court.	Injunction granted to maintain the competence of the Union, States and Municipalities to impose restrictive health measures during the pandemic[1].
2. Federal State of São Paulo.	To unblock the roads on the coast of Caraguatatuba.	São Paulo State Court of Justice.	Suspension of the injunction and the judgment that blocked the roads[2].
3. Brazilian Federal District.	Mandatory submission to diagnostic examination and home isolation in one necessary case.	Federal district court of justice.	Injunction granted[3].
4. Municipality of Ariquemes Rondônia	Injunction and judgment suspension to permit open trade within the city.	Superior Court of Justice.	Suspension not granted[4].
5. Citizen 1[a]	Preventive *Habeas Corpus* not to be submitted to social isolation.	Superior court of justice.	Injunction not granted[5].
6. Citizen 2[b]	Home Prison.	Superior court of justice.	Measure approved[6].
7. Citizen 3[c]	Home Prison	São Paulo state court of justice.	Measure not approved[7].

Source: Data collected and prepared by the authors in the named courts' databases, after search and scraping data in the Google database with options described in the 'Data Selection' section above.

Chart legend: A: Citizen 1 did not want to be hypothetically submitted by a government rule to social isolation in case of infection by the novel coronavirus. The court decision did not permit the citizen avoidance of the health measures adopted by the government. B: Citizen 2 was a male jail prisoner accused of drug trafficking caught with 101 g of crack and 99 g of cocaine and would have

committed the crime without violence and was preventively arrested without conviction—overdue preventive detention. The court understood that in exception, because of the COVID-19 pandemic, and the fact that the crime was committed without violence or serious threat, to substitute the institutionalized prison to the home prison measure, according to pandemics guidelines recommended by the CNJ (National Counsel of Justice), prevailing a preventive measure to the health benefit (cope the coronavirus infections) over the criminal procedural law enforcement of the maintenance of the jail prison decree due to the gravity of the crime (great amount of drug apprehended) and general reasoning of jail preventive imprisonment in the protection of the public order. C: Citizen 3 was a female jail prisoner, mother of a child, condemned for drug trafficking with a community service punishment not complied to. This was replaced by arrest for 2 years, and the measure required was not approved due to the judgment consideration of the child's best interest in maintaining distance from the mother. 1: Direct Action of Inconstitutionality (ADI) n◦6341 from the Supreme Federal Court (STF) stf.jus.br, search of law suit tool by class (ADI) and number (6341). 2: Suspension of Injunction and Sentence (SLS) n.◦2054679-18.2020.8.26.0000 from the Court of Justice of the São Paulo State (TJSP) tj.sp.jus.br, search of law suit tool with the number. 3: Civil litigation n.◦0701858 04.2020.8.07.0018 from the Court of Justice of the Federal District (TJDF) tjdft.jus.br, search of consultations tool, public consultations, 1st instance, with the number. 4: Suspension of Injunction and Judgement (SLS) 2697 RO from the Superior Court of Justice (STJ) stj.jus.br, search of law suit tool with SLS 2697 descriptor. 5: Habeas Corpus (HC) 576058 DF 2020/0095453-4 from the Superior Court of Justice (STJ) stj.jus.br, search of law suit tool with HC 576058 descriptor. 6: Habeas Corpus (HC) 564736 SP 2020/0054426-4 from the Superior Court of Justice (STJ) stj.jus.br, search of law suit tool with the descriptor HC 564736. 7: Habeas Corpus (HC) 20602463020208260000 from the São Paulo State's Court of Justice (TJSP) tj.sp.jus.br, search of law suit tool with the number.

This can also be demonstrated in the science denial discourse of the head of the State (29).

On the other hand, the Senate of Brazil decreed, after the President of the Republic requested, based on the Constitution, a state of public calamity to cope with the pandemic using economic measures. A state of emergency in public health was determined by the Ministry of Health to cope with the pandemic and adopt necessary health measures.

It also established, by law, the possibility of the government adopting, among other measures, the restriction to movement of people, compulsory submission to diagnostic tests, social isolations, quarantines, lockdowns, and the request of private assets for the use of the State. It was also declared by law that all people in the scope of the pandemic have the right to be treated free of charge. These are the main potential measures to be taken by the country's government to face the pandemic (30), at federal and local levels.

State and Municipal governments in Brazil, within the scope of their constitutionally guaranteed competence in health issues, have addressed normative and administrative acts (pandemic measures) to restrict the movement of people, established compulsory isolation of individuals, and have made determinations to carry out diagnostic tests on specific individuals. They likewise established quarantines, social distancing rules, and other restrictions such as road and street blocking, as well as specific lockdown measures.

There have been judicial decisions on conflicts related to the pandemic, and recurrent judicial rulings recognizing the prioritization of the right to health that justifies restrictions in freedom rights. The most important and iconic of the conflicts that have occurred so far was at the legislative initiative of the President of the Republic in which he aimed to prevent State and Municipal governments from adopting measures to restrict the exercise of freedom rights, such as social isolation, quarantine, and local lockdowns.

This was provisionally prevented by the Federal Supreme Court. The Brazilian President tried to avoid local governments having to balance the fundamental rights to health access under their constitutional competency and the freedom fundamental rights, in order to be capable of determining pandemic measures to cope with the spread of the virus, and the Brazilian Supreme Federal Court did not permit that limitation by the President, which would have been terribly unconstitutional.

There was a declaration by the court that State and Municipal governments, as well the Federal government, can legislate on health under the Constitution rules and principles, but especially in the pandemic scope, in order to face the emergency of public health.

Conflicts and collisions of rights have been judicialized in several Brazilian courts. The matters are diverse, such as lawsuits that have been filed to release prisoners from risk groups to avoid the damaging consequences of COVID-19. In this kind of situation, the right to health only sometimes prevailed over the State's right to punish in the precarious context of the pandemic, as demonstrated in Table 3.

There are also cases of compulsory testing and social isolation. In such cases, the right to health has prevailed to the detriment of individual liberties in the cases verified (Table 3).

It is interesting to note that, in a way to prioritize health rights in habeas corpus petitions, in order to maintain social distancing, the claim verified has been that house arrest (relative liberty compared to prison) is necessary for inmates, in the risk group or with special conditions, to serve out their sentences or provisional prison measures.

In a case in which the judicial decision was to concede the mandamus, the court understood that imprisonment during this pandemic conflicts with health rights protection, and so it made the prioritization of health rights (Citizen 2, Table 3).

Some of the most relevant types of lawsuits involving the collision of principles which establish fundamental rights that have been found in the Brazilian pandemic situation are listed in Table 3. The right to health in the majority of the cases selected (5–2) prevailed over the other interests in the context of the pandemic.

The Weighting and Balancing of Rights in Collision

There are theoretical guidelines in legal doctrine for making judicial decisions in the face of a collision of law principles and for conflicts of legal rules. On the other hand, in the theories of the field of justice there is a consensus that "A Theory of Justice" from John Rawls is a watershed moment[31, 32].

John Rawlsisthetheorist that, from thesecond half of the20th century onwards, changed thefocusof thejusticeissuein a liberal way, focusing on the fairness of the justice, placing it in a set of rules for the better stand of liberty to all (egalitarian liberty) and of democratic equality completed by the sense of the principle of difference[31, 32].

It is recognized in doctrine that justice was, in Rawls's theory, replaced in a different focus considering the distributive sense of just measures to all, and that Rawls conceived his theory based on criticizing the utilitarianism ethics.

In summary, the justice theories have developed since Plato's concept of justice as happiness of the city and of its guardians, and Aristotle's concept of justice as equity. Subsequently, justice was connected to Hobbes's and Locke's concepts of State and Justice, founded on the power of the strongest due to a necessary obedience of the sovereign, and based on the right to property, respectively.

Justice conception was completed in this chronology by the utilitarian theoriesof Jeremy Bentham and John Stuart Mill based on the principle of happiness. After this evolution until the 19th century there was not another widely relevant new theory of justice before John Rawls.

At the other side of the current approach of this research, hard decisions in which fundamental law principles that contain the fundamental rights of people collide, Ronald Dworkin sets the problem assuring that rights only apparently collide because constitutional rights, at his notion, are neat and clear concepts that need to be known by the interpreter, from a point of view of the internal theory, without external influence of other fundamental rights, according to the concept that the principles are found in their internal content[4,33].

But Dworkin accepts the balancing and weighting of the interests involved in such cases, but in a hidden way, with justification deficiency to the theory[33]. At his side, Robert Alexy delivered an interpretation of law rules and principles, and in his conception of these optimization commandments (constitutional principles), from an external theory, it is necessary to balance and weigh principles and assume rights collisions, in a construction of a well-accepted technique to solve collision of rights and principles in court and state decisions [4,33,34].

Supported by the theory of principles by Robert Alexy, and the concepts of rules and principles by Ronald Dworkin, and also the horizon of liberty and equality borrowed from John Rawls's "A Theory of Justice," it is possible to discuss the established rules created to face the COVID-19 pandemic in the context of the scenarios given by the selected PubMed searcher articles, in several countries in the world and different legal systems considering also the Brazilian constitutional context in comparison.

Fundamental rights are essentially relative in the sense that there is no fundamental right, based on a principle, of absolute nature, according to the prevalent interpretation of the Constitution. For Pildes[35], although constitutional theory and political philosophy understand that rights are individual trumps for autonomy, dignity, and liberty against decisions in the common good, constitutional practice indicates that rights function in another sphere rather than acting in atomistic protection of individual interests. For thistheorist, rightsserveas tools for courts to evaluate the social meanings and dimensions of governmental action. In this way, rights are means of realizing the common good.

The exceptional situation of the COVID-19 pandemic and the need to face the public health emergency make it possible for authorities to balance constitutional principles, and to create and enforce legal rules that impose direct restrictions on the exercise of individual and social rightsin theprioritization of thecommon good. Thus, greater constitutional and democratic values can prevail amid the pandemic.

The rights to life, public health, and human dignity are examples of fundamental rights of unquestionable social and legal importance. Dueto thepandemic thesefundamental human rights take precedence in a weighting of values in comparison to the mere right to freedom dissociated from the values of solidarity, self-protection, precaution, and care.

For most general liberty exerciserightsto prevail over theright to health during a pandemic, they must be linked to solidarity, self-protection, precaution, and care. Examples are the cases of health professionalsthat refuseto assist COVID-19 patients, or of prisoners in Brazil, or of migrants in Europe or near the Mexican border in North America, whose restrictions to liberty in prison institutions render them unable to protect themselves from the virus spread in the pandemic, which is unacceptable.

These findings are based onthe legal system, on constitutionalism, and the normative nature of constitutional principles, and are observed in the literature. In cases of collision of rights, the fundamental rights thatcarry a social relevant value, notably the rights to health, to liberty with solidarity and self-protection, to equality, protection of all human lives, promotion of human dignity, and social justice efficacy, must be, in all of these cases, prioritized as a necessary respect of the rule of ethics and rule of law that must e necessarily attended.

ACTIONABLE RECOMMENDATIONS

In his Theory of Justice, Rawls[32] locates political action at the encounter between the rationality of the modern political social contract and geometric morality.

In his work “A Theory of Justice,” Rawls[32] assumes that in each society all individuals must be equally free, autonomous, and democratically equal (principles of egalitarian liberty and democratic equality). No onemay besubject to discrimination or exclusion, and institutional objectivesmust movein thedirection and primary purpose of poverty reduction and, therefore, of social ills.

This theory of justice is complemented by the principle of difference, according to which institutions must be structured based on the observation of social inequalities, and institutional practice must produce, in the long run and in the future, greater benefits to the least favored in society.

From the viewpoint of the theory of principles, by Robert Alexy, according to Virgílio Afonso da Silva[34], there is a possibility of conflict between legal rules and of collision between legal principles which make up the fundamental rights. But it is also possible that a collision occurs between rules and principles, which isanother way in which a collision between principles may take place[34].

Ronald Dworkin, in his work “Taking Rights Seriously”[36] addresses the issue of balancing law principles and the weighting of them as a need to decide, e.g., hard cases for which there are no decisions made yet but they certainly must be made. Some bases of these themes were previously addressed by the author earlier, in 1967, in an article entitled “The Model of the Rules”[37].

Dworkin establishes, in a way that is also indicated by Alexy, and is vastly accepted in law theory that a conflict between two rules has to be solved at the level of validity, with only one possible answer: one of the rules is valid, and the other rule is not valid.

On the other hand, Alexy indicates that in a collision between two principles, the nature of the collision is based in the “factual supports” of the principles, which includes in it the “protection scope ofthe principle” and the “governmental intervention”[34].

The “factual support” in Virgílio Afonso da Silva[4], on the other hand, also includes the “constitutional reasoning” in the conception of the constitutional principle to define whether the rightsrestriction based on rightscollision, e.g., isconstitutionally permitted or not.

Therefore, the technique to solve rights collision is to weigh the related principles, balance them, and select the one with greater weight, applying theproportionality principleconception to decide which is the most relevant principle to prevail for the governmental action to face the issue (facts) addressed, in order to restrict fundamental rightsexercisesin a constitutionally respectful pattern. And this weight and importance must be in accordancewith thefairnessof thedecision for that situation[32,34,36].

Virgílio Afonso da Silva developed his own concept of the “factual support” based on Alexy’s theory to clarify the constitutional permission of the fundamental rights restriction under a necessary verification: Scope of protection of the fundamental right + Governmental intervention + Constitutional Reasoning = Constitutional and Acceptable restriction of a Fundamental Right Exercise, case by case, necessarily considered the proportionality principle[4]. If there is no constitutional reasoning for the measure/intervention adopted to restrict fundamental rights, the State’s intervention in this case will be unconstitutional.

When two principles collide, e.g., the principle of individual liberty and the principle of public health, it must be assessed which principle should prevail in that specific scenario, considering and deciding in favor of themost fair decision to take (according to Alexy, themaximum protection of thefundamental right), always balancing and describing the weights of the law principles(rights) related to thesituation. From thenotion of the right to liberty that can belimited, in aTheory of Justiceby Rawls, it is considered that liberty can be limited in favor of everyone's own equal liberty[32].

Added to the notion of the emergency of public health, everything indicates that the right to health in the context of the current pandemic must prevail over the right to unrestricted liberty of movement of people, because the health right in this pandemic carries more legal and moral weight than the liberty exercise with some necessary restrictions, considering also that the liberty exercise can never be without any restriction, for the common good of all people.

Thus, the legality and legitimacy of the extreme measures that restrict freedom rightsin thestrict duty to copewith theCOVID-19 pandemic are well-justified if they are based in fairness and on solid facts, better scientific evidence, acceptable rules and constitutional principles, and if they are made by the competent authorities. Those measures can also be accepted if they use the least aggressive and restrictive measures possible to achieve the public health goal, if they do not cause direct or predicable harm to the life, dignity, and health of anybody, if they prioritize the health rights protection of the most vulnerable in the first instance, and if themeasuretaken isproportional to therisk faced and to the better protection of indivisible and interconnected fundamental rights.

In the Brazilian case, there is a regulation of social restrictions based on Federal and Local normative acts that settles legal rules during the pandemic. These rules inform other normative acts, improved per locality, which can bemorerestrictivebut not more flexible than the Federal rules or the Federal State's rules. Hence, thenormativeprescriptionscan beimproved and adapted in local rules, on the level of the State, the Municipal, and the Federal District governments.

Accordingly, a potential collision of norms of broad spectrum of freedom rights exercises in the face of the established rules of health protection, in the context of the pandemic, to better protect health rights and healthcare systems demonstrates the possibility of the collision of a constitutional principle (rights to freedom) with a rule of protection of the right to health (restriction measures).

In this case, as described for similar abstract situations by Virgílio Afonso da Silva disserting on Dworkin's and Alexy's concepts[34], a principle (of liberty) is restricted by a rule (pandemic extreme measures set by law) so that other principles can prevail—in this case the principle of public health (which is the foundation of the right to health).

The Supreme Federal Court in Brazil has several precedents establishing that whenever health and life collide with constitutional principles less important than life (life with dignity is the most important democratic principle)[5], the rights to life and to health must prevail.

The US Supreme court on May 29, 2020 rejected a church challenge to California's COVID-19 restrictions by a 5–4 vote. Chief Justice John Roberts joined the liberals and said in his opinion that he would not join conservative judges escalating effortsto overridepublic health measuresin thenameof religious freedom. It was set that "the Supreme Court will not facilitate the spread of a deadly virusin thenameof thefirst amendment"[38].

In the context of the pandemic, the acceptable measures to restrict individual and social rights are strictly intended to contain the spread of the SARS-CoV-2 virus always with the aim of preserving public health and people's lives.

In an ethical approach there is the necessity to consider the argument of utilitarianism decisions to achieve major happiness as a finality (principle of happiness), at least to most people. The point defended by John Stuart Mill's utilitarianism[39] can be a point of departure, but not the foundation of the ethical decision. Other important legal and ethical implications must be considered for decision-making during a pandemic.

No life can be forgotten, that is the point. Decisions in such situations that involve freedom rights exercise, health rights access, and protection of healthcare systems during pandemics, must be decisions that do not directly affect anyone with imminent risk of death or health injury, and it must also predict the consequences of extreme decisions, in its foundations for not to put in real and imminent risk thehuman dignity of any person. For example, an extreme pandemic measure that put someone in imminent risk of death to protect the health right of most people is not a feasible and fair ethical or legal decision.

That iswhy the"ruleutilitarianism" is, till today, agood way to make ethical decisions guided by law, as it establishes that "an act ismorally right if and only if it is(or islikely to be) in accordance with an acceptable rule (or set of rules), where the acceptability of a rule is determined on utilitarian grounds"[40].

The present study developed Table 4 with resumed information of the recommendations found within this research for a guideline on taking pandemic measures fairly to the fundamental human rights and based on acceptable ethical rules.

CONCLUSIONS

It is legal and legitimate for governments to adopt extreme measures by balancing and weighting constitutional principles to adopt restrictions on the fundamentalrights exercise that collide with the fundamental rights to health in situations of a pandemic, on the level of the Constitution. It is extremely necessary to protect rights to life, dignity, and the health of all. The prioritization of them in the face of freedom rights divorced from the solidarity, self-protection, care, and respect of autonomy, values that are important to societies, must be considered in health decisions.

To face the collision of rights (on the level of constitutional principles) it is necessary that facts have not yet being legislated specifically by a rule, or the specific rules are imprecise or incomplete, or if the rules (indirectly the principles that forged the rules) collide with other fundamental principles based on the Constitution. For that reason, these situations need the constitutional principles that address fundamental human rights to complement or define the legal significance of the governmental intervention to be applied. Pandemic occurrences must require this special legislation (rules) and precedent rulings of courtsto determinethelegal conformation of rightsrestriction measures for decision-making.

The conflict of general legal rules and special rules for a pandemic, at the other side, must be decided at the validity level, in which a pandemic rule must prevail when applied to the current situation, by the application of the prevalence of a special rule instead of a general rule, according to the *Latin sentence lex specialis derogat generali*.

If one intends to achieve a state of social justice during a pandemic, at the same time the government must first protect the most vulnerable. Then it is necessary to protect all people's rights to health and liberty with solidarity, or health equity will not be possible, mainly in impoverished communities, in prisons, and in peripheral regions of the world.

Most of the articles selected in the present study legitimize social restraint measures to face the increase in the number of infected casesin thepandemic by factual evidenceof contribution to decreasing the contagion and spread of the virus.

The same direction is noted in Table 3 data, in which seven court decisions face extreme measures related to the pandemic, and in its majority (5–2) they give precedence to the protection of the rights to health related in the case (only the cases 2. and 7., the"unblock of roads" and the"Citizen 3" cases, werenot decided invoking the need of the extreme measure adopted to protect the right to health, as described in Table 3).

TABLE 4 | Guidelines of conditions to orient authorities to take pandemic measures respecting acceptable ethical issues and fundamental human rights.

Extreme measures and its flexibilizations orders in pandemics must be, concomitantly:	**BASED IN:** Solid facts **OR** Better scientific evidence **AND** Better protection of all people **OR** Minor public health risks **AND** Minor individual health risks **OR** Prioritization of individual or collective health rights protection	**NOT CAUSE INJURY DIRECTLY TO:** Life **AND** Health **AND** Dignity **OF ANYBODY; OR IS LIKELY TO (PREDICTABLE TO):** Cause no harm to anybody **AND** Better and in first place favor the most vulnerable	**FAIR IF VALID TO:** All persons in the same conditions **OR** One person or group in specific condition	**TAKEN WITH:** The least aggressive effort to achieve the aimed public health benefits.	**RESPECTFUL TO:** Proportionality between the public health measure taken and the pandemic related risk faced.
Home quarantine					
Off-site quarantine**					
Social distancing					
Social isolation**					
Compulsory testing**					
Compulsory treatment**					
Compulsory vaccination**					
Person apprehension*					
Schools closure					
Schools reopening					
Travel restrictions					
Closure of clinics					
Closure of stores					
Closure of services					
Jail prison order*					
Home prison order*					

De-hospitalization	
Confinement* detention	
Cities closure	
Contact tracing	
Temperature Checks	
Streets closures	
Roads closure	
Lockdown measures	
Private and health goods/materials apprehensions	
Compulsory use of masks	
Commerce, stores, services reopening	

Table Interpretation: (A) These measures must be decreed by a criminal judge, in the Brazilian law system, after a requirement of a competent public authority, and must be related to a crime investigation on course or related to a conviction settled by a criminal judge (21). (B)** These measures can be taken by public administrative authorities due to the COVID-19 exceptional Federal and States legislations in Brazil, but, for a systematic view of fundamental rights, in case of enforcement measures with the use of public force against individuals physical liberty exercise, it is strongly recommended, for involving people's direct subtraction of liberty, to count with an ongoing criminal investigation and legal order emanated by a criminal judge after the occurrence of a crime related to the pandemic theoretically practiced by the individual (except in the cases such as of vaccination and of treatments with no iminent risks to life, that cannot be forced by physical strength). Isolation measures recommended are obligatory but if physical use of force to make it effective is not needed, the judicial order is also not necessary. But further criminal effects can arise if the individual deliberately do not accomplish with the measure determined by the public administrative authority (isolation after testing positive for COVID-19). These recommendations are founded on the due process of law principles and it's criminal law procedure rights and guarantees (21). (C) The measures of compulsory collecting samples and vaccination do not need a medical doctor prescription to be obligatory in Brazil. On the other hand, the measures of medical examinations, laboratorial tests and treatments, and social isolation must be abiding to medical prescription to be obligatory to the individual in Brazil due to the pandemic legislation in effect (30)., (D) The other measures in the Brazilian scenario can be made by public administrative action, due to Executive and Legislative authorities' norms, under their competency to legislate and administrate the health subject of law, also with the use of police force. (E) In case that the competent authorities do not act in their public duty or act against it, the Judiciary power can be provoked to act and deliberate in all these measures, regarding to its legal competencies, by court decisions, also founded in the principle of prohibition of the non-liquet (and the principle of no judgement avoidance) according to which the Judiciary Power in Brazil has the duty to decide in all questions that are demanded in courts (21). (F) If the pandemic exceptional/extreme measure and its flexibilization measure has all five affirmatives to the conditions above, the related measure is fair and accomplish with the fundamental human rights of all, aiming to protect and to promote rights to health in a pandemic scenario. In this case, according to the "Rule utilitarianism," the measure taken in the case fact is also accordant with an acceptable and ethical rule and that is a moral right act also based on utilitarian grounds. Source: Data prepared, interpreted from the research findings, and formatted by the authors, from the data related on the references section of this research.*

Nevertheless, there are some selected articles in this study that claim the alleged ineffectiveness or limited effectiveness of containing the transmissibility of the virus by restricting the movement of people, and there are also respectful researches advocating the contradiction of the travel restrictions to the rules of international law. These viewpoints are worth considering despite their limited influence due to the adoption of extreme measures since the SARS pandemic of 2002-2004, but they make an important point by indicating that it is necessary to consider the balance between the health protection of everyone and the preservation of the rights to freedom of all and all related fundamental rights that can be restricted in their exercise by pandemic extreme measures adopted by governments based on scientific evidence.

Restrictive measures must abide by the legal and constitutionalsystems, the social condi-tions and must be in harmony with the notion of relativity of fundamental rights. There exists the feasibility that health rights rules must take precedence over general freedom rights in the scope of a pandemic. Thepresent research created guidelinesfor authorities to take during a pandemic when adopting extreme measures that affect fundamental rights exercises in a way of respecting the fundamental human rights of all and for the consideration of acceptable ethical decisions in this same direction. The guide is summarized in Table 4.

AUTHOR CONTRIBUTIONS

JS concepted the theme and idea of the research, indicated a law science author for consideration, and redacted its first manuscript. PS made the research of scientific articles used within this article, selected and interpreted them, selected the law science authors to be cited, concepted the structure of the research, and comparison of data. Also designed the tables, the article type, format, sections, headings and their nomenclatures, the abstract, the keywords, and the others sections of the article. Wrote the final version of the manuscript submitted, prepared the template for the journal submission, and designed its english version that was revised by experienced translators. FA coordinated the research and the writing process of the manuscript. IB, PM, and ET-C analyzed the data collected and suggested modifications and made revisions. LA conducted the process of creation, coordinated the authors, made suggestions in the conception and writing of the manuscript, and contributed within the data analysis. All authors contributed to the article and approved the submitted version.

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CONFLICT OF INTEREST

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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CHAPTER 13

OLFACTORY SENSORY EVALUATION IN NEWBORN CHILDREN OF WOMEN INFECTED WITH COVID-19 DURING PREGNANCY

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Abstract

Introduction: In adults, olfactory loss is one of the earliest and most frequent acute clinical manifestations of SARS-CoV-2 infection. The number of children infected with SARS-CoV-2 is relatively small, perhaps due to the lower expression of Angiotensin Converting Enzyme 2 (ACE2) in children compared to adults. Little is known about foetal impairment in mothers infected with SARS-CoV-2. This paper describes an ongoing scientific project on smell perception in infants. **Objective:** The goal of the study is to develop and validate a behavioural evaluative scale of olfactory perception in healthy newborns and to apply this scale to newborn children of women infected with COVID-19 during pregnancy comparing to newborn children of women without COVID-19 infection history, in order to compare these groups. **Methods:** This is a retrospective comparative analytical cohort study of 300 newborns exposed and unexposed to COVID-19 during pregnancy. The data collection will follow the experimental procedure in a previous study that explored odours of the maternal breastmilk, vanilla (sweet) and distilled water (neutral). A coffee smell was implemented as an addition to this previous study in order to include acid/bitterness category to the categories of stimuli. **Discussion:** It is feasible to argue the hypothesis of the involvement of the foetus' olfactory bulb as one of the indelible pathophysiological manifestations to the clinical diagnosis of COVID-19 with neurosensory olfactory deficit in foetuses and newborns affected by intrauterine infection. This study aims to investigate if newborn children of women infected with COVID-19 during pregnancy have olfactory sensory changes. The clinical trial was registered in the Brazilian Registry of Clinical Trials (ReBEC- RBR-65qxs2).

Keywords: Newborn; Perception; Odors; COVID-19; SARS- CoV-2.

Resumo

Introdução: Em adultos, a perda olfativa é uma das manifestações clínicas agudas mais precoces e frequentes da infecção por SARS-CoV-2. O número de crianças infectadas com SARS-CoV-2 é pequeno, talvez devido à menor expressão da Enzima Conversora da Angiotensina 2 (ACE2) em crianças em comparação com adultos. Pouco se sabe sobre o comprometimento fetal em mães infectadas com SARS-CoV-2. Este artigo descreve um projeto em andamento sobre a percepção olfativa em bebês recém-nascidos. **Objetivo:** o objetivo do presente estudo é desenvolver e validar uma escala de avaliação comportamental da percepção olfativa em recém-nascidos saudáveis e aplicá-la a recém-nascidos de mulheres infectadas com COVID-19 durante a gravidez e comparar a recém-nascidos de mulheres sem histórico de infecção por COVID-19. **Método:** Este é um estudo de coorte analítico comparativo retrospectivo de 300 recém-nascidos expostos e não expostos ao COVID-19 durante a gravidez. A coleta de dados seguirá o procedimento experimental de estudo anterior que explorou odores do leite materno, baunilha (doce) e água destilada (neutro). Um cheiro de café foi implementado como um complemento a este estudo anterior, a fim de incluir a categoria ácido / amargo nas categorias de estímulos. **Discussão:**

É possível argumentar a hipótese do envolvimento do bulbo olfatório do feto durante a vida intrauterina como uma das manifestações fisiopatológicas indeléveis para o diagnóstico clínico de COVID-19 com déficit olfatório neurossensorial em fetos e recém-nascidos afetados por infecção intrauterina. Este estudo tem como objetivo investigar se filhos recém-nascidos de mulheres infectadas com COVID-19 durante a gravidez apresentam alterações sensoriais olfativas. O ensaio clínico foi registrado no Registro Brasileiro de Ensaios Clínicos (ReBEC- RBR-65qxs2).

Palavras-chave: Recém-nascido; Percepção; Odores; COVID-19; SARS-CoV-2.

INTRODUCTION

The natural history of COVID-19, caused by the SARThe natural history of COVID-19, caused by the SARS- CoV-2 virus, is still being explored. Little is known about its effects on pregnancy, the puerperium and the health of the mother and foetus, as well as the impact on the long- term development of the children of infected mothers during pregnancy. Based on the positive data to date, the clinical picture of COVID-19 during pregnancy does not seem to differ when observed outside this period. The disease can be asymptomatic or present with clinical manifestations that vary in severity and symptomology, with the most common symptoms being fever (67%) and cough (66%), accompanied less frequently by malaise, dyspnoea, and diarrhoea[1].

Vertical transmission of SARS-CoV-2 was previously thoroughly assessed in six pregnant women affected by the disease in the third trimester[2]. This study tested the amniotic fluid, umbilical cord blood, breast milk and nasopharyngeal swab of newborns, which were all negative for the virus. Subsequently, two systematic review and two studies describing cases of pregnancy infection in hospitals of Wuhan, China and New York City, United States, found no evidence of vertical transmission[1,3–5]. Inconclusive reports of vertical transmission include that of newborns with specific anti-SARS-CoV-2 IgM, but with negative RT-PCR[5], as well as that of a 16h newborn with positive RT-PCR with 16h of life, but specific IgG and IgM remained negative until the 5th day6. The interpretation of these results requires prospective studies, which are known for the accuracy of molecular tests and the kinetics of anti-SARS-CoV-2.

Maternal SARS-CoV-2 infection does not expose the foetus and newborn only to the effects caused directly by the virus, but also to a variety of indirect effects. The consequences of the maternal and foetal inflammatory response, with the production of potentially cytotoxic cytokines, as well as the effect of the use of antiviral medications, have not been studied to date. Another important aspect concerns the risk of contamination of the newborn during or shortly after birth. Practices such as delayed cord clamping and skin-to-skin contact between mothers and newborns are not universally recommended and evidence on the risk of contagion during breastfeeding is still limited[7,8].

There are studies reporting infected adults who developed neurological diseases, such as mental confusion, stroke, seizure, or loss of smell, due to a direct or indirect effect on the central nervous system (CNS). Likewise, a picture of acute haemorrhagic encephalopathy diagnosed through magnetic resonance imaging was reported in a woman in the sixth decade of life affected by COVID-199. The prevalence of neurological impairment by the disease is still being observed, but a study of 214 patients in Japan showed that 36% had some clinical finding related to the nervous system10. Though, not enough data is provided about the risk of fetuses or newborn infants being vulnerable to neurological sequels due to the COVID-19 infection.

Problem

Among the symptoms provided by carriers of the new coronavirus, is an olfactory sensory alteration. Olfactory loss in adults is one of the earliest and most frequent acute clinical manifestations of SARS-CoV-2 infection. It is feasible to hypothesize the involvement of the foetus' olfactory bulb during intrauterine life as one of the indelible pathophysiological manifestations to the clinical diagnosis of COVID-19 with neurosensory olfactory deficit in

foetuses and newborns affected by intrauterine infection. Based on these evidences, the following research question was raised: do newborn children of women infected with SARS-CoV-2 during pregnancy have olfactory sensory changes? Hence, this work is based on the scientific literature on the sensory-perceptual development of smell in foetuses and newborn babies[11-18] and aims to replicate methodological procedures of studies such as Bartocci et al.[12], adapting this to the hospital context and expanding it as categories of olfactory stimulus for the implementation of a measure of discrimination sensitivity.

The main goal of the study is to assess the olfactory sensory perception of newborn children of women infected with SARS-CoV-2 during pregnancy. The specific objectives are to develop a behavioural evaluation scale of olfactory perception in infants; to validate this scale in healthy newborns; and to compare the responses with that of newborn children of women infected with COVID-19 during pregnancy.

METHODS

Study Design

The present study is a retrospective comparative analytical cohort research of 300 newborns as part of a major project aiming to follow-up the development of children born from mothers that tested positively for COVID-19 during pregnancy entitled “Clinical outcomes of children of mothers exposed to SARS-CoV-2 infection during pregnancy”.

Sample size calculation

No precise figure is available about the prevalence of SARS-CoV-2 infection among pregnant women in Brazil, but international reports estimate up to 15.3% of all pregnancies being exposed[1-4]. Recent data accounts for a birth rate of 44,195 newborns per year in the Federal District area, where Brasilia the capitol of Brazil, is located. Thus, considering an “infinite” population (>20.000 pregnant women), and assuming a 15% prevalence of SARS-CoV-2 exposed pregnancies, a confidence level of 95% and margin of error of 5%, the minimum size for a random sample of exposed women would be 195, yielding an expected similar figure for the exposed children. Taking into consideration an expected drop-out rate of up to 20% in the BORN sub-study, the required number of exposed mothers (to give birth to the BORN participants) would raise to 234.

Nevertheless, our sampling approach is based on convenience, not random chance, as eligible subjects present to the recruitment centres. The aforementioned calculations served primarily as a reference, so as not to overestimate the inclusion of participants. Given the limited available knowledge regarding the effects of SARS-CoV-2 on pregnancy and child development, thus conferring upon the study an eminently exploratory character, we adopted an approach of “as much as feasible, but no more than reasonable” for the sample size definition.

Everything considered, we set an a priori number of 300 exposed women in the PREGNANT phase, which would result in expected 300 exposed children in the BORN phase. We adopted a 1:1 allocation rate between exposed and controls, thus implying another 300 mothers and 300 children who did not test positive for COVID-19 to constitute the non-exposed control group. Hence, the overall sample size of the PROUDEST study was finally set at 1200 participants (600 mother-child dyads: 300 exposed, 300 control).

Study Location and Period

This study would take place at the outpatient clinic for newborns born to pregnant women with COVID -19 (and Regular Growth and Development Outpatient clinic with newborns born to pregnant women without Covid-19). This outpatient clinic was developed at the University Hospital of Brasília (HUB) aiming at accompanying these

newborns up to five years of age. It is composed of a multidisciplinary team, such as paediatric doctors, nurses, occupational therapists, speech therapists and neuropsychologists. This study will investigate infants born between July 2020 and March 2021.

Study Population and Eligibility Criteria

The target group will be composed of newborns up to 14 days old, whose mothers tested positive on a test that detects genetic material of the virus using a laboratory technique called polymerase chain reaction (PCR) for SARS-CoV-2 during pregnancy. The control group will be composed of newborns up to 14 days old, whose mothers did not test positive for SARS-CoV-2 during pregnancy. The inclusion criteria for exposed mother-baby dyads are a maternal age of ≥18 years and laboratory evidence of SARS-CoV-2 infection during pregnancy through RT- PCR or serology (searching for IgG and IgM antibodies) markers. The results of the rapid test accompanied by information about the clinical symptoms or characteristic tomography were collected as supplementary data. For the control group of unexposed mother-baby dyads, the inclusion criteria are a maternal age of ≥18 years and serology for SARS-CoV-2 (IgG and IgM antibodies) at admission for delivery assistance. Exposed newborns will be included evidence of maternal SARS-CoV-2 infection during pregnancy.

Exclusion criteria for exposed women and unexposed women are: pre-existing chronic diseases requiring continuous use of medications, except diabetes and hypertension; smoking and / or alcohol consumption; suspected or confirmed other congenital infections such as toxoplasmosis, syphilis, rubella, herpes, Chagas and ZIKA; and impossibility of sequential follow-up until delivery. Exposed and unexposed newborns will be excluded if there are indications or confirmation of genetic disorder; suspected or confirmed other congenital infections, such as toxoplasmosis, syphilis, rubella, herpes Chagas and ZIKA; and impossibility of sequential follow-up until the age of five.

Data Collection

The maternal epidemiological data will be obtained at the first meeting with the pregnant woman or her legal representative and are those contained in the “Epidemiological data spreadsheet”. Clinical data will be obtained during prenatal care, which will occur in consultations with the following maximum interval: monthly between 0 and 34 weeks, twice a week between 34 and 36 weeks and weekly between 36 weeks and delivery. The data referring to childbirth and puerperium assistance will be obtained during hospitalization in the maternity hospital from medical reports. The monitoring of child growth and development will follow the intervals determined by the Ministry of Health of Brazil and will take place in an outpatient clinic specifically created for this purpose, composed of a multidisciplinary team of paediatrics, psychologists, occupational therapists, speech therapists, physiotherapists and nurses. The assessment of child neurodevelopment up to 42 months of life will include cognitive, motor, socioemotional aspects, and aspects related to language and adaptive behaviour and will be carried out with the validated version of the Bayley III Child Development Scale19. As of two and a half years of age, aspects related to intellectual performance will also be assessed through the Wechsler Pre-School and Primary Intelligence Scale20, with a half-yearly interval.

The metabolic evaluation will be carried out by measuring blood glucose, insulin, lipid profile (total cholesterol and fractions, triglycerides), thyroid function (TSH, free T4) and basal cortisol at the end of the 12th and 24th months of life. Blood, CSF and placenta samples will be stored following the current rules for handling biological materials until their analysis.

Data Collection Procedure

The data collection will follow an experimental procedure from Bartocci et al.12 that explores odours of the maternal breastmilk, vanilla (sweet), coffee (acid/ bitter) and distilled water (neutral). The coffee smell is an addition to the previous study in order to include the acid/ bitterness category to the categories of stimuli. Each test epoch consists of 30 s of baseline definition followed by 30 s of smell exposure with a two-minute interval for washout effect (figure 1).

The research assistants will wear surgical gloves for each handling of the solutions, and they will be prepared in an auxiliary room to avoid the spread of the smell of the solutions in the environment. Each solution will be kept in a hermetically sealed flask before and during all session to avoid smell impregnation. The room temperature will be maintained between 19-21ºC. The baby will be accommodated and cuddled on the lap of a familiar caregiver to prevent social stress and in a calm, relatively quiet (between 40 and 50dB(A)) environment reserved inside the Hospital Paediatric Follow-Up facility. The behavioral state21 during the session will be monitored and registered for each stage of smell exposure ranging from state 1 (deep sleep) to sate 6 (crying). In case of the baby achieving state level six (cry – intense cry or high motor activity) or in need of a diaper change, the session will be paused and resumed as soon the baby returns to the state five or less. Mothers will be instructed to not use moisturizers or perfumes and to bring the babies already breastfed at least 15 min before the session.

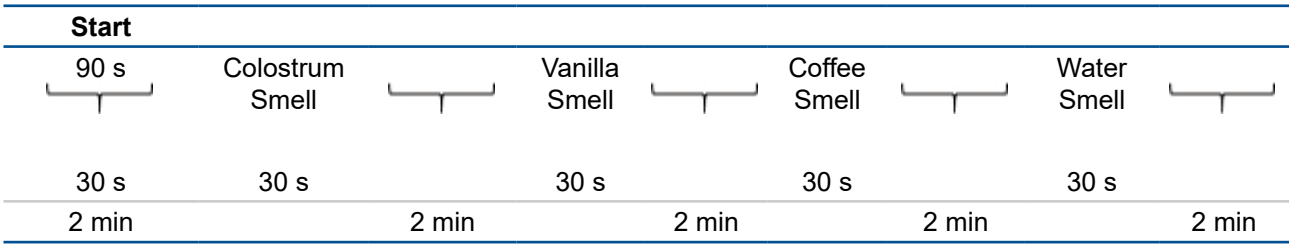

Figure 1: Timeline of odour exposure during one session adapted from Bartocci *et al*.[12]

Session phases

Step I

Collection of socio-demographic and clinical information through specific instruments and consultation of the electronic medical record.

Step II

1. Select the sample according to the inclusion criteria – participant invitation.
2. Explain to the mother how the research will be carried out and collect the consent form from the person responsible for the newborn.
3. Ask if the mother had followed the requirement to not use moisturizers or perfumes.
4. Ask the mother to remove 1 ml of breast milk and put it on a hermetic flask.
5. Turn on the video recorder.
6. Follow the following steps with the baby sitting on the companion's lap (not the mother):
    A. Basal Phase: start filming the baby's face for at least 30 seconds before the first odour presentation and keep filming the entire session.
    B. Stimulus Phase I: present the cotton swab soaked in breast milk for 30 seconds 2 cm from the baby's nose, maintaining the filming throughout this period, discard the cotton swab.

C. Wash out phase I: continue filming the baby for 2 minutes while the research assistant discards the cotton swab dipped in breast milk.
D. Stimulus Phase II: present the cotton swab soaked in vanilla solution for 30 seconds 2 cm from the baby's nose, maintaining the filming throughout this period, discard the cotton swab.
E. Wash out phase II: continue filming the baby for 2 minutes.
F. Stimulus Phase III: present the cotton swab soaked in coffee solution for 30 seconds 2 cm from the baby's nose, maintaining the filming throughout this period, discard the cotton swab.
G. Washout phase
I: continue filming the baby for 2 minutes.
H. Control Phase: present the cotton swab soaked in water for 30 seconds 2 cm from the baby's nose, maintaining the filming throughout this period, discar d the cotton swab.
J. Washout phase II: continue filming the baby for 2 minutes.

Step III - Image coding

1.Phase I coding: will be carried out for the development of the olfactory sensory evaluation scale. The videos will be analyzed frame by frame to survey categories of behavioural responses to the four different olfactory stimuli. The rating levels will consider two response categories "yes" or "no", for present and absent reaction to the smell. Factor Analysis will be performed with analyses of the main components for the construction of the instrument and analysis of the sample data.

2.Phase II coding: will be carried out for comparative evaluation of newborn children of pregnant women with and without a diagnosis for Covid-19.

Data Analysis

A mixed design will be run, with treatment (colostrum, vanilla, coffee, water) as within-subject variable and COVID-19 (covid vs. noncovid babies) as between-subject variable (group variable). The dependent variable will be the dichotomous responses. Continuous variables will be described as mean and standard deviation or median and interquartile range (IQR), as appropriate. Categorical variables will be described as frequencies and percentages. The analyses will be run to determine the perception thresholds, sensitivity parameters, and ROC curves (Receiver Operating Characteristic). In addition to fixed effects models, random effects models are estimated and also adjusted for possible confounders. Statistical significance will be considered when the p value is less than .05. The data will be stored in a SPSS-21 file, with an alphanumeric code that prevents the identification of the patient; curve fitting will be done with the MATLAB curve-fitting tool. To control for possible selection bias, propensity score matching (PSM) will be performed, followed by re-analyses as part of the robustness analyses.

Ethical and Legal Aspects of the Research

The study was approved by the Research Ethics Committee from the University of Brasilia School of Medicine (http://www.fm.unb.br/cep-fm - CAAE 32359620.0.0000.5558) and was registered in the Brazilian Registry of Clinical Trials (ReBec) under number RBR- 65qxs2. The complete protocol can be accessed at ReBec "Effects of COVID-19 on pregnancy, childbirth, puerperium, neonatal period and child development" [cited 2020 Sep 17]. Available from: http:// ensaiosclinicos.gov. br/rg/ RBR-65qxs2/).

DISCUSSION

Pregnant women can be infected with SARS- CoV-2, with a possible consequent infection of their foetuses and newborns. SARS-COV-2 infection can cause an immune overreaction that is manifested by the excessive activation of immune cells and the production of a large amount of interferon and cytokines that can affect foetal development and increase the risk of neurological diseases in the neonatal period[5].

Like SARS-CoV, SARS-CoV-2 uses angiotensin converting enzyme 2 (ACE2) as a functional receptor to infect human cells. Studies have shown that ACE2 is expressed mainly in the respiratory, cardiovascular and digestive systems, which makes these organs more susceptible to this new virus. ACE2 is less mature in the youngest children and thus may not function as an appropriate receptor for SARS-CoV-2. The number of children infected with SARS-CoV-2 is relatively small. Thus, one hypothesis for this low infection rate is the low expression of ACE2 in children. Bunyavanich[22] conducted a retrospective study that examined the nasal epithelium of 305 individuals aged 4 to 60 years and observed that the gene expression of ACE2 in the nasal epithelium was age dependent. ACE2 gene expression was lower in younger children and increased with age.

A neurological symptom that has been frequently described in patients who tested positive for COVID-19 is a temporary impairment of taste and smell, which has been reported in 49-70% of infected people[23]. Somekh et al.[24] evaluated sensory function in patients (children and adults) who had COVID-19 documented by laboratory tests. Of the 73 patients, 37 (51%) reported having had a change in taste or smell, 25.8% of which were children. Children aged 5 to 10 years did not report sensory impairment[23]. However, there are still no reports about infants, especially newborn infants on the risk of being infected during pregnancy or delivery time.

One of the proposed mechanisms for altering smell and taste related to COVID-19 is the ability of SARS- CoV-2 to bind to ACE2 in the nasal and oral mucosa. Among people who tested positive for COVID-19, olfactory sensory sensation was significantly less impaired in children than in adults ($p = .00014$). The significant difference in olfactory sensory impairment between children and adults, and particularly between younger children and middle-aged adults, is in line with the finding that the expression of ACE2 in the nasal epithelium and in the oral cavity is more intense among adults, corroborating the possibility that the distribution and expression of ACE2 in the oral cavity and nasal epithelium may contribute to differences in sensory impairment22. Little is known about foetal impairment in mothers infected with SARS-CoV-2. By evaluating the olfactory sensory perception of newborns of women infected with COVID-19 during pregnancy, we can quantify such involvement.

Author Contributions

RMT, GMF KSFC and LRM devised the original study protocol, which was amended by TL, JS, JALJ and KNC. RMT, KNC, KSFC wrote the first draft of the manuscript that was then critically reviewed and revised by the other co-authors. All authors approved the final version of the manuscript for submission. RMT is the guarantor, and affirms that the manuscript is an honest, accurate and transparent account of the study being reported; and that any discrepancies from the study as planned have been explained.

Conflicts of Interest

The authors have no conflict of interest to declare.

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CHAPTER 14

THREE URGENT NEEDS IN THE BATTLE AGAINST COVID-19: SPECIFIC MEDICATIONS, INFORMATION AND ACCEPTANCE OF PANDEMIC

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Abstract

The first confirmed case of COVID-19 was notified to the Brazilian Ministry of Health on February 26, 2020. On November 20, 2021, by the end of Epidemiological Week-46 (EW-46) 257,168,692 confirmed cases of COVID-19 reported worldwide. Among the countries with the highest number of accumulated cases the United States of America ranks number one (47,701,872), followed by India (34,510,413), Brazil (22,012,150), the United Kingdom (9,857,658), and Russia (9,135,149). Concerning deaths, 5,146,467 were confirmed worldwide until November 20, 2021. The United States was the country with the highest accumulated number of deaths (771,013), followed by Brazil (612,587), India (465,662), Mexico (292,145), and Russia (257,891).

Keywords: COVID-19; Lethality; Mortality; Time-Series.

Resumo

Introdução: O primeiro caso confirmado de COVID-19 foi notificado ao Ministério da Saúde do Brasil em 26 de fevereiro de 2020. Em 20 de novembro de 2021, ao final da Semana Epidemiológica 46 (SE-46), haviam sido notificados 257.168.692 casos confirmados de COVID-19 em todo o mundo. Entre os países com o maior número de casos acumulados, os Estados Unidos da América ocupavam a primeira posição (47.701.872), seguidos pela Índia (34.510.413), Brasil (22.012.150), Reino Unido (9.857.658) e Rússia (9.135.149). Em relação aos óbitos, até 20 de novembro de 2021 foram confirmadas 5.146.467 mortes no mundo. Os Estados Unidos eram o país com o maior número acumulado de mortes (771.013), seguidos pelo Brasil (612.587), Índia (465.662), México (292.145) e Rússia (257.891).

Palavras-chave: COVID-19; Letalidade; Mortalidade; Série Temporal.

EPIDEMIOLOGY AND BACKGROUND

The first confirmed case of COVID-19 was reported to the Ministry of Health (MS) of Brazil on February 26, 2020. Based on daily data reported by the State Health Departments to the Ministry of Health and compiled by the COVID-19 Brazil/Ireland Observatory, 22,012.150 COVID-19 cases and 612,587 COVID-19 deaths were confirmed in Brazil in less than two years (from February 26, 2020 to November 20, 2021). The cumulative incidence rate of COVID-19 was 10,367.5 cases per 100,000 inhabitants, while the cumulative mortality rate was 288.6 deaths per 100,000 inhabitants.

COVID-19 is a global public health problem and is the most extensive pandemic in the recent history. It is caused by the new coronavirus (SARS-CoV-2) and is characterized by being a potentially severe respiratory infection with global distribution and presents a high transmissibility between people by respiratory droplets, airborne or contact with contaminated objects and surfaces.

Having information about the behavior of COVID-19 is essential for prevention of the disease and care of the population using public health measures implemented by Federal, State and Municipal Brazilian governments. Measuring and monitoring the numbers of cases and deaths of the disease and analyzing these numbers allows public health workers to present mortality and lethality rates for the whole populations and for segments of the population[1].

Using health indicators and other epidemiological data constructed from data collection and their analysis by statistical methods, health diagnoses are made to support the implementation of health promotion and disease prevention measures collectively[2,3]. Therefore, it is important for every health care professional, particularly for those working on the frontline of the fight against COVID-19, to develop their capacity to implement the epidemiological method with the aim of reducing diseases, promoting health and improving health care in the population. Moreover, it is essential for everyone involved in combating the COVID-19 pandemic to work with two indices: mortality and lethality. The mortality rate is a demographic index and is the ratio between the number of deaths and the number of population within a specific period of time (weeks, months, a year). Frequently, the rate is represented as the number of deaths in every 100 inhabitants (%). Lethality is a measure of the severity of the disease, estimated by dividing the number of deaths by a given disease by the number of cases of the same disease (%)[2].

From the beginning of the pandemic through November 6, 2021, there were 249,546,001 confirmed cases of COVID-19 worldwide, with the United States of America (USA) being the country with the highest number of accumulated cases (46,465,823), followed by India (34,355,509), Brazil (21,874,324), the United Kingdom (UK) (9,317,072) and Russia (8,613,533)[4,5].

During the same period, there were 5,044,871 confirmed deaths worldwide, with USA being the country with the highest number of accumulated deaths (754,310), followed by Brazil (609,388 deaths), India (460,791), Mexico (289,674) and Russia (241,095)4,5. The gross incidence rate in the world through November 6, 2021, was 31,688.5 cases for every million inhabitants.

In Brazil, the cases of new deaths related to COVID-19 were different in the different regions of the country. The number of new cases of COVID-19 was 21,179 in the Southeast, 19,087 in the Northeast, 18,611 in the South, 6,778 in the Central-West region and 4,584 in the North (Ministry of Health, 2021). The number of new deaths was 945 in the Southeast, 327 in the South, 189 in the Central-West region,188 in the Northeast, and 45 in the North. Thus, the Southeast was the region with the highest absolute number of cases and new deaths[4].

The estimation of the rates takes into consideration the number of inhabitants per location, thus removing the effect of the population's size on the comparison between

regions. Until November 6, 2021, the Southern region of Brazil was the one with the highest incidence rate, reaching 61.6 cases/100,000 inhabitants. The Central-West region had the second highest rate of incidence (41.1 cases/100,000 inhabitants), followed by the Northeast (33.3 cases/100,000 inhabitants), the North (24.5 cases/100,000 inhabitants) and the Southeast (23.8 cases/100,000 inhabitants). The overall incidence in Brazil was 33.2 cases/100,000 inhabitants in the 44th epidemiological week[4,5].

Through November 6, 2021, the Central-West, South and Southeast regions recorded a mortality rate of 1.1 deaths/100,000 inhabitants, with the Northeastern region having a rate of 0.3 deaths/100,000 inhabitants. The overall mortality rate for Brazil through November 6, 2021 was 0.8 deaths per 100,000inhabitants[4].

For both years 2020 and 2021, almost 80% of people infected by SARS-CoV-2 recovered from the disease, not requiring hospital management and nearly 15% had severe forms of the disease (COVID-19), particularly those who were older and/or with comorbidities, such as cardiac or pulmonary problems, diabetes or cancer[4].

Prevention and Control:

During the early days of the pandemic, there were joint efforts globally to slow down viral transmissibility and contain the new coronavirus transmission by using non-pharmacological measures, such as face masks6. Despite these actions, Brazil recorded approximately 615 thousand deaths, officially registered in the Ministry of Health with COVID-19 as the primary cause of death[4].

This devastating COVID-19 pandemic required the fast development of sanitary processes which are capable of preventing deaths and reducing complications in people infected by SARS-CoV-2. Mass vaccination is the natural candidate for this goal, and in fact there has been significant reduction in COVID-19 lethality and mortality indicators in the Brazilian regions with the increasing number of individuals vaccinated against COVID-19[6].

Based on scientific evidence, vaccination seems to be the proper and safe process to prevent severe cases of COVID-19 and to reduce the number of deaths. Vaccines have proven over time to be the best intervention in public health for the control, removal and eradication of infectious diseases. Similarly, published research to date indicates that there is enough evidence to support using immunization to prevent COVID-19 to control the ongoing pandemic[7].

The platforms for COVID-19 vaccine development, particularly those approved by the World Health Organization (WHO), have reported an increasing number of new vaccines being developed against COVID-19 throughout the world, focused on new technologies, not overlooking those already being used, such as the vaccine using inactivated whole-cell vaccines, since they represent a tested and safe long-term vaccination method[7,8].

A representative of this type of vaccine, widely used in Brazil, is CORONAVAC, which is produced from the inactivated and weakened SARS-CoV-2 virus. The rest of the vaccines produced in Brazil are of the replicating and non-replicating viral vector vaccines, nucleic acid vaccines (DNA, RNA), and protein-based vaccines (with protein subunits and particles similar to the virus)[8,9].

The epidemiological data recorded worldwide through November 6, 2021, show that the vaccines using the inactivated and weakened virus, such as CORONAVAC, have been efficient to control SARS- CoV-2 virus transmissibility[7,8]. This type of vaccine (CORONAVAC) stands out because it has the potential to trigger a wider immune response against the virus, not restricted to the S protein (from “spike”), like vaccines against COVID-19 from other platforms (such as the Pfizer non-replicating viral vector vaccine, and the AstraZeneca and Janssen vaccines, that have been authorized by the National Agency for Sanitary Surveillance (ANVISA - Agência Nacional de Vigilância Sanitária) in Brazil, with the potential of being more effective against the new coronavirus variants (SARS-CoV-2)[7,8].

According to Bargieri and Boscardin (2021), CORONAVAC is quite different from other vaccines, since it not only uses the Spike protein, but the whole virus. This means that it induces an immunological response against the Spike protein but also against the other 25 proteins of the virus. CORONAVAC induces low levels of antibodies in general, and low levels of neutralizing antibodies. Also, it is efficient to prevent COVID-19[9].

In recent findings, with 85 patients who recovered from COVID-19, there was an indication that the CORONAVAC, produced in Butantan and from the Sinovac pharmaceutical company is capable of doubling the amount of neutralizing antibodies and multiplying by 4.4 times the level of immunoglobulin (IgG) in people who already had the disease, suggesting that CORONAVAC stimulates the humoral immunologic memory of recovering patients, accelerating the production of neutralizing antibodies and their circulation levels in the bloodstream10. Thus, every dose of the inactivated virus vaccine is made up of trillions of particles of the virus, and stimulates the immune system to identify the virus as soon as it gets in contact with it. As CORONAVAC contains the whole inactivated SARS-CoV-2 virus, the immune system produces antibodies that identify many antigens (proteins) of the new coronavirus. The S protein is the main one, used by the SARS-CoV-2 to penetrate within human cells, but not the only one[11].

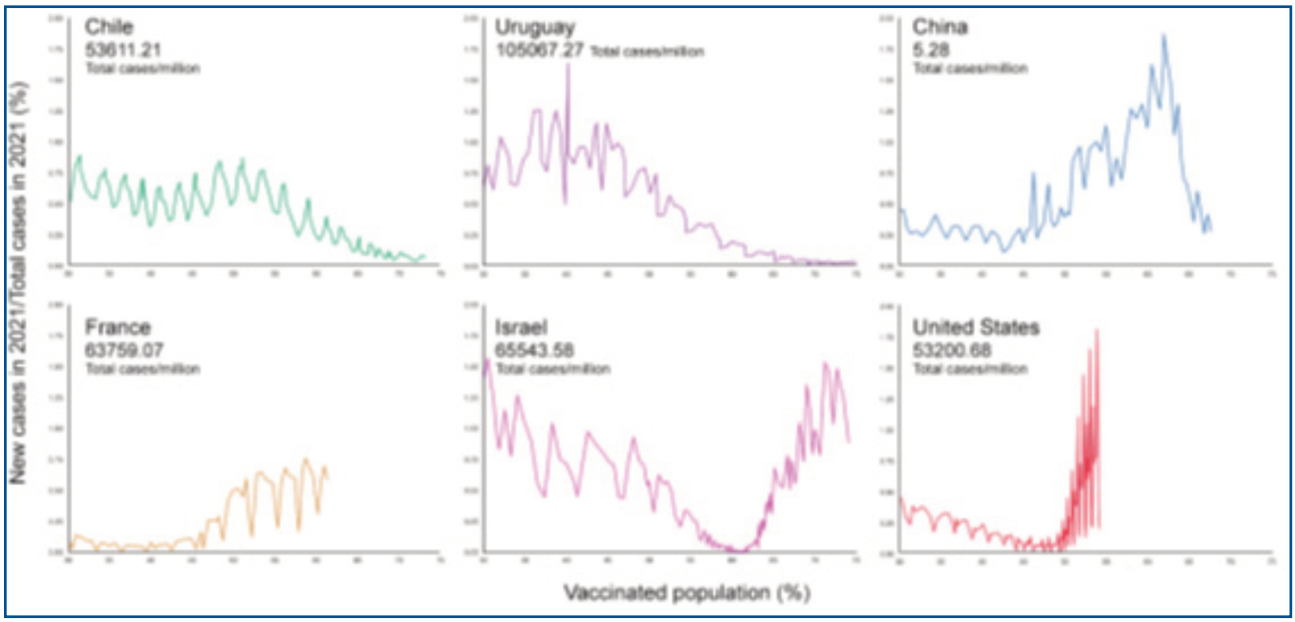

Figure 1: New cases of COVID-19 versus the percentage of vaccinated population. The numbers under the name of the country indicate the total of reported cases since the beginning of 2021. For the comparison, the same axes, X and Y, were used in all graphs. The file with the data used in the construction of the graphs was taken from official data storages reported by each country (check the “Statement of data availability” below).

Figure 1 shows the new COVID-19 cases versus the percentage of vaccinated population. The data (collected up to August 24, 2021) were selected using 30% of the vaccinated population as limit. In the countries of Chile, Uruguay and China, the CORONAVAC vaccine was predominantly used. In France, Israel and the US, only mRNA/AV vaccines were used[11].

Coronavirus has 25 proteins in total, mostly responsible for regulating the multiplication and exit of the virus from human cells. Thus, a variant that presents S-protein alteration (mutation) is no longer identified by specific vaccines containing only the S protein[11].

Likewise, we should highlight a post-COVID-19 condition occurring in individuals with a history of probable or confirmed infection by SARS-CoV-2, generally 3 months after the onset of COVID-19, with symptoms lasting for at least 2 months, which cannot be explained by an alternative diagnosis.

The characterization of this post-COVID-19 condition is ordinary symptoms, including fatigue, shortness of breath, cognitive dysfunction, and others, which generally have an impact on daily life. The symptoms could be new after the initial recovery of an acute COVID-19 episode or persist after the initial disease. The symptoms may also fluctuate or recur over time.

Thus, these symptoms may fluctuate (modify over time in terms of quantity or quality), they may recur (a return of the manifestations of the disease after the period of improvement), or manifest as a cluster (two or more symptoms related to each other and occurring jointly).

CONCLUSIONS AND RECOMMENDATIONS

When fighting against the COVID-19 pandemic, on November 1, 2021, there was a total of 6,893,866,617 doses of the vaccine administered in the world population[4]. As we don't have a specific medication for the treatment of COVID-19, COVID-19 continues to be a challenging condition for public health at the global level for the foreseeable future. It is therefore reasonable to consider vaccination as the natural candidate to be the intervention of choice to slow down viral transmission, and to consider the vaccines that are produced with the inactivated virus as the vaccines of choice to combat the spread of COVID-19 at the present time.

There continues to be many questions related to COVID-19 infection and its sequelae. Research on COVID-19 behavior in the Brazilian population will help to advance both the prevention and the research, and will probably change as new scientific evidence emerges.

The JHGD has been contributing to a better understanding of the challenge of COVID-19 through the publication of the papers published in this 31.3 issue[12-30] about lethality and mortality of COVID-19, the laboratory diagnosis, and the scale of evaluation of the fear of COVID-19.

From our point of view, the consequences of COVID-19 will continue to evolve, with scientific dissemination being the only way to fight against misinformation and the absence of scientific knowledge. Health education provides knowledge about transmission, as well as the ongoing search for new strategies for global health in the fight against COVID-19.

In science, truth is transient. This is the greatest scientific legacy of humanity. We believe that today, the vaccine produced from the inactivated and weakened SARS-CoV-2 virus is our greatest hope to control the COVID-19 pandemic.

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CHAPTER 15

COVID-19 FEAR SCALE – TRANSLATION AND VALIDATION INTO BRAZILIAN PORTUGUESE

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Abstract

Introduction: fear is one of the main factors associated with psychopathological disor-ders evidenced in the context of the COVID-19 pandemic. **Objective:** translate and validate Fear of COVID–19 Scale (FCV-19S) into Portuguese Brazilian version, named Covid-19 Fear Scale (EMC-19). **Methods:** cross-sectional study with 364 individuals recruited through social networks, considering as inclusion criteria: being over 18 years old and fluent in Portuguese. After participant consentment an electronic form was completed, which included the prelimi-nary Portuguese version and EMC-19, in addition to sociodemographic variables. Data processing was performed using the SPSS 26 version. For parametric measures, Pear- son's coefficient and Student's T were used, and for non- parametric measures the U of Mann Whitney. The magnitude of the correlation coefficients was classified according to Cohen's criteria and the confirmatory factor analysis using AMOS 26.0. For internal con-sistency, Cronbach's alpha. **Results:** mean age of 33.11 years (±10,047), most of them female (n=332; 91,2%), with higher education (n=286; 78,6%), married (n=225, 61,8 %) and with children (n=300, 82,4%). Exploratory factorial analysis/EFA and confirmatory factor analysis/CFA made. Only one component emerged from the CFA, with an explained variance of 55,49%, re-sulting in a one- dimensional model with satisfactory adjustment indexes (X2/ gl=2,135; RMSEA=0,061; CFI, TLI, GFI<0,095). Cronbach's alpha coefficient is 876. **Conclusions:** the construct validity of the one-dimensional structure of the EMC-19 was demonstrated, as well as its good internal consistency.

Keywords: COVID-19; Fear; Psychometry; Validation Study.

Resumo

Introdução: o medo é um dos principais fatores associados aos transtornos psicopatológicos evidenciados no contexto da pandemia da COVID-19. **Objetivo:** traduzir e validar a Fear of COVID–19 Scale (FCV-19S) na versão portuguesa (do Brasil), denominada como Escala de Medo da COVID-19 (EMC-19). **Método:** estudo transversal com 364 indivíduos recrutados de maneira virtual através das redes sociais, considerando-se como critérios de inclusão na pesquisa: ter mais de 18 anos de idade e ser fluente em português. Após o consentimento informado, os participantes preencheram um formulário eletrônico, que incluía a versão portuguesa preliminar da EMC-19, além de variáveis sociodemográficas. O tratamento dos dados foi realizado através do pacote estatístico do SPSS versão 26. Para medidas paramétricas, utilizou-se o coeficiente de Pearson e o T de Student e nas medidas não-paramétricas U de Mann Whitney. A magnitude dos coeficientes

de correlação foi classificada segundo os critérios de Cohen e a análise fatorial confirmatória por meio do AMOS 26.0. Para consistência interna, o alfa de Cronbach. **Resultados:** os participantes tinham idade média de 33,11 anos (±10.047), a maioria do sexo feminino (n=332; 91,2%), com escolaridade superior (n=286; 78,6%), casados (n=225, 61,8%) e com filhos (n=300, 82,4%). Da análise fatorial exploratória/AFE e da análise factorial confirmatória/AFC emergiu apenas um componente, com variância explicada de 55,49%, resultando num modelo unidimensional com índices de ajustamento satisfatórios (X2/gl=2.135; RMSEA=0,061; CFI, TLI, GFI<0,095). O coeficiente alpha de Cronbach foi de de 0,876. **Conclusão:** foi demonstrada validade de construto da estrutura unidimensional da EMC-19, bem como sua boa consistência interna.

Palavras-chave: COVID-19; Medo; Psicometria; Estudo de Validação.

INTRODUCTION

On March 11, 2020, the World Health Organization decreed the SARS-COV-2 virus pandemic, responsible for COVID-19[1]. The first case in Brazil occurred on February 26, 2020, when the pandemic had already shown its expansion strength and lethality in China and in several countries in Asia and Europe.

In Brazil, although the pandemic arrived in late February, in mid March the inability of the federal government to manage epidemiological information was already evident, contributing to what has been called underreporting[2].

After a year and a half of the pandemic, official information shows that Brazil accumulates more than 20 million notified cases of COVID-19 and surpassed the number of 570 thousand deaths from the disease, according to data from the Ministry of Health[3]. The country occupies fourth place in the world ranking of people affected by the pandemic[4], still adding difficulties in implementing measures to contain the spread of the infection, in particular actions to immunize the population.

Despite all the sanitary measures adopted to control the dissemination of the coronavirus in the national territory, the psychosocial impact of the COVID-19 pandemic stands out, which, in its least relevant space among the adopted measures, represents a significant issue for the field of research and comprehensiveness of health care[5].

According to Ornel et al.[6], the repercussions of a global health crisis of this magnitude, from the perspective of mental health, can last for many years, even after the disease has been contained.

It is observed that, as the pandemic advances, several elements of significant importance for the installation of a crisis situation from the point of view of mental health were consolidated, considering both the individuals who were affected by COVID-19 , as for the general population[7,8].

Quarantine, physical distance, the risk of contamination, the increase in the number of deaths, including family members and close people, changes in the domestic and work routine, job loss, aggravated by loneliness, fear and grief, increase susceptibility to problems such as anxiety, posttraumatic stress disorder, panic syndrome, social isolation, among other disorders[6,8].

Crisis is understood, as defined by Slakieu, Mejía and López[7], the state of disorganization produced by the impact of a life altering situation that exceeds people's usual capacity to face problems.

Efforts to respond to the crisis context require effective mental health resources to improve the quality of care, and reduce the global burden of mental disorders caused by missed opportunities for preventive actions and timely treatment, especially in developing countries[9].

Discussing mental health in the face of COVID-19 and physical distancing, Galea, Merchant and Lurie[10] warn that, as populations become physically and socially isolated, strategies must be used to plan the inevitability of loneliness and prevent its sequels.

The first systematic review and metaanalysis of the psychiatric consequences of coronavirus infection identified 72 independent studies, which provided data on acute psychiatric and neuropsychiatric characteristics and post coronavirus infection[8].

Initially, the review suggests that most people do not suffer from any psychiatric disorder after coronavirus infection, and adds that to date, there is little to suggest that common neuropsychiatric complications, in addition to shortterm delirium, are a feature8. However, this review alerts physicians to the possibility of later development of depression, anxiety, fatigue, post-traumatic stress disorder and rarer neuropsychiatric syndromes[8].

Thus, the increase in psychopathological disorders[11,12] puts pressure on health systems to develop resources and rapid response strategies to deal with the COVID-19 pandemic. The imminent risk of successive "waves" of COVID-19, or the aggravation caused by the emergence of new variants of the coronavirus, further affect the mental health of individuals[13].

In fact, in addition to the resurgence of the virus, in a few months, public health systems may have to face, simultaneously, the consequences of the pandemic on mental health[14]. Mental health problems (depression, stress, panic, anxiety, etc.) can, in more extreme situations, result in suicidal ideation, suicide attempts and actual occurrence of suicide[15-16].

The most common repercussions for mental health, such as anxiety and depression, also tend to last longer, possibly six months after the end of the illness) and are associated with a higher prevalence of fear[6,17].

It should be noted that the dominant psychological aspect of the COVID-19 pandemic is fear. This constitutes a central emotional response to imminent threats, such as COVID-19[18]. Fear is defined gone as an unpleasant emotional state that is triggered by the perception of threatening stimuli[19].

From an evolutionary perspective, this emotional response constitutes a basic component of the human experience, conceived as a shock emotion due to the perception of present and urgent danger that threatens the preservation of that individual; caus-ing a series of physiological effects in the body, which make it capable of a defense reaction, such as escape[20].

Thus, fear can be adaptive and determine the degree of protection and prevention to be adopted against the threat, as is the case with COVID-19[19]. On the other hand, when the intensity of fear is too intense or too weak, disproportionately to what the stimulus actually represents, maladaptive behaviors can be triggered, such as excessive exposure to the virus or paralysis in the face of the crisis, making access to resources difficult internal for coping[19,20].

Increased fear can amplify the damage caused by the disease itself and can be directly associated with its transmission rate, as well as its morbidity and mortality[18]. The development of fear is not a strictly interindividual process, but the result of a complex interaction of biological, psychological and social factors, which can also lead to other psychosocial challenges, including stigmatization, discrimination and loss[21].

With high levels of fear, individuals may not think clearly and rationally when reacting to COVID-19, resulting in irrational processing of information related to the pandemic[22], which considerably increases suffering and psychosocial challenges[21,23-25].

With regard to the motivating role of fear, there was a significant relationship between scores on the Fear of COVID–19 Scale (FCV-19S) and adherence to mitigation rules implemented in New Zealand[26], namely compliance with the social distance of two meters and physical activity in outdoor places that can be easily accessed on foot. This finding is consistent with the results of Harper et al.[26], who reported a positive correlation between FCV-19S scores and participants' perceptions of the degree to which various behaviors and practices were changed due to the pandemic (eg, hygiene, care of children and the elderly)[26].

Effectively, it has been shown that high levels of fear, along with self efficacy, positively affect adaptive behavioral changes; low levels of fear and self efficacy were associated with the involvement of avoidant behaviors[27].

Thus, it is essential to have a tool to measure the level at which fear of COVID–19 can affect individuals. The FCV-19S was developed at the beginning of the pandemic, precisely with this objective[23], having been translated into several languages and validated in several countries, namely Italy28; New Zealand29; Russia and Belarus[30];

Turkey[31]; Peru[32]; Israel[33]; Arab Countries[34]; Spain[35] and France[36] always with positive results for their psychometric properties.

In this sense, this study aims to translate and validate the Portuguese version (from Brazil) of the FCV– 19S[23], which is called the COVID-19 Fear Scale (EMC- 19). After analyzing its main psychometric properties, such as validity and reliability, in addition to measuring, this scale can be used in clinical practice and in research, to better understand and intervene on the psychosocial repercussions of COVID-19.

It will still be possible to carry out crosscultural comparative studies between the different countries that have already translated and validated it. The knowledge produced in this way can help to promote health behaviors to prevent the impacts of COVID-19 on mental health, and to support public policies that are adequate to fight the pandemic.

METHODS

The Fear of Covid-19 Scale (FCV19S)[23] is a self-administered questionnaire consisting of seven items to be answered on a 5-point Liberte scale, from “Strongly Disagree” to “Strongly Agree”. In the original psychometric study, a one dimensional scale was considered, with factor loadings ranging from 0.66 to 0.74. As for internal consistency, Cronbach’s alpha of α= 0.82 was favorable, as well as the correlation coefficients be- tween items and the corrected total, from 0.47 to 0.74. The test-retest stability of 0.72 was also acceptable. The FCV19S scores correlated significantly and positively with perceived vulnerability and anxiety and depression, assessed using the Likert scale[23].

The process of translating the FCV19S into Brazilian Portuguese was as follows: first, the original scale in English (v1) was translated into Portuguese by two of the Brazilian researchers (v2). Then, the translated Portuguese version (v2) was translated back to English by a Google Translator (v3) translation software. Finally, the 2 Brazilian researchers compared the English version (v3) with the original version (v1), item by item, verifying the equivalence of meanings. Subsequently, a Portuguese researcher carried out a new review, so that the proposed version could be used in Brazil and Portugal. A total of 3 researchers participated in the process of translating the instrument in an interdependent manner, thus obtaining its final version in Portuguese (Brazil), called the COVID-19 Fear Scale (EMC-19).

Participants were recruited online, through social networks and invited to participate in the study, stating its objective and inclusion criteria, namely: being over 18 years of age and fluent in Portuguese. Participants who agreed to participate voluntarily gave their informed consent. They then filled out a form in Google Forms, which, in addition to the Portuguese version of the EMC19, asked about some sociodemographic variables, including: age in years, gender (male and female), education (elementary, graduation, master’s doctorate, other) , race with which they identified (white, black, brown, indigenous or yellow), marital status (single, stable, married, divorced, other), in the case of women, if they were pregnant at the time of the research and the number of living children.

Statistical treatment was performed using the IBM SPSS Statistics program, version 26 for Windows. Data processing began by determining descriptive statistics, measures of central tendency and dispersion.

As the sample size is sufficient, and taking into account the central limit theorem, measures and parametric tests, such as Pearson’s correlation coefficient and Student’s T, were used to compare mean scores.

The magnitude of the correlation coefficients was classified according to Cohen’s criteria: low if less than 0.19; moderate if between 0.20 and 0.49 and high if greater than 0.50.

In the Exploratory Factor Analysis (EFA), it was guided by the Kaiser Criteria (1958)[37] and the scree test by Cattell[38]. Following Kline’s[39] suggestion, it is considered that “weights” (loadings) with values > 0.30 are associated with the factor and that “weights” > 0.60 are high.

Before proceeding with the factor analysis, the KMO test (Kaiser-Meyer-Olkin) and the Bartlett sphericity test were performed, which are two statistical procedures that allow to measure the quality of the correlations between the variables, in order to know if it is plausible perform the factor analysis[40]. To carry out this analysis safely, the first should approach one, being "good" if >0.80; the second should lead to rejecting the null hypothesis, which also happened with our data (p <0.001).

The AMOS 26.0 software was used for the confirmatory factor analysis (CFA). Violation of the normal distribution was verified with the skewness and kurtosis coefficients. The adjustment of the models was made from modification indices greater than 11, p < 0.001, produced by AMOS and based on theoretical considerations[41]. To assess the fit of the model, the following fit indices were used: X2/gl, Comparative Fit Index (CFI), Goodness of Fit Index (GFI), Tucker-Lewis Index (TLI), Root Mean Square Error of Approxima-tion (RMSEA).

For the analysis of internal consistency, Cronbach's alpha coefficient was used. In order to determine the particular contribution of each item to the internal consistency of the dimension, Cronbach's alpha coefficients were determined excluding the respective items, and then compared with the global alpha of the dimension. To ascertain the discriminative power or internal validity of each item, the correlation coefficients were analyzed between each item and the total (excluding the item).

The study was approved by the National Research Ethics Committee of Brazil - CONEP, in accordance with the attributions defined in CNS Resolution No. 510 of 2016, in CNS Resolution No. 466 of 2012 and Operational Standard No. 001 of 2013 of the CNS, which manifested itself for the approval of the proposed research project with the CAAE number: 32934720.3.0000.5556, under the title: Perinatal Psychological Disorder in times of COVID. Data were treated with conditionality, equality and fairness. All procedures followed were in accordance with ethical standards. Informed consent was obtained from all participants included in the study. Case number: 4,179,143.

RESULTS

Sample characterization

During the period of data collection, between June 19th and July 23rd, 2020, 364 valid responses were obtained.

The mean age of participants was 33.11 years (±10.047), ranging from 18 to 67 years. The majority were female (n=332; 91.2%), with a degree of education or more (n=286; 78.6%); regarding marital status, most were married or in a stable relationship (n=225, 61.8%) and had children and/or were pregnant (n=300, 82.4%). Regarding the race with which they identified, the distribution was as follows: white, n=182 (50.0%); brown, n=119 (32.7%); black, n=52 (14.3%); indigenous, n=2 (5.0%) and yellow, n=9 (2.5%).

A little more than a quarter of the participants (n=95, 26.1%) were health professionals, and of these, 42 (11.5% of the total sample) are "frontline professionals", that is with direct contact with patients.

Construct validity

To establish the construct validity a random division of the sample into two subsamples was performed; with one of them, EFA was performed (n=192; 52.7%) and, with the other, AFC (n=172; 43.3%). Mean age (33.29±10.41 vs. 32.91±9.68; t=0.311, p=0.756) and the proportions of females (91.3% vs. 90.4%; X2=0.002, p =0.557), of having children (55.5% vs. 45.0%; X2=3.474, p=0.073), of being a health professional (22.4% vs. 30.2%; X2=2.889, p =0.067) and being of black/brown race (91.3% vs. 90.4%; X2=0.002, p=0.557) did not vary significantly in these two subsamples, confirming their equivalence.

Preliminary to AFE it was verified that the KMO was equal to 0.860 and that the Bartlet test resulted in significant (p<0.001).

The exploration of the factor analysis, carried out without any rotation and without defining the number of factors (the only criterion was that components with latent roots greater than one were extracted), resulted in only one component, with an explained variance of 55.49%. The graph corresponding to the Scree plot of Catell is shown below (Figure 1).

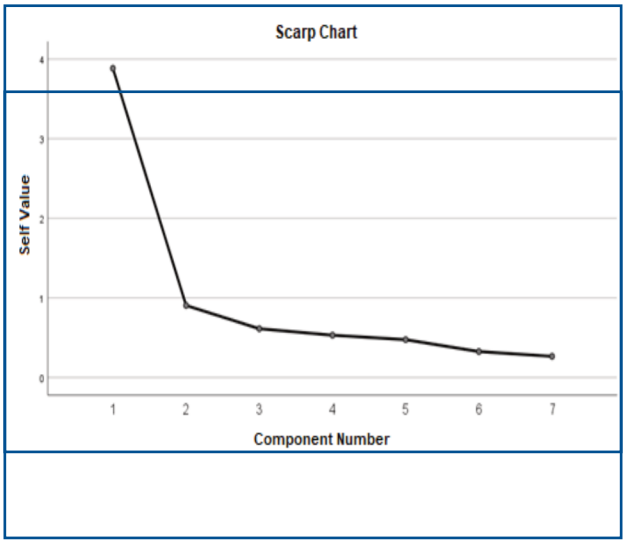

Figure 1: Scree plot of Catell from EMC19 (N=192).
Brazil, 2021.

The observation of the scree plot also favors the option for a one-dimensional structure.

Table 1 corresponds to the factorial matrix obtained with the items arranged in descending order of their respective weight in the (single) factor. With this subsample, the alpha coefficient of internal consistency was a=0.865.

Table 1: Factorial matrix related to EMC-19 and respective weights in TAA-25 (N=364). Brazil, 2021.

Items	Factor loading
2. It makes me uncomfortable to think about coronavirus-19	0,811
7. My heart races when I think I can get coronavirus-19	0,797
1. I'm very afraid of the coronavirus-19	0,790
4. I'm afraid of losing my life because of the coronavirus-19	0,767
5. When watching news and stories about coronavirus-19 in the media, I get nervous or anxious	0,696
6. I can't sleep because I'm worried about getting the coronavirus-19	0,672

Table 2: Fit indices of EMC-19 to the tested models (N=364). Brazil., 2021

Models	Indexes	χ2/g.l	RMSEA	CFI	TLI	GFI
Initial model	Fit indices	4,996	0,111	0,884	0,826	0,864
	Interpreta-tion of val-ues [23]	Suffera-ble	Unac-ceptable	Suffera-ble	Suffer-able	Sufferable
final model*	Fit indices	2,135	0,061	0,981	0,960	0,965
	Interpreta-tion of val-ues [23]	Good	Accepta-ble	Very good	Very good	Very good

Notes: χ2/g.l = ratio between chi-square (χ2) and degrees of freedom (gl); RMSEA= Root Mean Square Error of Approximation; CFI= Comparative Fit Index; TLI= Tucker-Lewis Index; GFI=Goodness of Fit Index. *With four pairs of correlated errors.

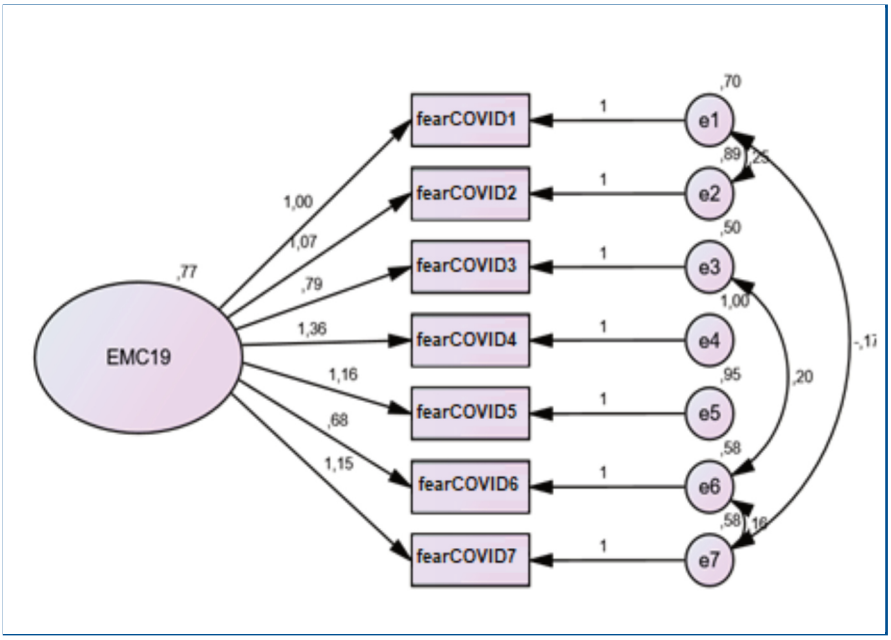

Figure 2: Confirmatory factor analysis of the final EMC-19 model, with 4 pairs of correlat-ed items (N=364).Brazil, 2021.

With the AFC, unsatisfactory adjustment indices were obtained from the initial one dimensional model with seven items (Table 2). After correlating fourth pairs of item errors (1 and 2, 1 and 7, 3 and 6 and 6 and 7) with modification indices greater than 1140, there was a very good overall fit (Table 2, Figure 2). Cronbach's alpha coefficient in this subsample (n=172) was a=0.898.

Cronbach's alpha coefficient in the total sample (N=364) was a=0.876.

The table 3 presents, in addition to the mean score and standard deviation of each item, the Cronbach's alpha if each item is excluded and the corrected item total correlation. It was found that all items in the scale contribute to internal consistency, as they presented corrected item total correlations greater than 0.40, ranging from 0.589 (item 6) to 0.709 (item 7) and that the exclusion of each one would cause the full scale Cronbach's alpha/ decreases slightly.

The mean total score on the EMC19 was 18.53 (±6.63), with a range from 7 to 35, that is, equivalent to the theoretical variation.

In Table 4, we present the values corresponding to the percentiles (and quartiles) of this sample.

Table 3: Corrected item-total correlations and Cronbach's alpha coefficients excluding the item (N=364) and mean score and standard deviation of each item on the COVID-19 Fear Scale (EMC-19). Brazil, 2021.

COVID-19 Fear Scale Items (EMC-19)	Average	standard deviation	Corrected item-total correlation	Cronbach's alpha excluding item
1. I'm very scared of coronavirus-19.	3,70	1,213	0,688	0,849
2. It makes me uncomfortable to think about coronavirus-19.	3,31	1,353	0,708	0,846
3. My hands get clammy when I think about coronavirus-19.	1,54	0,971	0,608	0,861
4. I'm afraid of losing my life because of coronavirus-19.	3,16	1,521	0,675	0,853
5. When watching news and stories about coronavirus-19 in the media I get nervous or anxious.	3,24	1,404	0,629	0,858
6. I can't sleep because I'm worried about getting coronavirus-19.	1,56	0,942	0,589	0,863
7. My heart races when I think I can get coronavirus-19.	2,00	1,293	0,709	0,846

Table 4: Values corresponding to the 5, 10, 15, 25, 50, 75, 85, 90 and 95 Percentiles of the EMC-19 (N = 364). Brazil, 2021.

Percentile	EMC-19
5	8,0000
10	10,0000
15	11,0000
25	13,0000
50	18,0000
75	24,0000
85	26,0000
90	28,0000
95	29,7500

The mean total score was significantly higher in females (18.76±6.62) than in males (16.03±6.26) [t=2.243 (362), p=0.026)].

By age groups, organized into two categories, aged under 35 years (n = 192, 52.7%) vs. older than 36 years (n = 172, 47.2%), there was no significant difference in the mean total score on the EMC19 [t = 2017 (362), p = 0.065)].

Having children, not having children or being pregnant also does not seem to influence fear of COVID19, measured by EMC19 [t= 1.200 (362), p=0.231)].

Race, categorized as white (n = 182, 50.0%) vs. others (n = 171, 47.0%) also did not result in previous scores beyond fear of COVID19 [t = -1386 (351), p = 0.167)].

When compared to other professional categories, it appears that health professionals did not present higher scores in the total CME19 [t= -0.524 (362), p=0.601)]. How-ever, if only the "professionals at the top" are considered, it will be possible to notice that they have significantly lower scores for fear of COVID-19 (16.40±6.31) than the rest of the sample (18.80± 6.62) [t=- 2.218 (362), p=0.027)].

DISCUSSION

The present study sought to ensure the validity and reliability of the COVID-19 Fear Scale, through its translated and validated version into Portuguese (Brazil), as a measure of the severity of fear of COVID-19 among a population of Brazilian adults, according to psychometric variables.

The results confirmed the construct validity of the one dimensional structure of the EMC-19, as well as its good internal consistency. In addition, normative values, means and percentiles are presented, which can be used to compare scores of individuals or groups, including across countries[23].

The good psychometric properties of the scale offer confidence, rigor and objectivity in the assessment of this important component of the population's mental health during the pandemic, both in clinical practice and in research[23,43].

No significant differences were found in scores when compared according to the sociodemographic variables selected in the study, with the exception of gender. Being a woman was also a variable that was associated with higher levels of fear of COVID-19, in the results obtained in other studies that used FCV-19S, as well as being married[44,45,46]. they also corroborate the findings in the literature regarding education that did not influence the perception of fear of the people in the sample[23,44,47].

It is important to highlight that fear represents a stimulus strongly associated with triggering the stress response, which, in turn, interferes with the adaptive process in face of potentially life threatening situations[48].

The ability to respond to stress is an individual characteristic. There are people who are robust to stress. That is, they are able to understand their experience, trigger effective emotional selfregulation strategies and adapt successfully[48,50].

Others, in turn, present maladaptive coping that, in addition to denying or naturalizing stress, include behaviors and attitudes such as working too hard; hyperactivity; abusive use of legal and illegal substances; overeating; cultivate dysfunctional and depressive thoughts[48,50].

It was found that the group of health professionals, particularly those who work in a different line, have lower levels of fear of COVID-19, which may be related to a phenomenon of desensitization or habituation, related to the reduction of fear and with cognitive changes[49]. That is, a set of coping strategies that some people end up developing in an attempt to maintain balance and deal with the pressures of life[49,50].

On the other hand, these low levels of fear can be one of the signs of maladaptive coping that, in longerlasting situations, can lead to physical and mental illness[49,50].

Furthermore, individuals with a low level of fear may not adhere to the sanitary measures recommended for the prevention of COVID-19, increasing their exposure to the risk of becoming ill[18].

In addition to the personal risks involved in the provision of services, health professionals do not have, in the immediate future, a forecast about the end of this situation of pressure and psychoemotional overload.

Thus, it is essential to adopt preventive and care measures at an opportune time, considering that the context of the pandemic itself interferes with stress levels and can worsen the mental health of individuals already predisposed to psychoemotional disorders[51].

Duan & Zhu (2020)[52], propose that interventions aimed at mental health care should be broad and based on the careful assessment of risk factors, such as history of mental suffering, experience of mourning, selfinjury or violent behavior in relation to others people, panic, separation from the family and low family income.

The emotional experience of health professionals, as well as adaptive coping with stress, represent important questions for future studies, considering that coping styles and psychological growth are important for the maintenance of everyone's mental health[42].

It is important to understand that the greater perception of fear can have repercussions as a motivational element in the adoption of preventive behavior, which constitutes

a positive and functional response with regard to containing the advance of the pandemic[26,53]. However, these individuals with higher levels of fear may adopt mistaken preventive measures that are not based on scientific evidence, making them more susceptible to infection[18], as well as to the development of more severe mental disorders[51].

These results overlap with those of other validation studies carried out in Iran, New Zealand, Paraguay, Russia, Saudi Arabia, Canada, France, Italy, Bangladesh, Israel[28-36]; among which, depression and/or anxiety scales were included to test the convergent validity, with positive, significant and moderate magnitude associations.

The availability of a valid and reliable instrument will support future correlational studies, already underway, in order to contribute to a better understanding of the correlates of fear of COVID-19. These correlational studies may also serve for additional validation of the instrument.

The findings of the present study must be considered in light of some limitations. First, this is not a population study and, therefore, the results apply only to the selected sample and do not allow generalizations. The sample was mostly represented by the female sex, which affects

its representativeness. Although data collection through social networks facilitates the recruitment of volunteers for the research, it can lead to a selection bias, from the point of view of sociodemographic variables, such as education and socioeconomic level, and problems cannot be excluded. social and convenience factors may have influenced participants' responses to the questionnaire.

It is noteworthy that the temporal stability was not properly analyzed, considering that such analysis requires a longer term that allows for a valid instrument for this issue. In other words, it is considered that, given its urgency, it was not justified to wait two months for the retest.

Future studies should also assess whether individuals with underlying medical conditions associated with an increased risk of death from COVID-19 (eg, diabetes, hypertension, coronary heart disease, preexisting respiratory conditions) might have increased levels of fear from COVID-19.

It is important to collect a more representative sample of the Brazilian population to confirm the preliminary results provided by this study. However, the evidence that the total scores on the EMCV-19 do not differ significantly by age suggests that the EMC-19 can be used to assess fear of COVID-19 among Portuguese speaking individuals. The phrases used in each of the items are exactly the same in the Portuguese versions of Brazil and Portugal, in order to enable multicentric and crosscultural studies.

CONCLUSION

The Covid-19 Fear Scale (EMC-19) in its Portuguese (Brazil) version is a reliable and valid tool to assess the severity of fear of COVID-19 among Brazilian adults.

The EMC-19 validation process demonstrated the questionnaire's construct validity and internal consistency, characterized by the robustness of its psychometric qualities.

The EMC-19 is an instrument that is easy to apply by health teams, which will al-low the assessment of behaviors in the face of the COVID-19 pandemic, in order to provide subsidies for mental health care, from planning to the implementation of preventive actions, educational and rehabilitation activities that aim to overcome fear and the impacts of psychoemotional disorders of COVID-19.

Author contributions

All authors contributed to the conception and design of the study. Material preparation, data collection and analysis were performed by Monalisa NS Barros, Ana Telma Pereira, Marcella Aguiar and António Macedo. The first draft of the manuscript was written by Monalisa N. S. Barros and Ana Telma Pereira. All authors commented on previous versions of the manuscript. Maria Inês Puccia made a final review of the article. All authors read and approved the manuscript.

Conflict of interest statement

The inexistence of a conflict of interest is declared, as so far, the existence of conflicts, whether financial or not, is not known.

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CHAPTER 16

ANALYSIS OF VACCINATION COVERAGE DURING THE COVID-19 PANDEMIC IN VITÓRIA, BRAZIL

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Abstract

Introduction: with the current situation of measles outbreak in Brazil and the sharp drop in immunization coverage nationwide, it is necessary to think about ways to intervene in the face of so many difficulties, since the expansion of immunization coverage is the most effective and safe for the control of infectious diseases. **Objective:** to analyze vaccine coverage of two National Campaigns during the COVID-19 pandemic in Vitória/ES. **Methods:** a descriptive experience report on the implementation of an intervention plan to expand vaccination coverage of two National Vaccination Campaigns in 2020 in a Family Health Unit (FHU) during the Curricular Internship I (EC-I). It was based on the Situational Strategic Planning. Descriptive and bivariate statistical analyzes were performed. **Results:** there was an increase of 5.79 times in the vaccination coverage of the National Measles Vaccination Campaign 2020 in the territory, from 0.86% (vaccination coverage of the triple viral before the start of EC-I) to 4.98% at the end of EC-I (p = 0.438). When comparing the vaccination coverage of the National Multivaccination Campaign 2020 of immunobiologicals administered before and after the EC-I period at the FHU, we observed that there was a statistically significant difference (p = 0.0049). **Conclusion:** the proposed and implemented intervention plan had a positive outcome on the FHU, as the vaccination coverage of the two campaigns were expanded, despite all the challenges of the pandemic.

Keywords: Coronavirus Infections; Prevention & Control; Vaccine Preventable Diseases; Vaccine Coverage.

Resumo

Introdução: com a conjuntura atual do sarampo no Brasil, além da queda acentuada da cobertura vacinal em âmbito nacional, faz-se necessário pensar sobre as formas de intervir frente a tantos desafios, compreendendo que a ampliação da cobertura vacinal é a forma mais efetiva e segura para o controle de doenças infectocontagiosas. **Objetivo:** analisar a cobertura vacinal de duas Campanhas Nacionais durante a pandemia de COVID-19 em Vitória/ES. **Método:** relato de experiência descritivo, sobre a implementação de um plano de intervenção de ampliação de cobertura vacinal de duas Campanhas Nacionais de Vacinação em 2020 em uma Unidade de Saúde da Família (USF) durante a Disciplina de Estágio Curricular I (EC-I). O plano de intervenção foi alicerçado no Planejamento Estratégico Situacional. Análises estatísticas descritivas e bivariadas foram realizadas. **Resultados:** houve um aumento de 5,79 vezes da cobertura vacinal da Campanha Nacional de Vacinação contra o Sarampo 2020, passando de 0,86% (em março de 2020) para 4,98% no final de outubro de 2020 (p=0,438). Ao comparar a cobertura da Campanha Nacional Multivacinação 2020 dos imunobiológicos administrados antes e após o plano de intervenção, observamos que houve uma diferença estatisticamente significante (p=0,0049). **Conclusão:** verificou-se um aumento nas coberturas vacinais da Campanha Nacional de Vacinação contra o Sarampo 2020 e da Campanha Nacional Multivacinação 2020. O plano de intervenção proposto e implementado surtiu efeito positivo na USF, pois, foi ampliado a cobertura vacinal das duas Campanhas, mesmo com todos os desafios da pandemia.

Palavras-chave: Infecções por Coronavírus; Prevenção & Controle; Doenças Preveníveis por Vacina; Cobertura Vacinal.

INTRODUCTION

Immunization is the most relevant cost-effective intervention for the global control of infectious diseases, through which it is possible to promote the reduction of mortality and the incidence of preventable diseases[1,2]. With the creation of the Brazilian Public Health System (SUS) in 1988, within the scope of the Federal Constitution, the way of thinking about health in Brazil, as well as the ways of acting in relation to immunization, were recycled. In 1973, the National Immunization Program (PNI) was formulated, which emerged as a form of organization to coordinate actions related to immunization in the country[1,3].

In 2010, the Information System of the National Immunization Program (SIPNI) was implemented, allowing access to the vaccination record of each individual within the national territory, thus reducing locoregional barriers. The system allows the inspection of several indicators, such as doses received by each individual, post- vaccination adverse effects, and information regarding vaccination coverage[4].

In recent years, the PNI has identified a drop in vaccination coverage[5]. The determinants and requirements associated with this low vaccination coverage are mainly linked to misinformation and users' lack of interest in immunization[5,6]. Added to that, there are the recent threats of SUS dismantling, the technical-operational aspects of the SIPNI, as well as the sociocultural aspects interfering with the acceptance of vaccination, the growing anti- vaccination movements worldwide, which are being strengthened with the increase in the spread of fake news shared especially on social midia[7].

Aiming at increasing vaccination coverage, the Ministry of Health announced two important campaigns in 2020. On March 23, the National Measles Vaccination Campaign began for people aged 20 to 49 years, with the objective of applying an Measles, Mumps, and Rubella (MMR) vaccine booster dose in adults of this age group. According to the regular vaccination schedule established by the Ministry of Health, MMR vaccine shall be applied as follows: one dose of the vaccine at 12 months; a dose of MMRV at 15 months; two doses between 20 and 29 years, and one dose of the same vaccine between 30 and 49 years of age[8].

Since 1968, measles has been a mandatory notification condition. To achieve the eradication of this disease, Brazil implemented, in 1992, a national plan for the elimination of measles, and the intensification of continued vaccination actions that same year led to a great reduction and control of the contagion. In 2015, with these actions established, measles transmission was eliminated, and in 2016 the country received the disease eradication certificate[9]. However, in recent years, there has been a return of circulation of the virus in the country, revealing a major problem of Public Health, as measles is a viral disease with a high rate of contagion and one of the main causes of childhood morbidity and mortality in individuals under 5 years of age[10].

In 2017, in Venezuela, there was an outbreak of the disease and, due to the geographical proximity to the northern region of Brazil, and the political and economic situation experienced by the country, there was a migratory movement that triggered the return of the circulation of the virus in the Brazilian territory. In 2018, in the state of Roraima, the first confirmed case of an unvaccinated Venezuelan child was notified, starting a chain of transmission and dissemination throughout the territory[11]. Until October 2019, there were 49,613 suspected cases in Brazil, 10,429 of which were confirmed[12].

On October 5, the National Multivaccination Campaign for children and adolescents under 15 years of age began, based on the regular vaccination schedule established, to expand vaccination coverage in times of pandemic of the new coronavirus[10]. In 2020, with the COVID-19 pandemic caused by the new coronavirus, in- person attendance at health services dropped dramatically in many countries, including child vaccination and that for the adult and elderly population, due to social distancing measures to mitigate virus transmission[13-19].

Efforts to contain the COVID-19 pandemic, which involve telehealth practices and the use of other technologies to continue home health care, greatly affected vaccination actions, which require people to go to the health service facilities[13]. Parents' concern to expose children to SARS-CoV-2 when taking them to health services for vaccination also contributed to the decline in vaccination coverage in the year 2020[13,15-18]. A recent risk-benefit study in African countries showed that deaths preventable by routine vaccination outweigh the excess risk of death from COVID-19 associated with attendance at the health service for vaccination, highlighting the need for efforts to increase vaccine coverage at this time[13].

On March 26, 2020, the WHO and the Pan American Health Organization (PAHO) published recommendations on vaccination during the COVID-19 pandemic. The measures considered three scenarios of availability of health services and included the temporary suspension of mass vaccination campaigns during this period. It was recommended that routine vaccination be maintained in places where essential health services had the preserved operational capacity regarding human resources and supply of vaccines, respecting physical distancing and other measures to control the transmission of Sars-CoV-2[20,21].

In Brazil, there was a recommendation to suspend routine immunization in the first 15 days after the start of the influenza vaccination campaign, a period dedicated to elderly groups and health professionals, which, although valid for the protection of the elderly, caused concern on the part of Brazilian medical societies[22]. Taking the current situation of measles in Brazil into account, as well as the sharp drop in immunization coverage nationwide, it is necessary to think about ways to intervene in face of so many difficulties, understanding that expanded immunization coverage is the most effective and safe way to control infectious diseases, to promote the reduction of mortality, and the incidence of preventable diseases.

Thus, the objective of this study is to analyze vaccine coverage of two National Campaigns during the COVID-19 pandemic in Vitória/ES.

METHODS

A descriptive experience report was carried out on the implementation of an intervention plan to expand vaccination coverage of two National Vaccination Campaigns in 2020 in a Family Health Unit (FHU) during the Curricular Internship I (EC-I). It was based on the Situational Strategic Planning.

Municipal Health Department of Vitória has a computerized system called "Rede Bem Estar", which helps monitoring the citizens' health, since health information related to these users is recorded in a single, electronic medical record. This system registers all families in the area covered by each territory in the capital. The study was carried out at the Family Health Strategy (FHS) São Cristóvão - opened in December 2012, which serves residents of the neighborhoods Tabuazeiro and São Cristóvão, and a small portion of residents from the neighborhood Maruípe, in the city of Vitória, ES, Brazil. According to "Rede Bem Estar", the FHS São Cristóvão had 4056 registered families, totaling 13,077 people in 2020.

Data collection procedures took place in the second half of 2020. The group of researchers consisted of six nursing students from the Federal University of Espírito Santo (UFES), the manager of the FHS, three specialist nurses in Public Health, and professors of the Public Health from UFES.

The intervention plan consisted of prior scheduling and vaccination of individuals in the city commerce – all registered in the territory covered by the FHS and registered in Rede Bem Estar. In the period between 09/29/2020 and 10/30/2020, the researchers in this study actively sought users to expand vaccine coverage with a focus on commerce in the territory.

Before going to the stores to give the vaccines, the researcher responsible for the Vaccine Room at the FHS unit contacted retailers via telephone to schedule and program vaccination. Following vaccination, the information was registered by the researchers at Rede Bem Estar. Information on the vaccination status of the population in the territory covered by the FHS São Cristóvão in the period from March to October 2020 was collected from the Rede Bem Estar Information System at the FHS. The vaccine coverage, according to the doses received and to whether they were administered at the recommended age, was analyzed, following the guidelines of the National Immunization Program. The number of vaccine doses applied monthly from March to October 2020 was also evaluated and a comparison between the beginning and end of the campaign was performed.

For the feasibility of the intervention plan, the Situational Strategic Planning (SSP)[23] was used as a theoretical framework. At the first moment of SSP (explanatory moment), there was an abrupt drop in relation to vaccination coverage in 2020, due to the new coronavirus pandemic.

In the second moment of the SSP (normative moment), after identifying the problem with the health team and the nurse preceptors, the intervention plan was made with the health team and researchers. The structured plan was presented and discussed at the team meeting for assessment and feasibility. The established goals were of short term (1 month) – period in which the 2020 National Measles Vaccination Campaign would end and the 2020 Multivaccination Campaign would begin.

In the third moment of the SSP (strategic moment), the team discussed the operationalization of material and human resources for the implementation of the intervention plan to expand vaccination coverage in the territory. An important point of this moment was the awareness, flexibilization, and collaborative practice related to the presentation of the intervention plan by the FHS health team. Therefore, all notes by each member of the team were considered, to enhance the intervention plan. In the fourth moment of SSP (tactical-operational moment), the intervention plan was put into effect, including immersion in the field to vaccinate individuals in the stores in the territory (figure 1).

Authorization was obtained from the Municipal Health Department of Vitória/ES, as well as from the Direction of the FHS São Cristóvão for the collection of secondary data via Rede Bem Estar. It should be noted that the present study involved only the description and analysis of secondary data collected from the Information System of Rede Bem Estar. In particular, no information with individual identification was obtained for this study. Therefore, being in line with Resolution No. 510/2016, of April 7, 2016, of the National Health Council, this study was neither registered nor evaluated by the Research Ethics Committee/National Research Ethics Committee (CEP/CONEP) system.

Descriptive statistical analyses were performed using the Statistical Package for the Social Sciences (SPSS®) version 20.0. Data were presented by absolute frequencies and percentages. Student's t test was used to compare vaccination coverage before and after the intervention plan. The significance level adopted was 5% ($p < 0.05$).

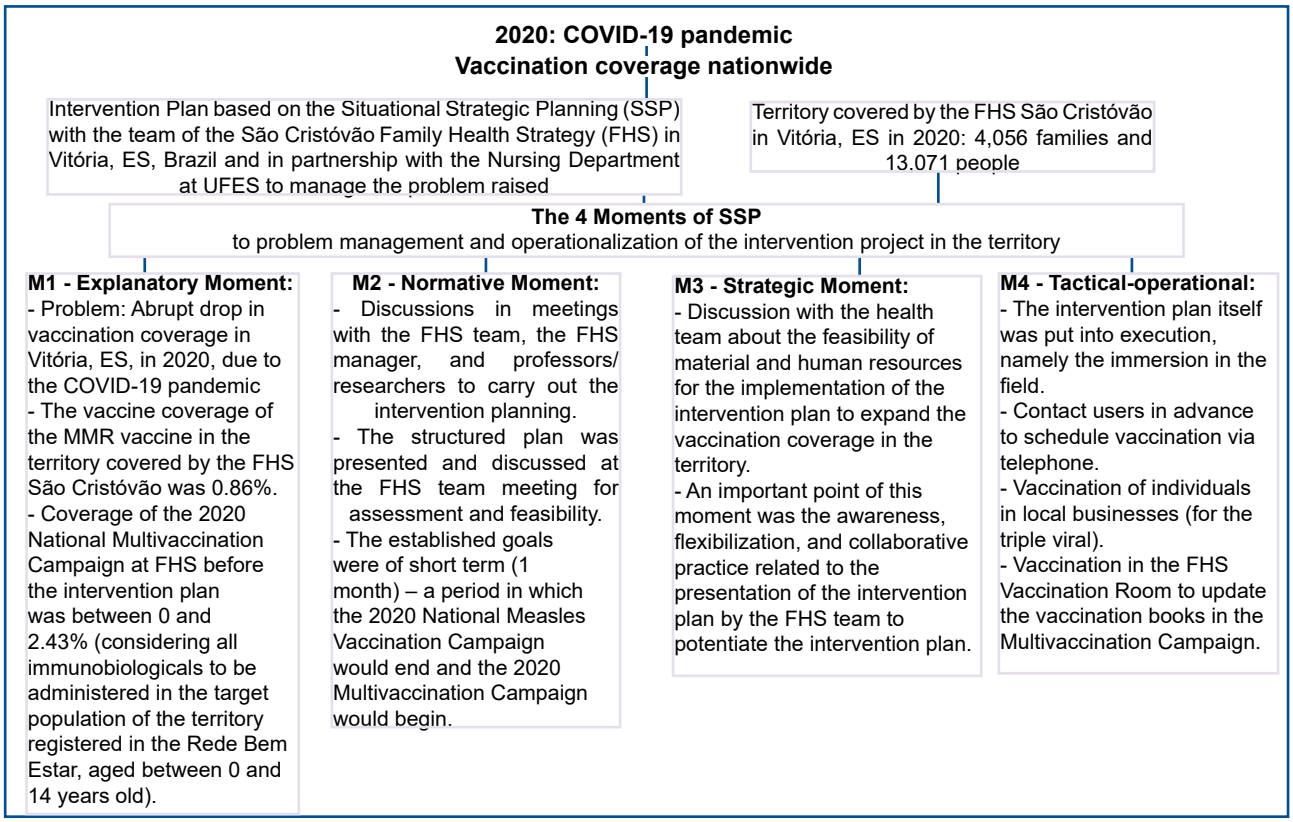

Figure 1: Research flowchart according to the four moments of Situational Strategic Planning

RESULTS

For the 2020 National Measles Vaccination Campaign, the total number of MMR vaccines administered and analyzed was 393. Table 1 shows the absolute frequencies related to the variables age, MMR vaccine dose, manufacturer, place of application, and vaccine schedule.

Regarding the Multivaccination Campaign, 794 vaccines were administered and analyzed. Table 2 shows the absolute frequencies related to the variables age, dose of the different vaccines received, immunobiological, manufacturer, site of administration, route of administration, and vaccination schedule.

Table 3 shows the characterization and quantification of vaccination coverage achieved in the 2020 National Measles Vaccination Campaign at the Family Health Strategy São Cristóvão during the study period.

Table 1: Characterization of the study population according to age, dose of the MMR vaccine, manufacturer, place of application, and vaccination schedule, during the National Measles Vaccine Campaign from March to October 2020. Vitória, ES, Brazil.

Variables	n	%
Age		
0 months - 1 year	58	14.75
2 years - 11 years	2	0.50
12 years - 22 years	46	11.70
23 years - 33 years	109	27.73
34 years - 44 years	111	28.24
45 years - 55 years	57	14.50
56 years - 60 years	10	2.54
Vaccine dose		
1st dose	149	37.91
2nd dose	36	9.16
3rd dose	1	0.25
Campaign dose	207	52.67
Manufacturer		
Fundação Oswaldo Cruz	126	32.06
Serum Institute of India	267	67.93
Site of administration		
Left deltoid	384	97.70
Right deltoid	8	2.05
Left thigh vastus lateralis	1	0.25
Vaccination schedule		
Updated	380	96.70
Delayed	13	3.30

Table 2: Characterization of the study population according to age, dose of different vaccines received, immunobiological, manufacturer, site of administration, route of administration, and vaccination schedule, during the 2020 Multivaccination Campaign in October 2020. Vitória, ES, Brazil.

Variables	n	%
Age		
0 months - 3 months	21	2.64
4 months - 7 months	74	9.31
8 months -11 months	25	3.14
1 year - 5 years	571	71.91
6 years - –10 years	37	4.65
11 years - 14 years	66	8.35
Vaccine dose		
1st dose	123	15.49
2nd dose	136	17.13
3rd dose	20	2.52
Campaign dose	285	35.90
Booster	230	28.96
Immunobiological		
Oral Polio vaccine	291	36.65
Inactivated polio vaccine	21	2.65
DPT/HB/Hib	23	2.89
Td	4	0.51
Yellow fever	64	8.06
Pediatric Hepatitis A	17	2.15
Hepatitis B	5	0.62
Quadrivalent HPV	41	5.17
Trivalent Influenza	52	6.55
Meningococcal ACWY	36	4.54
Meningococcal C conjugate	41	5.17
Pneumococcal 10V	33	4.16
MMRV	1	0.12
dTpa	54	6.80
MMR	53	6.67
Human Rotavirus	11	1.38
Varicella	47	5.91
Manufacturer		
Biological	4	0.50
Butantan	110	13.86
Fiocruz	440	55.42
Fundação Ezequiel Dias	41	5.17
Serum Institute of India	87	10.96
Glaxosmithkline Brazil	18	2.27
Green Cross - Pharmaceutical BM Corp.	15	1.89
Pfizer Laboratories	19	2.39
Lg Chemical Investment Ltd	5	0.62
Merck Sharp E Dohme Farmaceutica Ltda/Go	32	4.03
Panacea Biotec Ltd	23	2.89
Site of administration		
Ignored	306	38.54
Right deltoid	152	19.15
Left deltoid	136	17.13
Right thigh vastus lateralis	101	12.72
Left thigh vastus lateralis	99	12.46
Route of administration		
Ignored	1	0.12
Oral	302	38.03
Subcutaneous	160	20.16
Intramuscular	331	41.69
Vaccination schedule		
Updated	687	86.53
Delayed	107	13.47

Table 3: Vaccination Coverage of the 2020 National Measles Vaccination Campaign at the Family Health Strategy São Cristóvão, Vitória, ES, Brazil.

Immunobiological	Vaccination coverage before the intervention plan			Vaccination coverage after the intervention plan			Increased coverage
MMR	n*	%	N**	n*	%	N**	%
	52	0.86	6.025	300	4.98	6.025	579
p-value***				p=0.438			

*n= population of the vaccinated territory; **N= target population of the territory of 6,025 individuals registered at Rede Bem Estar, aged between 20 and 49 years old to be vaccinated. ***p-value= based on student's t-test.

Table 4 shows in details the characterization and quantification of vaccination coverage achieved in the 2020 National Measles Vaccination Campaign at the Family Health Strategy São Cristóvão before and after the intervention plan.

Table 4: Vaccination Coverage of the 2020 National Measles Vaccination Campaign at the Family Health Strategy São Cristóvão, Vitória, ES, Brazil.

Immunobiological	Vaccination coverage before the intervention plan			Vaccination coverage after the intervention plan			Increased coverage
	n*	%	N**	n*	%	N**	%
Hepatitis B	1	0.04	2.306	6	0.26	2.306	650
Inactivated Polio Vaccine - IPV	56	2.43	2.306	32	1.39	2.306	57
Oral Polio Vaccine - OPV	22	0.95	2.306	76	3.29	2.306	346
Human Rotavirus	32	1.39	2.306	17	0.74	2.306	53
Pentavalent (diphtheria, tetanus, pertussis, hepatitis B and infections caused by Haemophilus influenzae B)	58	2.50	2.306	35	1.50	2.306	60
10-valent Pneumococcal (conjugated)	56	2.43	2.306	41	1.78	2.306	73
Meningococcal C (conjugate)	49	2.12	2.306	51	2.21	2.306	104
Yellow fever	29	1.26	2.306	67	2.90	2.306	230
MMR (measles, mumps and rubella)	37	1.60	2.306	61	2.64	2.306	165
MMRV (measles, mumps, rubella and varicella)	0	0.00	2.306	1	0.04	2.306	100
Pediatric Hepatitis A	17	0.74	2.306	21	0.91	2.306	122
Triple Bacterial - DPT (diphtheria, pertussis, and tetanus)	38	1.65	2.306	63	2.73	2.306	165
Adult double - Td	3	0.13	2.306	5	0.22	2.306	169
Attenuated Varicella	34	1.47	2.306	52	2.25	2.306	153
Quadrivalent HPV	23	1.00	2.306	43	1.86	2.306	186
Trivalent Influenza	0	0.00	2.306	60	2.60	2.306	650
Meningococcal ACWY	0	0.00	2.306	36	1.56	2.306	390
p-value***				p=0.049			

*n= population of the vaccinated territory; **N= target population of the territory of 2,306 individuals registered at Rede Bem Estar, aged between 0 and 14 years old to be vaccinated; ***p-value= based on student's t-test.

DISCUSSION

The Brazilian vaccination schedule in the territory covered by the Family Health Strategy (FHS) São Cristóvão in the city of Vitória, ES, Brazil, was behind schedule in relation to the vaccination coverage defined by the Brazilian Ministry of Health (MS). During the period comprising the beginning of the 2020 National Measles Vaccination Campaign, the vaccine coverage of the MMR vaccine in the territory covered by the FHS São Cristóvão was of 0.86% vaccinated. With the implementation of the intervention plan, this vaccination coverage reached 4.98%, with 300 individuals vaccinated. However, this difference was not statistically significant (p=0.438). Nevertheless, we found that coverage was 5.79 times greater after the intervention plan was carried out at FHS São Cristóvão.

There was also a percentage increase in the vaccination coverage of the 2020 National Multivaccination Campaign, after an intervention plan, of the following immunobiologicals, in descending order: 650% of the hepatitis B vaccine; 346% of the oral polio vaccine; 186% of the quadrivalent HPV vaccine; 169% of the Td vaccine; 165% of both MMR vaccine and DPT vaccine; 153% of the attenuated varicella vaccine; 130% of the yellow fever vaccine; 122% of pediatric hepatitis A vaccine; 4% of meningococcal C vaccine. When comparing the vaccine coverage of the 2020 National Multivaccination Campaign of immunobiologicals administered before and after the intervention plan, we observed a statistically significant difference (p=0.0049).

The new coronavirus pandemic has challenged health systems around the world in providing essential services, including immunization programs, as routine vaccination and mass vaccination campaigns could contribute to the spread of COVID-197,[24]. In fact, the COVID-19 pandemic had a significant impact on vaccine coverage, leading to high risks of resurgence of vaccine- preventable diseases[25].

The expansion of vaccination coverage is one of the contemporary challenges for ensuring the population's health. Vaccination should be compulsory, a citizen's duty, as the collective well-being is what is at stake when seeking to prevent diseases. Since the 1970s, vaccination of children and adolescents has been the most effective and cost-effective measure of preventive health in the world. The vaccine schedule with availability of vaccines was developed to be one of the most successful and cost-effective public health measures to prevent diseases and save lives. Since the last half of the 20th century, diseases that were once very common have become rare in the developed world, mainly due to generalized immunization[26,27]. Vaccination is a public health priority even in times of pandemic and shall be maintained, whenever possible, with the adoption of strategies adapted to local and regional realities. These strategies shall preserve health professionals', the community's and caregivers' safety, and comply with the rules of social distancing defined for each period of the pandemic[28].

With the spread of the new coronavirus pandemic, measures such as social isolation, the use of masks, and an increase in hand hygiene were required[20]. While isolation and limited circulation of people reduce the spread of COVID-19, they also reduce the spread of other pathogens (Measles, Respiratory Syncytial Virus, and Influenza). However, the non-attendance of children, adults, and the elderly to health facilities to update the vaccination schedule can impact vaccination coverage and put everyone's health at risk, especially in light of the current Brazilian epidemiological situation of measles, yellow fever, and pertussis[29].

The drop in the vaccination coverage is one of the main health problems faced by men. The COVID-19 pandemic has worsened this problem even further. Health professionals shall be aware and updated in what regards vaccination schedules of different population groups and risk groups. They shall spread knowledge about the importance of vaccines, fight false news and, above all, ensure that vaccination opportunities are not missed[30-32].

According to an alert from UNICEF and WHO, due to COVID-19, more than 117 million children in 37 countries may not receive the measles vaccine. Measles vaccination campaigns have already been postponed in several countries, which

increases the chance of outbreaks. Brazil remains with an outbreak of measles in the five regions of the federation. The North Region has five (71.4%) states with an outbreak, the Northeast Region six (66.7%), the Southeast Region three (75.0%), the South Region three (100.0%), and the Midwest region four (100.0%) states. In Brazil, within the epidemiological weeks 01 to 25 of 2020 (12/29/2019 to 06/20/2020), 11,405 measles cases were reported, 4,958 confirmed (43.5%), 4,740 (41.5%) were ruled out, 1,707 (15.0%) were under investigation. The states of Pará, Rio de Janeiro, São Paulo, Paraná, and Santa Catarina concentrate the largest number of confirmed measles cases, totaling 4,804 (96.9%) cases. Deaths from measles occurred in the states of Pará (3, 60.0%), Rio de Janeiro (1, 20.0%) and São Paulo (1, 20.0%)[8].

A recent ecological study that aimed to analyze immunization coverage and measles incidence in the Northern Region of Brazil, using secondary data on immunization coverage of Td vaccine, MMR and MMRV, and measles incidence in residents of the Northern Region States, Brazil, from 2010 to 2018, showed a reduction in vaccination coverage during the study period, not reaching the percentage recommended by the Ministry of Health, and an increase in the incidence of measles in the Northern Region of Brazil[33].

The sharp drop in vaccine coverage, especially for children during the COVID-19 pandemic, was a phenomenon experienced by several countries in various regions of the world[15,18]. In the USA, a considerable decline in the vaccination coverage of children was found, starting in the week after the declaration of COVID-19 as a pandemic by the World Health Organization on March 11, 2020, being greater among children under two years of age[17]. Particularly in the State of Michigan, in the United States, there was a decrease in vaccination coverage and a delay in all age groups analyzed when compared to the historical series of previous years. Coverage for measles was 70.8%[14].

In England, three weeks after the introduction of social distancing (March 20, 2020), there was a 19.8% drop in doses of measles-mumps-rubella vaccine, compared to the same period in 2019[16]. In Michigan (USA), the completeness of the vaccination schedule for children at five months of age dropped from 67.0% to 49.7% in May 2020. At 16 months, it was found that measles vaccine coverage dropped from 76.1% to 70.9%16. In Indonesia, where immunization takes place in schools, an important drop in coverage of the basic vaccination scheme was estimated after the closing of schools in March 2020[19]. Moreover, this impact is much more significant in families of unfavorable socioeconomic conditions, as well as those living in situations of vulnerability[18].

There are several factors related to the drop in vaccine coverage. Among them, we can list the main ones, such as the population's lack of perceptions of the risk of vaccine-preventable diseases, changes in the data collection systems of the National Immunization Program (PNI), the increase in the number of available vaccines, and updates on the recommendations by the Ministry of Health. The lack of education and training of professionals to work in vaccine rooms, the opening hours of vaccination sites, the momentary shortages for some immunobiologicals, the emergence of the anti-vaccination movement and fake-news have also contributed to the drop in the population vaccination coverage[25].

The WHO recognizes this weakness and recommends efforts to ensure high vaccine coverage, seeking herd immunity for vaccine-preventable diseases, so that immunization programs adopt innovative measures[20,21]. Vaccination strategies in vehicles, at home, or in specific rooms well separated from other clinical care locations could be used, as well as the identification of absentees and recruitment for vaccination with the aid of computerized immunization records[14-18].

Furthermore, safe strategies shall be developed to allow the maintenance of routine vaccination. Among them are knowledge of local epidemiology on vaccine- preventable diseases. It is also necessary to know how the circulation of COVID-19 is (transmissibility, number of new cases, number of deaths, number of hospital admissions, use of intensive care beds), what the demographic data and the availability of vaccines and supplies are, and the personnel capacity and structure of the vaccination service[28,34-36].

Each local manager shall define the strategy to maintain immunization activities in accordance with the COVID-19 transmission rates in their area of residence. It is imperative that Primary Health Care is strengthened with investments and inputs for the active search and vaccination in the territories, especially for people with risk factors or the vulnerable ones. The surveillance system for vaccine-preventable diseases shall receive investments in inputs and personnel to detect cases early and track them when necessary[37-43].

It should be noted that the health care network was greatly harmed by COVID-19[38,43], both due to the health professionals who fell ill and continue being infected by the virus, and the difficulties faced with restrictions on urban mobility and the closing of some units. An active search and follow-up of people who were not vaccinated is required to update their vaccination schedule. When the vaccine capacity is limited, priority shall be given to risk groups, children under 5 years of age, pregnant women, and people with comorbidities. Priority becomes more important in institutionalized people and in areas of difficult access. When there is a spontaneous demand by the population in visits to clinics, hospitals, or through family health, it is essential to encourage vaccination in view of this opportunity[31].

In health services, there shall be a change in people the inflows and outflows, changes in the routines of the health professionals involved, scheduling to avoid overcrowding, appointments for people from risk groups, and staff hiring to increase vaccine supply. Vaccination of residents of nursing homes, prisons, long-stay institutions of high or medium complexity, and companies with essential service workers/health professionals, among others, shall also be encouraged[28].

Regarding the organization of health services at the time of vaccination, a vaccination waiting place in an outdoor and open place shall be found. A 2-meter distance between the individuals in the waiting line is essential. There needs to be a professional at the entry for screening of symptoms related to COVID-19 and rescheduling of vaccination. Gloves shall not be used at the time of vaccination, it is essential to clean the hands correctly with soap and water or 70% alcohol hand sanitizer gel. The use of masks is recommended to reduce transmission. A uniform shall be used in the work environment, instead of clothes used for transport to work. Wearing closed shoes, no accessories, fastening long hair, not using phones during the service and frequently cleaning them are other important actions[29].

The dissemination of information about the importance of maintaining high rates of vaccination coverage for the population is essential. The training of credible information multipliers related to health and immunizations and the mobilization of community leaders strengthen the vaccine goals. The message that vaccines are safe, service at health care units, information about service hours shall be part of advertising campaigns on the national network. Vaccination is a priority in public health and should be maintained, whenever possible, with the adoption of strategies adapted to local realities and focused on the territory. These strategies shall preserve health professionals', the community's and caregivers' safety, and comply with the rules of social distancing defined for each period of the pandemic. There shall be a fight to re-establish adequate vaccination coverage levels for the entire population, especially for the most vulnerable[28].

The proposed and implemented intervention plan had a positive effect on the FHS São Cristóvão, since the vaccination coverage of the two Campaigns was significantly expanded, despite all the challenges of the new coronavirus pandemic. This confirms that the intervention plan facilitated the management and organization of the work process, as well as the improvement of FHS indicators, based on the teaching-service-community integration within the Brazilian Public Health System. These indicators are important to determine the strategies to be carried out by the National Immunization Program and the Health Surveillance at the municipal level.

CONCLUSION

The proposed and implemented intervention plan had a positive outcome. During the study period, an increase in the vaccination coverage of the 2020 National Measles Vaccination Campaign and the 2020 National Multivaccination Campaign was observed in the territory covered by the FHS São Cristóvão in the city of Vitória, ES, Brazil. The vaccination coverage of the two Campaigns was significantly expanded, despite all challenges of the COVID-19 pandemic.

Author contributions

LCLJ, participated in the conception and design of the study; data interpretation elaboration and critical review of the manuscript; approval of the final version of the manuscript; and has public responsibility for the content of the article. TMS, LBS, CLVD, IRD, NBM, TLCD participated in data collection and interpretation, drafting and critical review of the manuscript; approval of the final version of the manuscript. LCR, EAM, VRS and FMS participated in data interpretation and critical review of the manuscript; approval of the final version of the manuscript.

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CHAPTER 17

COVID-19 MORTALITY AND LETHALITY IN THE STATE OF PARÁ, LEGAL AMAZON, BRAZIL

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Abstract

Introduction: the growth of coronavirus indices in the North region highlights the region's historical social inequalities and the problems in accessing citizenship. **Objective:** to analyze the mortality and lethality of COVID-19 in the state of Pará, Brazil. **Methods:** this is an ecological study with a time series design of secondary data. All registered cases and deaths reported by COVID-19 in the period from March 2020 to June 2021, in the state of Pará, Brazil, were considered. The incidence and mortality and lethality rates were used. The daily percentage variation and their respective 95% confidence intervals were estimated. **Results:** the total number of confirmed cases and deaths from COVID-19 in the state of Pará was 552,937 and 15,469, respectively, from March 2020 to June 2021. Incidence and mortality rates from March 2020 to June 2021 were, respectively, 6,407.9 and 179.3 per 100,000 inhabitants and the lethality was 43.3. Regarding the analysis of the daily trend of rates in the period from March 2020 to June 2021, both mortality and incidence increased. **Conclusion:** it was found that the behavior of the trend of rates in the first wave was increasing in the incidence of confirmed cases and the lethality decreasing, and in the second wave, the mortality and lethality rates were increasing.

Keywords: COVID-19; SARs-CoV-2; Mortality; Lethality; Lockdown; Quarantine.

Resumo

Introdução: o crescimento dos índices do coronavírus na região Norte evidencia as desigualdades sociais históricas da região e os problemas no acesso à cidadania. **Objetivo:** analisar a mortalidade e letalidade da COVID-19 no estado do Pará, Brasil. **Método:** trata-se de um estudo ecológico com delineamento de série temporal de dados secundários. Foram consideradas todos os casos registrados e óbitos notificados por COVID-19 no período de março de 2020 a junho de 2021, no estado do Pará, Brasil. Foi utilizado a taxa de incidência, mortalidade e letalidade. Estimou-se a variação percentual diário e seus respectivos intervalos de 95% de confiança. **Resultado:** o total de casos confirmados e óbitos por COVID-19 no estado do Pará foi de 552.937 e 15.469, respectivamente, no período de março de 2020 a junho de 2021. As taxas de incidência e mortalidade do período de março de 2020 a junho de 2021 foram, respectivamente, 6.407,9 e 179,3 por 100.000 habitantes e a letalidade foi 43,3. Com relação à análise de tendência diária das taxas no período de março de 2020 a junho de 2021 tanto a mortalidade quanto a incidência foram crescentes. **Conclusão:** constatou-se que o comportamento da tendência das taxas na primeira onda foi crescente na incidência de casos confirmados e a letalidade decrescente e, na segunda onda, as taxas de mortalidade e letalidade foram crescentes.

Palavras-chave: COVID-19; SARs-CoV-2; Mortalidade; Letalidade; Lockdown; Quarentena.

INTRODUCTION

In the year 2020, an outbreak of the new Coronavirus in China became an international public health problem. In a short period, a pandemic was declared with different impacts signaled by the World Health Organization (WHO). COVID-19 had a remarkable impact on global economic development, harmed health systems, the political and social field[1].

Approximately 180 million cases have been registered around the world. South America was recently declared by the World Health Organization as a new epicenter of the SARS-CoV-2 pandemic[2].

The Unified Health System (SUS), despite the hospital and health crisis, guarantees access to millions of inhabitants, in person and digitally, developing an artificial intelligence system for non-presential care. Despite all measures, the pandemic had a profound impact on the Brazilian population, especially its population in a vulnerable situation, aggravated by the high rate of unemployment[3]. With death records exceeding 500 thousand victims of the disease, the lack of control of the pandemic in the country is worrying[4]. It began in 2021 without effective intervention measures, strategies for health promotion and combating the virus, overloading the hospital system, general beds, and intensive care units (ICU)[5].

One of the concerns linked to the COVID-19 pandemic refers to the capacity of the health system structure to support the demand for care and treatment of people affected by this disease[6].

In Brazil, one of the countries most affected by the COVID-19 pandemic, mortality data do not reflect the actual number of deaths from the disease. Between February 23 and August 8, 2020, 46,028 deaths from respiratory causes were recorded in the eight cities (Rio de Janeiro, São Paulo, Manaus, Belém, Fortaleza, Recife, Cuiabá, and Curitiba). The high and heterogeneous percentage of excess respiratory deaths suggests high underreporting of deaths from COVID-19, reinforces regional inequalities and the need to review deaths associated with respiratory symptoms[6,7].

The growth of coronavirus indices in the North region, therefore, highlights the historical social inequalities of the region and the problems in accessing citizenship[8].

With few epidemiological studies in the northern region of Brazil, the gaps in information on the epidemiology of COVID-19 show the highest incidence rates of COVID-19 in this region[9,10]. The Northern region took the third place early in the COVID-19 pandemic outbreak, with confirmed cases at approximately 16% as of May 5, 2020[11].

In the State of Pará, 4,756 cases were registered, with an incidence rate of 788 cases in 49 days after confirmation of the first COVID-19 infection. The first confirmed case of the disease was reported on March 18, 2020, in the city of Belém, capital of the state. The first notification of death occurred on April 1, 2020, and since then the curve of new cases and incidence of deaths has been frequent and recorded with high rates in the region[11].

The investigation and characterization of epidemiological aspects, analyzing the temporal variations of COVID-19 mortality and lethality in the North region to understand the disease behavior in the population of the State of Pará, can lead to timely and adequate interventions for the prevention of worse outcomes.

Therefore, the objective is to analyze the mortality and lethality of COVID-19 in the state of Pará, Brazil.

METHODS

This is an ecological study conducted according to the protocol proposed by Abreu, Elmusharaf and Siqueira (2021)[12], using time series of public and official data available on the website of the Department of Health of the State of Pará, Brazil (https://www.covid-19.pa.gov.br/#/).

The Legal Amazon comprises nine states, Acre, Amapá, Amazonas, Mato Grosso, Pará, Rondônia, Roraima, Tocantins, and part of Maranhão, totaling 772 municipalities. Its territorial extension corresponds to about 59% of the Brazilian territory, its population is equivalent to 13% of the total inhabitants of Brazil and 60% of the country's indigenous population live in the region[12,13]. Pará has an estimated population of 8,777,124 inhabitants, an HDI of 0.646[14] (figure 1).

Data were classified according to notification date and deaths according to closing date. All cases and deaths registered by COVID-19 in the period from March 2020 to June 2021, in the state of Pará, Brazil, were considered. Extracted by two researchers independently, to minimize the collection bias and ensure the quality and reliability of the data obtained.

All notifications of cases and deaths related to COVID-19 were considered, using the International Classification of Diseases, 10th edition (ICD-10), of "U07.1 COVID-19, identified virus", associated with the diagnosis of the disease, confirmed by clinical and/or laboratory diagnosis.

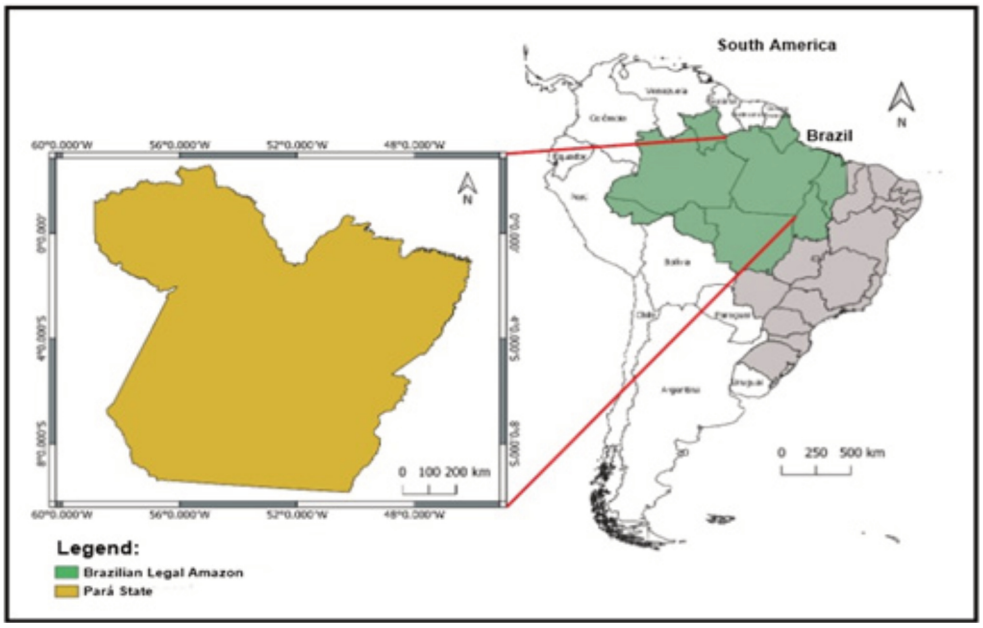

Figure 1 : Map of Brazil with the states of the Brazilian Legal Amazon.

The collected data were distributed in an Excel spreadsheet. Incidences (cases/population x 100,000) and mortality rates (deaths/population x 100,000) expressed per 100,000 inhabitants, and lethality (total deaths/total cases x 100), expressed as a percentage, were calculated. Mortality rates were also calculated throughout the period, stratified by sex and age.

For trend analysis, the periods were divided into first wave (1st wave - March to November 2020) and second wave (2nd wave - December 2020 to June 2021), to define the end of the first wave, the month with the lowest rate of mortality was considered, which suggested the end of a first wave in the curve.

Trends were analyzed using the methodological guidelines of Antunes and Cardoso[15]. The Prais-Winsten regression model for population mortality rates was used to construct time series, which allowed the correction of first-order autocorrelation in the analysis of the values of the organized time series. The following values were estimated: probability (p) and Daily Percentage Change - DPC, considering a significance level of 95%. This procedure allowed for the classification of mortality and lethality, assessing whether it increased, decreased or was flat.

Statistical analyzes were performed using STATA 14.0 software (College Station, TX, U.S. 2013).

Due to the use of public domain data, there was no need to submit the work to the National Research Ethics Commission (CONEP) and to analyze the Research Ethics Committee (CEP) system.

RESULTS

The total number of confirmed cases and deaths from COVID-19 in the state of Pará was 552,937 and 15,469, respectively, in the period from March 2020 to June 2021. The months with the highest frequencies of confirmed cases for COVID-19 were June 2020 (65,245/11.8%), April 2020 (54,036/9.77%) and March 2021 (52,880/9.56%). Regarding death, they were May 2020 (2,715/17.55%), April 2021 (2,555/16.52%) and June 2021 (1,997/12.91%). The incidence and mortality rates for the period from March 2020 to June 2021 were, respectively, 6,407.9 and 179.3 per 100,000 inhabitants and the lethality was 43.3% (table 1).

Table 1: Incidence, mortality, and lethality rate due to COVID-19 per month in the state of Pará, Brazil, March 2020 to June 2021.

Data	Cases	%Cases	Deaths	%Deaths	Incidence	Mortality	Lethality
03/2020	32	0.01	0	0.00	0.37	0.00	0.00
04/2020	2,844	0.51	208	1.34	32.96	2.41	7.31
05/2020	35,085	6.35	2,715	17.55	406.60	31.46	7.74
06/2020	65,245	11.80	1,997	12.91	756.12	23.14	3.06
07/2020	51,479	9.31	808	5.22	596.59	9.36	1.57
08/2020	44,781	8.10	418	2.70	520.01	4.84	0.93
09/2020	30,893	5.59	427	2.76	358.02	4.95	1.38
10/2020	22,470	4.06	170	1.10	260.40	1.97	0.76
11/2020	17,629	3.19	172	1.11	204.30	1.99	0.98
12/2020	22,992	4.16	273	1.76	266.45	3.16	1.19
01/2021	35,766	6.47	448	2.90	414.49	5.19	1.25
02/2021	35,337	6.39	955	6.17	409.52	11.07	2.70
03/2021	52,880	9.56	1,835	11.86	612.82	21.27	3.47
04/2021	54,036	9.77	2,555	16.52	626.22	29.61	4.73
05/2021	45,055	8.15	1,523	9.85	522.14	17.65	3.38
06/2021	36,323	6.57	935	6.04	420.95	11.18	2.66
Total	552,937	100.00	15,469	100.00	6,407.97	179.27	2.80

Source: Secretaria Estadual de Saúde do Pará. COVID-19, 2021. Projeção da população Brasil e Unidades de Federação por sexo e grupos de idade: 2000-2030 do Instituto Brasileiro de Geografia e Estatística (IBGE) do Departamento de Informática do Sistema Único de Saúde (DATASUS). Taxa de incidência: número de casos confirmados da COVID-19 dividida pela população residentes por 100.000 habitantes. Taxa de mortalidade: número de óbitos confirmados da COVID-19 dividida pela população residentes por 100.000 habitantes. Taxa de letalidade: número de óbitos confirmados da COVID-19 dividida por casos confirmados da COVID-10 por 100, expresso por porcentagem.

Regarding the analysis of the daily trend of rates in the period from March 2020 to June 2021, both mortality and incidence increased. With the division into two periods, it was found that the incidence remained increasing and the lethality decreasing in the first wave and in the second wave the mortality rate and lethality increasing (table 2).

Table 2: Prais-Winsten and Daily Percent Change (DPC) regression estimates of mortality, lethality, and incidence rates of COVID-19 in the state of Pará, Brazil, from March 2020 to June 2021.

Rate	Beta	95% CI Beta		p	DPC	95% CI DPC		Tendency
Total Period (March 2020 to June 2021)								
Mortality	0.001316	0.0003	0.002333	0.011	0.30	0.07	0.54	Increasing
Lethality	0.000014	-0.00063	0.000655	0.966	0.00	-0.14	0.15	Stationary
Incidence	0.003034	0.001804	0.004263	<0.001	0.70	0.42	0.99	Increasing
1st Wave (March 2020 to November 2020)								
Mortality	-0.00142	-0.00403	0.001188	0.284	-0.33	-0.92	0.27	Stationary
Lethality	-0.00436	-0.00553	-0.00318	<0.001	-1.00	-1.27	-0.73	Decreasing
Incidence	0.008661	0.004007	0.013316	<0.001	2.01	0.93	3.11	Increasing
2nd Wave (December 2020 to June 2021)								
Mortality	0.003803	0.002304	0.005302	<0.001	0.88	0.53	1.23	Increasing
Lethality	0.002975	0.001815	0.004135	<0.001	0.69	0.42	0.96	Increasing
Incidence	0.000813	-0.00052	0.002147	0.231	0.19	-0.12	0.50	Stationary

Source: Pará State Health Secretariat. COVID-19 Dashboard, 2021. Population projection for Brazil and states by sex and age groups: 2000-2030 from the Brazilian Institute of Geography and Statistics (IBGE) from the Computer Department of the Unified Health System (DATASUS). Incidence rate: number of confirmed cases of COVID-19 divided by the resident population per 100,000 populations. Mortality rate: number of confirmed deaths from COVID-19 divided by resident population per 100,000 inhabitants. Case fatality rate: number of confirmed deaths from COVID-10 per 100, expressed as a percentage. CI (Confidence Interval). p (p-value). DPC (Daily Percent Change).

DISCUSSION

In the state of Pará, 552,937 confirmed cases and 15,469 deaths were reported from COVID-19 from March 2020 to June 2021. There was a characterization of two waves of disease incidence (classified by 1st and 2nd wave). The months with the highest frequencies of confirmed cases for COVID-19 were June 2020 (65,245/11.8%), April 2020 (54,036/9.77%) which coincides with the first wave and the next highest increase was in the second wave in March 2021 (52,880/9.56%).

Regarding death, there was a higher frequency in the first period, which was in May 2020 (2,715/17.55%) and in the second period it was concentrated in the months of April 2021 (2,555/16.52%) and June 2021 (1.997/12.91%). The behavior of the trend of rates in the first period was that the incidence remained increasing and the lethality decreasing and in the second period it presented an aggravation, both the mortality rate and the lethality were increasing.

Recent studies have been carried out observing the incidence of COVID-19 in Brazilian municipalities and verified specific flows in each region[16-20]. And possibly, these variations can be influenced by aspects related to socioeconomic, cultural and health inequalities, thus, it can be understood that COVID-19 has a syndemic nature[21]. The term syndemic means the biological and social interaction so that a prognosis, treatment, public policy, and social protection can be established, and these determinants can interfere with the incidence of COVID-19, and this characterizes how this disease behaves in Brazil[22,23].

In Northern Brazil, the most affected states on May 5, 2020, in reported cases of COVID-19 and mortality per 1 million inhabitants, were Amazonas (2,327.5 and 251.7) and Pará (627.4 and 49 .5). The capital of Pará has the highest incidence (1,816.4/1,000,000 inhabitants) and mortality (240/1,000,000 inhabitants) with a mortality rate of 9.9% such rates remain after one year of the pandemic in the state of Pará, corroborating the present study[11].

Regarding the spatial distribution of incidence and mortality, the north and northeast are among the regions with the highest rates. Both regions had cities with incidence rates two to 10 times higher than the incidence rates of cities in the Midwest, South and Southeast regions, and this heterogeneity of the disease corroborates to validate the hypothesis that the incidence and mortality from COVID-19 are associated with a combination of geographic, economic, social, and cultural factors that express the way of life of the population[24].

In the Northern region, the high mortality rate may be linked to the presence of the indigenous population[25]. All people are immunologically susceptible to COVID-19, however, this population is more vulnerable to epidemics due to worse social, economic and health conditions, increasing the spread of diseases[26]. In addition, the difficulty of accessing health services, geographic distance, scarcity of human resources in the areas of health and language, and a lifestyle that allows them to be more exposed to infectious diseases, such as living in collective houses and sharing personal utensils are all favorable factors. Many indigenous people have already been victims of COVID-19, but the difficulty in diagnosing and notifying the inhabitants of indigenous areas contributes to the underreporting of the number of cases and deaths[25-27].

The rates of intensive care unit beds in the Brazilian territory per 10,000 inhabitants is another factor in relation to the capacity of the health system, which the northern region has a much lower rate than other regions, with 0.9 beds[27]. The high incidence of mortality can be justified by conditions related to health care, socioeconomic and demographic conditions, and factors peculiar to the population (age, presence of comorbidities and lifestyle habits)[28-31].

To minimize the increase in new cases and mortality, and the spread to the interior, the government of Pará instituted a blockade decree in the capital and nine other municipalities. This measure aimed to impose social isolation as there were municipalities that had a higher incidence than the Capital[11].

The insufficiency in the capacity of hospital care and emergency care units, health professionals and adult beds, ICU beds and ventilators, and the lack of rapid testing possibly contributed to the advancement of COVID-19 in the state of Pará for both increase in cases and deaths[11,32].

The state of Pará started vaccination on January 19, 2021, and until September 24, 2021, there is a total of 7,036,152 applied doses, which represents 46.04% of vaccination coverage for the first dose and 29.02% for second or single dose[33]. It is known that vaccination will take more time to reach most of the population, which is why social distancing, isolation, the use of face masks and quarantine are still the best ways to prevent transmission of the virus.

This study had some limitations: the methods and analyzes applied cannot infer causality; secondary data analysis may be limited by incompleteness of the dataset[34]; do not consider individual-level variables such as age/ gender/race and therefore limit conclusions.

CONCLUSION

It was found that the behavior of the trend of rates in the first period was increasing in the incidence of confirmed cases and the lethality decreasing, and in the second period both mortality and lethality rates were increasing. The contribution of this analysis supports preventive actions, control and treatment, reduction of mortality and definition of priorities within the area of public health.

Authors' Contributions

All authors participated in all stages of the work, study design and manuscript design. All authors agreed with the final version of the manuscript.

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Conflict of Interest

There are no conflicts of interest.

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CHAPTER 18

EFFECTS OF THE SOCIAL ISOLATION GENERATED BY COVID-19 ON THE QUALITY OF LIFE OF THE POPULATION IN RIO BRANCO -ACRE AND SANTO ANDRÉ - SÃO PAULO, BRAZIL

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Abstract

Introduction: COVID-19 is a highly transmissible virus that is causing very serious problems in the world's health, generating major political and financial problems. There are numerous risk factors related to this disease, ranging from morbidities to social and family issues. **Objective:** to evaluate the effects of the social isolation generated by Covid-19 on the quality of life in the population of two Brazilian cities. **Methods:** cross-sectional study. This survey with an online platform uses the drive's Google Forms tool to assess the population's quality of life through the SF-36 protocol. The research was carried out in two different cities of the Brazilian confederation. One in Santo André in São Paulo and Rio Branco in Acre State. The selection was carried out randomly in both groups (Acre and São Paulo), with 109 and 62 participants respectively in this first moment. **Results:** regarding gender, women are in greater numbers participating in the city of Santo André, than in Rio Branco, with (80.6% and 48.6%), respectively. Likewise, Santo André has an average age younger than in Rio Branco in relation to the age group. When we compared the dimensions between the two states, performing a Mann-Whitney statistical analysis, statistical differences appeared in three dimensions: functional capacity, pain, and vitality, with better quality of life in these three domains for the city of Rio Branco. **Conclusion:** the city of Rio Branco, has a positive score compared to the city of Santo André, in most of the domains analyzed.

Keywords: Quality of Life; COVID-19; Social Isolation; SARS- CoV-2.

Resumo

Introdução: Introdução: o COVID-19 é um vírus altamente transmissível e que estar causando problemas gravíssimos na saúde do mundo, gerando com isso, grandes problemas políticos e financeiros. Existem inúmeros fatores de risco relacionados a esta doença, que vai desde morbidades até questões sociais e familiares. **Objetivo:** avaliar os efeitos do isolamento social gerado pelo Covid-19 na qualidade de Vida na população de duas cidades Brasileiras. **Método:** estudo transversal. A pesquisa foi realizada em duas cidades diferentes da confederação brasileira. Uma em Santo André – SP e a outra em Rio Branco-AC. Trata-se de uma pesquisa com uma plataforma online, utilizando a ferramenta do Google Formulários do drive para avaliar a qualidade de vida da população pelo protocolo SF-36. A seleção foi realizada de forma aleatória em ambos os grupos (Acre e São Paulo), tendo respectivamente 109 e 62 participantes neste primeiro momento. **Resultados:** em relação ao gênero, as mulheres estão em maior número participando na cidade de Santo André - SP do que em Rio Branco-AC, com (80,6% e 48,6%), respectivamente. Da mesma forma, em relação a faixa etária Santo André encontra-se com uma média de idade mais jovem do que em Rio Branco. Quando realizamos uma comparação das dimensões entre os dois estados realizando uma análise estatística de

Mann-Whitney apareceram diferença estatística em três dimensões, que foram a capacidade funcional, a Dor e a vitalidade, apresentando nestes três domínios melhor qualidade de vida para a cidade de Rio Branco. **Conclusão:** a cidade de Rio Branco-Acre encontra-se com um escore positivo quando comparado com a cidade de Santo André - SP na maioria dos domínios analisados.

Palavras-chave: Qualidade de Vida; COVID-19; Isolamento Social; SARS-CoV-2.

INTRODUCTION

Known as SARS-CoV-2 (acute severe respiratory syndrome coronavirus 2), it has spread globally rapidly to the present day, without until the present moment, we do not have a concrete and definitive solution[1,2]. Although the virus genome has been sequenced, which has allowed for the development of various diagnostic tests and the initiation of vaccines and data around clinical features grow daily, the clinical spectrum of the disease remains to be defined (including the potential for spread asymptomatic)[3].

The quarantine and isolation currently imposed throughout the world due to COVID-19, which acts to separate and restrict both symptomatic and asymptomatic people, seeking to avoid a potentially greater exposure to the virus, thus reducing the risk of infecting other people as well as being infected, is often an unpleasant experience for those who go through it. Separation from loved ones, loss of freedom, uncertainty about the status of the illness, and boredom can occasionally create dramatic effects. The successful use of quarantine as a public health measure requires us to reduce the negative effects associated with it as much as possible. Given the evolving situation with coronavirus, policymakers urgently need evidence synthesis to produce guidance for the public. In the circumstances like these, rapid tests are recommended by the World Health Organization (WHO)[4].

According to the WHO, the infection cases by COVID-19 are only increasing worldwide, where a globalized pandemic has already been characterized. There are countless works carried out by scientists looking for a definitive cure (in principle, a vaccine). Research is as varied as possible, in the clinical area and epidemiological, social, human aspects, etc. Because the population is being reached in all its dimensions[1].

Research on quality of life (QOL) is a growing research topic in health studies[7]. Since the mid-twentieth century, the Health and QOL of populations, with and without a clinical diagnosis, have been discussed together, often taking place with a conceptual understanding of one by the other[5,6]. The study of QOL has assumed importance in several aspects in recent years, particularly regarding its assessment and measurement, either individually or collectively[8].

The QOL theme is one of the great questions and challenges for the health area at the beginning of this century. Much has been said about QOL, and there are many attempts to find the best definition for the term, approached from the most different perspectives, whether from the perspective of science or individuals[9]. Given the need to formulate a concept focused on the health perspective, the WHO in 1994 defined QOL as the individual's perception of their position in life in the context of the culture and value system in which they live and in concerning your goals, expectations, standards and concerns[4].

Health-Related Quality of Life (HRQOL) is a subset of the term QOL, often used to distinguish QOL in a more general sense and QOL related to medical and clinical parameters. HRQOL addresses relevant aspects that may vary from study to study. Still, in general, they include health, physical symptoms, physical, emotional, cognitive and sexual functions, functional status, and the possible consequences of these factors[10].

The health-related quality of life (HRQOL) assessment has been an increasingly frequent practice in medicine today. This assessment aims to monitor the health of a given population, diagnose the nature, severity, and prognosis of the disease, in addition to evaluating the effects of treatment[11].

Within this perspective, the HRQOL assessment is a tool capable of verifying the impact of the disease, health, and treatment, consisting of multidimensional indicators, allowing the assessment of different people who have the same problem and different levels of health physical well- being and emotional[12]. Although there is no consensus on the meaning of the term QOL, as it deals with concepts related to subjective and individual perception, it is possible to measure it through standardized and validated instruments used in each population[13-15].

Although there are several definitions, the main concept is the definition of quality of life proposed by the WHO[16]. QOL is not only related to the resolution of basic survival problems, it must also include the guarantee of conditions of comfort and psychological, physical, individual and family satisfaction of individuals. It must be understood as the sense of well-being of each one, that is, it must be understood about objective material aspects and subjective emotional aspects[17].

HRQOL is the value attributed to lifetime when changed by the perception of physical and psychological limitations, social functions and opportunities influenced by the disease, treatment and other health problems, becoming the main indicator for evaluative research on the outcome of interventions[18].

The assessment of the HRQOL and aspects surrounding it is paramount to understand the citizen in the aspects associated with illnesses or linked to therapeutic interventions. This type of assessment maintains a multidimensional character, even though the emphasis is on symptoms, disabilities, or limitations caused by illnesses[19].

Taking into account the above about quarantine and its possible side effects, as well as that the North region (Acre) is considered the neediest in the country, where there are many difficulties in conditions ranging from housing, sanitation, financial and social issues, government assistance and support, how is the QOL of this population affected by COVID-19 in the State of Acre? What are the main epidemiological and clinical characteristics of this population? How will the quality of life of the population of Acre be compared to another population of another state in Brazil?

Given the described context, we aimed to evaluate the effects of the social isolation generated by COVID-19 on the quality of life of the population of two Brazilian states.

METHODS

Cross-sectional study. The research was carried out in two different cities of the Brazilian confederation. In Santo André, São Paulo and Rio Branco, Acre, both in Brazil. This is a survey with an online platform, using DRIVE's Google Forms tool to assess the quality of life of the population, the selection was carried out randomly in both groups, with 109 and 62 participants respectively at this first moment.

This study was carried out following the guidelines that regulate research on human beings, in Resolution No. 466/12 of the National Health Council. The research was approved by the Ethics Committee of the Centro Universitário FMABC/Fundação do ABC, under number 4,184,251. All participants who agreed to participate in the research signed the free and informed consent form.

Inclusion criteria

Participants aged over 18, literate of both sexes and in full mental health. People who were in social isolation caused by COVID-19.

Exclusion criteria

Minors, indigenous and illiterate people, and people with mental disabilities could not participate in the research. Also people who were not in social isolation.

Instrument used

The SF-36 assesses the QOL of the population, where we have the “Brazilian Version of the Quality-of-Life Questionnaire - SF-36”. This protocol works with eight dimensions, as follows: physical functioning (10 items), limitations caused by physical health problems (4 items), limitations caused by emotional health problems (3 items), social function (2 items), well- emotional being (5 items), pain (2 items), energy/fatigue (vitality) (4 items), general health perception (5 items) and an item about the current health status compared to a year ago which is computed to part. In general terms, to evaluate the results, a score is given for each item (or question), later transformed into a scale from 0 to 100, in which the value 0 reflects a worse QOL and the value 100 reflects a better QOL. The internal consistency estimated by the SF-36 exceeded 0.80 (range 0.61 to 0.90). The SF-36 is considered a generic measure and is supplemented with multi-item type scales.

In this study, the scores of the dimensions present will be distributed into ranges: 1st range – scores from 0% to 25%; 2nd range – scores from 25.001% to 50%; 3rd range – scores from 50.001% to 75%; 4th range – scores from 75.001% to 100%. To analyze the prevalence of participants in the different dimensions, the 1st and 2nd ranges will represent low QOL and the 3rd and 4th ranges, good QoL.

The SF-36 was developed to measure HRQOL, satisfying two essential properties: the assessment of the dimensions that are important for the health condition and the integration of information from the domains, enabling a more complete analysis. The scoring procedure is done by dimension and is therefore analyzed separately. Thus, there is no single value resulting from the global assessment of the health-related quality of life, but average scores for each dimension. This analysis makes it possible to identify the real health-related problems of the participants and verify which ones impact the QOL.

Statistical analysis

Data were analyzed using the Statistical Package for Social Science (SPSS), version 23.0. Descriptive analysis was performed for all variables. Data were expressed as mean ± standard deviation or median (interquartile range), when appropriate. To compare each group’s initial and final values, the paired t-test and the Wilcoxon test were performed for non-parametric data. Comparisons between groups were performed using the unpaired t-test or the Mann-Whitney test, when appropriate. In this sense, we carried out both evaluations of the same sample group and compared two related samples as much as possible. For comparison between groups, the Mann- Whitney test for non-parametric distributions was applied. Statistical significance was considered at the level of $p < 0.05$ (or 5%). Sample distribution was tested with the Shapiro-Wilk test. The data collected were analyzed: a) descriptive: frequency tables, with position measurements (mean, median, minimum and maximum) and standard deviation; Cronbach’s alpha coefficient: checks the internal consistency of KDQOL-SF. Good reliability is considered for alpha values equal to or greater than 0.6020.

RESULTS

The sociodemographic characteristics found in this study are described in table 1. Regarding sex, proportionally, participants from Santo André have a much higher number of women than in the city of Rio Branco (80.6% and 48.6%) respectively. Also at a proportional level, the age group in Santo André, is much younger than the city of Rio Branco, having, for example, no participants in the age group above 65 years old. In terms of education, the averages are equal. A very interesting fact is about family income, as the state of Acre has almost 50% of participants with income up to the minimum wage. On the contrary, São Paulo has only a percentage of 6.5% in this range.

Table 1: Sociodemographic characteristics of research participants on quality of life related to social isolation due to COVID-19 in the cities of Rio Branco, Acre, and Santo André, São Paulo, both in Brazil, 2020.

	Rio Branco, Acre		Santo André, São Paulo	
Variables	**n**	**%**	**n**	**%**
Sex				
Male	56	51.4	12	19.4
Female	53	48.6	50	80.6
Total	109	100	62	100
Age group (in years)				
18-30	16	14.7	26	41.9
31-40	31	28.4	13	21.0
41-50	25	22.9	13	21.0
51-65	23	21.1	10	16.1
More than 65	14	12.8	0	0
Total	109	100	62	100
Education				
Elementary School	0	0	0	0
Incomplete High School	4	3.7	1	1.6
Complete High School	24	22	15	24.2
Higher Education	81	74.3	46	74.2
Total	109	100	62	100
Family income				
Up to 1 minimum wage	54	49.5	4	6.5
Between 1 and 2 minimum wages	22	20.2	10	16.1
Between 2 and 4 minimum wages	15	13.8	22	35.5
Between 5 and 10 minimum wages	17	15.6	13	21.0
More than 13 minimum wages	1	0.9	13	21.0
Total	109	100	62	100

Source: Author.

Table 2 shows the anthropometric characteristics of the participants from both states, the average of all variables being equal (height, weight, and Body Mass Index (BMI)), and the assessment of the BMI in Santo André is slightly above the ideal classification according to the literature.

With table 3, which shows the eight dimensions of the SF-36 for the State of Acre, we identified only two domains considered as “Low QOL”, which were those of limitation by physical aspects and limitation by emotional aspects with averages of 35.55 and 40.96 respectively. We recall that the dimensions “General health status”, “Vitality”, “Social Aspects” and “Mental Health”, despite having been classified as good quality of life, their values were close to the 50% average. As for the internal consistency of the SF-36, the dimensions obtained satisfactory Cronbach’s Alpha values (≥0.60).

In table 4, where the SF-36 dimensions of the participants from São Paulo were evaluated, three domains were classified as “Low QOL”, which were “Limitation by Physical Aspects”, “Vitality” and “Limitation by Emotional Aspects”, with means 39.11; 44.03 and 42.99 respectively. Also, when evaluating the internal consistency of the SF-36, the dimensions obtained satisfactory Cronbach’s Alpha values (≥0.60).

In table 5, when we compared the dimensions between the two cities, performing a Mann-Whitney statistical analysis, statistical differences appeared in three dimensions, which were functional capacity, pain, and vitality, presenting in these three domains better quality of life for the state of Acre. The Mann-Whitney test showed that the position of the functional capacity domain in the State of Acre is better than in the State of São Paulo ($U = 2186.00$; $p<0.01$) in Pain ($U = 2522.00$; $p<0.01$) and in vitality ($U = 2604.00$; $p<0.01$), but not in the other dimensions.

Table 2: Anthropometric characteristics (height in centimeters; weight in kilograms and BMI percentage) of research participants on quality of life related to social isolation due to COVID-19 in the cities of Rio Branco, Acre, and Santo André, São Paulo, both in Brazil, 2020.

Variables	N	Minimum	Maximum	Media	SD
Heigh – Rio Branco	109	150	184	167.82	8.522
Heigh – Santo André	62	147	185	164.82	8.768
Weight - Rio Branco	109	43	116	72.71	15.661
Weight - Santo André	62	46	145	72.56	19.033
BMI - Rio Branco	109	18	38	25.67	4.551
BMI - Santo André	62	19	43	26.44	5.019

Source: Author.

Table 3: Assessment of the dimensions of Quality of Life with SF-36 with participants from the city of Rio Branco, Acre, Brazil, 2020.

SF-36 – Domains	N	Media %	SD	Min	Max	Range	Classification (QoL)	Alpha de Cronbach
Functional capacity	109	81.56	17.489	10	100	4ª range	Good QoL	0.753
Limitation by physical aspects	109	35.55	36.688	0	100	2ª range	Low QoL	0.768
Pain	109	69.94	23.209	12	100	3ª range	Good QoL	0.739
General health status	109	59.28	14.728	27	95	3ª range	Good QoL	0.758
Vitality	109	52.94	23.612	0	100	3ª range	Good QoL	0.717
Social aspects	109	52.75	26.969	0	100	3ª range	Good QoL	0.755
Limitation by emotional aspects	109	40.96	39.444	0	100	2ª range	Low QoL	0.743
Mental health	109	59.38	22.451	4	100	3ª range	Good QoL	0.735

Source: Author.

Table 4: Assessment of the dimensions of Quality of Life - SF-36 with participants from the city of Santo André, São Paulo, Brazil, 2020.

SF-36 - Domains	N	Media %	D/P	Min	Max	Range	Classification (QoL)	Alpha de Cronbach
Functional capacity	62	72.02	17.093	20	100	3ª range	Good QoL	.840
Limitation by physical aspects	62	39.11	40.393	0	100	2ª range	Low QoL	.804
Pain	62	59.10	21.569	11	90	3ª range	Good QoL	.815
General Health Status	62	62.95	19.355	20	100	3ª range	Good QoL	.824
Vitality	62	44.03	22.990	5	100	2ª range	Low QoL	.804
Social aspects	62	56.25	25.582	0	100	3ª range	Good QoL	.825
Limitation by emotional aspects	62	42.99	38.353	0	100	2ª range	Low QoL	.815
Mental health	62	54.26	19.936	16	96	3ª range	Good QoL	.816

Source: Author.

Table 5: Comparison of the dimensions of the SF-36 between the states of Acre and São Paulo performed using the Mann-Whitney U test with a significance level of $p<0.05$, Brazil, 2020.

SF-36	Rio Branco, Acre			Santo André, São Paulo				
		Media			Media			
Domain	N	%	SD	N	%	SD	p-value	U-value
Functional capacity	109	81.56	17.489	62	72.02	17.093	0.000	2186.00
Limitation by physical aspects	109	35.55	36.688	62	39.11	40.393	0.797	3302.00
Pain	109	69.94	23.209	62	59.10	21.569	0.006	2522.00
General Health Status	109	59.28	14.728	62	62.95	19.355	0.151	2933.50
Vitality	109	52.94	23.612	62	44.03	22.990	0.013	2604.00
Social aspects	109	52.75	26.969	62	56.25	25.582	0.377	3106.50
Limitation by emotional aspects	109	40.96	39.444	62	42.99	38.353	0.680	3256.00
Mental health	109	59.38	22.451	62	54.26	19.936	0.110	2883.00

Mann-Whitney U test. Asymptotic significances are displayed. The significance level is 0.05.
Source: Author.

DISCUSSION

In general, the population in isolation due to COVID-19 in the city of Rio Branco, Acre has a better QOL than the population of the city of Santo André, São Paulo when evaluated from the domains of SF-36 protocol. The dimensions with low QOL in Rio Branco, were “limitation by physical aspect” and “limitation by emotional aspect”, with an average score of 35.55 and 40.96 respectively. While the city of Santo André obtained as low QOL in the dimensions “Limitation by physical aspects”, “Vitality” and Limitation by emotional aspect” with an average score of 39.11; 44.03 and 42.99 respectively.

By carrying out a comparative analysis between the two cities, Rio Branco obtained better results in terms of QOL. Three dimensions had a statistically significant difference, all being positive with good QOL for the city of Rio Branco compared to Santo André, which were: “functional capacity”, “Pain” and “Vitality”. The other domains had no statistical difference, although in an overall score, the means were better for the state of Acre compared to the state of São Paulo.

The sociodemographic characteristics concerning sex, proportionally, participants in São Paulo have a much higher number of women than in Acre. Also at a proportional level, the age group in Santo André is much younger than the city of Rio Branco, having, for example, no participants in the age group above 65 years. In terms of education, the averages are homogeneous. A very interesting fact is about family income, as the state of Acre has a percentage of almost 50% of participants with income up to the minimum wage, while on the contrary, São Paulo has only a percentage of 6.5% in this range, showing with that, a much greater purchasing power. The body mass index of Santo André is higher, slightly above the classification recommended by the scientific literature.

SARS-CoV-2 is reaching all age groups, social classes and ethnic groups around the world, without distinction[21]. A large part of this population is recovering at home, and are often in isolation with the virus without knowing it, as it goes unnoticed[21,22]. Another specific audience, such as the elderly, pre-existing diseases have a higher risk of developing serious illnesses and even death21, including pregnant women who may also be more susceptible to COVID-19, as they are generally vulnerable to respiratory infection[23]. A large part of this population is in social isolation. This is what our research demonstrates, having two groups from different places in Brazil.

An interesting data to be analyzed in our research was the dimension “limitation by physical aspect”, where in the two analyzed states they gave a low score classified as “Low QOL”, leaving the city of Rio Branco, Acre with 35.55 and Santo André, São Paulo with 39.11. Which means that they are not taking proper care to exercise in any way, thus affecting this dimension. Corroborating these results, the dimension “Vitality” in the result for São Paulo is also found with Low quality of life, with a score of 44.03, what correlates with the first domain cited.

Well-oriented and developed physical activity can benefit the whole body, even helping to prevent diseases[24,25] and defend the body[26,27]. The social isolation caused by the COVID-19 pandemic can cause various body functions, consequently affecting possible aspects of quality of life[28]. Thus, the great importance of developing some sport, even if adapted in this isolation, can help benefit other dimensions of QOL that go hand in hand in this isolation phase, such as psychological and cognitive issues, among others[29], as well. as in the improvement in physical aspects[30].

Corroborating the studies by Li Z, et al.[31], when evaluating health professionals who were in contact with patients with Covid-19, they had great emotional problems, anguish and anxiety because they were insecure about the disease, as well as because they were in direct contact with infected patients. The emotional dimensions in both cities (Rio Branco and Santo André) had a low QOL, demonstrating the high impact that the concern with being in isolation is causing psychologically. Another factor to be taken into account with these professionals is knowing that there is still no definitive cure and little information on the subject[32].

In their study, CHEN Q, et al.[33] with a medical team, identified many professionals who demonstrated a poor general health status due to the possibility of being transmitters of the disease to other people and the lack of protective material and inefficiency against the patients. Differently, in our case, the domain “General Health Status” had a good QOL. This may be because the circumstances are averse to the hospital environment regarding social isolation.

The fear of dying, the insecurity due to the lack of a vaccine to cure the disease caused by the pandemic in Italy has caused great psychological impacts on the population34. Although our studies have provided a good QOL in both cities (Rio Branco and Santo André), in both cases the scores in the Social Aspect domains were similar, with 52.75 and 56.25 respectively, demonstrating that there is also insecurity in the population that is in social isolation on the subject.

Conversely, studies showed cases of suicide among health professionals who were infected by COVID-19 in India and Italy. In the mental health aspect of our study, the means were considered as having good QOLin both states, which demonstrates that this population is enduring the moment of social isolation in their homes. Possible psychiatric problems intensify with psychological wear, thus increasing the suicide rate[35-37].

Ornell F, et al.[36] considers that there will be changes in the daily lives of families, in their work, cultural environments, among others. Our studies demonstrate that despite the changes in daily life due to isolation, in social aspects in both states, people continue to maintain active social relationships, even if it is with other mechanisms such as lives, virtual conversations, etc. this domain was classified as good QOL.

Many areas of knowledge consider the quality-of- life component important to know how we can identify, assess, and treat the so-called silent diseases. In this phase that the world is going through, all aspects must be considered to alleviate the population's life in a moment of social isolation. In our case, Rio Branco, had a better QOL on average than the city of Santo André. Several aspects can be considered, such as housing aspects, where in Acre most of the houses are houses with land and not apartments like São Paulo. Thus, people have more mobility, which was demonstrated in the domains "functional capacity", "pain" and "vitality", where these three variables even gave significant positive differences to the State of Acre compared to the State of São Paulo. All related by aspects of larger physical spaces.

CONCLUSION

The results indicate that both cities have their QOL compromised due to social isolation. Rio Branco, had better QOL than the city of Santo André, in the domains of functional capacity, pain and vitality. Both cities showed similar results in the rest of the domains.

Author's contribuitions

Francisco Naildo Cardoso Leitão - writing the manuscript, following the guidelines of the magazine; Maura Bianca Barbary of God - Manuscript Writing; Carlos Roberto Teixeira Ferreira - data collection, experiments and manuscript writing; Ocilma Barros de Quental - data collection, carrying out the experiments and writing the manuscript; Mauro José de Deus Morais - data collection, carrying out the experiments and writing the manuscript.

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Conflicts of interest

We declare no potential conflicts of interest.

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CHAPTER 19

EPIDEMIOLOGICAL PERSPECTIVE OF THE EVOLUTION OF THE COVID-19 PANDEMIC IN AMAPÁ STATE, NORTHERN BRAZIL

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Abstract

Introduction: COVID-19 impacted health systems worldwide; the virus quickly spread in Brazil, reaching its 27 Federative units peculiarly. The northern country region recorded the lowest number of cases and accumulated deaths from the disease. However, it is a region of sizeable territorial extension and low demographic density, marked by socioeconomic inequalities and vulnerable groups, such as indigenous tribes, riverine peoples, and quilombolas. Sociodemographic factors may contribute to the dissemination of the coronavirus in this territory; thus, studies are needed to analyze the epidemiological indicators related to the pandemic. **Objective:** to evaluate incidence, mortality, and case fatality of COVID-19 trends in the state of Amapá, Brazil, from March 2020 to April 2021. **Methods:** an ecological time-series study was conducted with publicly accessible data from the Health Department of the State of Amapá. Incidence and mortality rates per 100,000 inhabitants and percentage case fatality were calculated. Crude rates were calculated by municipalities, age, and sex, per month. The Prais-Winsten regression test was performed, and the trends of monthly rates were classified as increasing, decreasing, or flat. **Results:** during the study period, there were 99.936 cases and 1,468 deaths accumulated by COVID-19 in the State of Amapá, Brazil. Macapá and Santana's cities, which have the highest demographic density and Human Development Index (HDI), had the highest number of cases and deaths. The most vulnerable population was elderly males aged 70 years or over; these individuals had the highest cumulative incidence, case fatality, and mortality rates. The second wave of the disease (October 2020 to April 2021) illustrated a more aggravating scenario, with increasing incidence and mortality rates. **Conclusion:** the COVID-19 pandemic in the state of Amapá, Brazil, is in increasing evolution, which illustrates that non-pharmacological prevention measures and acceleration of vaccination must be strengthened to avoid the development of future waves of the disease.

Keywords: COVID-19; Incidence; Case Fatality; Mortality; Amapá.

Resumo

Introdução: a COVID-19 impactou os sistemas de saúde em todo o mundo, rapidamente o vírus disseminou-se no Brasil, atingindo de modo distinto as 27 unidades Federativas do país. A região norte do Brasil registrou o menor número de casos e óbitos acumulados da doença. Entretanto, trata-se de região de grande extensão territorial e baixa densidade demográfica, marcada por desigualdades socioeconômicas, presença de população vulnerável como tribos indígenas, povos ribeirinhos e quilombolas. Os fatores sociodemográficos podem contribuir para a disseminação do coronavírus na região, assim, fazem-se necessários estudos que analisem os indicadores epidemiológicos relacionados à pandemia. **Objetivo:** avaliar as tendências da incidência, mortalidade e letalidade da COVID-19 no estado do Amapá, durante o período de março de 2020 a abril de 2021. **Método:** foi realizado um estudo ecológico de séries temporais, com dados de livre acesso, oriundos da Secretaria de Saúde do Estado do Amapá. Foi calculado a taxa de incidência e mortalidade por 100.000 habitantes e letalidade percentual. As taxas brutas foram calculadas por municípios, idade e sexo e por mês. Foi realizado o teste de regressão de Prais-Winsten, as tendências das taxas mensais foram classificadas em crescentes, decrescentes ou estacionárias. **Resultados:** houve 99,936 casos e 1,468 óbitos acumulados por COVID-19 no Estado do Amapá durante o período estudado. As cidades de Macapá e Santana, que apresentaram densidades demográficas e Índice de Desenvolvimento Humano (IDH) mais elevados, apresentaram o maior número de casos e óbitos. A população mais vulnerável foi constituída pelos idosos do sexo masculino, com idade igual ou superior a 70 anos, estes indivíduos apresentaram as maiores taxas acumuladas de incidência, letalidade e mortalidade. A segunda onda da doença (outubro de 2020 a abril de 2021) ilustrou um cenário mais agravante, com crescentes nas taxas de incidência e mortalidade. **Conclusão:** a pandemia da COVID-19 no estado do Amapá está em crescente evolução, o que ilustra que medidas de prevenção não farmacológicas e aceleração à vacinação devem ser fortalecidas para evitar o desenvolvimento de futuras ondas da doença.

Palavras-chave: COVID-19; Incidência; Letalidade; Mortalidade; Amapá.

INTRODUCTION

In February 2020, the Brazilian Ministry of Health, through Law 13.979, declared a state of public health emergency due to infection by the SARS-CoV-2[1]. Since then, COVID-19 cases have increased, and the country has suffered drastically from the pandemic attack[2]. By July 2021, Brazil exceeded 550.000 fatalities and has surpassed 19 million cases of COVID-19[3].

Before the pandemic, it was speculated that Brazil was better prepared to face situations of public calamity. One of the reasons is the solid presence of the Unified Health System (SUS - Sistema Único de Saúde), which provides free access healthcare to the population, through its primary care network, through the Family Health Strategy.

Besides that, Brazil exhibited examples of well- implemented vaccination programs in the past[4]. However, the exposure sustained by Brazil since the beginning of the pandemic of COVID-19 revealed several structural and management problems in making pandemic control decisions. Several factors influenced this, including the lack of non-pharmacological measures at the beginning of the pandemic to prevent community contagion, coupled with the lack of massive tests to diagnose infected people[5] and isolate them.

There is also evidence of a lack of beds in the Intensive Care Unit to take care of patients with high severity of COVID-19, limitations to refer patients to health centers with better infrastructure[6]. Brazil is classified as an upper-middle-income country[7]. However, its vast territorial extension shows great diversity in terms of economic development; these regional differences became more evident during the COVID-19 pandemic.

The country's areas present different scenarios; the North region has been characterized as one of the territories showing significant social inequalities and poor health services[8]. Amapá is a northern Brazilian state located in the context described above. It is noteworthy that 6.1% of its population is over 15 years old, and about 50,000 people do not read or write[9].

According to data from the National Information System on Basic Sanitation (Sistema Nacional de Informação sobre Saneamento Básico - 2019), only 38% of the population of the state capital, Macapá, has potable water supply, with the worst percentage of this indicator. There is a shortage of health workforce; for example, the number of doctors per thousand inhabitants in the state is 0.75; in comparison with the Federal District, it is 3.61, Rio de Janeiro, 3.52, and São Paulo, 2.5[10].

Under these circumstances, the pandemic of COVID-19 reached Amapá, and its first confirmed case was reported on March 20, 2020. By the end of May of the same year, the state recorded 163 cases, representing the highest infection rate in Brazil (751 per 100,000 inhabitants), followed by the already collapsed state of Amazonas, whose rate was 721 per 100.000. COVID-19 patients occupied Ninety-eight percent of the beds in the Intensive Care Unit.

The situation was so critical that patients hospitalized for suspected COVID-19 were mixed with patients with other diseases due to lack of space, increasing the risk of contagion[11]. In early August 2021, the Amapá government has registered more than 121,00 cases and 1,900 cumulative deaths from COVID-19[12]. All this complex scenario makes it necessary to monitor the indicators that determine the trends of the pandemic COVID-19 in the different regions of Brazil. Therefore, the objective of this study is to analyze the evolution of mortality, lethality, and incidence of COVID-19 in Amapá State from March 2020 to April 2021.

METHODS

Following the protocol of Abreu and Siqueira (2021)[13], a time series ecological study was conducted with information on cases and deaths of COVID-19 notified by the Department of Health of the State of Amapá, the northern region of Brazil. Inclusion criteria for the study were all cases and deaths that occurred in that state in the period from March 2020 to April 2021, which used the International Classification of Diseases, 10th edition (ICD-10), cause U07 (COVID-19, identified virus) or U07.2 (COVID 19, unidentified virus). Cases were confirmed using laboratory (molecular biology and immunology), clinical epidemiological, clinical by imaging (chest CT scan) and/ or laboratory (in asymptomatic individuals) criteria[14]. Cases were classified according to the notification date and deaths according to death; cases without this information were excluded. Data were obtained with the information available in a public access database by the Health Secretariat of the State of Amapá. The study population consisted of data on 99,936 cases and 1,468 deaths in Amapá from March 2020 to April 2021[12].

The collected data were transported to an Excel spreadsheet. Incidence rates were calculated (new cases/population) expressed as new cases per 100,000 inhabitants; mortality (deaths/population) expressed as the number of deaths per 100,000 inhabitants; and lethality (total deaths/total cases), expressed as a percentage. The estimate from the Population Projection of the Federation Units by sex and age groups: 2000-2030, was used for the calculation, considering the resident population of the state of Amapá for the year 2020, a total of 842,914 inhabitants. The resident population according to sex and age group is illustrated in the table 1[15].

Table 1: Projection of resident population of Amapá State according to sex and age range.

Age Group	Total	Male	Female
0 to 19 years	330.184	165.523	164.661
20 to 29 years	160.666	81.055	79.611
30 to 39 years	131.633	65.809	65.824
40 to 49 years	99.763	50.330	49.433
50 to 59 years	64.706	34.031	30.675
60 to 69 years	35.441	18.067	17.374
70 to 79 years	14.576	7.008	7.568
80 years and over	5.945	2.494	3.451
Total	842.914	424.317	418.597

Source: Resident population of Amapá State in the year 2020, estimate 2020- 2030[15].

The population used to calculate incidence and mortality per municipality was estimated for 2020 as described by the Brazilian Institute of Geography and Statistics[15], as illustrated in table 2.

Table 2: Projection of the resident population in the municipalities that make up Amapá State.

Municipalities	Population
Amapá	9.187
Calçoene	11.306
Cutias	6.101
Ferreira Gomes	7.967
Itaubal	5.617
Laranjal do Jari	51.362
Macapá	512.902
Mazagão	22.053
Oiapoque	27.906
Pedra Branca do Amapari	17.067
Porto Grande	22.452
Pracuúba	5.246
Santana	123.096
Serra do Navio	5.488
Tartarugalzinho	17.769
Vitória do Jari	16.254

Source: Estimate of the resident population in the municipalities of Amapá State in the year 2020[16].

The trends of incidence, mortality, and lethality indicators were conducted following the methods proposed by Antunes and Cardoso (2015)[17]. Prais-Winsten regression model was used to calculate the rates for building time series. This method allows the first-order autocorrelation corrections to be performed on the values, organized by time.

Thus, the values of the angular coefficient (β) and respective probability (p), were estimated, considering a significance level of 95% confidence interval (95% CI). The results of the log-ratios (β) of the PraisWinsten regression allowed us to estimate the Daily Percent Change (DPC), with the respective confidence intervals (CI 95%). The trends of the calculated rates were classified as increasing, decreasing, or stationary. The trend was considered stationary when the p-value was not significant, p>0.05.

RESULTS

A total of 99.936 cases (100.00%) and 1.468 deaths (100.00%) were found to have accumulated per COVID–19 in Amapá State from March 2020 to April 2021. The new cases and new deaths distributed per day are illustrated in figure 1. The number of cases and deaths and the accumulated gross incidence, mortality, and lethality rates according to the municipality, demographic density, and HDI are shown in table 3.

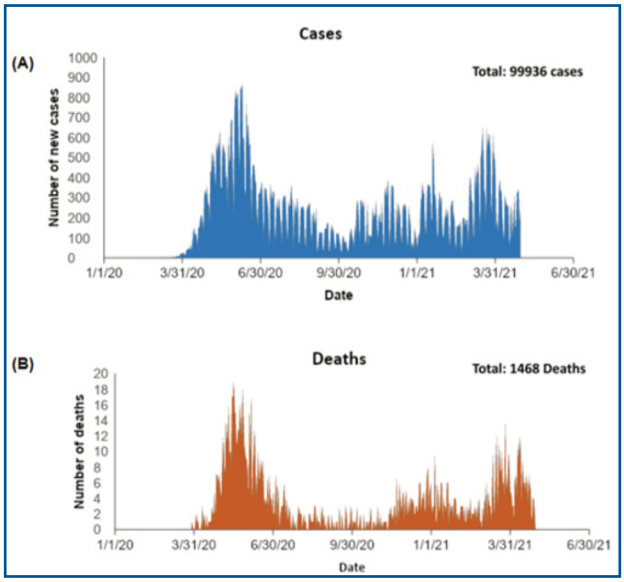

Figure 1: Number of daily cases and deaths from COVID-19 in Amapá state, from March 2020 to April 2021. Source: Cases and deaths extracted from the Amapá State Health Secretariat[18].

It was observed that cities with higher population density and HDI showed a high percentage of cases and deaths. Macapá presented 50.81% of cases and 75.14% of deaths by COVID-19, followed by Santana, which had 17.53% of patients and 8.38% of deaths (table 3). The cumulative number of cases and deaths from COVID-19 and the respective incidence rates (per 100,000 inhabitants), lethality (%), and mortality (per 100,000 inhabitants) according to age group and sex were described in table 4. Among the 99812 (100.00%) cases and 1467 (100.00%) deaths by COVID-19, information regarding sex and age is presented. It was observed that in Amapá state, in the period March 2020 to April 2021, there were 54.90% (n= 54,799) female cumulative cases and 45,10% (45013 cases) in male individuals. Moreover, the highest incidence, lethality, and mortality rates were described in males' elderly (80 years or more) (table 4).

Table 3: Distribution of cases, deaths, incidence, mortality, lethality, per municipality, according to demographic density and Human Development Index.

Municipality	Cases	Deaths	Incidence	Mortality	Lethality	Density	MHDI
	N (%)	N (%)	(Per 100.000 inhabitants)	(Per 100.000 inhabitants)	(%)	(Hab./ Km2)	
Amapá	1429 (1.43)	9 (0.61)	15554.59	97.96	0.63	0.88	0.642
Calcine	1598 (1.60)	10 (0.68)	14134.09	88.45	0.62	0.63	0.643
Cutias	781 (0.78)	5 (0.34)	12801.18	81.95	0.64	2.22	0.628
Ferreira Gomes	1309 (1.31)	5 (0.34)	16430.27	62.76	0.38	1.15	0.656
Itaubal	461 (0.46)	3 (0.20)	8207.23	53.41	0.65	2.50	0.576
Laranjal do Jari	7193 (7.20)	89 (6.06)	14004.52	173.28	1.24	1.29	0.665
Macapá	50779 (50.81)	1103 (75.14)	9900.33	215.05	2.17	62.14	0.733
Mazagão	2588 (2.59)	13 (0.89)	11735.36	58.95	0.50	1.30	0.592
Oiapoque	5028 (5.03)	35 (2.38)	18017.63	125.42	0.70	0.91	0.658
Pedra Branca do Amapari	2999 (3.00)	8 (0.55)	17571.92	46.87	0.27	1.13	0.626
Porto Grande	1436 (1.44)	20 (1.36)	6395.87	89.08	1.39	3.82	0.640
Pracuúba	295 (0.30)	6 (0.41)	5623.33	114.37	2.03	0.77	0.614
Santana	17521 (17.53)	123 (8.38)	14233.61	99.92	0.70	64.11	0.692
Serra do Navio	1099 (1.10)	5 (0.34)	20025.51	91.11	0.45	0.56	0.709
Tartarugalzinho	2010 (2.01)	13 (0.89)	11311.83	73.16	0.65	1.87	0.592
Vitória do Jari	3409 (3.41)	21 (1.43)	20973.30	129.20	0.62	5.01	0.619
Total	99935 (100.00)	1468 (100.00)	-	-	-	-	-

Dens.= Population density (Habitants/ Km2)[16]; MHDI = Municipal Human Development Index[16].

Table 4: Incidence rate (per 100,00 inhabitants), mortality (per 100,00 inhabitants), and lethality (%) of COVID-19 in Amapá State, by sex and age group.

Age group (years)	Cases		Deaths		Incidence (Per 100.000 inhabitants)		Mortality (Per 100.000 inhabitants)		Lethality (%)	
	M	F	M	F	M	F	M	F	M	F
0-19	6409	7736	2	6	3871.97	4698.14	1.21	3.64	0.03	0.08
20-29	8045	10633	18	20	9925.36	13356.19	22.21	25.12	0.22	0.19
30-39	10311	12983	51	26	15668.07	19723.81	77.50	39.50	0.49	0.20
40-49	8999	10994	113	62	17879.99	22240.20	224.52	125.42	1.25	0.56
50-59	5867	6759	169	78	17240.16	22034.23	496.61	254.28	2.88	1.15
60-69	3361	3590	210	122	18602.98	20663.06	1162.34	702.20	6.25	3.40
70-79	1435	1418	225	97	20476.60	18736.79	3210.62	1281.71	15.68	6.84
≥ 80										
586	686	167	101	23496.39	19878.30	6696.07	2926.69	28.50	14.72	
Total	45013	54799	955	512	10608.34	13091.11	225.07	122.31	2.12	0.93

Source: Cases and deaths extracted from Amapá State Health Secretariat18, N= 99812 cases; N= 1467 deaths.

The monthly distribution of cases and deaths from COVID-19 in the state of Amapá, with the respective incidence rates (per 100.000 inhabitants), percentage lethality, and mortality (per 100.000 inhabitants) are shown in the table 5. The trend analyses of incidence, lethality, and mortality rates and their respective percentages of daily change were described in table 6.

We observed that the incidence rate per 100,000 inhabitants was increasing in both periods analyzed ($p<0.05$), with percentage lethality transitioning from decreasing during the first wave to stationary during the second wave ($p>0.05$) and increased mortality rate during the second wave ($p<0.05$) (table 6).

Table 5: Number of Cases, deaths, incidence rates (per 100,000 population), lethality (%) and mortality (per 100.000 inhabitants) of COVID-19 during the period March 2020 to April 2021.

Wave	Date	Cases	Deaths	Incidence (per 100.000 inhabitants)	Mortality (per 100.000 inhabitants)	Lethality (%)
1st Wave	March	107	1	12.69	0.12	0.93
	April	3731	58	442.63	6.88	1.55
	May	14238	366	1689.14	43.42	2.57
	June	16263	209	1929.38	24.79	1.29
	July	8063	73	956.56	8.66	0.91
	August	6496	39	770.66	4.63	0.60
	September	3586	24	425.43	2.85	0.67
2nd Wave	October	4165	25	494.12	2.96	0.60
	November	5725	59	679.19	7.00	1.03
	December	5406	117	641.35	13.88	2.16
	January	8049	102	954.90	12.10	1.27
	February	4732	58	561.38	6.88	1.23
	March	12373	179	1467.88	21.23	1.45
	April	7002	158	830.69	18.74	2.26

Source: Cases and deaths extracted from the Amapá State Health Secretariat[18]. First wave: March to October 2020. Second wave: November 2020 to April 2021.

Table 6: Prais-Winsten regression estimates and percent change per day (PCD) of incidence and mortality rate per 100.000 inhabitants and lethality (%) of COVID-19 in Amapá state during the first wave (March to October 2020) and second wave (November 2020 to April 2021).

Period	DPC (CI 95%) Incidence	p	Trend Incidence	DPC (CI 95%) Lethality	p	Trend Lethality	DPC (CI 95%) Mortality	P	Trend Mortality
1st Wave	2.43 (0.76: 4.12)	0.004	Crescent	-0.33 (-0.60: -0.06)	0.016	Descending	-0.35 (-0.78: 0.08)	0.113	Stationary
2nd Wave	0.34 (0.05: 0.62)	0.022	Crescent	0.14 (-0.18: 0.47)	0.383	Descending	0.49 (0.23: 0.74)	<0.001	Crescent

Source: Cases and deaths extracted from the Amapá State Health Secretariat18. DPC – Daily Percent Change (%); CI 95% – Confidence Interval 95%; * Statistical difference detected by Prais-Winsten Regression test, $p<0.05$. First wave: March to October 2020. Second wave: November 2020 to April 2021.

DISCUSSION

COVID-19 in Amapá state from March 2020 to April 2021 spread through all state municipalities, affecting 99,936 cases and 1.468 deaths accumulated by the disease. The cities with higher population density, such as Macapá and Santana, recorded the highest number of cases and deaths. The elderly males aged 70 or more presented high vulnerability for COVID-19, registering the highest incidence, lethality, and mortality rates. Moreover, there was a characteristic formation of two waves of the disease. The second wave (October 2020 to April 2021) presented a more alarming scenario, with increasing incidence and mortality rates trends. Given the global public health emergency due to the rapid increase in the number of cases of COVID-19 and the occurrence of oligosymptomatic cases of difficult identification, SARS- CoV-2 spread worldwide. The disease reached the state of Amapá in March 2020, with the first case confirmed on the 20th, in the city of Macapá, the state capital. The patient was a 36-year-old female with a history of travel to Para State, where the patient had contact with a friend from São Paulo. Concomitantly, new cases were registered in other cities of the state[19]. Currently, the disease has impacted all cities in Amapá, with records of cases and deaths by COVID-19[18]. This study found that the cities with higher population density were the ones that presented a high percentage of cases and deaths.

The state capital, Macapá, registered 50,81% of cases and an alarming number of 75,14% of deaths from the disease, followed by Santana, which had 17,53% of cases and 8,38% of deaths. According to the scientific literature, demographic density can influence the epidemiological profile of COVID-19[20-23]. In a study that identified predictors of early until the beginning of May 2020 in municipalities in the interior of the state of São Paulo, southeastern Brazil, it was found that high population density is associated with early introduction of the disease and elevation in its incidence and mortality rates[20].

The relationship between COVID-19 and population density was also verified in counties of the United States of America (USA). Counties with higher population density had higher levels of SARS-CoV-2 transmission due to increased contact rates in these regions. Moreover, a population density limit of 22 people/ km2 was sufficient to sustain an outbreak[23].

It is noteworthy that this value is lower than that found in the current study in the Brazilian cities of Macapá (62,14 inhabitants/km2) and Santana (64,11 inhabitants/ km2), which might be associated with maintenance of the outbreak that led to the higher number of cases and deaths observed in these cities. However, the impact of population density may vary according to the region and the pandemic period. During the period of intrusion or importation of COVID-19, the initial cases of the disease were found in places that were made up of large transportation networks and their surroundings, regions where travelers and vectors of the disease were located. These transportation centers and surrounding areas did not necessarily have the highest levels of population density. However, over time, as the virus began to spread, the most populated regions were more likely to register the highest number of cases of the disease[21,22].

However, divergent results were described by Hamidi, Sabouri, Ewing (2020) in a study that evaluated the impacts of population density on viral infection rates and COVID-19 mortality rates for 913 metropolitan counties in the USA. The authors reported that population density was not related to the infection rate due to greater adherence to social distancing guidelines in these regions. Furthermore, residing in a metropolitan area was one of the most significant predictors influencing infection rates. The authors found that when considering metropolitan population, and not only population density, it was observed that the county population density was no longer related to the infection rate. It is possible that the divergences between the studies verified in the scientific literature are associated with sociodemographic factors of each region.

According to Fortaleza et al.,[20] the distance between the municipalities and the State metropolitan area represented by its Capital is inversely associated with the time of introduction of COVID-19 in the region and its incidence rate. The authors reinforce the

hypothesis that there are two patterns of geographical dissemination of the virus, one spatial (from the metropolitan area to the interior of the state) and the other hierarchical (from urban centers of regional relevance to the smaller and less connected municipalities).

Within this context, there is a need to consider sociodemographic variables for adequate planning and resource allocation to mitigate the impacts and dissemination of SARS-CoV-2[23]. Thus, it is possible to identify risk areas and intensify disease prevention strategies using non-pharmacological measures[20]. Social distancing represents one of the most promising means to prevent viral spread until the entire population is vaccinated.

However, the possibility of adopting this measure in practice is limited by population density and behavioral issues. Therefore, population density needs to be considered in the models used to estimate the spread of SARS-CoV-2[21,22]. It is evident that although, in theory, the most populated areas are those with greater chances of face-to-face interaction between individuals, making them more prone to viral infection, these places also have better access to health services and greater implementation of policies and practices of social distancing[24].

Thus, it is possible that the population has sought the most populous state regions, such as Macapá and Santana looking for a better health infrastructure. In the North of Brazil and the Northeast, there is great heterogeneity in the distribution of beds; new beds for COVID-19 were practically concentrated in the state capitals[24,25]. The state of Amapá had a 312.5% increase in the number of beds, but despite this expansion, this number is still low compared to other locations in the country. By the end of the first semester of 2020, Amapá had an average of 8,9 beds destined for COVID-19 patients per 100 thousand inhabitants, while Espírito Santo, Rio de Janeiro, Minas Gerais, and São Paulo, states of the southeastern region of the country, recorded higher indexes, with the respective numbers of COVID-19 beds per 100 thousand inhabitants: 18.8; 17.1; 16.7; e 15.6[25].

Amapá has six COVID-19 Care Centers that provide free assistance through Unified Health System (SUS) to patients affected by the pandemic. Among these Centers, three are located in Macapá with 80 beds, while 42 are offered by the Care Center located in Santana, followed by Laranjal do Jari (17 beds) and Oiapoque (2 beds). Overall, the state has available to care for patients with COVID-19, 129 adults, 17 pediatric clinical beds, and 146 adult and four pediatric ICU beds11. However, most of the beds for patients with COVID-19 are concentrated in Macapá, followed by Santana.

The current study found that the state capital had the highest notification of cases, deaths and the highest mortality and lethality rates among all municipalities. However, the incidence rates were not the highest in the region. Probably, many patients sought care in the state capital and, for fear of not being attended, they informed that they resided in this municipality. Moreover, the state capital receives patients from other cities and has a better infrastructure to care for severe disease cases.The cities of Macapá and Santana also presented the highest HDI scores of this state. It is known that HDI is an essential measure of the level of development of a municipality, for encompassing factors on income, education, and longevity conditions, but it has some limitations, such as not considering its social variations. According to the scientific literature, there are different results on the influence of HDI on the epidemiological indicators of COVID-19.

In a study that evaluated the spatial dynamics of COVID-19 and its relationship with living conditions in the state of Alagoas, northeastern Brazil, the authors highlighted that the highest incidence rates were observed in municipalities with better HDI and in those with greater social vulnerability. The high number of deaths was verified in poorer municipalities[26].

In research on the analysis of socio-spatial inequality and the impact of COVID-19 in residents of Rio de Janeiro, southeastern Brazil; it was verified that areas with higher HDI scores presented lower mortality rates when compared to areas with lower HDI[27]. However, it is known that HDI can also be related to a higher proportion of confirmed cases among the population and high lethality rates of COVID-19. In these regions, there

may also be higher concentrations of individuals with comorbidities, which is what happens in countries like Italy, France, and Spain[28]. Besides Macapá and Santana, the municipality of Laranjal do Jarí stood out, presenting the second-highest mortality rate by COVID-19 with an index of 173,28 deaths per 100.000 inhabitants. It might be that its international border with French Guiana and Suriname[29], the low technological capacity, and deficiencies in healthcare staff in the southwestern region[19] contributed to the observed results.

Besides sociodemographic factors, sex and age influenced the epidemiological indicators of incidence, mortality, and lethality. During the analyzed period, most cases (n=54.799) and the highest gross incidence rate were verified in female individuals. However, male patients had the highest number of deaths (n= 955) and the highest gross mortality (255.07 deaths per 100,000 inhabitants) and lethality (2.12%) rates. Moreover, the older people, especially male individuals aged 70 years or more, were the most vulnerable to COVID-19, presenting the highest incidence, mortality, and lethality rates. It is noteworthy that the risk of contamination by COVID-19 does not differ according to sex.

However, older adults, mainly men and patients with comorbidities have a higher risk of developing severe disease and a worse prognosis[30,31]. Men also have behaviors that negatively impact their health, such as alcoholism, smoking, poor hygiene, and resistance to seek health services and adopt public health measures[8]. On the other hand, the female population has more protective health behaviors. They have greater adherence to non- pharmacological control measures, such as hand washing, that significantly reduces the risks of contamination[32].

In this sense, the higher number of cases observed in women may reflect the higher demand for health services in search of testing for the disease. Moreover, biological variations interfere in antiviral and antiinflammatory immune responses to SARS-CoV-2 among different biological sexes and age groups[28]. The impacts of COVID-19 on the population of Amapá are still uncertain; therefore, it is essential to recognize the most vulnerable groups so that prevention policies are intensified for this specific public, besides the acceleration of vaccination in the entire population.

Furthermore, analyzing temporal variations of epidemiological indicators of this disease is also essential to prevent the formation of new outbreaks and the dissemination of new variants. In the period analyzed, the formation of two waves of the disease was observed. The first wave (March to September 2020) recorded the highest cumulative incidence rate in June 2020 (1929.38 new cases per 100.000 inhabitants), with higher mortality rates (43.42 deaths per 100.000 inhabitants) and lethality (2.57%) of COVID-19, described in May of the same year. It is noteworthy that the incidence suffers limitations arising from the number of tests performed.

The increase in mortality and lethality seen in May 2020 may have contributed to an increase in testing to detect new cases observed in the following month, thus reflecting the higher incidence rate seen in this period. At the beginning of the pandemic, Amapá did not have the autonomy to perform exams for viral confirmation, so the patients' tests were sent outside the state, and the Evandro Chagas Institute Pará[18] performed the testing. This fact may have contributed to an initial delay in detecting and isolating cases, thus favoring the dissemination of SARS- CoV-2 in the region. Later, the state started to perform the virus detection tests, and measures to increase the testing capacity were adopted.

In June 2020, the State Government signed a partnership with the Oswaldo Cruz Foundation (Fiocruz), in Rio de Janeiro and the Evandro Chagas Institute (IEC), in Belém to perform mass testing and decrease the queue, which was responsible for the increased incidence observed in June 2020. In this period, Amapá stood out as one of the states that most evaluated its population; it also presented a lethality rate with lower values than the one observed in May 2020, similar to the findings of the current study, being the lowest lethality of COVID-19 among those verified in the states of the northern region of Brazil[33].

During the second wave of the disease, considering the period from October 2020 to April 2021, the month of March stood out for concentrating the highest rates of incidence (1467.88 new cases per 100,000 inhabitants), mortality (21.23 deaths per 100.000 inhabitants), and lethality (1,45%). According to the Ministry of Health, on April 3, 2021, 130,769,607 cases of COVID-19 were reported worldwide. During this period, Brazil ranked second in the world in cumulative cases (12,953,597) and deaths (330,193) due to the disease, behind only of United States. The number of cases and deaths of COVID-19 in the country were heterogeneous among the country's different regions.

It was noteworthy that the northern region reported the highest incidence of cases and deaths of the disease[34]. The peak of cases and deaths observed in March 2021 in the state of Amapá reflects the acceleration of the pandemic in the Brazilian territory. According to the epidemiological indicators analysis of COVID-19 conducted by FIOCRUZ35, the pandemic moved to a new level, increasing the number of cases, deaths, and high permanence in the positivity of the tests. Furthermore, the country faced collapse in Health Systems, 70% of the country's Federal Units had an alert classified as critical for the occupation of hospital beds, and Amapá had an occupation rate of 100% of beds.

It is emphasized that the second wave analyzed in this study, which encompasses March 2021, presented a more aggravating profile, with incidence and mortality rates with increasing trends at the end of the analyzed period, suggesting a daily growth percentage of 0.34% and 0.49% respectively indicating that efforts are still needed to mitigate the impacts of COVID-19 in the state of Amapá. The dissemination of new SARS-CoV-2 variants in Amapá, as well as in Brazil, contributed to the scenario found.

There were found three types of coronavirus variants in viral genomic sequencing of samples from individuals from that state: P.1, P.2 (VOI), and N.9. The latter two variants are not considered an elevated risk but need attention and studies to assess their degree of transmissibility. However, the variant P1, also known as Gamma (501Y.V3), needs attention, as it has been responsible for health breakdowns in the state of Amazonas, where it was identified for the first time. Amapá identified the presence of this variant in March 2021, and it is already circulating throughout the national territory.

Currently, the country is concerned about the spread of the coronavirus delta variant, which has not yet been identified in Amapá state, Brazil, by mid-July 2021[36]. The presented scenario shows that the pandemic is not over yet and impacts Health Systems even in the most distant regions. Thus, non-pharmacological measures to control the disease, double masking and hand hygiene[35-37], must be strengthened in the entire population and maintained even after vaccination of Amapá until the spread of SARS-CoV-2 is controlled.

Studies are needed to evaluate this constantly changing pandemic scenario. Only with the development of public policies with a scientific basis can we create strategies to mitigate the impacts of the pandemic within this complex context, considering the regional variations presented in the most distinct regions of Brazil.

Limitations

The study has limitations arising from population database analysis. The data came from the Covid-19 Amapá Panel, which is subject to errors and delays in notifications. This region has technological difficulties related to internet access by municipalities in the state's interior.

CONCLUSION

There were reported 99.936 cases and 1.468 deaths by COVID-19 in Amapá State from March 2020 to April 2021. The cities with higher population density and higher HDI recorded the highest number of cases and deaths from the disease. The older males, aged 70 years or over, were the most vulnerable individuals to COVID-19. They presented higher incidence, lethality, and mortality rates. Considering the period from October 2020 to April 2021, the second wave of the disease showed a more aggravating scenario, with increasing incidence and mortality rates. For this reason, daily data are subject to revisions and updates.

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CHAPTER 20

LETHALITY AND MORTALITY OF COVID-19 IN AN IMPORTANTE INDUSTRIAL CENTER IN LATIN AMERICA, REGION OF GRANDE ABC, SÃO PAULO, BRAZIL

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Abstract

Introduction: the new coronavirus (COVID-19) disease has been causing economic and health system impacts worldwide, triggering humanitarian crises in vulnerable regions, marked by high mortality rates of the disease. Brazil has been suffering an increase in the number of cases, characteristic of the formation of a second wave, with great epidemiological differences observed in the most diverse regions of the country. Many studies illustrate the behaviour of COVID-19 in the state of São Paulo, but there are gaps in the scientific literature on the epidemiology of COVID-19 in municipalities of the São Paulo metropolitan region that constitute an important industrial pole in Latin America, such as the region of Grande ABC. **Objective:** to evaluate mortality and lethality trends of COVID-19 during the period March 2020 to July 2021, in municipalities on region of Grande ABC, metropolitan region of São Paulo, Brazil, divided into two periods (March to November 2020 and December to July 2021). **Methods:** we conducted an ecological time series study with population data from the Brazilian Ministry of Health. We collected the number of cases and deaths confirmed for COVID-19 in the municipalities that make up the region of Grande ABC (Diadema, Mauá, Rio Grande da Serra, Ribeirão Pires, Santo André, São Bernardo do Campo, and São Caetano do Sul) from March 2020 to July 2021. Prais-Winsten linear regression was performed, and the percentage of daily change was calculated. Differences were considered significant when $p<0.05$. **Results:** in region of Grande ABC, in the period analysed, 217,264 cases and 10,004 deaths of COVID-19 were recorded. Although the mortality rate remained stationary during the first wave (March to November 2020) and the second wave (December 2020 to July 2021); lethality transitioned from decreasing during the first wave to increasing during the second wave, with rates varying according to municipality. **Conclusion:** trend analyses in incidence, mortality, and lethality rates assist in understanding the behaviour of the COVID-19 Pandemic in the region known as Grande ABC. Efforts must be maintained throughout the region to control the Pandemic.

Keywords: COVID-19; Lethality; Mortality; Trend.

Resumo

Introdução: a doença do novo coronavírus (COVID-19) vem ocasionando impactos econômicos e nos sistemas de saúde mundiais, desencadeando crises humanitárias em regiões vulneráveis, marcadas por elevadas taxas de mortalidade da doença. O Brasil vem sofrendo por um aumento no número de casos, característicos da formação de uma segunda onda, com grandes diferenças epidemiológicas observadas nas mais diversas regiões do país. Muitos estudos ilustram o comportamento da COVID-19 no estado de São Paulo, mas há lacunas na literatura científica sobre a epidemiologia da COVID-19 em municípios da região metropolitana de São Paulo que constituem importante polo industrial da América latina, como por exemplo a região do Grande ABC. **Objetivo:** avaliar as tendências de mortalidade e letalidade da COVID-19 durante o período de março de 2020 a julho de 2021, em municípios do Grande ABC, região metropolitana de São Paulo, Brasil, dividindo em dois períodos (março a novembro de 2020 a dezembro a julho de 2021). **Método:** foi realizado um estudo ecológico de series temporais com dados populacionais oriundo do Ministério da Saúde do Brasil. Foram coletados o número de casos e óbitos confirmados para COVID-19 nos municípios que compõe a região do Grande ABC (Diadema, Mauá, Rio Grande da Serra, Ribeirão Pires, Santo André, São Bernardo do Campo e São Caetano do Sul) no período de março de 2020 a julho de 2021. Foi realizado a regressão linear de Prais-Winsten, e calculado o percentual de mudança diária. Foram consideradas diferenças significativas, quando $p<0,05$. **Resultados:** na região do Grande ABC, no período analisado, foram registrados 217.264 casos e 10.004 óbitos de COVID-19. Apesar da taxa de mortalidade ter se mantido estacionária durante a primeira onda (março a novembro de 2020) e a segunda onda (dezembro de 2020 a julho de 2021); a letalidade transitou de decrescente durante a primeira onda para crescente durante a segunda onda, com índices variando segundo o município. **Conclusão:** as análises de tendência nas taxas de incidência, mortalidade e letalidade auxiliam na compreensão do comportamento da Pandemia da COVID-19 na região conhecida como Grande ABC. Esforços devem ser mantidos em toda à região para o controle da Pandemia.

Palavras-chave: COVID-19; Letalidade; Mortalidade; Tendência.

INTRODUCTION

The Coronavirus Disease (2019) (COVID-19) is an urgent Public Health Problem, which even after the World Health Organization declared on March 11, 2020, the disease as a Pandemic and instigated global efforts to contain the spread of the SARS-CoV-2[1] virus, its impacts are still directly affecting political, social, and economic structures of countries[2].

COVID-19 brought to light a scenario of a world that is beset by many crises and in need of effective changes. Its arrival in Latin America highlighted a region with weaknesses in public sectors (such as health, science, and education), in addition to scarce investments in public policies, significant fiscal austerity, fragile ties between official regional institutions, weaknesses in the instruments of national and regional government systems, which were already suffering the impact of weaknesses in global governance mechanisms[3]. In addition, political instability, corruption, social unrest, fragile health systems and socio-economic inequalities contributed to the fact that the Pandemic COVID-19, which began as a health crisis, is now, for Latin American countries, a humanitarian crisis, marked by one of the highest mortality rates in the world[4].

Approximately 130 million cases of COVID-19 were registered in the world until the beginning of April 2021, with most cases concentrated in the Americas, with evidence for Latin American countries, especially Brazil, which leads the rank in number of cases in the region[5]. In that period, the Ministry of Health of the country recorded about 13 million cases of the disease; the southeast region, especially the state of São Paulo the most affected place[6].

It is noteworthy that Brazil has been facing the biggest hospital and health crisis in its history, with accumulated death records of more than 300,000 victims of the disease and records of daily deaths that reflect the lack of control of the pandemic in the country. Among the 26 states and the Federal District, 20 regions are with high lethality and mortality rates, which make large percentages of global deaths by the disease[7].

The region continues to break records for the wrong reasons, while it has experienced the deadliest episode faced since the beginning of the pandemic, due to the dissemination of new variants[8,9]. These, resulting from genetic mutations, may be responsible for the increase in the number of cases and the emergence of new waves of the disease[10]. This is a worrisome fact, since this second wave was even more lethal because the Brazilian population was already tired of the virus and lacked, for the most part, minimum educational and health measures[7].

Despite the efforts and advances to minimize possible impacts of the pandemic, little is known about the spatial-temporal patterns of COVID-19, especially in urban spaces of highly affected regions, such as the metropolitan region of São Paulo[11].

It is noteworthy that many studies evaluate epidemiological patterns of the municipality of São Paulo, or the state. However, there are information gaps on the epidemiology of COVID-19 in important metropolitan regions, such as the region known as the Grande ABC.

The region of Grande ABC, located in the state of São Paulo, is a widely known region due to its socioeconomic importance. Its industrial park constitutes the largest industrial agglomeration in Latin America, with a focus on the automotive sector, in addition to petrochemical potential, with upstream (the Capuava Refinery) and downstream (the chemical, plastics segments and some others) ramifications[12].

Thus, there is an emerging need for regional studies to address the epidemiology of COVID-19 in the municipalities that make up the region of Grande ABC, highlighting the first and second waves of the Pandemic. Therefore, the objective of this study was to evaluate the mortality and lethality trends of COVID-19 during the period from March 2020 to July 2021, in municipalities of region of Grande ABC, metropolitan region of São Paulo, Brazil, dividing it into two periods (1st Wave and 2nd Wave).

METHODS

The protocol developed by Abreu, Elmusharaf and Siqueira (2021)[13] was the base to conduct this ecological study of population-based time series of public access with information on cases of COVID-19 in the region of Grande ABC.

This region consists of the municipalities of Diadema (423,884 inhabitants), Mauá (472,912 inhabitants), Rio Grande da Serra (50,846 inhabitants), Ribeirão Pires (123,393 inhabitants), Santo André (718,773 inhabitants), São Bernardo do Campo (838,936 inhabitants), and São Caetano do Sul (161,127 inhabitants), constituting a total population of 2,789,871 inhabitants. The population of each city was described based on data from the Ministry of Health, that considered the resident population used by the Federal Audit Court (TCU), according to estimates of 2019[6].

The municipalities that make up the region of Grande ABC were characterized according to the analysis of the socioeconomic profile, using the Índice Paulista de Resposabilidade Social (Paulista Index of Social Responsibility/IPRS), which was thought to measure the degree of human development in the state of São Paulo. This index uses indicators of longevity, education, and wealth of a municipality, characterizing and allocating them into 5 distinct groups (Dynamic, Unequal, Equitable, In Transition, and Vulnerable)[14].

The municipalities of region of Grande ABC presented a total of 217,264 cases and 10,004 deaths by COVID-19, notified during the period from March 2020 to July 2021. The new cases and new deaths were classified according to the location and date of disease notification.

The information was collected in August 2021. All notification of cases and deaths that referred to COVID-19 were included, using the International Classification of Diseases, 10th edition (ICD-10) of “U07.1 COVID-19, identified virus” or “U07.2 COVID-19, unidentified virus”, associated with the diagnosis of the disease, by laboratory and/or clinical-epidemiological confirmation[15].

The data were extracted in a panel created by the Brazilian Ministry of Health, which was developed to be the official vehicle of communication on the epidemiological situation of COVID-19 in the country. This system uses the number of cases and deaths recorded by the Municipal and State Health Secretariats in that period and is updated daily[6].

The collected data were distributed in Excel spreadsheet, illustrated in figures and tables.

Effective reproductive numbers (Rt) were calculated using the R studio software package EpiEstim version 2.2.416, Effective reproductive number (Rt) were calculated using the R studio software package EpiEstim version17. A mean serial interval of 2.97 days with a mean standard deviation of 3.29 days was used, as described in previous studies[18,19], and in a window of 7 days.

Incidence rates were calculated (new cases/population) expressed as new cases per 100,000 inhabitants; mortality (deaths/population) expressed as number of deaths per 100,000 inhabitants, and lethality (total deaths/total cases), expressed as a percentage.

For the trend analyses, the period was divided into first wave (March to November 2020) and second wave (December 2020 to July 2021); to define the period, the month with the lowest mortality rate was considered, which suggested the end of the first wave in the curve.

The incidence, mortality and lethality rate trend analyses were performed using the methods proposed by Antunes and Cardoso (2015)[20].

The Prais-Winsten regression model was used to calculate the time series construction rates. This method allows the first order autocorrelation corrections to be performed on the values, organized by time.

Thus, the values of the angular coefficient (β) and respective probability (p) were estimated, considering the significance level of 95% confidence interval (CI 95%). The data modeling process included the transformation rates (dependent variable = Y value) in a logarithmic function of base 10. The independent variable (X value) was the months of the historical series.

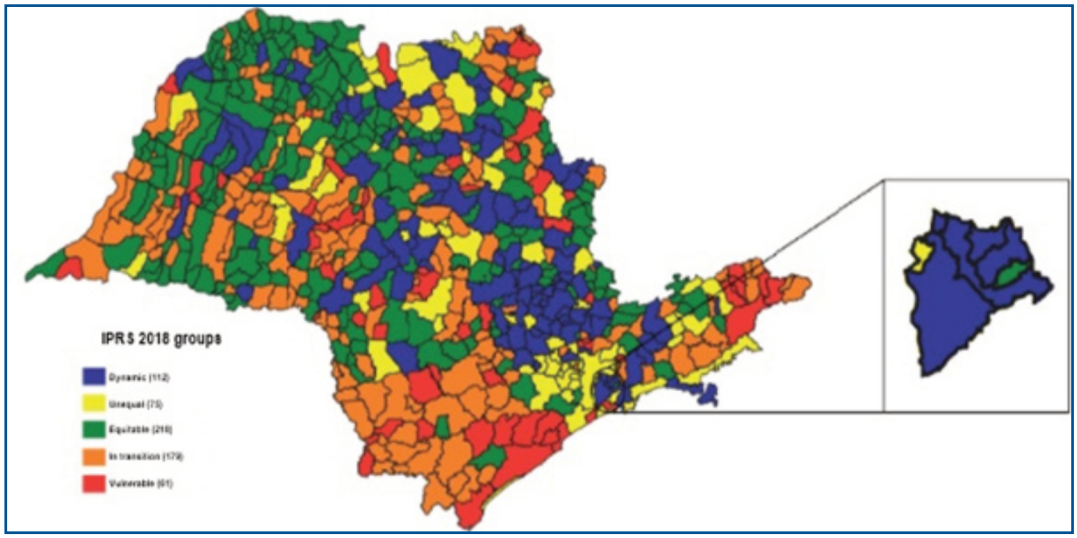
The results of the log rates (β) of the Prais-Winsten regression allowed us to estimate the Daily Percent Change (DPC) in each region, with the respective confidence intervals (95% CI).

This procedure made it possible to determine the rates as increasing, decreasing, or stationary and to quantify the percentage variation in daily incidence, mortality, and lethality rates. The trend was considered stationary when the coefficient was not significantly different from zero ($p>0.05$).

Statistical analyzes were performed using the STATA 14.0 software (College Station, TX, U.S. 2013).

RESULTS

The socio-demographic analysis of the component municipalities of the Grande ABC region, via IPRS, illustrated that the municipalities of Mauá, São Bernardo do Campo, São Caetano do Sul and Santo André presented the highest level of IPRS (Dynamic level), while, Diadema is at the Unequal level and Rio Grande da Serra presented the lowest index (equitable level) among the municipalities (figure 1).



Local	Wealth	Longevity	Schooling	IPRS
Diadema	42	66	56	Unequal
Mauá	40	74	57	Dynamic
Ribeirão Pires	41	77	66	Dynamic
Rio Grande da Serra	37	74	58	Equitable
São Bernardo do Campo	47	76	60	Dynamic
São Caetano do Sul	53	77	82	Dynamic
Santo André	45	75	58	Dynamic

Figure 1: Municipalities in the State of São Paulo, according to groups in the São Paulo Social.
Responsibility Index (IPRS), with emphasis on the region of Grande ABC Source: Fundação Seade. Paulista Social Responsibility Index - IPRS, 2019 (adapted)13. RPS - Paulista Index of Social Responsibility, Wealth - 15 to 62, Longevity - 43 to 94, Schooling - 30 to 94. Dynamic - High Wealth, Longevity and Medium or High Schooling. Equitable – Low Wealth, Longevity and Medium or High Schooling. Unequal - High wealth, low longevity and medium or high schooling or medium or high longevity and low schooling.

There were 217,264 cases (100.00%) by COVID-19 in the region of Grande ABC in the period from March 2020 to July 2021, and 10,004 cases evolved to death. Among the cities that constitute the region it was São Bernardo do Campo that presented the highest number of cases (32.90%) and deaths (31.06%), followed by the city of Santo André with 61,568 cases (28.34%) and 2,905 (29.04%) deaths; the city of Rio Grande da Serra constituted only 0.96% of the cases of COVID-19 in the region and 0.81% of the deaths.

The reproductive number effect (Rt) during the analysis period (March 28, 2020, to July 31, 2021) in the region of Grande ABC of São Paulo started at values close to 1.6 in early April and remained similar until July 2020 with a predominance of Rt greater than 1, followed by a reduction in transmissibility in August 2020. However, in early November 2020, there was a high peak in transmissibility, reaching values of Rt of approximately 2.8 (the highest value observed in the analyzed period). After this period, Rt values were maintained below 1.4 until July 2021.

Table 1: Number of cases, recovered cases, and deaths by COVID-19, in metropolitan region of the State of São Paulo, Grande ABC, in the period March 2020 to July 2021.

Grande ABC Region	Cases		Deaths	
	N	%	N	%
Santo André	61,568	28.34	2,905	29.04
São Caetano do Sul	18,405	8.47	862	8.62
São Bernardo do Campo	71,481	32.90	3,107	31.06
Diadema	25,139	11.57	1,256	12.55
Mauá	30,198	13.9	1,459	14.58
Ribeirão Pires	8,377	3.86	334	3.34
Rio Grande da Serra	2,096	0.96	81	0.81
Total	217,264	100.00	10,004	100.00

Source: Cases and deaths extracted from the Ministry of Health

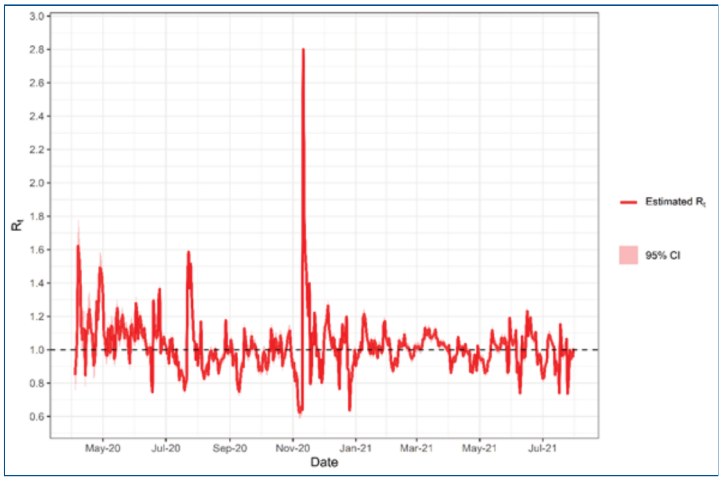


Figure 2: estimated Rt. during the period March 28, 2020 to July 31, 2021
CI = Confidence Interval.

The temporal distribution of the incidence rate of COVID-19 in the analyzed period was illustrated in figure 3.

It was observed that the municipality of São Caetano do Sul presented the highest incidence rates of the disease, except in June and July, with a maximum peak registered in March 2021, with a rate of 1,387.72 cases per 100 thousand inhabitants.

At the end of the period analyzed (July 2021), the lowest incidence rates were presented by the municipalities of Rio Grande da Serra (171.09 cases per 100,000 inhabitants) and Diadema (270.18 cases per 100,000 inhabitants) (figure 3).

The analyses of the trends of the incidence of COVID-19 in the region of Grande ABC were evidenced in table 2.

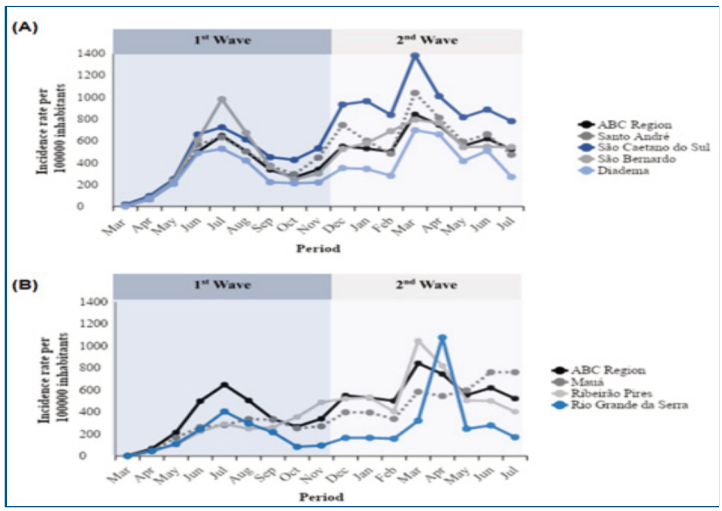


Figure 3: Incidence rate per 100 thousand inhabitants of COVID-19, in the period from March 2020 to July 2021, in cities of the metropolitan region of São Paulo (ABC Region) and the contribution of each component municipality (A) Santo André, São Bernardo, São Caetano do Sul, Diadema, (B) Mauá, Ribeirão Pires, Rio Grande da Serra in their outcomes.

It was found that the incidence of the disease in the region of Grande ABC showed increasing trends in the period from March 2020 to November 2020 (First Wave), $p<0.05$, and stationary trends during the second wave, considering the period from December to July 2021 ($p>0.05$). The municipalities of Mauá, Ribeirão Pires, São Bernardo do Campo, São Caetano do Sul, and Santo André also presented increasing trend of incidence rate at the end of the first wave ($p<0.05$). While, during a possible second wave, in the period from December to July 2021, only Mauá presented incidence rate with increasing trend, with daily increase of 0.23%, $p<0.05$ (table 2).

The mortality rates of the region of Grande ABC and its component municipalities were described in figure 4.

Table 2: Prais-Winsten regression estimates and Daily Percent Change (DPC) of incidence rates per 100,000,000 inhabitants of COVID-19 in São Paulo Metropolitan Region (region of Grande ABC) in the period March 2020 to July 2021.

Local	DPC (95% CI) Incidence	p	Incidence Trend	Period
ABC Region	0.59 (0.21 : 0.97)	0.002	Crescent	1st Wave
Santo André	0.68 (0.34 : 1.02)	<0.001	Crescent	
São Bernardo do Campo	0.46 (0.04 : 0.89)	0.034	Crescent	
São Caetano do Sul	0.47 (0.14 : 0.80)	0.005	Crescent	
Diadema	0.22 (-0.14 : 0.57)	0.227	Stationary	
Mauá	0.65 (0.36 : 0.95)	<0.001	Crescent	
Ribeirão Pires	0.59 (0.32 : 0.85)	<0.001	Crescent	
Rio Grande da Serra	-0.07 (-0.33 : 0.19)	0.593	Stationary	
ABC Region	0.04 (-0.14 : 0.22)	0.671	Stationary	2nd Wave
Santo André	-0.10 (-0.28 : 0.08)	0.272	Stationary	
São Bernardo do Campo	0.04 (-0.15 : 0.23)	0.680	Stationary	
São Caetano do Sul	0.04 (-0.23 : 0.31)	0.772	Stationary	
Diadema	0.13 (-0.12 : 0.38)	0.306	Stationary	
Mauá	0.23 (0.03 : 0.42)	0.021	Crescent	
Ribeirão Pires	-0.08 (-0.32 : 0.17)	0.545	Stationary	
Rio Grande da Serra	0.19 (-0.08 : 0.46)	0.165	Stationary	

DPC – Daily Percent Change (%); CI 95% – Confidence Interval 95%; p – p value: probability of statistical significance, * Means statistical difference - Prais-Winsten regression test, p <0.05. Source: Cases, deaths extracted from the Ministry of Health.

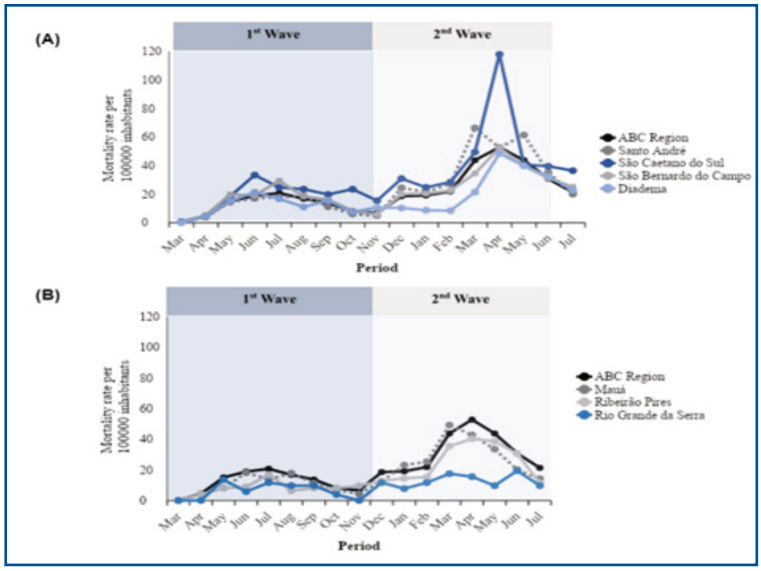


Figure 4: Comparison of mortality rate (per 100 thousand inhabitants) of COVID- 19, in the period March 2020 to July 2021, among cities of the Metropolitan Region of São Paulo (Region of Grande ABC) and the contribution of each component municipality (A) Santo André, São Bernardo, São Caetano do Sul, Diadema, (B) Mauá, Ribeirão Pires, Rio Grande da Serra in their outcomes.

The highest mortality rate for the region of Grande ABC was verified in April 2021, with records of 52.78 deaths per 100,000 inhabitants; it should be noted that in this same period, the municipalities of São Caetano do Sul, followed by Santo André and São Bernardo do Campo presented mortality rates higher than those presented by the region of Grande ABC, with the respective values: 117.93, 52.54 and 52.46 deaths per 100,000 inhabitants (figure 4).

The Prais-Wisten Regression estimates of the mortality rate were illustrated in table 3.

It was verified that there were stationary trends for mortality rates for the region of Grande ABC and its municipalities during the first wave (March to October 2020) ($p>0.05$). But, during a possible second wave, it was highlighted that the Municipality of Diadema showed an increasing trend in mortality ($p<0.05$) and daily growth rate of 0.45% (table 3).

The lethality rate of COVID-19 in the region of Grande ABC and constituent municipalities were described in figure 5.

Table 3: Prais-Winsten regression estimates and Daily Percent Change (DPC) of mortality rates (per 100 thousand inhabitants) of COVID-19 in São Paulo Metropolitan Region (Region of Grande ABC) in the period March 2020 to July 2021.

Local	DPC (95% CI) Mortality	p	Mortality Trends	Period
ABC Region	0.22 (-0.10 : 0.54)	0.178	Stationary	1st Wave
Santo André	0.04 (-0.24 : 0.33)	0.759	Stationary	
São Bernardo do Campo	0.08 (-0.18 : 0.34)	0.555	Stationary	
São Caetano do Sul	0.10 (-0.16 : 0.36)	0.452	Stationary	
Diadema	-0.05 (-0.31 : 0.20)	0.675	Stationary	
Mauá	-0.08 (-0.33 : 0.18)	0.543	Stationary	
Ribeirão Pires	-0.05 (-0.26 : 0.15)	0.602	Stationary	
Rio Grande da Serra	0.00 (-0.13 : 0.13)	0.988	Stationary	
ABC Region	0.24 (-0.07 : 0.55)	0.134	Stationary	2nd Wave
Santo André	0.23 (-0.11 : 0.56)	0.184	Stationary	
São Bernardo do Campo	0.10 (-0.16 : 0.36)	0.452	Stationary	
São Caetano do Sul	0.04 (-0.24 : 0.33)	0.759	Stationary	
Diadema	0.45 (0.18 : 0.71)	0.001	Crescent	
Mauá	0.04 (-0.24 : 0.32)	0.771	Stationary	
Ribeirão Pires	0.27 (-0.01 : 0.55)	0.057	Stationary	
Rio Grande da Serra	0.06 (-0.15 : 0.28)	0.564	Stationary	

DPC – Daily Percent Change (%); CI 95% 95% Confidence Interval; p - p value: probability of statistical significance, * Means statistical difference - Prais-Winsten regression test, $p <0.05$. Cases, deaths and population extracted from the Ministry of Health.

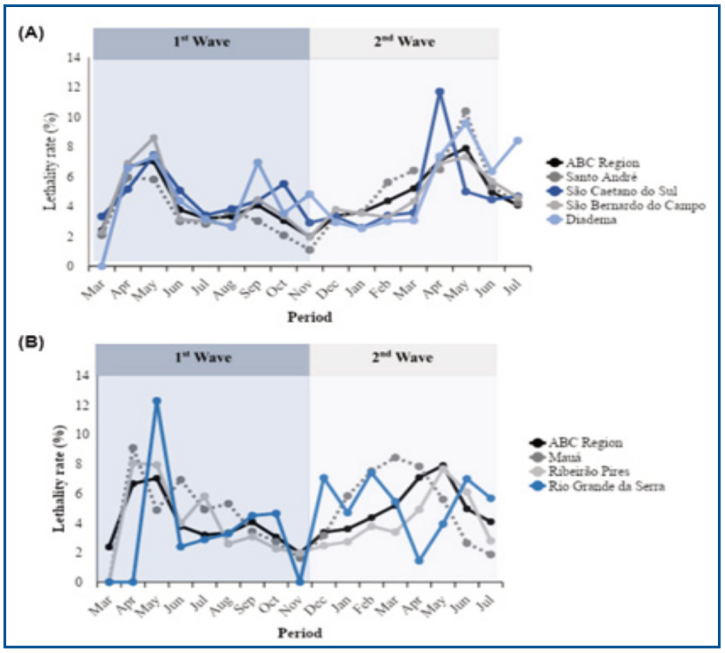


Figure 5: Comparison of the lethality rate (%) of COVID-19, in the period from March 2020 to July 2021, among cities of the metropolitan region of São Paulo (ABC region) and the contribution of each component municipality (A) Santo André, São Caetano do Sul, São Bernardo do Campo, Diadema, (B) Mauá, Ribeirão Pires, Rio Grande da Serra, in their outcomes.

It was observed that the highest lethality percentage for the region of Grande ABC was in May 2021 (7.90%). In this same period, the city of Santo André had the highest lethality (10.39%) by COVID-19 among all analyzed regions. The end of the 1st wave (month of November 2020) illustrated lower lethality percentages for the region of Grande ABC and most of the studied municipalities, being respectively: ABC - 1.97%, Santo André - 1.09%, São Bernardo do Campo - 1.93%, Mauá - 1.63%, Ribeirão Pires - 1.98 and Rio Grande da Serra - 0.00% (figure 5), trends in lethality rates are illustrated in table 4.

The first wave of COVID-19 (March 2020 to November 2020) was marked by decreasing trend of the lethality percentage, and a negative daily variation percentage for the region of Grande ABC and its component municipalities ($p<0.05$), except for Diadema and Rio Grande da Serra, that presented stationary trend ($p<0.05$). During the second wave, Santo André and Diadema showed an increasing trend of lethality of COVID-19 ($p<0.05$), while the other municipalities studied showed lethality with stationary trends during the second wave ($p> 0.05$) (table 4).

Table 4: Prais-Winsten regression estimates and the Dialy Percent Change (DPC) of lethality (%) of COVID-19, in São Paulo Metropolitan Region (ABC Region) in the period March 2020 to July 2021.

Local	DPC (95% CI) Lethality	p	Lethality Trend	Period
ABC Region	-0.50 (-0.69 : -0.30)	<0.001	Descending	1st Wave
Santo André	-0.78 (-1.07 : -0.49)	<0.001	Descending	
São Bernardo do Campo	-0.60 (-0.93 : -0.27)	<0.001	Descending	
São Caetano do Sul	-0.52 (-0.93 : -0.11)	0.013	Descending	
Diadema	-0.21 (-0.57 : 0.15)	0.253	Stationary	
Mauá	-0.49 (-0.80 : -0.19)	0.002	Descending	
Ribeirão Pires	-0.64 (-1.04 : -0.24)	0.002	Descending	
Rio Grande da Serra	-0.57 (-1.47 : 0.34)	0.207	Stationary	
ABC Region	0.22 (0.00 : 0.44)	0.046	Crescent	2nd Wave
Santo André	0.35 (0.03 : 0.67)	0.034	Crescent	
São Bernardo do Campo	0.25 (-0.01 : 0.52)	0.064	Stationary	
São Caetano do Sul	0.18 (-0.18 : 0.54)	0.318	Stationary	
Diadema	0.42 (0.17 : 0.67)	0.001	Crescent	
Mauá	-0.23 (-0.52 : 0.06)	0.115	Stationary	
Ribeirão Pires	0.32 (-0.05 : 0.70)	0.091	Stationary	
Rio Grande da Serra	-0.19 (-0.79 : 0,41)	0.527	Stationary	

DPC – Dialy Percent Change (%); CI 95% – Confidence Interval 95%; p - p value: probability of statistical significance, *Means statistical difference - Prais-Winsten regression test, p<0.05. Source: Cases, Deaths and Population extracted from the Ministry of Health.

DISCUSSION

The trend analyses of incidence, mortality and lethality rates in the studied municipalities help in understanding the behavior of the COVID-19 pandemic in the region of Grande ABC. Although the incidence rate in this region went from increasing (1st wave - March to November 2020) to stationary (2nd wave - December 2020 to July 2021), the mortality rate remained stationary, while the lethality rate went from decreasing in the first wave to increasing in the second wave, with rates varying according to the period and municipality.

It is noteworthy that the incidence rate is a fundamental concept in the epidemiology of infectious diseases, since it describes the frequency of new cases of the disease in each period. However, this index suffers direct limitations due to the number of tests for infection detection[21]. Thus, it is possible that the stationary trends of new cases of COVID-19 observed for Diadema and Rio Grande da Serra, during the first wave, and for the region of Grande ABC and its component municipalities (except Mauá) during the second wave, are a reflection that the percentage of testing of cases did not follow the actual increase in the incidence of the disease.

It is noteworthy that, during the period studied, the state of São Paulo was enacting the emergency phase of the pandemic, with the adoption of harsh restrictive measures to curb the increase in the number of new cases, hospitalizations, and deaths by COVID-19 and to contain the overload of hospital beds observed throughout the state[22].

Although efforts are being made to contain the spread of SARS-CoV-2 infections in São Paulo, differences in mortality rates from the disease among regions are observed. Therefore, it is essential that geographic triages are performed in different locations, so that this information can guide intervention strategies aimed to promote the reduction of the pandemic in the metropolitan region of São Paulo[8].

In this study, it was observed that the municipalities of the metropolitan region of São Paulo, which constitute Grande ABC, presented stationary mortality during the first and second waves, except for the municipality of Diadema, which presented an increasing trend in the mortality rate by COVID-19. However, it was highlighted that the lethality of the disease suffered significant variations in the periods evaluated according to the period and municipality.

It was found that the municipalities of Ribeirão Pires, São Bernardo do Campo, São Caetano do Sul and Mauá went from a lethality rate that presented decreasing trends in the first wave (March to November 2020), to stationary in the second wave (December 2020 to July 2021); while the municipality Rio Grande da Serra remained with the lethality with stationary trend in both periods. Moreover, the municipalities of Santo André and Diadema were the only places where the lethality rate of COVID-19 presented increasing trends at the end of the second wave, illustrating a more alarming scenario.

In this context presented, there is a need for future monitoring throughout the ABC region, especially in the municipalities of Santo André and Diadema, which showed lethality rates indicating daily increase even after the pandemic year. It is possible that during the second wave, the viral action has triggered in these places a more lethal scenario of the disease. Moreover, in regions where the lethality rate remained stationary at the end of the period studied, efforts should also be intensified to reduce the dissemination and aggravations of the disease caused by the new coronavirus.

It is noteworthy that the evolution of the pandemic can trigger greater impacts in places of São Paulo with worse socioeconomic conditions[8], that is, with higher rates of social vulnerability, corroborating the results of the current study. It was found that the two municipalities of the ABC Region that presented different IRPS indices, which were the municipalities of Diadema and Rio Grande da Serra, which had indices classified as unequal (high wealth, low longevity and medium/high education or low education and medium/high longevity) and equitable (Unequal - Low Wealth, Longevity and Medium or High Education), were the only municipalities that, during the first wave, the trends of incidence and lethality remained stationary. It is possible that the socioeconomic conditions of these cities reflected in some deficit in the number of testings for the disease and even in the quality of care provided by the Health services.

Studies still show the need for control of the pandemic of COVID-19 in regions of the state of São Paulo[22,23]. Similarly, in the region of Grande ABC, even after more than a year of the pandemic, there were periods when the Rt indices showed high transmissibility, suggesting that the pandemic was out of control. These results corroborate the Rt values verified for the state of São Paulo, it is known that at the beginning of April 2021, this state had the Rt for the disease equal to 1.1 (CI: 0.93 - 1.2), with expected changes in daily cases probably increasing[24].

It is emphasized that measures adopted in metropolitan regions of that state, such as social distancing and improvement of testing protocols, use of masks and standard health safety, can decrease the effective reproduction rate of COVID-19. However, this scenario suffers variations throughout regions and period and may not be enough to contain the epidemic[23].

Given the oscillation in health indicators, mainly due to the growing tendencies in the lethality of the COVID-19 verified during the second wave for the ABC region, with daily growth rates of 0.22%, it is emphasized the importance of the precepts of health promotion in search of the reorientation of hygiene practices, after all, the current situation experienced by the population demands an agile and preventive posture25. Moreover, it is necessary that investments be directed to the development of vaccines and, especially, to the weak health systems that suffer the impacts of the onus arising from the pandemic. After all, this health crisis cannot be defeated without robust national health systems; however, these are the places that have received the least political attention or funding[13,26].

Although our spatial analysis is subject to methodological limitations arising from ecological studies and secondary database analysis, such as delays in notifications or underreporting of cases of the disease, the results contribute to a better understanding

of the evolution of the disease in the metropolitan region of São Paulo, a region that has been facing numerous challenges in the face of a disease that undergoes daily changes in its health indicators. The analyses illustrate the beginning of a second wave faced by the population of the region, so it is essential to remember that the Pandemic is not over, thus, it is necessary the constant analysis of epidemiological data to update and monitor the COVID-19 in all regions of Brazil.

CONCLUSION

The trend analysis of important health indicators that are associated with disease severity revealed that there was no decrease in mortality and lethality of COVID-19 in the region of Grande ABC, even after one year of the pandemic. Mortality maintained a stationary trend in the first and second wave of the pandemic in this region, while the lethality changed from decreasing trends in the initial period to increasing in the second wave.

It was highlighted that during the second wave of COVID-19 only the municipality of Diadema presented increasing tendencies in mortality, evidencing a daily increase rate of 0.45%. Diadema also presented increasing tendencies in lethality during the second wave, as well as the municipality of Santo André.

These results together are important indicators for monitoring the behavior of the Pandemic in the ABC Region and its component municipalities, although this scenario is constantly changing. Thus, it is emphasized that efforts remain necessary to contain the spread of the disease in all municipalities analyzed until the disease does not represent a threat to Public Health, for which the data presented in this paper can be useful.

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CHAPTER 21

EVOLUTION OF MORTALITY AND LETHALITY DUE TO COVID-19 IN THE STATE OF RORAIMA, BRAZIL, FROM MARCH 2020 TO JULY 2021

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Abstract

Introduction: the context of the Covid-19 pandemic in the Brazilian North region is worrying. There is a lack of resources for Public Health, a low human development index, and poverty indicators above the national average. **Objective:** to analyze mortality and lethality from COVID-19 in the State of Roraima, Brazil. **Methods:** this is an ecological time-series study of secondary data on COVID-19 in Roraima, Northern Brazil, from March 2020 to July 2021. The incidence, mortality, and lethality rates due to COVID-19 were calculated. The Prais-Winsten regression model was used to calculate the time series trends. Trends were classified as increasing, decreasing, or stationary. The trend was considered static when the p-value was not significant ($p>0.05$). **Results:** in the state of Roraima, from March 2020 to July 2021, there were 123,125 cases and 1,903 accumulated deaths due to COVID-19. The first wave (March 2020 to October 2021) of COVID-19 recorded the incidence rate (2,995.30 new cases per 100,000 inhabitants - July 2020) and mortality (56.32 deaths per 100,000 inhabitants - June 2020) higher lethality. However, in the second wave (November 2020 to July 2021), the highest lethality rate was observed (3.47% - February 2021). It was observed that during the first wave, the incidence rate of COVID-19 showed increasing trends. During this period, the mortality rate had a stationary tendency ($p>0.05$) and the percentage lethality with a decreasing trend ($p<0.05$). During the second wave, there was a more aggravating scenario for lethality, which changed from a daily reduction rate of 0.90% to stationary trends. **Conclusion:** the pandemic in the state of Roraima is not yet under control, so it is necessary to strengthen strategies to mitigate the spread of the pandemic in the region and prevent the formation of new waves.

Keywords: SARS-CoV-2; COVID-19; Mortality; Epidemiology; Incidence.

Resumo

Introdução: o contexto da pandemia da Covid-19 na região Norte é preocupante, visto que há falta de recursos para a Saúde Pública, baixo índice de desenvolvimento humano e indicadores de pobreza acima da média nacional. **Objetivo:** analisar a letalidade e mortalidade por COVID-19 no Estado de Roraima, Brasil. **Método:** trata-se de um estudo ecológico de séries temporais de dados secundários sobre a COVID-19 no estado de Roraima, região Norte do Brasil, no período de março de 2020 a julho de 2021. Foram calculadas as taxas de incidência, mortalidade e letalidade por COVID-19. Utilizou-se o modelo de regressão de Prais-Winsten para calcular as taxas de construção de séries temporais. As taxas foram classificadas como crescen-

tes, decrescentes ou estacionárias. A tendência foi considerada estacionária quando o p-valor não foi significativo, (p>0,05). **Resultados:** no estado de Roraima, durante o período de março de 2020 a julho de 2021, houve um total de 123.125 casos e 1.903 óbitos acumulados devido a COVID-19. A primeira onda (março de 2020 a outubro de 2021) da COVID-19 foi registrada a taxa de incidência (2.995,30 novos casos por 100.000 habitantes - julho de 2020) e de mortalidade (56,32 óbitos por 100.000 habitantes - junho de 2020) letalidade mais elevada. Entretanto, foi na segunda onda (novembro de 2020 a julho de 2021) que foi observada a taxa de letalidade mais elevada (3,47% - fevereiro de 2021). Observou-se que durante a primeira onda, a taxa de incidência da COVID-19 apresentou tendências crescentes. Neste período, a taxa de mortalidade encontrava-se com tendência estacionária (p>0,05) e a letalidade percentual com tendência decrescente (p<0,05). Durante a segunda onda, observou-se um cenário mais agravante para a letalidade, que transitou de uma taxa de redução diária de 0,90%, para tendências estacionárias. **Conclusão:** a pandemia no estado de Roraima ainda não está controlada, assim faz-se necessário o fortalecimento de estratégias para mitigar o avanço da pandemia na região e evitar a formação de novas ondas.

Palavras-chave: SARS-CoV-2; COVID-19; Mortalidade; Epidemiologia; Incidência.

INTRODUCTION

Coronavirus 2019 disease (COVID-19) is an acute respiratory infection caused by a beta-coronavirus, SARS-CoV-2, identified in Chinese patients with potentially severe pneumonia in 2019. This family of viruses is commonly found in different animals, including primates, bats, cats, and camels[1]. In addition, it has high transmissibility and global distribution.

By August 2021, in the global context, there were more than 200 million confirmed cases and 4 million deaths from COVID-19. The highest incidence of cases is concentrated in the United States of America, with 35,957,692 million confirmed cases, India with 32,077,706 million, and Brazil with 20,212,642 million[2].

The Board of Directors of the Pan American Health Organization (PAHO) noted a low vaccination rate in Latin America. It stated that if current trends continue, health, social and economic disparities will grow even more significant, and it will take years for the virus. Therefore, it highlights the importance of access to vaccines, adoption of Public Health measures, and non- pharmacological preventive attitudes, such as the use of masks, hand hygiene, and physical distance, in addition to robust surveillance systems. These actions are necessary for controlling the virus, even with the expansion of vaccine coverage and reducing cases in Brazil and the world[3].

Currently, Brazil is in remission concerning the number of cases of COVID-19, mainly due to the increase in vaccination coverage in the country. This decrease was predicted by authors who suggested greater rigidity to non- drug prevention measures, in addition to the development and purchase of vaccines[4].

The context of the pandemic in the North region is worrying. There is a lack of resources for Public Health, a low Human Development Index, and poverty indicators above the national average. This profile worsened during the arrival of the COVID-19 disease when a large part of the resident population did not have access to the Unified Health System (SUS), and the few hospitals were overloaded[5].

The epidemiological bulletin of Roraima dated August 12, 2021, confirmed 121,666 positive cases of COVID-19, of which 115,982 people were considered to have recovered from the disease[6].

Amid the drop in the number of cases, hospitalizations, and deaths from COVID-19 in Roraima, it is noteworthy that viral transmission is still high. Thus, to avoid the formation of new waves of disease and daily records of cases and deaths, it is crucial to combine vaccination with masks and social distancing to maintain and obtain further illustrated advances in the direction of pandemic control[7].

The government agents have put in place several measures to reduce the effects of the pandemic experienced in several states and countries. One of them is accelerating the vaccination campaign that will reach the public aged 12 to 17 years, with and without comorbidities, from August 16, 2021[8]. Thus, it is possible to mitigate the impacts of the

The government agents have put in place several measures to reduce the effects of the pandemic experienced in several states and countries. One of them is accelerating the vaccination campaign that will reach the public aged 12 to 17 years, with and without comorbidities, from August 16, 2021[8]. Thus, it is possible to mitigate the impacts of the pandemic in the region. In 2020 Roraima was one of the states with the highest number of cases and deaths in Brazil, mainly in Boa Vista, the capital, with an increased incidence and mortality compared to other regions[9].

Regarding knowledge gaps present about the epidemiology of the SARS-CoV-2 virus, specifically in the North region, and for the characterization of the typical behavior of the disease, this study aims to analyze the mortality and lethality from COVID-19 in the State of Roraima during the pandemic established by the international Public Health authorities, considering the period from March 2020 to May 2021.

METHODS

An ecological time-series study on COVID-19 was carried out in the State of Roraima, Northern Brazil, from March 2020 to July 2021 , following the protocol of Abreu, Elmusharaf and Siqueira (2021)[10].

Data on cases and deaths of COVID-19 were obtained from a public database, made available by the Department of Health of Roraima.

The inclusion criteria for the study were all cases and deaths that occurred in the state of Roraima, from March 2020 to July 2021, which used the International Classification of Diseases, 10th edition (ICD-10), from U07.1 COVID-19 (identified virus) or U07.2 (COVID-19, unidentified virus)[11], considering laboratory or clinical, epidemiological confirmation criteria. Thus, the study population consisted of 123,125 cases and 1,903 deaths of COVID-19 in the state of Roraima.

Cases were classified according to notification date and deaths according to death date; those without such information were excluded.

The collected data were further organized into an Excel spreadsheet to analyze incidence, mortality, and lethality rates.

Incidence rates were calculated by dividing the number of cases that occurred in a period by the population multiplied by 100,000. Thus the results were expressed as the number of new cases per 100,000 inhabitants. Mortality rates were calculated by dividing the number of deaths in the period by the number of inhabitants multiplied by 100,000; the results were expressed in number of deaths per 100,000 inhabitants. The lethality was calculated as the total of deaths in the period divided by the number of cases and multiplying by 100; the results were expressed in percentage.

For the calculations, we used the estimate of the Population Projection of Federation Units by sex and age groups: 2000-2030, considering the population residing in the state of Roraima in July 2020, which consisted of 546,891 inhabitants[12].

Trend analyzes of incidence, mortality, and lethality rates were performed using the methods proposed by Antunes and Cardoso[13]. The Prais-Winsten regression model was used to calculate the time series construction rates. This method allows first-order autocorrelation corrections to be performed on values organized by time. Thus, the values of the angular coefficient (β) and respective probability (p) were estimated, considering a 95% confidence interval (95% CI).

The results of the logarithmic rates (β) of the Prais- Winsten regression allowed us to estimate the percentage change in daily change (Daily Percent Change - DPC), with the respective confidence intervals (95% CI). Rates were classified as increasing, decreasing, or stationary. The trend was considered stationary when the p-value was not significant ($p>0.05$).

RESULTS

The sociodemographic aspects of the state of Roraima are shown in table 1.

The state of Roraima has a territorial extension of 223,644,527 Km2, a population density of 2.01 inhabitants per Km2, an estimated population of 546,891 inhabitants, being constituted in a minority of elderly individuals.

Table 1: Sociodemographic characteristics of the state of Roraima.

Sociodemographic characteristics	Description
Number of municipalities*	15 counties
State's capital*	Boa Vista
International borders *	Venezuela and Guiana
Territorial extension*	223,644,527 km²
Demographic density*	2.01 inhabitants/km²
Population (2020)**	546,891 inhabitants
0 to 4 years	47,945
5 to 9 years	51,098
10 to 14 years	53,960
15 to 19 years	56,759
20 to 29 years	105,208
30 to 39 years	87,309
40 to 49 years	62,810
50 to 59 years	43,653
60 to 69 years	25,489
70 to 79 years	9,634
80 years or more	3,026
household income	$USD 177.76
Human Development Index (HDI), according to the last census, 2010)*	0.707
Average number of people per household***(2019)	3.5 people
Number of basic health units #	111 units

Source: *Instituto Brasileiro de Geografia e Estatística (IBGE, 2021). **DATASUS - Projeção da População das Unidades da Federação por sexo e grupos de idade: 2000-2030. *** Sistema IBGE de Recuperação Automática – SIDRA. #Cadastro Nacional de Estabelecimentos de Saúde – CNESNet – Ministério da Saúde, Brazil.

Furthermore, the average monthly household income per capita is less than a minimum wage (983 reais) (table 1).

The characterization of COVID-19 cases notified by the state of Roraima according to sex, age group, and comorbidities is illustrated in table 2. In the examined period, there were a total of 123,125 cases of COVID-19, of which 1.55% (n=1,903) evolved to death (table 2).

It was observed that 55.41% of cases (n = 68,224) were female and 44.59% (n = 54,896) were male. Furthermore, cases were predominant among young adults, especially among individuals aged between 30 and 39 years (23.36%) and between 40 and 49 years (20.08%) (Table 2).

There were 11,570 reported comorbidities or special health conditions described among the cases of COVID-19. It was highlighted that the most prevalent comorbidities were chronic heart diseases (49.50%), followed by diabetes (28.13%) and chronic respiratory diseases (28.13%) (Table 2).

The daily distribution of and deaths from COVID-19 in the state are described in figure 1.

In the daily distribution of new cases and deaths, it was observed that the highest peak of daily cases of COVID-19 occurred in June 2020, with records of 1,052 new cases described on June 24, 2020. Meanwhile, on January 26, 2021, the state reached the highest number of registered deaths per day (n=18 deaths), as seen in figure 1.

Table 2: Characterization of COVID-19 cases in the state of Roraima, Brazil, reported from March 2020 to July 2021, distributed according to evolution to death, sex, age group and comorbidities.

Confirmed cases of COVID-19	Absolute frequency (n)	Relative frequency (%)
Accumulated cases	123.125	100.00
Accumulated deaths	1.903	1.55
Sex*		
Male	54.896	44.59
Female	68.224	55.41
Age group		
0 to 19 years	17.474	14.19
20 to 29 years	23.139	18.79
30 to 39 years	28.757	23.36
40 to 49 years	24.718	20.08
50 to 59 years	15.633	12.70
60 to 69 years	8.532	6.93
70 to 79 years	3.485	2.83
80 years or more	1.387	1.13
Comorbidities or health conditions**		
Chronic Heart Disease	5.727	49.50
Diabetes	3.255	28.13
Chronic Respiratory Disease	1.501	12.97
Immunosuppression	453	3.92
Pregnant	427	3.69
Kidney Diseases	193	1.67
Risk Management	7	0.06
Immune Fragility	7	0.06

Source: Data on cases and deaths were extracted from Secretaria de Saúde do Estado de Roraima.

*Sex – n= 123,120 cases – 5 were excluded for not containing information about sex. ** Comorbidities or health conditions – An individual could have more than one comorbidity.

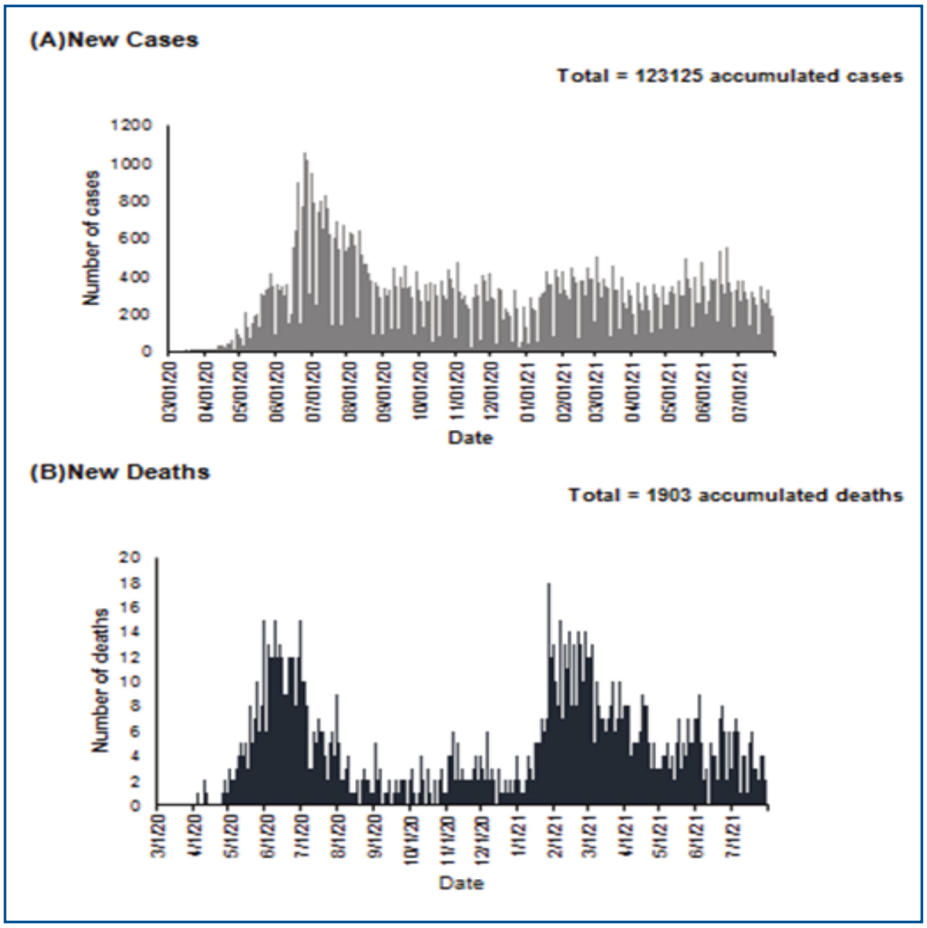

Figure 2: Number of new cases and daily deaths of COVID-19 in the state of Roraima, from March 2020 to July 2021 Source: Cases and deaths extracted from Secretaria de Saúde o Estado do Roraima.

The new cases and deaths and the respective incidence rates (per 100,000 inhabitants), mortality (per 100,000 inhabitants) and lethality (%) are described in table 3.

There was the formation of two possible waves of COVID-19 in the state of Roraima. The first wave (March 2020 to October 2020) of COVID-19 in the studied region had the highest incidence rates, verified in June (2,389.69 new cases per 100,000 inhabitants) and July 2020 (2,995.30 new cases per 100,000 inhabitants). During the first wave, the highest mortality rate of the entire period was also verified, which occurred in June 2020, with a rate of 56.32 deaths per 100,000 inhabitants. However, during the second wave (November 2020 to July 2021), the state had the highest peak of lethality, as observed in February 2021, a lethality of 3.47% (table 3).

Trend analyzes of incidence, mortality and lethality rates and their respective Percentage of daily change (DPC) were shown in table 4.

It was observed that during the first wave (March to October 2020), the incidence rate of COVID-19 in the state of Roraima showed increasing trends ($p<0.05$), with a daily growth rate of 1.68%. During this period, the mortality rate was in a stationary trend ($p>0.05$), and the percentage lethality was in a decreasing trend, registering a daily decrease rate of -0.90% ($p<0.05$) (table 4).

Table 3: Monthly number of cases, deaths, incidence and mortality rates per 100,000 inhabitants and percentage lethality of COVID-19 from March 2020 to July 2021.

Date	Cases	Deaths	Incidence (per 100.000 inhabitants)	Mortality (per 100.000 inhabitants)	Lethality (%)	Period
Mar-20	28	0	5.12	0.00	0.00	1ª wave
Apr-20	860	9	157.25	1.65	1.05	
May-20	5.551	142	1.015.01	25.96	2.56	
Jun-20	13.069	308	2.389.69	56.32	2.36	
Jul-20	16.381	145	2.995.30	26.51	0.89	
Aug-20	10.085	50	1.844.06	9.14	0.50	
Sept-20	8.009	31	1.464.46	5.67	0.39	
Oct-20	7.017	32	1.283.07	5.85	0.46	
Nov-20	6.275	58	1.147.40	10.61	0.92	2ª wave
Dec-20	5.004	48	914.99	8.78	0.96	
Jan-21	6.632	138	1.212.67	25.23	2.08	
Feb-21	7.491	260	1.369.74	47.54	3.47	
Mar-21	8.016	225	1.465.74	41.14	2.81	
Apr-21	6.240	138	1.141.00	25.23	2.21	
May-21	7.577	112	1.385.47	20.48	1.48	
Jun-21	8.496	111	1.553.51	20.30	1.31	
Jul-21	6.394	96	1.169.15	17.55	1.50	
TOTAL	123.125	1903	22.513.63	347.97	1.55	

Source: Cases and deaths extracted from Secretaria de Saúde o Estado de Roraima.
First Wave: March to October 2020; Second Wave: December 2020 to July 2021.

Table 4: Prais-Winsten regression estimates and percentage change in daily change (DPC) of the incidence and mortality rate per 100,000 population and mortality (%) of COVID-19 in the state of Roraima, Brazil, during the first (March to October 2020) and second waves (November 2020 to July 2021).

Period	DPC (95% CI) Incidence	p	Tendency Incidence	DPC (95% CI) Mortality	p	Tendency Mortality	DPC (95% CI) Lethality	p	Tendency Lethality
1st wave	1.68	<0.001	Crescent	-0.39	0.059	Stationary	-0.90	<0.001	Decrescent
	(1.01; 2.35)			(-0.79; 0.02)			(-1.38; -0.43)		
2nd wave	0.15	0.113	Stationary	0.12	0.208	Stationary	-0.03	0.827	Stationary
	(-0.04; 0.34)			(-0.07; 0.31)			(-0.29; 0.23)		

DPC – Daily Percent Change (%); 95% CI – Confidence Interval 95%; * Statistical difference detected by the Prais-Winsten Regression test, p<0,05. First wave: March to October 2020. Second wave: November 2020 to July 2021.
Source: Cases and deaths extracted from Secretaria de Saúde o Estado de Roraima.

During the second wave (November 2020 to July 2021), a profile with a predominance of stationary trends for incidence, mortality, and lethality rates (p>0.05) is indicated in table 4.

DISCUSSION

In the state of Roraima, 123,125 cases and 1,903 deaths were reported due to COVID-19 from March 2020 to July 2021. It was during the first wave (March to October 2020) of the disease that the region had the highest rate of high mortality, observed in June (56.32 deaths per 100,000 inhabitants), and incidence, verified in July 2020 (2,995.30 new cases per 100,000 inhabitants). However, during the second wave (November 2020 to July 2021), the highest lethality rate was evidenced, recorded in February 2021 (3.47%).

COVID-19 had its first suspected cases in residents of the state of Roraima in March 2020; it was on the 20th of that month that the first two confirmed cases of the disease in patients from the capital, Boa Vista, were notified by the State Health Department[14]. In the same month, the community transmission of the disease was announced, and 30 days later, more than 1,000 cases of COVID-19 were reported[15]. The State Government decreed an emergency in Public Health from this date due to the pandemic; the first fatal victim notification occurred on April 3, 2021.

However, an epidemiological study that analyzed the pattern of spatial and temporal dissemination of COVID-19 cases and deaths in Brazil concluded that the virus was possibly circulating in the state of Roraima earlier as happened in Amazonas State. Probably, the release of the reports took place after a large part of the population was already infected, or there were multiple introductions of the rapidly spreading virus in space[16].

After the rapid dissemination of SARS-CoV-2, COVID-19 caused cases and deaths in all municipalities in the state. According to the State Health Department, the epidemiological profile of COVID-19 in Roraima is characterized by a higher proportion of cases in female individuals (55.5%) and adults aged between 30 and 39 years (23.1 % male 24.1% female). While deaths affected more male individuals (58.9%), elderly aged 60 to 69 years (27.1%), brown individuals (64.4%), and comorbidities such as hypertension (38.4%), followed by diabetes (28.5%) and obesity (10.8%)[15].

The presence of comorbidities and biological factors such as sex and age represent risk factors associated with COVID-19 and are variables that cause significant clinical implications and are related to a worse prognosis of the disease[17,18]. Although women are at greater risk of being infected by SARS-CoV-2 at younger ages (<35 years), they have a greater chance of recovery when compared to males. However, the chances of recovery decrease with increasing age[18].

Numerous factors may be associated with biological differences due to sex and age[17,19]. Some of these elements are related to differences in the inflammatory response developed during COVID-19. In elderly male patients, there is an increase in inflammatory markers, compared to women of the same age group, demonstrating that the hormonal influence mediates the different functional responses to the virus, especially in components of the innate immune system20. Furthermore, sex and age can influence the levels of angiotensin II converting enzyme - ACE2 receptors, which are binding sites that facilitate the replication of SARS-CoV-2[21,22].

Another factor contributing to the biological differences observed in patients with COVID-19 is the presence of comorbidities seen in a more significant proportion in the elderly, the most common being atherosclerotic cardiovascular disease (56.5%) and hypertension (43.5%)[23].

Regarding the increased risk of comorbidities, cardiovascular diseases have high mortality rates for patients who develop Acute Respiratory Syndrome (SARS) since SARS-CoV-2 uses ACE2 receptors to enter cells. These receptors are predominantly found in the lung and heart, so SARS-CoV-2 invades lung cells, causing respiratory symptoms. These symptoms are much more intense in patients with cardiovascular diseases, who have a greater expression of these receptors. Thus, in these individuals, COVID-19 can lead to a severe coronary syndrome, acute myocardial infarction, and heart failure[19,24].

In addition to cardiovascular diseases, metabolic diseases such as diabetes mellitus and obesity are also reported in the scientific literature as risk factors for severe COVID-19. They are associated with a high rate of hospitalization and mortality from COVID-19[25,26].

Probably the aggravating factors of COVID-19 observed in patients with diabetes mellitus come from the physiological impacts due to the effects of prolonged hyperglycemia. It induces a chronic pro-inflammatory state, causing systemic vascular damage and compromise of the immune system. Furthermore, the virus can also cause damage to the pancreas, aggravating the hyperglycemic condition[25].

Similar mechanisms are verified in obese people. These individuals are three times more likely to develop the most severe form of COVID-19. Obesity can promote a chronic pro-inflammatory condition that favors systemic damage and aggravations in the patient's prognosis. Furthermore, SARS-CoV-2 enters fatty tissue cells, which can serve as a viral reservoir[26].

Notably, the factors that impact the diseases arising from COVID-19 are far behind only biological factors. Demographic and Public Health characteristics may explain part of the differences in the evolution of the pandemic in each region. It is known that population density, degree of urbanism, socioeconomic aspects, and the capacity of the Health Systems to provide care are factors that may be associated with mortality from COVID-19[27].

The state of Roraima is located in the northern region of Brazil. This macro-region does not have the highest populations at risk for COVID-19, such as a high proportion of older adults and a high burden of patients with chronic diseases. But it has a high social vulnerability, marked by socioeconomic differences and a scarcity of hospital resources, both in the public and private sectors. Furthermore, the northern region presents inequality in the number of ICU beds and the number of human resources; there is a low number of ICU doctors per capita compared to states in other regions of the country[28].

As for the capacity of the structure of Health Systems to support the demand for the care of patients affected by COVID-19 without suffering a collapse in the health systems, Roraima presents unsatisfactory rates. In a study that created and mapped the Health Infrastructure Index (IIS) in Brazilian states, the authors found that there are regional disparities in the spatial distribution of the health system infrastructure, with the lowest indices being registered in the northern region, in states such as Amapá and Roraima, places belonging to the macro-region where COVID-19 had an impact on health and funeral systems[29].

It is noteworthy that the state of Roraima has only one reference hospital available for the care of critically ill patients who need admission to the Intensive Care Unit (ICU) and in wards for the treatment of COVID-19, which is the General Hospital of Roraima[30].

In critical moments faced by the pandemic, as verified in the current study, in July 2020 (which had the highest incidence rate of the entire period) and February 2021 (which illustrated the highest fatality rate), the state had a different rate of occupation of beds COVID-19. At the end of July 2020, Roraima had a rate of 54.8% of adult beds occupied, and Tocantins, another state in the North region, had a very high occupancy rate (83%)[31]. In early March 2021 Roraima had an occupancy rate of 80% of ICU beds, following the worrying scenario in most states that had a critical alert for the occupation of hospital beds[32].

July 2020 was the month that represented the peak of the first wave of COVID-19 in the state. This month, the highest incidence rate was described (2,995.30 new cases per 100,000 inhabitants) in the period analyzed, with significant mortality (26.51 deaths per 100,000 inhabitants), but it was in June 2020 that the highest mortality rate was described of the entire period analyzed, illustrating a rate of 56.32 deaths per 100,000 inhabitants

According to the Ministry of Health of Brazil (2020), in mid-July 2020 (12 to July 18) the state of Roraima had the third highest mortality rate in the country (70.8 deaths per 100,000 inhabitants), being surpassed only by Ceará (78.5 deaths per 100,000

inhabitants) and Amazonas (75.5 deaths per 100,000 inhabitants). It is possible that the differences in the mortality rates described are due to the different periods evaluated.

It is noteworthy that the high incidence of cases and deaths verified in Roraima may be associated with low adherence to sanitary protocols, as well as administrative negligence that occurred in the state, such as the lack of investment of Federal public resources that were made available for the use of needs from COVID-19[9].

At the end of the first wave, from March to October 2020, a profile of increasing trends in incidence rates was observed, which corroborated the formation of a second wave. From November 2020 to July 2021, this new wave presented a scenario marked with stationary trends in incidence, mortality, and lethality rates.

It is noteworthy that even the epidemiological indicators illustrate stationary trends, it was after a year of the pandemic that Roraima registered the highest lethality rate of the entire period analyzed, which was verified in February 2021 (3.47%), followed by significant mortality (47.54 deaths per 100,000 inhabitants). The values remained significant in March 2021, with an incidence of 1465.74 new cases per 100,000 inhabitants, mortality of 41.14 deaths per 100,000 inhabitants, and a mortality rate of 2.81%.

Brazil experienced an acceleration of the pandemic in early 2021, with the formation of a second wave of the disease, impacting changes in the epidemiological profile characterized by an increase in the number of infected adults (20-59 years), with an increase in young adult mortality. There was an increase in ICU hospitalizations and the need for Mechanical Ventilators. They are reflexes arising from the high infectivity of the P.1 variant, which, in January 2021, had a genetic sequencing frequency of 91% in samples from patients in the state of Amazonas[33,34].

According to records until February 20, there were 7 cases of COVID-19 caused by the VOC P.11 variant. This fact suggests that since February 2021, the new variant was circulating in the region and probably was responsible for the high lethality and mortality rates observed in February and March 2021.

In that period, the country faced the worst scenario brought by the pandemic; the number of cases and deaths broke daily records, accompanied by situations of collapse in health systems in most states and municipalities. It is noteworthy that the country never achieved a significant reduction in the viral transmission curve, remaining, during the pandemic, at high levels of daily incidence when compared to other countries10,35. This event illustrates that the pandemic is not over; a scenario that is in constant change is still being experienced. Thus it is necessary for continuous epidemiological monitoring of COVID-19 in Roraima and throughout Brazil.

Only with strategies based on science, with the engagement of government authorities, and with the population's adhesion will we be able to mitigate the impacts arising from COVID-19 and contain the advances in the mortality of the disease in the state of Roraima.

Limitations

Although we have precise data and statistically significant trends, there are always data limitations, which may be subject to underreporting in COVID-19 cases and deaths. Furthermore, some municipalities in the State of Roraima are located in places of difficult access, resulting in deficiencies in infrastructure and internet access, resulting in delays in notification.

CONCLUSION

COVID-19, from March 2020 to July 2021, affected the health of 123,125 confirmed cases of the disease, being responsible for death in 1,903 individuals. The temporal distributions of the COVID-19 epidemiological indicators illustrated the formation of two possible waves, the first wave being considered from March to October 2020 and the second wave from November 2020 to July 2021. The second wave having presented incidence, mortality, and lethality rates, with stationary trends, there was a more aggravating scenario for lethality from COVID-19. The disease lethality in the state transitioned from decreasing trends, such as a daily reduction rate of 0.90% (DPC= -0.90%), to stationary. Furthermore, one year after the pandemic, Roraima had the highest lethality rate (3.47%) of the entire period analyzed. Thus, it is evident that the pandemic in Roraima is not yet under control, so it is essential to strengthen and expand preventive non- pharmacological measures and the immunization of the population.

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JUDICIALIZATION OF HEALTH CARE IN THE WESTERN AMAZON: COLLECTIVE DECISIONS OF THE JURISDICTIONAL COURT OF JUSTICE IN THE STATE OF ACRE, BRAZIL

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Abstract

Introduction: the judicialization of health is an alternative to the health services in Brazil, despite criticism of judicial decisions and control of public health policy. The large number of actions that demand health services is a health problem that characterizes the political, social, ethical, legal, and health systems of the Public Health Policy. **Objective:** to analyze the judicialization of health care in the Acre State, Brazil, from 2010 to 2016. **Methods:** it is a documentary and cross-sectional study of collegiate decisions, with final judgments, in the period from 2010 to 2016, issued by the Court of Justice of the State of Acre. **Results:** all proposed actions were Writ of Mandamus. The use of preliminary injunction was the most common strategy (n = 34; 94.44%). One third of the respondents were not questioned by the State of Acre (n = 9; 25%) as decisions of the Court of Justice on health concern medicines, examinations, and procedures, in these cases, it only manages interests, with no litigation per se. (n = 25, 69.44%). Men and women demanded in the same proportion, all of them characterized by living in poverty (n = 28; 77.78%). **Conclusion:** the collective health decisions handed down by the State Court of Justice Acre, Brazil, guarantee access to health goods and services to the claimants, with emphasis on preliminary injunctions and grounds based on the principle of human dignity, physical integrity and life, and on medical prescriptions in each specific case and, in a third of the cases, serving as a mere administration of interests.

Keywords: Public Health Policy; Judicial Decisions; Legal Procedural Law; Health Judicialization.

Resumo

Introdução: a judicialização da saúde é uma alternativa aos serviços de saúde no Brasil, apesar das críticas às decisões judiciais e ao controle das políticas públicas de saúde. O grande número de ações que demandam serviços de saúde é um problema de saúde que caracteriza os sistemas político, social, ético, jurídico e de saúde da Política Pública de Saúde. **Objetivo:** analisar a judicialização da saúde no Brasil, Amazônia Ocidental, de 2010 a 2016. **Método:** estudo documental e transversal de decisões colegiadas, com sentenças definitivas, no período de 2010 a 2016, proferidas pelo Tribunal de Justiça do Estado do Acre, cujo foco principal é o contexto, fatores e consequências que os conduzem ao seu direito à saúde no Judiciário. **Resultados:** todas as ações propostas eram mandatos de segurança. O uso de liminar foi uma estratégia comum entre os autores (n = 34; 94,44%). um terço dos respondentes não foi contestado pelo Estado do Acre

(n = 9; 25%). Já as decisões do Tribunal de Justiça em matéria de saúde dizem respeito a medicamentos, exames e procedimentos (n = 25, 69,44%). Homens e mulheres propõem a mesma proporção e uma característica básica dos autores é a pobreza (n = 28; 77,78%). **Conclusão:** as decisões coletivas de saúde proferidas pelo Tribunal de Justiça do Estado são legais, constitucionais e refletem a alteração entre todos os órgãos que integram a relação em que se estabelece a judicialização, que pode ser alcançada por meio do aprimoramento do processo de incorporação. tecnologias ao SUS, para a boa execução da política pública de saúde, com a manutenção dos princípios da universalidade e integralidade do Sistema Único de Saúde.

Palavras-chave: Políticas Públicas de Saúde; Decisões Judiciais; Direito Processual Jurídico; Judicialização da Saúde.

INTRODUCTION

The judicialization of health is the search for the judicial system as the ultimate alternative to obtain the drug prescription or service denied by the public or private health provider, either for out of stock or budgetary issues. It reflects a flawed health system, which can not fully satisfy the protection of this fundamental right[1].

Since 1990, the judicialization process has been present in South and Central America. Still, in Brazil, it exhibits many demands attended by the Judiciary, involving discussions among managers and health professionals, politicians, lawyers, in the most varied political, social, ethical and legal contexts[2].

The scope and social repercussion of the theme caused the Federal Supreme Court (STF) to categorize the judicialization of health as a public health problem present in all Brazilian states[3,4].

The Unified Health System (SUS) is responsible for the creation and implementation of public health policies. It is administered, executed, and controlled by the Executive Branch at all three levels of government (Federal, State, and Municipal), with established hierarchy and decentralization of actions and responsibilities, promoting health for all in the national territory, regardless of the requirement[5].

Brazil recorded 1.346,931 processes in the health area as of December 2016, with 214,947 lawsuits related to medical-hospital treatment or medicine supply by the SUS[6]. In the same year, the State of Acre presented 320 legal actions, 82 related to hospital medical treatment or supply of medical drugs (SUS)[7].

The structuring of the right to health through public policy makes the Executive Branch responsible for creating infrastructure and human resources to guarantee a good quality health service to the citizen. It is the responsibility of the Judiciary to control it without prejudice to all criticisms regarding the capacity technique and social effectiveness of judicial decisions[8,9] affecting SUS management and financing systems.

It is evident that the search for judicial intervention for access to medicines, services, treatments reflects a mismatch between public health needs and the provision of universal, integral, and equitable care to citizens[10].

In the context of judicial control of the public health policy by the Judiciary, the Executive Branch's challenge is the reduction of the number of judicial litigation. Hence, it is essential to understand the causes and effects of judicialization in the public health policy system[8], mainly due to the regional diversity of the Brazilian states, such as Distrito Federal[11], Pernambuco, Rio Grande do Sul, and Minas Gerais[12-14].

In this way, the Executive Branch must adopt approaches to the political and collective construction of the right to health, distinguishing the legitimate interests of each actor involved, establishing an effective institutional dialogue in resolving public health conflicts[15,16]. In addition ethical commitment, must be adopted to ensure the balanced performance of each actor, governmental organization, and social organization involved in guaranteeing the right to health[17].

Regional approaches to the judicialization of health are necessary to understand the problems of access to health in Brazil and adopt an efficient and effective public health policy.

The present study is based on the premise that collegiate decisions on Health Judicialization are legal and constitutional. Moreover, understanding that the apparent divergence between Public Authorities and users is the result of a conflict directed at the resilience of the Judiciary, aiming at the realization of Brazilian SUS principles and human dignity above all.

Thus, the objective of this study is to analyze the collegiate decisions on the of health's judicialization in the State of Acre, Brazil, from 2010 to 2016.

METHODS

Study Design

It is a cross-sectional documentary study[18] with secondary data collected in the judgments of the Court of Justice of the State of Acre (TJ / AC), Western Amazon, Brazil, whose decisions were related to health services in the SUS from 2010 to 2016. It defined legal terms for this data collection as follows:

- Monocratic decisions: they are judicial decisions pronounced by a single magistrate;
- Infringing embargoes: it is an appeal filed against a monocratic decision of the rapporteur and is intended to review the decision[19];
- Amendment of Judgment: refers to a legal instrument (appeal) whereby a party to a judicial process asks the judge (or Court) to clarify particular aspect (s) of a decision given when there is any doubt, omission, or contradiction in judgments[20];
- Writ of Mandamus: are lawsuits that seek to protect a clear legal height; being this the right whose proof of the factual support is pre-constituted, when there is no need to demonstrate the facts that sustain it by the instruction of the process[21];
- Out-of-home treatment: these are situations in which the State can not guarantee health treatment in its locality, needing to be referred from its locality to centers referenced within or outside the State, at the discretion of the Acre medical committee[22];
- Plaintiff: it is the part of the process that holds a right or interest and seeks, by legal action, to obtain a good, to ensure protection and others[19];
- Defendant: it is the part of the process that is legally responsible for the safeguard and guarantee of a right[19];
- Interest: it is the condition for filing the lawsuit qualified by the necessity and utility, since the actual situation of the plaintiff admits the service of a need in a helpful and timely manner by judicial means[19];
- Claim: it is the request of the satisfaction of an interest (a right) of the plaintiff with the Judiciary Power;
- Dispute: it is the defendant's resistance resistance to the satisfaction of an interest (a right) of the plaintiff sought from the Judiciary Branch[19].

Study Location and Period

The data were collected in the Service Portal of the Judicial Automation System (e-SAJ) of the State of Acre, (http://esaj.tjac.jus.br/cjsg/resultadoCompleta.do), for the period 2010-2016.

Study Population and Eligibility Criteria

The e-SAJ portal is an automation system that promotes the integration of information among institutions of the justice ecosystem and brings the justice of all citizens closer together, adopted by the Court of Justice of the State of Acre (TJ / AC) to exchange information and streamline procedures through online services for use by lawyers, citizens, and court officials.

The data extraction was performed using the following descriptors: Health - Medical-Hospital Treatment 10069 and / or Drug Supply. In the following, the operating system of the Court of Justice of the State of Acre, Brazil offers the following fields: judicial body (Court of law), origin (second degree), type of publication (judgment), order by date of publication.

Data Collection

The information of 47 judgments were found during the examined period. After applying the inclusion and non-inclusion criteria, 11 decisions were excluded because they were monocratic. Subsequently, thirty-six (36) decisions were considered on judicializing the right to health.

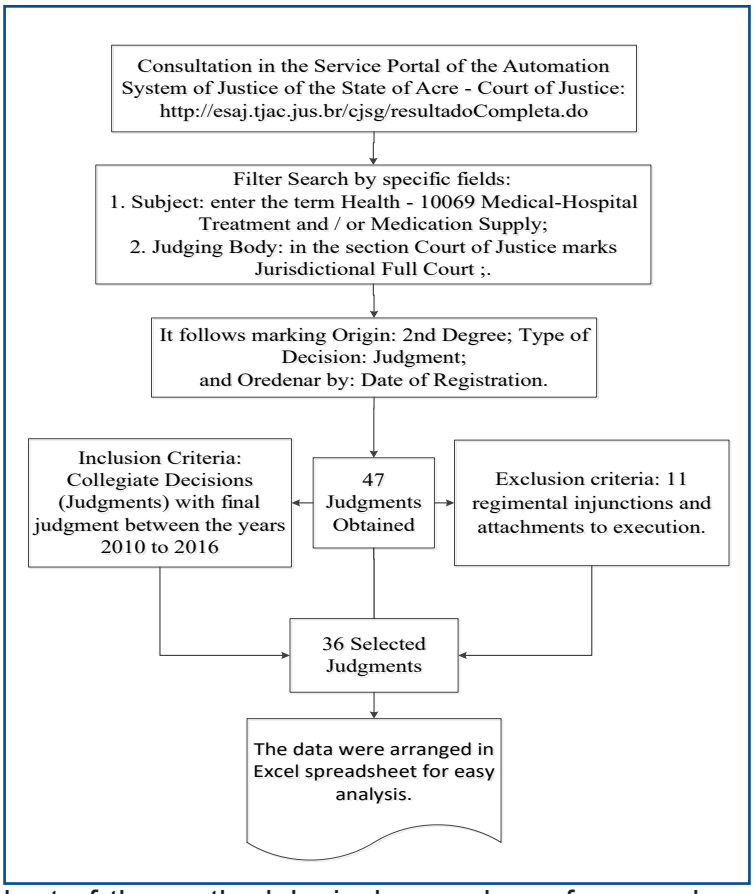

Figure 1. Flowchart of the methodological procedures for sample selection with the Court of Justice of the State of Acre, from 2010 to 2016.

Source: Documentary research with the judgments of the Court of Justice of the State of Acre (TJ/AC).

The criteria for inclusion were judgments (decisions of collegiate courts) delivered by the Full Court of the Court of Justice of the State of Acre. A collegiate decision does not allow further discussion in higher Court in medical treatment and / or supply of medicines. The exclusion criteria were: internal appeal by a court (infringing liens) and declaration liens.

Data Analysis

The data were tabulated in Microsoft Excel, and the descriptive statistic was applied to consider the percentage of the judicialization of health requirements.

Ethical and Legal Aspects of the Research

CEP CEA CAAE approval: 60249316.0.0000.5624, Opinion no. 1.802.271.

RESULTS

Judicial decisions on a writ of mandamus are preceded by the failure or omission of the State of Acre to provide essential health services to the citizens, who seek in the Judiciary to meet their needs and fulfill their health rights (figure 2).

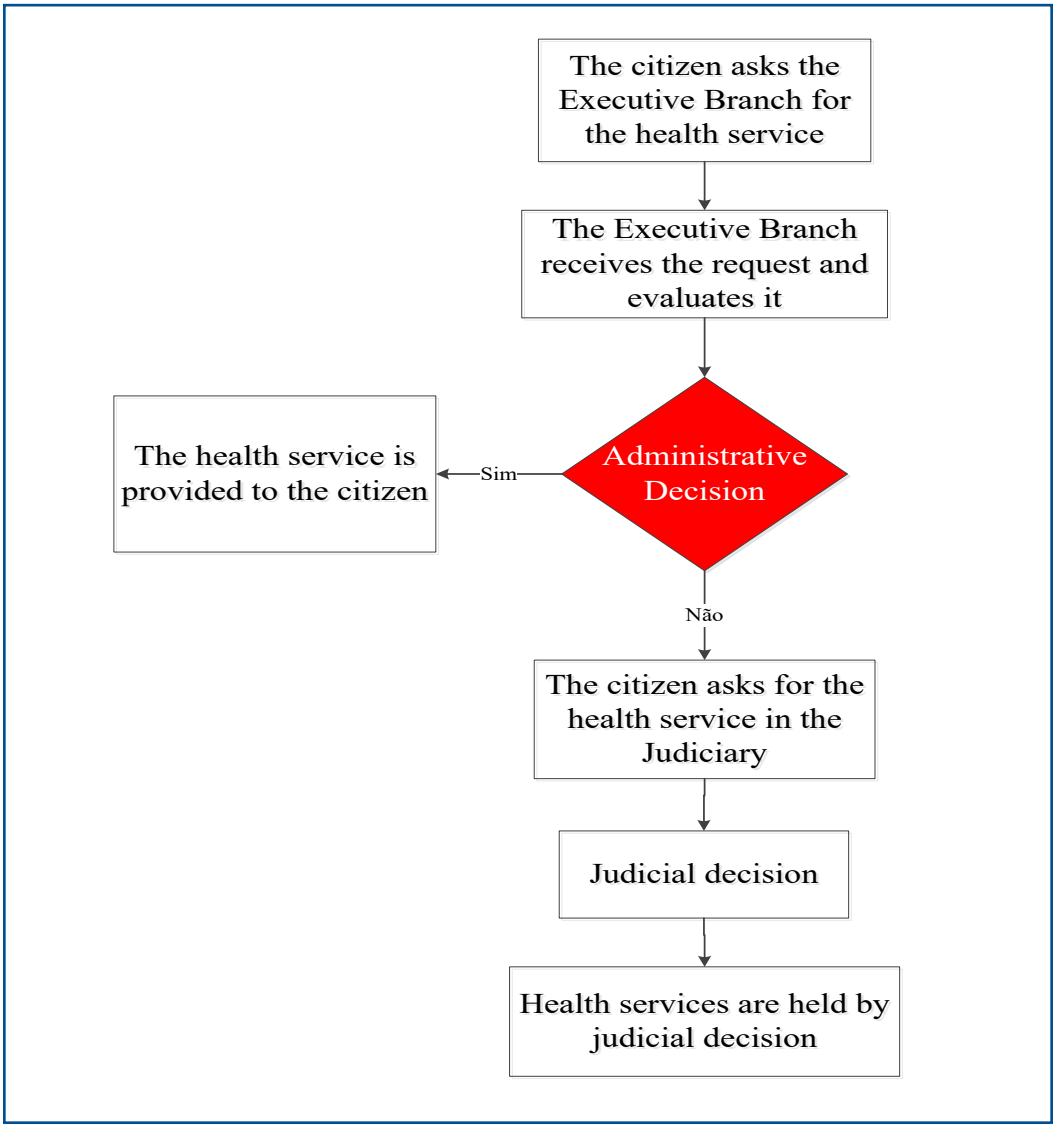

Figure 2. Flow diagram of the Health Judicialization process in the State of Acre.
Source: Documentary study in collegiate decisions in the Court of Justice of the State of Acre (TJ/AC).

Thirty-six (36) collegiate decisions were found to analyze and evaluate the legal steps to assure their right to health. They identify the factors and circumstances that motivated the demand, the profile of the plaintiff and the nature of his judicial representation (public or private), the legal principles used by magistrates, and the outcome.

The analyzed writs of mandamus had the objective to access medicines, examinations, and the referral of the plaintiffs to the treatment of care outside the home. The most frequent diagnoses are viral hepatitis B or C. The most requested applications are pegylated interferon-alpha two or alpha 2 b, ribavirin, protease inhibitor Victrelis (Boceprevir), Telaprevir 375 Entecavir 0.5 mg. In contrast, the second most frequent diagnosis was osteoporosis, which had Teriparatide Fortéo 250 mg (table 1).

Table 1: Characterization of the Judicialization of Health in the Collective Decisions of the Court of Justice of Acre, Western Amazon, Brazil, from 2010 to 2016.

Collective Decisions	Doctor's Prescription	Diagnosis
6111	TOH	Retinopatia diabética com deslocamento de retina e hemorragia
6183	Colonoscopy	Intestinal Disease
6290	Physiotherapeutic Treatment + TOH1	Locomotion Problem
6549	Imipramine 75mg e Normosang	Porphyria in Acute Neuronal Lesion
6676	Pegylated Interferon Alpha 2 A or Alpha 2 B Ribavirin and the Victrelis Protease Inhibitor (Boceprevir)	Hepatitis "C"
6792	Cardiac Catheterization + TOH	Cardiopatia
6799	Antibody Examination CCP e FAN	Daily suffering for unexplained cause
6977	Clexane 40 mg	Thrombophilia
6986	Testosterone Udecanoate 250mg	Testicular retention in the abdominal cavity causing sterility and serious diseases
7066	Telaprevir 375mg	Hepatitis "C" Genotype I
7083	Alfapeginterferone 2B 180mcg ampoule, Ribavirin 250mg capsule and Boceprevir 200mg	Hepatitis "C" Chronic
7104	Alfapeginteride 2B 180mg ampoule; Ribavirin 250mg capsule; Boceprevir 200mg	Hepatitis "C" Chronic
7106	Telaprevir 375mg	Hepatitis "C"
7179	Boceprevir 200 mg	Chronic Obstructive Pulmonary Disease, Type Emphysema, Class IV
7204	Spiriva Respimat (Brometo de Tiotrópio 2,5 mg)	Chronic Obstructive Pulmonary Disease, Type Emphysema, Class IV
7293	Interferon Pegylated 180mg, Ribavirin 250mg - Capsule and Telaprevir 375mg	Hepatitis "C" Chronic
7419	Teriparatide Fórteo 250 mg	Severe Osteoporosis, having suffered fracture in several vertebrae in the dorsal and lumbar spine
7426	Leg graft + TOH	Queimadura da perna esquerda, necessidade de enxerto.
7427	Enoxaparin 40mg	Thrombophilia
7429	Risperidone 1mg e Imipramina 75mg	Psychotic Disorder
7431	24-Hour Holter and Nasosinusal Videoendoscopy	Adenoide and Extra-Systoles
7466	Electroneuromyography MMSS e MMII	Repetitive Strain Injury - "READ OUT"
7482	Entecavir 0,5 mg	Hepatitis "C" Chronic Viral "B"
7510	Teriparatide 250 mg	Osteoporosis with Vertebral Fractures and Wrist
7513	Teriparatide 250 mg	Severe Lumbar Osteoporosis with Risk of Pathological Fracture
7570	Cardiology of Peripheral Blood Band G	Microcephaly
7592	Exame + TOH	Microcephaly
7594	Spiriva Respimat 2,5mg	Chronic Respiratory Failure 3rd Degree and Chronic Pulmonary Disease
7596	Entecavir 0,5 mg	Cirrhosis
8161	Sandostatin LAR-20 IM	Gallbladder Cancer

Continuation - Table 1: Characterization of the Judicialization of Health in the Collective Decisions of the Court of Justice of Acre, Western Amazon, Brazil, from 2010 to 2016.

Collective Decisions	Doctor's Prescription	Diagnosis
8186	Teriparatide 250 mg	Advanced Lumbar Osteoporosis with Pathological Fracture
8225	Genetic CGH-ARRAY	Chronic Non-Evolutionary Encephalopathy
8708	Entecavir 0,5 mg	Hepatitis "B" and Renal Insufficiency
8718	Doxorubin and Vimblastine EV	Hodgkin's lymphoma ICD 10 n. C81.9
8724	Slelazini 5mg e Léptico 100 mg	Psychotic Disorder
9565	TOH	Cancer

1. TOH - Treatment Outside the Home.

Source: Documentary study in collegiate decisions in the Court of Justice of the State of Acre (TJ / AC).

All the actions proposed in the period under study were imposed by writ of mandamus (MS). Most of the cases supported the right to health of the plaintiffs by injunctions, duly confirmed in a final merits decision (table 2).

Nine lawsuits were not contested by the State, which contemplated the sale of medicines, followed by examinations and treatments.

Table 2: Characterization of the Judicialization of Health in the Collective Decisions of the Court of Justice of Acre, Western Amazon, Brazil, from 2010 to 2016.

Variables	Nº	%
Action Kind:		
WM[1]	36	100.00
Court Jugment:		
Right to Health ensured	34	94.44
Right to Health not ensured	2	5.56
Legal Dispute:		
WM contested	27	75.00
WM uncontested	9	25.00
Requests:		
Drugs	25	69.44
Exame and therapeutic treatment	11	30.56
Sex:		
Male	19	50.00
Female	19	50.00
Claimant's representation by a lawyer:		
Public Attorney	28	77.78
Private Attorney	10	22.22
Defense's representation by a lawyer:		
Public Attorney	36	100.00

1. Writ of Mandamus.

Source: Documentary study in collegiate decisions in the Court of Justice of the State of Acre (TJ/AC).

DISCUSSION

In the analysis of the collective health judicial decisions issued by the Court of Justice of the Acre State, from the Full Jurisdictional Court, the results report that all actions proposed in the period under study were writ of mandamus (WM). And, 94, 4% (n = 34) of the requests were granted by injunctions, duly confirmed on merits in these same cases (table 1).

There is evidence of a high level of legal health demands, such as those reported by Travassos[12] (91.2%) and Gomes[8] (93.6%), noting that judicial measures are urgent and emerging, requiring rapid action the Judiciary to safeguard the plaintiff's physical integrity and life.

The study reveals a regional peculiarity that a quarter of the demands, 25% (n = 9), have not been contested by the State of Acre. There are no similar records in the literature, and in this case, despite the possibility of interfering with the judicial action of the State of Acre. It is possible that the Executive Branch uses judicial channels for the purpose of granting the health service or input under the scrutiny of legality, but without due administrative proceedings for public procurement, a time-consuming and laborious procedure, especially in the case of medicines.

The absence of litigation in health actions transforms the Judiciary into a mere administrator of public-private interests, which distorts the judicial function and reveals the need for a new mechanism of state action to resolve public health litigation. In this context, the judicialization of health legitimizes the expenses in front of the control organs, allowing the purchase of medicines and the solicitation of medical exams without bidding.

The absence of litigation in health demands induces the adoption of institutional arrangements that favor conciliation and / or mediation[23].

The health demands, in most cases, are about the judicial discussion of access to medicines, observing this situation in other States of the Federation, motivated by the divergence between the medical prescription and the indications contained in the Clinical Protocols and Therapeutic Guidelines (PCDT) of the SUS[11-13].

The divergences of PCDT from SUS and medical prescriptions, which are always prevalent over those in the cases studied, bring as possible consequences the risk to the health of the applicant because there is no scientific proof as to the suitability and efficacy of the drug and / or service and / or procedure for the treatment of the health need of the petitioner. A clear example of this situation was the granting of 13,000 preliminary injunctions for the supply of synthetic phosphoethanolamine[24], an experimental drug, at the time considered a remedy by the Judiciary, without the protection of CPTGs, violating the principles of bioethics[25,26] and endangering of thousands of people.

In order to provide greater legal certainty to judicial decisions on health, the National Council of Justice (CNJ) issued Recommendation No. 31 of October 30, 2010, establishing to the Courts the adoption of measures aimed at better subsidizing judges and other to ensure greater efficiency in the resolution of lawsuits involving health care, including the adoption of technical assistance centers in health[27] and that the basis of the decisions consider scientific evidence[27,28].

The judicialization of health can not be a prejudicial factor to society[29] and the judicial granting of health services, inputs and procedures with observance of the PCDTs of the SUS, with the assistance of health technical assistance centers and based on scientific evidence are objective and firm criteria for provide the universality, completeness and equity of SUS.

The resolution of the difficulties regarding the incorporation of technologies in the SUS goes through legal, administrative and technological evolution issues, noting that advances in Brazilian legislation have sought to reduce the time of evaluation and incorporation of services and inputs[30], but the time of management never will be the time of need and urgency of health care.

It is also worth noting that the health court in the State of Acre concerning requests for services of examinations and procedures, which occurred in 30.56% (n = 11),

emphasizing that in six cases the request was associated with the referral of the petitioner to the treatment of care outside the home. This association is not observed in other states such as Brasília[11], and Rio Grande do Sul[13].

Five were associated with receiving treatment outside the home in the eleven cases concerning the requests for examinations and services (TOH). The TOH associated with judicial health claims is a peculiar condition deriving from the geographical location of the State of Acre in the westernmost part of the Amazon Brazilian population, with 54.19% (397,521 inhabitants) settled in distant areas from urban centers. The main urban centers are Rio Branco, capital of the State of Acre, and Cruzeiro do Sul, where the main health centers are located[31].

Most of the population of the State of Acre lives in the forest. However, the largest urban concentrations are in the cities of Rio Branco (336,038 inhabitants), and Cruzeiro do Sul (78,507 inhabitants)[31]. If not completely isolated, remote locations sometimes present transit difficulties during rainy periods, which hampers public health interventions in the vast majority of the 22 municipalities of the State of Acre.

A strategy to solve the problem can be itinerant health and video medicine, for example, that can mitigate conflicts and adequately meet social needs, especially regarding primary health care, efficiently meet health demands, as a fundamentally guaranteed constitutional right[32].

It is also important to note that CCE cases considerably increase health costs for public claimants because they are associated with the services and expenses, such as housing and food. In 2017, the State of Acre spent more than R$ 12 million (the US $ 5 million) on TOH[33].

It is noticed that 16.66% (n = 6) of the processes involve vulnerable population: children, older adults, pregnant women, and people with disabilities. They request medicines already included in the National List of Essential Medicines (RENAME), for example, Rispiridone and Imipramine, to treat mental disorders; Teriparatide 250mg, for osteoporosis treatment; and the G. Band Peripheral Blood Cardiotype test.

The concept of vulnerability in health is shaped by a dynamic of reciprocal interdependencies that express multidimensional values - biological, existential, and social[34]. This research reports the health vulnerability in six analyzed cases that show that the violation of fundamental rights is aggravated when there is an absence or delay in health care, as well as when their vulnerable condition have been neglected, directly violating equity, one of the basic principles of SUS.

It is perceived that the situation of vulnerability in the health of the claimants is transferred to their capacity of exercise of postulation in Court, which is treated like the other petitioners of the other cases analyzed.

The socioeconomic profile of the prosecutors of the health judiciary in the State of Acre is poor since in 77.78% (n = 28) of the actions, the prosecution of these cases is performed by the Public Defender, acting in view of the urgency and necessity of the judicial measure in health. The Court, considering the factual support of the case, deferred gratuitousness for presumption, whereas the law requires objective proof of the insufficiency of financial resources of the author postulation in court[35].

The judicialization of health is a means of accessing health services and inputs through the most varied social levels. The demands are related to high-cost drugs, hospitalizations, and procedures from the most complex to the simplest[8,36]. The characteristics of poverty and extreme need for health care are also observed in other regions of Brazil, such as Rio Grande do Sul, Minas Gerais, and the Federal District[11,12,37,38].

The research data also show the dynamic performance of the Public Defender's Office and the judicial manifestations of the Public Ministry in the health demands of Acre State, frequently in favor of the defendants of the demands as observed in the judgments analyzed. Note that the hyposufficiency of the claimants is evidenced by a signed selfdeclaration of poverty[35]. In contrast, the health need of the impetrates is proved by medical prescription, seen in the cases analyzed as the primary evaluation parameter of the judgment.

When the Judiciary considers medical prescription as the main evaluation parameter for the judgment of health demands brings out the intense controversy about the concept of essential medicine in the face of that available to the World Health Organization (WHO).

It is noticed in the analyzed demands that essential medicine is one that the patient needs, prescribed by a qualified doctor, which conflicts with the definition of essential medicine from the WHO, that defines it as that either satisfies the need priority of health of the population[39]. The judicial position of the TJ/AC conflicts with the collective conception of health concerning essential medicine. Bucci et Duarte (2017)[40] criticize the individual concession of treatments for interfering in public health policy management and systematic financing.

The study results showed that the implementation of public health policy requires programming, systematicity, tactics, and management strategy to achieve healthcare, under the principles of universality, completeness, and equity, with a fundamental social right of the citizen.

Even the judicialization serves as an alternative instrument to health access, the resolution of conflicts involving public policies control, requires mechanisms of institutional dialogue between political and legal actors to reduce lawsuits, which may increase even more given the broad concept of health built after the Declaration of Alma-Ata(1978)[41] and the Ottawa(1986) Charter[42].

An example of an initiative of communicative institutional dialogue was carried out in the Municipality of Lages, Santa Catarina State, Brazil, with Conciliation Centers[43]. In specific cases, the judge promotes the reduction of the health claim litigation through the mediation of conflicts, strengthening the dialogue among the various local actors, despite the resistance of the Court of Justice of that State.

In the State of Acre, a similar initiative was performed in 2012, through the Technical Cooperation Agreement No. 017/2012, which drew technical cooperation between the Executive Branch, Judiciary Branch, Public Prosecutor's Office, and Public Defender's Office, intending to guarantee technical subsidies to the demands and procedures that involve the provision of health services[44].

The interactivity between all the organs that are part of the relationship in which the judicialization is established is indispensable for constructing actions that serve the common good, considering the possibility and reality of each of the organs involved in this chain[45]. The initiative of institutional dialogue in the State of Acre had no practical solutions. It should be re-evaluated and resumed to rationalize relations between the Executive Branch, Judiciary, and users of the health system.

The foundation of institutional arrangements lies in communicative theories and cooperative constitutionalism, which are based on balance and reasonableness in the relationship between power and citizenship as an effective alternative for resolving issues involving the judicialization of public policies[26,43]. Thus, the conventional judicial model of conflict resolution in public health is dysfunctional to meet social health demands, and tends to aggravate violations of SUS principles and permanent increase in the number of requests in the Judiciary, harming the management of public health and intelligent allocation of scarce resources.

In referring to the thesis on the right to health as a fundamental social right of the citizen, the findings of the research report that the JB / AC bases its decisions on the principle of human dignity, physical integrity and life, affirming that the right to health must be guaranteed, regardless of budget constraints and bureaucratic requirements. But it reinforces the idea of the need for a new resolution mechanism in public health policy, since 25% of the health demands analyzed were not judicially resisted by the State of Acre in meeting the health interest of the user.

Access to healthcare is a fundamental citizen social right materialized by SUS, which serves more than 220 million people, and is characterized by three pillars of support: universality, integrality and equit[46].

Universality is bound to guarantee the right to health to all Brazilians, without meaning or discrimination, to access the health services offered by the SUS; while the integrity of care is understood as an articulated and continuous set of preventive and curative

actions and services, individual and collective, necessary for each case at all levels of system complexity[46].

The main causes of health judicialization in Acre are the divergences between medical prescriptions and the provisions established in the SUS PCDT, with prevailing injunctions as the main strategy of the applicants for access to health.

On the other hand, its main negative effects are the prevalence of individual rights over collective rights to health, with the credible commitment of the normative system of the SUS, and damages to the public order, public economy and systematicity of public health policy, especially consequences of double or triple violation of the fundamental rights of vulnerable groups, who must have differential and priority treatment.

In addition, the effects of the judicialization promote a direct violation of equity in SUS, which is characterized by valuation, fair judgment and virtue (attitude, behavior, fact, etc.) of who or what manifests a sense of justice, impartiality, respect for equal rights. Nevertheless, the judicialization directs the protection of the actions and services of the citizens that must be offered, regardless of the complexity of the service provision, the region in which the individual resides or his / her nationality[46].

The work of the Judiciary ensures compliance with SUS principles when the executive branch plans and effectively execute the public health policy. Still, the judicialization of health cannot be a mere administration of judicial interests in cases without conflicts, as was observed in cases not contested in the State of Acre.

The findings show that in the imposition of judicial decisions, there is no judicial evaluation regarding the predictability of the resources needed by the executive for health, and the damage to SUS's management and financing system is a serious consequence in the State of Acre.

According to Borges, mechanisms and/or dialogical approaches of the Judiciary and Executive Branch provide an environment of collaboration and partnerships between different state actors, such as state courts, state attorneys, public defenders, prosecutors, technical assistance centers, and conciliation chambers to reducing or responding better to individual health care disputes[47].

There is a lack of administrative and technical- scientific decisions that ensure the fundamental right to health by the Judiciary, and, above all, an instrument of institutional dialogue among the actors involved in litigation is necessary, to enabling a fairness service[48].

The institutional dialogue gap for resolving health disputes can be solved by improving the administrative process of incorporating technologies in the National Commission for the Merger of Technology (CONITEC)[49].

The institutional dialogue to mitigate the consequences of judicialization on public health policy can be achieved by improving the process of incorporating technologies into SUS, already existing and with legitimacy, competence and technical conditions to decide whether or not to incorporate technology (medication or procedure) to meet social needs in health, based on scientific evidence, efficiency and impersonality.

It is worth noting that preliminary health measures do not allow for an in-depth analysis of patients' health issues, striving for speed and not considering the State's bureaucratic and financial limitations, but promoting interference in the management and programming of public health policy.

However, understanding the factors and consequences of the judicialization of health in a regionalized way is essential for understanding the parts of a whole of Brazilian public health policy, for the collection of data and information that enable a more efficient and effective policy to propose services in terms of meeting health needs and filling health gaps.

CONCLUSION

Thus, collective decisions on the judicialization of health in the State of Acre ensure the right to health for citizens, in most cases (94.44%), through preliminary Injunctions

base dont he principle o fhumandignity,physical integrity and life, as well as in medical prescriptions in each specific case, regardless of assessments regarding financial, budgetary and bureaucratic constraints of the State.

About a third of cases (25%) go uncontested because the parties have common interests – health is a fundamental, universal and integral right for all. In these cases, health demands are no more than the mere administration of the public interest, where the citizen seeks health and the State grants health, considering the patient's clinical condition, contrary to good health management practices, which are generally silent and non-existent.

On these premises, also, considering the absence of litigation, the reduction of the judicialization of health can be achieved by cooperative procedures between powers and clinical management of diseases with the cooperation and development of due legal process that improves the standardization of patient health and clinical condition.

Author Contributions

All authors participated in all stages of the work, study design and manuscript design. All authors agreed with the final version of the manuscript.

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Conflicts of Interest

The authors declare that there are no competing interests.

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CHAPTER 23

GUILLAIN-BARRE SYNDROME RELATED TO COVID-19: MUSCLE AND NERVE BIOPSY FINDINGS

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Abstract

Background: the involvement of the peripheral nervous system (PNS) in COVID-19 is rare and, to date, morphological aspects from muscle and nerve biopsies have not been reported. Here, we describe a case of Guillain-Barré Syndrome (GBS) related to COVID-19 and demonstrate findings from peripheral nerve and skeletal muscle biopsies. A 79-year-old man presented with progressive weakness in both legs over one-week, evolving to both arms and urinary retention within 6 days. Four days earlier, he had a cough, febrile sensation and mild respiratory discomfort. On admission, his was afebrile, and without respiratory distress. A neurological examination disclosed asymmetric proximal weakness, diminished reflexes and no sensitive abnormalities. Three days later, the patient presented with bilateral facial weakness and proximal muscle strength worsened. Deep tendon reflexes and plantar responses were absent. Both superficial and profound sensitivity were decreased. From this point, oxygen saturation worsened, and the patient was placed on mechanical ventilation. CSF testing revealed one cell and protein 185 mg/dl. A chest CT showed the presence of ground-glass opacities and RT- PCR for SARS-CoV-2 was positive. The muscle biopsy revealed moderate neuromyopathic findings with positive expression for MHC- class I, C5b9, CD8 and CD68. The nerve biopsy showed inflammatory infiltrates predominantly with endoneurial compound formed by CD45 and CD68. The patient was treated with Oseltamivir for 9 days followed by IVIG for 5 days and died three days later of septic shock. **Discussion:** this is the first documented case of GBS associated with COVID-19 with a muscle and nerve anatomopathological study. A systematic review about neurological complications caused by COVID-19 described 11 patients with GBS. The morphological features reported in our patient showed signs of involvement of the immune system, suggesting that direct viral invasion could have played a role in the pathogenesis of peripheral nerve injury. Hereafter, further research will be necessary to understand the triggers for these cells migrating into the peripheral nerve.

Keywords: COVID-19; Peripheral Nervous System; Biopsies; Guillain- Barré Syndrome.

Resumo

Introdução: O envolvimento do sistema nervoso periférico (SNP) na COVID-19 é raro e, até o momento, os aspectos morfológicos de biópsias de músculo e nervo não foram relatados. Descrevemos um caso de Síndrome de Guillain-Barré (SGB) na vigência de COVID-19 destacando os achados na biopsia de músculo e nervo. Um homem de 79 anos apresentou fraqueza progressiva em ambas as pernas ao longo de uma semana, evoluindo para ambos os braços e retenção urinária em 6 dias. Quatro dias antes, apresentou tosse, sensação febril e leve desconforto respiratório. Na admissão, apresentava- se afebril e sem alteração respiratória. O exame neurológico mostrou fraqueza proximal assimétrica, reflexos diminuídos e sensibilidade preservada. Três dias após, o paciente evoluiu com fraqueza facial bilateral e piora da força muscular proximal. Reflexos tendinosos profundos e cutâneo plantar ausentes bilateralmente. A sensibilidade superficial e profunda estavam diminuídas. Evoluiu com piora na saturação de oxigênio sendo colocado sob ventilação mecânica. O exame de liquor revelou uma célula e aumento de proteína (185 mg / dl). A TC de tórax revelou a presença de opacidades em vidro fosco e o RT-PCR

para SARS-CoV-2 foi positivo. A biópsia muscular mostrou achados neuromiopáticos moderados com imunoexpressão positiva para MHC classe I, C5b9, CD8 e CD68. A biópsia de nervo revelou infiltrado inflamatório inflamatórios predominantemente endoneural composto por CD45 e CD68. O paciente foi tratado com Oseltamivir por 9 dias seguido de IVIG por 5 dias indo a óbito após três dias por choque séptico. Discussão: Este é o primeiro caso documentado de SGB associada a COVID-19 com estudo anatomopatológico de músculo e nervo. Uma revisão sistemática de complicações neurológicas associadas à COVID-19 descreveu 11 pacientes com SGB. As características morfológicas em nosso paciente mostrando sinais de envolvimento do sistema imunológico sugere que a invasão viral direta pode ter colaborado no processo patogênico da lesão neuromuscular. A partir daí, mais pesquisas serão necessárias para entender os gatilhos para essas células migrarem para o nervo periférico.

Palavras-chave: COVID-19; Sistema Nervoso Periférico; Biópsias; Síndrome de Guillain-Barré.

BACKGROUND

The primary manifestation of COVID-19 is respiratory, but neurological features are also being reported in the literature as case reports and case series. However, the mechanism involved in the induction of neurological manifestations is not well known[1]. Peripheral nervous system (PNS) involvement is notably scarce and morphological aspects from muscle and nerve biopsies have been scarcely reported[2,3]. Here, we describe a case of Guillain-Barré Syndrome (GBS) related to COVID-19 and present the findings from nerve and muscle biopsies.

REPORT OF A CASE

A 79-year-old man presented with progressive weakness in both legs evolving over one-week to both arms, and urinary retention within 6 days. Four days earlier he had cough, febrile sensation and mild respiratory discomfort. Relevant conditions of his medical history included hypertension, hypothyroidism and controlled type 2 diabetes. No previous neurological history was reported. On admission, he was afebrile, oxygen saturation was 96% and the respiratory rate was 16 breaths per min. Neurological examination disclosed asymmetric proximal weakness (3/5 right upper limb and left lower limb; 2/5 left upper limb and 1/5 right lower limb) and diminished reflexes. There were no sensitive abnormalities. Three days later, the symptoms progressed, presenting with bilateral facial weakness, and proximal muscle strength worsened. Deep tendon reflexes and plantar responses were absent. Superficial and profound sensitivity were decreased. From this point, oxygen saturation worsened (under 94%), the patient was placed on mechanical ventilation and transferred to an intensive care unit. Laboratory results, including creatine kinase, were normal except for an increased erythrocyte sedimentation rate of 60 mm. CSF testing revealed one cell, protein 185 mg/ dl, glucose 60 mg/dl, with normal cytology and sterile cultures. Recent infection of CMV, HIV, HTLV, syphilis and hepatitis were also negative. Conduction studies and EMG were not done due the peak of this pandemic. Brain computed tomography (CT) was normal and a chest CT showed the presence of ground-glass opacities with severe pulmonary involvement. Oropharyngeal and nasopharyngeal swabs were positive for SARS-CoV-2 on the RT-PCR assay. A muscle fragment from tibialis anterior revealed moderate to intense variation in muscle fibre size; hypertrophied fibres with internalised nuclei, nuclear clumps, small group atrophy and atrophy of both types. Immunohistochemical results showed positive immune expression for MHC-class I and C5b9, and scarce CD8 lymphocytes and CD68 macrophages. A sural nerve biopsy showed an inflammatory infiltrate, predominantly endoneurial, formed mainly by CD45 leucocytes and CD68; CD4, CD8, CD20 lymphocytes were rare. (Figure 1). The patient was treated with

Oseltamivir for 9 days followed by IVIG administration (0.4 g/kg) for 5 days. Although the pulmonary condition remained unchanged, the patient presented improvement in his neurological condition. Three days after IVIG administration, he died of septic shock.

DISCUSSION

To our best of knowledge, this is the first case of GBS associated with COVID-19 together with a muscle and nerve anatomopathological study. PNS manifestations are rare, with the most common being hypogeusia (5.6%) and hyposmia (5.1%), while skeletal muscle complaints were report in 10.3% of patients[2-4].

Recently, a systematic review about neurological complications caused by COVID-19 reported 6 publications about GBS, totalling 11 patients and only 2 cases of rhabdomyolysis[5]. Patients infected with COVID-19 showed significantly higher blood levels of cytokines and chemokines[6].

The morphological features described in our patient showed signs of involvement of the immune system, suggesting that direct viral invasion could have a role in the pathogenesis of peripheral nerve injury. However, one previous article analysed nerve biopsies from 35 autopsies who died with COVID-19 and demonstrated that Covid-19 immunohistochemistry was negative in muscle and nerve in all patients[2]. Both tissues, nerve and muscle showed inflammatory and immune-mediated damaged probably associated to cytokines activation[2,3].

The inflammatory cell infiltrate, characterised mainly by the presence of CD45 and CD68, confirmed the activation of phagocytosis and cytokine production which play an essential role as regulator of macrophages or T(Th) cells[7]. Also, the predominant cell infiltrate in endoneurial regions drew our attention to the similarities observed in nerve biopsies from patients with HIV, including polyneuropathy which shows inflammatory cell infiltrates affecting endoneurial and/or epineurial small vessels[8].

The muscle biopsy findings also favour the participation of the immune system in the pathogenesis of muscle lesions. Although the infiltrated cells were scarce (CD4, CD8, CD68, CD20), the expression of MHC-class I on the sarcolemma and C5b9 on the sarcolemma and sarcoplasm point to the activation of cytotoxic T cells and complement pathway, respectively. Lately, Aschman et al, studied muscle and myocardial inflammation in patients with COVID-19 in a series of 43 patients who died after COVID-19. Most saples showed signs od myositis ranging from mild to severe grade. The inflammatory process in skeletal muscle was related to duration of illness suggesting that the disease could be associated with a immune-mediated myopathy, postinfectious3. In our case, the muscle and nerve alterations was found from the beginning of the disease.

Hereafter, further research will be necessary to understand the triggers for these cells migrating into the peripheral nerve.

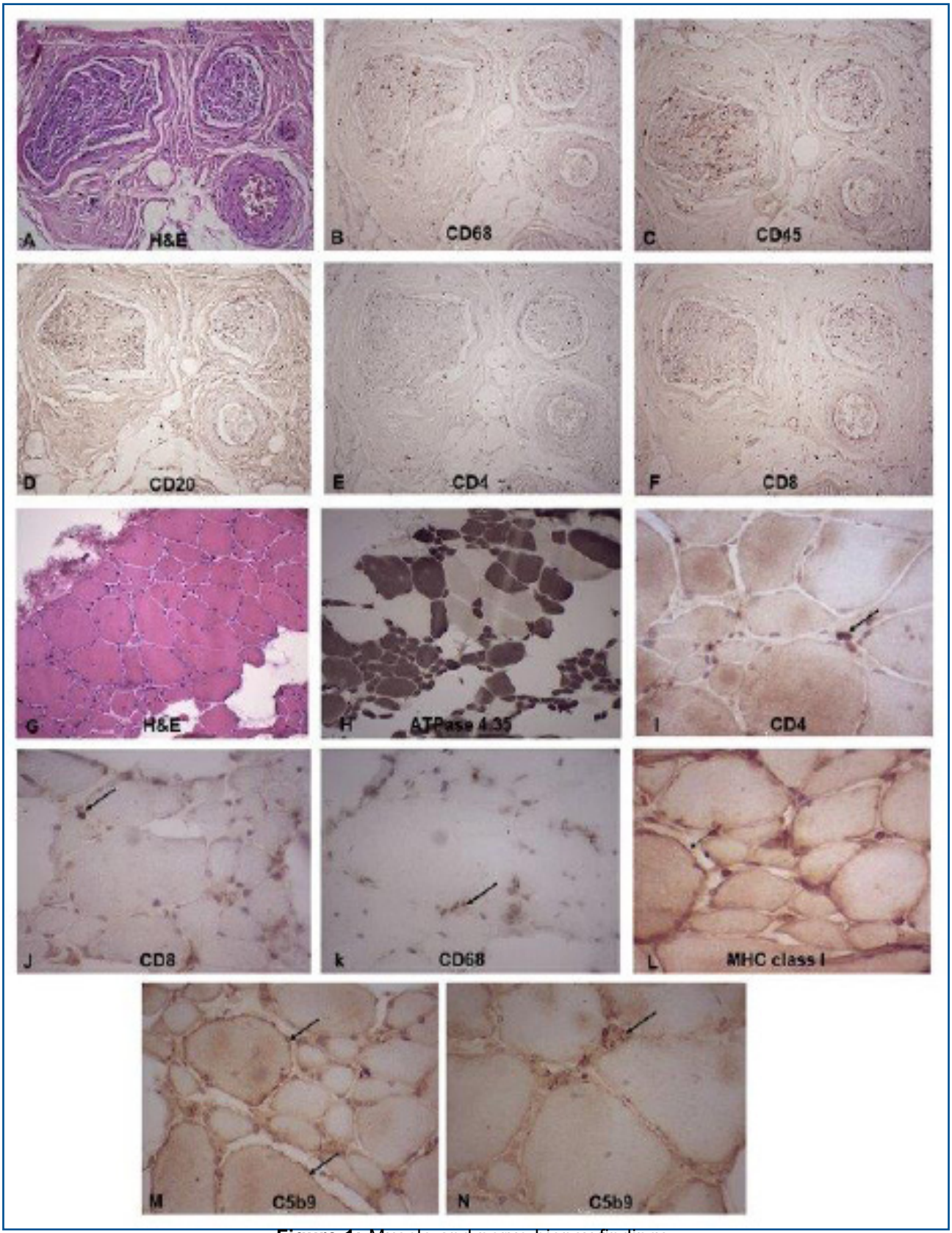

Figure 1: Muscle and nerve biopsy findings.

Legend Figure 1: A, B, C, D, E and F(nerve): A: presence of moderate endoneurial inflammatory infiltrate and mild perivascular infiltrate; B and C: moderate endoneurial immunoexpression of CD68/CD45; D,E and F: mild endoneurial immunoexpression of CD20 and CD8 and scarce immunoexpression of CD4. G and H(muscle): Moderate to severe variation of muscle fibres size; hypertrophied fibers with internalized nuclei; group atrophy and nuclear clumps; ATPase 4.3: atrophy of both types, type 1 predominance, group atrophy and type grouping; I, J, K, L, M, N (muscle): I,J,K: scarce CD4,CD8 and CD68; L: positive immunoexpression of MHC-class I; M, N: positive immunoexpression of C5b9 on the sarcolemma and inside of muscle atrophic fiber; L: positive immunoexpression of MHC class I on the sarcolemma.

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CHAPTER 24

MENTAL HEALTH STATUS AND QUALITY OF LIFE OF PEOPLE WITH DISABILITIES IN SOCIAL ISOLATION

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Abstract

Introduction: at this critical moment of the COVID -19 pandemic, we observe the social withdrawal and the break from the routine of individuals in society, for people with disabilities who need adequate support and a routine of more intense and effective activities may feel a greater need for care and attention of family support for solving everyday problems. **Objective:** to identify factors associated with the impact of the pandemic on the quality of life of individuals with disabilities and their caregivers. **Methods:** a virtual survey was carried out with parents and caregivers of people with disabilities to identify the main factors associated with the impact of the Pandemic on daily life and social relationships between family and community. **Results:** of the parents and caregivers we had access to and answered the questionnaire, 90% are residents of the ABC region of São Paulo. Their children and adolescents with disabilities are between 4 and 18 years old. The main scores of caregivers on difficulties in care during the pandemic, 70% felt helpless at some point, 17% had difficulties in performing self- care activities, 42% had anguish and fear during the period, 83% have the greatest responsibility for household decisions, and about 50% can share those decisions**. Conclusion:** the main complaints about the care of people with disabilities during the COVID-19 pandemic are related to the feeling of fear and anguish that affects decision-making and family relationships, which influences self-care activities and mental health of this population.

Keywords: Health Assessment; COVID-19 Pandemic; Mental Health; Quality of Life; Occupational Therapy.

Resumo

Introdução: neste momento crítico da pandemia de COVID -19, observamos o afastamento social e a quebra da rotina dos indivíduos na sociedade, para a pessoa com deficiência que necessita de suporte adequado e uma rotina de atividades mais intensas e efetivas podem sentir maior necessidade de cuidado e atenção do suporte familiar para resolução que problemas cotidianos. **Objetivo:** identificar os fatores associados ao impacto da pandemia na Qualidade de vida dos indivíduos com deficiência e seus cuidadores. **Método**: foi realizado um inquérito virtual com pais e cuidadores de pessoas com deficiência no para identificar os principais fatores associados ao impacto da Pandemia no cotidiano e nas relações sociais entre família e comunidade. **Resultados:** dos pais e cuidadores que tivemos acesso e responderam ao questionário, 90% são residentes da região do ABC de São Paulo, suas crianças e adolescentes com deficiência têm entre 4 e 18 anos de idade. As principais pontuações dos cuidadores sobre as dificuldades no cuidado durante a pandemia, 70% se sentiram desamparadas em algum momento, 17% tiveram dificuldades para realizar atividades de autocuidado, 42% tiveram angústias e medo durante o período,83% tem a maior responsabilidade nas decisões do lar, e cerca de 50%

conseguem compartilhar tais decisões. **Conclusão:** das principais queixas para o cuidado da pessoa com deficiência durante a pandemia de COVID-19, estão relacionadas a sensação de medo e angústia que afeta a tomada de decisão e as relações familiares, o que influencia as atividades de autocuidado e na saúde mental desta população.

Palavras-chave: Avaliação de Saúde; Pandemia de COVID-19; Saúde Mental; Qualidade de Vida; Terapia Ocupacional.

INTRODUCTION

At the end of 2019, we witnessed an event that the world has not faced for a long time, a new scenario motivated by the pandemic of a hitherto unknown microorganism. The newly discovered new strains of the new coronavirus were able to transform world history in a short period.

Coronavirus, named for thestructural conformation that gives it a coronal appearance belongs to a large family of positive single-stranded RNA viruses that parasitize and cause disease in mammals and birds, usually this class of virus, when it infects animals, it rarely affects humans[1]. This family of viruses was first isolated in early 1931; the coronavirus in question was the infectious bronchitis virus (IBV) and caused an acute and extremely contagious respiratory infection in birds2, already the first infection in people resulting from a coronavirus was identified in 1965 promoted by various strains of coronavirus and in almost 100% of cases involved upper airway infection[2].

Around 2003, a new variant of this virus family was responsible for an outbreak of severe acute respiratory syndrome, SARS-CoV. An individual admitted to the Prince of Wales hospital in Hong Kong was responsible for more than 100 minor disease cases. Other waves happened in the same country, at the Amoy Gardens housing complex, on Air China's flight from Hong Kong to Beijing, or at the Metropole Hotel, being the agent of the spread to Canada, Vietnam, and Singapore, resulting in hundreds of other confirmed cases of the disease[3].

In December 2019, a new variant of this family of microorganisms appeared, the so-called SARS-CoV-2 (Severe Acute Respiratory Syndrome-coronavirus 2), responsible for the development of the so-called coronavirus disease, currently known as COVID- 19 worldwide. This was first reported in China, in the state of Wuhan, Hubei province, spreading around the world extremely quickly, with less than three months, being declared a pandemic state by the World Health Organization (WHO) in March 2020[4,5].

During this critical moment of the COVID-19 pandemic, we observed the social withdrawal and the break in the routine of people in social life, considering that the person with a disability needs adequate support and a routine of activities, sometimes more intense and effective, and considering that researches point to a higher expectation of people with disabilities due to economic, social and affirmative policy advances.

Within the scope of health policies contemplated in Brazil, Health Promotion is the process that enables people to enhance control over their health. The central role of Public Health in confronting communicable diseases than communicable and others of a chronic nature, among other health threats[6,7].

When observing the numerous characteristics and comorbidities that can affect individuals with Cerebral Palsy and other disabilities such as Autism and Syndromes that cause some change in behavior and communication relationships, certain singularities of individuals affected by such conditions may feel the greater need of care and attention from family support for solving everyday problems[8].

Due to the repercussions arising from the COVID-19 Pandemic[9], which generated millions of deaths and hundreds of millions of infected people in the world, in Brazil, it highlighted the need for actions to contain the spread of the virus, with the application of social distancing to reduce transmission and this impacts the way we live and live, even with such measures we observe an important impact on the Unified Health System[10].

For people with disabilities, some determinants can be enhanced, according to the severity of the comorbidities that affect them. In some cases, its repercussions on daily life become very important, including for people who live and live with the person with a disability. Given the above, it is necessary to identify the impacts of the pandemic on Quality of life, especially among individuals with disabilities and their caregivers.

METHODS

This is a descriptive study with people who live and live with people with disabilities. In the face of physical and social isolation, they find themselves without face-to-face assistance to carry out activities, whether for educational or recreational purposes.

A virtual survey was carried out with about 20 parents and caregivers of people with disabilities to identify the main factors associated with the impact of the Pandemic on daily life and social relations between family and community.

Among the different analysis models, we chose to use the quality of life assessment method, through the SF-36 (The Medical Outcomes Study 36 - has Short- Form Health Survey), this generic instrument of easy administration, widely used in the literature[11,12].

Currently considered a health-related quality of life assessment model. This survey is based on a multidimensional instrument composed of 8 domains, with a scale from 0 to 100, in which 0 (zero) corresponds to the worst and 100 (one hundred) to the best perception of the individual's quality of life.

Questions related to the survey carried out with parents and caregivers can be found in the link on the electronic form: https://forms.gle/rQgpmreehbansZm1A

As this study is restricted to parents and caregivers of a Special Education Unit of a Municipality in the Greater ABC region, registration with the Research Ethics Committee was requested to resolve any conflicts of interest and procedures that could cause damage to the health of the participants in this study. The number of the respective research ethics committee follows CAAE: 56553816.4.0000.0082.

RESULTS

Of the parents and caregivers, we had access to and answered the questionnaire, 90% are residents of the ABC region of São Paulo, their children and adolescents with disabilities are between 4 and 18 years old.

Of the findings related to the survey carried out with the SF-36 quality of life questionnaire, the analysis parameters present the following results, as shown in Table1.

Table 1: Results of the domains observed by the SF- 36 Quality of Life questionnaire with individuals who live and live with people with disabilities and their impact on health during the pandemic period.

Domains	Score
Functional capacity	48.60
Limitation of physical aspects	99.00
Ache	19.38
general health status	24.13
Vitality	19.30
Social aspects	24.25
Limitation by emotional aspects	98.33
Mental health	18.84

Source: authors

From the main points observed in the study, we found that the issues related to responsibility and decision- making were presented in the following question.

When questioned about trust for decision making, we observed the main answers shown in Figure 2, with 1 representing RARELY and 5 ALWAYS.

DISCUSSION

The main scores of caregivers on difficulties in care during the pandemic, 70% felt helpless at some point, 17% had difficulties in performing self-care activities, 42% had anguish and fear during the period, 83% have the greatest responsibility for household decisions, and about 50% can share those decisions. 88% say they have a healthy relationship with their children and feel confident to solve domestic problems. However, 58% of the participants say they are mentally well at the time of the survey.

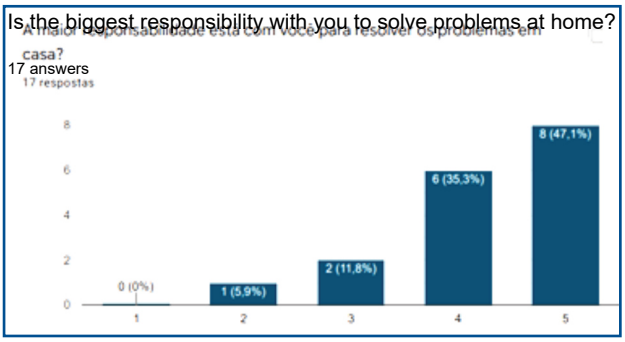

Figure 1: Questionnaire item carried out with families of people with disabilities, 1 represented with RARELY and 5 ALWAYS.
Source: authors

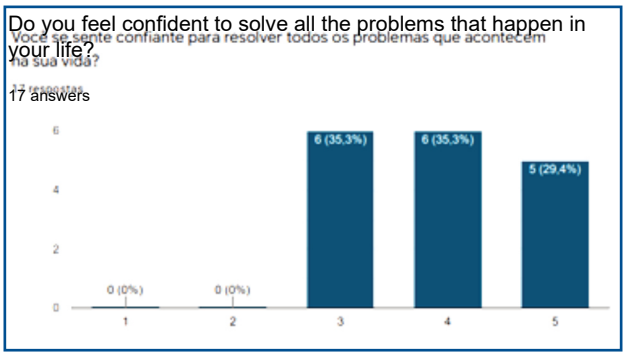

Figure 2: Item of the questionnaire carried out with families of people with disabilities, 1 represented with RARELY and 5 ALWAYS.
Source: authors

Translated and adapted for the Brazilian13 instrument encompasses generic data about the quality of life, its 36 items distributed in domains such as functional capacity related to the performance of daily activities (DA)[12].

These domains include self-care, dressing, bathing and climbing stairs, physical aspects that involve the impact of physical health on the performance of AD and/ or professionals, Pain and refers to the level of pain and the impact on the performance of AD and /or professionals, general health status and their subjective perception of the general health status, vitality that refers to the perception of the individual's energy and fatigue level, social aspects that show the reflection of the physical health condition in

social activities, aspects emotional conditions and how their emotional conditions affect the performance of AD and/or professionals, mental health that assesses their perception of mood and well-being[12].

This survey also involves a question of comparative assessment between the current health condition concerning the previous year[12]. Among these issues related to the quality of life, questions were also included at this time questions, topics related to sociodemographic data, and specific questions about their perception of mental health, decision-making and family relationships, so we can analyze more broadly their perception of pandemic and the social isolation of this population and what is the impact of this unhealthy condition on people.

Considering the results observed by the SF-36 instrument, in our study, we can identify that the main aspects in issues related to mental health and in the resolution of family conflicts are quite important and indicate that there may be a tensioning of the issues and at the time of the pandemic, but, it does not bring evidence about the difficulties in settling conflicts. These issues can influence the mental health of individuals when they are unable to solve problems in family relationships.

We observed in the analysis parameters the following results: functional capacity (48.60 points), a value far from the most important quality of life goal, considering that values closer to 100 points are as higher quality of life conditions, by example. The condition of limitation of physical aspects with 99 points indicates that, in general, this sample indicates that physical problems are not more important at the time of social isolation.

Limitation by emotional aspects (98.33 points) indicates that these findings demonstrate that the ability to solve problems and resolve family conflicts may not be affected to the detriment of social isolation, as observed in other studies such as the findings by Bezerra (2020)[14] in which shows us which issues of social isolation influence the behavior of individuals.

Mental Health (18.84 points) about the low value concerning the parameters of a better quality of life in terms of mental health (close to 100) indicate that factors influencing the progress of the pandemic and the fear proven by the possibility of the contamination may exert influence on this indicator.

The aspect related to pain (19.38 points) reveals important evidence regarding pain during this moment of the pandemic. For the general health status (24.13 points) it also indicates that there are problems that influence the health of individuals.

Vitality (19.30 points) shows that during this time of pandemic it also indicates that there are problems that influence the health of individuals, as we observed in Social Aspects (24.25 points) that influence the health of individuals, especially if we observe that social relationships were greatly affected due to the restrictive measures to contain the COVID-19 pandemic and its escalation of deaths.

Effects are resulting from the pandemic, such as anxiety and depression problems due to job loss, death of family, friends, and colleagues, financial insecurity, and social isolation, culminating in reduced quality of life and activities of daily living[15]. In addition, although clinical symptoms are predominantly respiratory associated with severe pneumonia, direct and indirect involvement of other organs is common. The main target after the lungs is the cardiovascular system, which makes heart disease a powerful group of risk, increasing the probability of developing severe infection[16].

Gao et al.[3] looked for relationships between mental health problems and excessive social media exposure during the COVID-19 outbreak. Compared to national data, there was a higher prevalence of depression, anxiety, or even the combination of these two psychological disorders during the outbreak of COVID-19. In the same direction, Zhang et al.[17] investigated the immediate impact of COVID-19 on the mental health and quality of life of patients in China. An association of the disease with a mild level of stress was found.

Depression and anxiety are intrinsically linked to the loss of quality of life, and the decrease in activities of daily living, which can worsen the prognosis of COVID-19 since psychological disorder and depression can affect the immune system's response[18]. In addition, depressed patients may have negative attitudes towards antiviral therapy, reducing treatment adherence and individual recovery[19-21].

These comorbidities, linked to COVID-19, are powerful indicators for compromised quality of life, whether due to psychological disorders related to the disease or even to decreased physical activity caused by social isolation, this association of events related to decreased health of the patient with coronavirus disease.

This study presents an outline of a specific group of parents and caregivers of people with disabilities, so we cannot emphasize that these results represent a larger group or class of individuals, as no statistical treatment was applied to evidence their expression in the population. Furthermore, the quality of life indicators present us with an overview of the perception of individuals in social isolation and may bring us new hypotheses for approaches to reduce the impact of the pandemic on the daily lives of these individuals.

CONCLUSION

One of the main complaints about the care of people with disabilities during the COVID-19 pandemic is the feeling of fear and anguish that affects decision-making in family relationships, which influences self-care activities and the physical and mental health of this population.

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CHAPTER 25

THE INFLUENCE OF SOCIAL ISOLATION ON THE INCIDENCE OF POSITIVITY IN COVID-19 TESTS IN A METROPOLITAN REGION OF SÃO PAULO, BRAZIL

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Abstract

Introduction: With the arrival of the SARS-CoV-2 (Coronavirus 2 of severe acute respiratory syndrome) pandemic in Brazil, especially in the city of São Paulo, there was a need to apply social isolation policies associated with testing, covering all municipalities. The Clinical Analysis Laboratory of Centro Universitário FMABC was one of the first laboratories to receive certification and qualification to perform RT-PCR (reverse transcriptase reaction followed by polymerase chain reaction) tests in the metropolitan region of São Paulo. **Objective:** Aim to analyze the influence of adopting social isolation on the incidence of positivity in COVID-19 tests in the metropolitan region of São Paulo, Brazil. **Methods:** a descriptive study carried out from March to May 2020, epidemiological data were collected from each unit served and organized by the data controllership team of the Clinical Analysis Laboratory of FMABC. Epidemiological, demographic, and laboratory data were extracted from the Matrix® outpatient data management system. Clinically suspected cases and confirmed by laboratory tests (RT-PCR and serological tests) were entered. The tests were divided into serological tests using the RT-PCR molecular test, on samples of nasopharyngeal mucosal scrapings collected with sterile Swab. **Results:** It were evaluated PCR test and antibody presence (IgA, IgM and IgG) in blood samples of 16.297 patients. 22.718 tests were performed for the diagnosis of COVID-19, both RT-PCR (10.410 tests) and serological tests to detect anti-SARS-CoV-2 antibodies, IgA, IgM and IgG, a total of 16.297 patients were assessed, 63% women and 37% men. It was observed that the social isolation policies adopted during this period contained the massive expansion of contamination, at least while the social isolation rates were above 55%. **Conclusion:** The data of this study demonstrated the effectiveness of social isolation in containing the positive contamination of SARS- CoV-2 in the metropolitan region of São Paulo, at least for the first three months.

Keywords: Coronavirus Disease 2019; Social Isolation; Brazil.

Resumo

Introdução: com a chegada da pandemia de SARS-CoV-2 (Coronavirus 2 da síndrome respiratória aguda grave) ao Brasil, especialmente na cidade de São Paulo, houve a necessidade de aplicar medidas de distanciamento social associado a testagem, que abrangesse todos os municípios. A região metropolitana de São Paulo compreende 39 municípios e possui uma rede de laboratórios habilitados a realizar a testagem para a detecção do coronavírus, tanto testes sorológicos quanto moleculares. O Laboratório de Análises Clínicas do Centro Universitário ABC/FMABC foi um dos primeiros laboratórios a receber a certificação e habilitação para realizar os testes RT-PCR (reação da transcriptase reversa seguida pela reação em cadeia da polimerase) na região metropolitana de São Paulo. **Objetivo:** analisar a influência da adoção do isolamento social na incidência de positividade nos testes de COVID-19 em região metropolitana de São Paulo, Brasil. **Método:** estudo descritivo realizado no período de março a maio de 2020, os dados epidemiológicos foram coletados de cada unidade atendida e organizada pela equipe de controladoria de dados do Laboratório de Análises Clínicas da FMABC. Os dados epidemiológicos, demográficos e laboratoriais foram extraídos do sistema Matrix® de gerenciamento de dados ambulatoriais. Foram inseridos os casos clinicamente suspeitos e confirmados por testes de laboratório (RT-PCR e testes sorológicos). Os testes foram divididos em testes sorológicos no teste molecular RT-PCR, em amostras de raspado de mucosa nasofaríngea coletada com Swab estéril. **Resultados:** foram avaliados o teste de RT-PCR e a presença de anticorpos (IgA, IgM e IgG) em amostras de sangue de 16.297 pacientes. Foram realizados 22.718 testes para o diagnóstico de COVID-19, tanto RT-PCR (10.410 testes), quanto testes sorológicos para detecção de anticorpos anti-SARS-CoV-2, IgA, IgM e IgG, um total de 16.297 pacientes foram avaliados, 63% mulheres e 37% homens. Observou- se que as políticas de isolamento social adotadas nesse período continham a expansão massiva da contaminação, pelo menos enquanto as taxas de isolamento social eram superiores a 55%. **Conclusão:** nossos dados demonstraram a efetividade do isolamento social na retenção da positividade da contaminação do SARS-CoV-2 nas cidades contempladas pelo serviço de testagem do Centro Universitário Saúde ABC, pelo menos nos três primeiros meses.

Palavras-chave: Doença do Coronavírus 2019; Isolamento Social; Brasil.

INTRODUCTION

In late November 2019, a new disease caused by coronavirus-2 (SARS-CoV-2) appeared in Wuhan, China. Infection with this new coronavirus results COVID-19, an acute respiratory syndrome with approximately 4% lethality[1,2]. On March 11th 2020, the World Health Organization (WHO) raised the status of SARS-CoV-2 contamination to pandemic, due to its geographical spread to most continents[3].

Brazil adopted the social distancing as one of the sanitary measures to pandemic control. This social distance is one of the preventive measures to control the extensive dissemination of COVID-19. Thus, these measures of social distancing, as a non-pharmacological intervention to combat COVID-19, are widely used around the world and promote better performance in flattening the COVID-19 pandemic curve. The intervention non-pharmacological to combat COVID-19 are widely used around the world and promote better performance in flattening the COVID-19 pandemic curve of social distancing is effective as a public health measure with individual, environmental and community reach, promoting the isolation of cases, reduced contact between individuals and a reduction in the number of deaths related to COVID-19[4].

In February 2020, the first case of contamination by SARS COV-19 emerged in Brazil, in the city of São Paulo[5]. This patient number 0 was a 61-year-old man who had just returned from the region of Lombardy in Italy a few days before. From this moment on, new cases emerged and the need for restrictive measures became imminent. On March 17th, the first fatal victim of COVID-19 happened in São Paulo; the patient was a 62-year-old man with type 2 diabetes mellitus, hypertension and prostatic hyperplasia[6].

Considering the imminent increase in the number of new cases in Brazil and the possibility of high lethality, the first social isolation policies were introduced in the country. Conceptually, social isolation is the measure applied for the separation of social contact from people considered as ‘suspect’ cases, or the restriction of social contact of people infected with COVID-19 with uninfected people. Quarantine, in turn, represents the restriction of restriction of movement of people who were exposed to a potentially

contagious disease[6,7]. At the start of quarantine in Brazil, the population was instructed to remain at home and to have as little contact as possible with people outside their daily interactions, in order to reduce the spread of the virus[8]. On March 16th, an official quarantine status was declared in Brazil. In the state of São Paulo, on that same day, classes and public service activities were suspended. Only services considered essential were kept in operation, such as: supermarkets, pharmacies, food distributors, basic health units and hospitals[6].

At the same time, the increase in testing to facilitate life-sustaining measures had become crucial[9]. In this sense, the Clinical Analysis Laboratory of the Centro Universitário FMABC initiated the validation processes of molecular tests for the detection of SARS-CoV-2 by RT-PCR, the gold standard in the diagnosis of COVID-19, and expanded investments to carry out serological testing for antibody detection. In this way, it could meet a great demand for tests.

São Paulo is the largest city in Brazil, with a territorial area of 1,521.110 km2, an estimated population of 12,252.023 people, with a demographic density of 7,398.260 inhabitants/km2. The Metropolitan Region of São Paulo comprises 39 cities in total. In this region, the Clinical Analysis Laboratory of the Centro Universitário FMABC/ABC Medical School was one of the first places to receive certification and authorization from the Adolfo Lutz Institute to diagnose COVID-19. This laboratory meets the demand for tests in 13 municipalities in the Metropolitan Region of São Paulo and on the coast of São Paulo. These municipalities have a population of approximately 3,190.000 inhabitants. The importance of studying this region is due to the fact that this is the largest metropolitan region in Brazil and the tenth, in this profile, most populous in the world. It comprises the largest economic hub in Brazil and is closely interdependent in relation to circulation and transport, so we hypothesized that social isolation would influence the increase in COVID-19 positive tests[10].

Considering the importance of social isolation and testing in the possible control of the dissemination of COVID-19. This study aimed to analyze the influence of adopting social isolation on the incidence of positivity in COVID-19 tests in the metropolitan region of São Paulo, Brazil.

METHODS

The diagnostic service performed by the Clinical Analysis Laboratory of the Centro Universitário FMABC met, during the first three months of the SARS-CoV-2 epidemic, the demand of 12 municipalities, these being: São Paulo (capital city), Francisco Morato, Franco da Rocha, Guarujá, Mairiporã, Caieiras, Mauá, Ribeirão Pires, Santo André, São Bernardo do Campo, São Caetano do Sul and Taboão da Serra. Laboratory tests were carried out through collections carried out in the Emergency Care Units (UPAs), Basic Health Units (UBSs), in the Municipal Hospitals of each municipality and University Hospitals, this is a reference laboratory for testing COVID-19 and referenced by the Brazilian Unified Health System.

This was a descriptive study carried out from March 7th, 2020 to May 31st, 2020; epidemiological data were collected from each serviced unit and organized by the data control team of the Clinical Analysis Laboratory at FMABC. The data obtained from each municipality were entered into spreadsheets for further analysis. Thus, it was possible to separate the patients seen at these health units according to the location of collection, age, gender and performed test. Subsequently, we verified the type of test used to detect COVID-19 performed in these regions. This study was approved by the Ethics Committee of Centro Universitário FMABC (process: 4.131.404). We ensure that this study has been carried out in accordance with Declaration of Helsinki.

Epidemiological, demographic and laboratory data were extracted from the Matrix® outpatient data management system. Clinically suspect cases were inserted and confirmed by laboratory tests (RT-PCR and serological tests). We divided the tests performed into serological tests, in which the presence of IgA, IgM or IgG antibodies in the patient's serum can be detected, and the RT-PCR molecular test, which identifies the presence of the SARS-CoV-2 RNA in samples of nasal and oropharyngeal mucosa secretion collected with sterile swab.

Additionally, maps of the city of São Paulo were generated using the Power BI® software with satellite information provided by Bing®, and divided by municipality. We used this data to design spatial databases, and thus, infer the incidence of positive tests for COVID-19 by municipality. To obtain the maps, we linked the databases via a spatial union operation.

Statistical Analysis

A descriptive analysis was performed and the qualitative variables were expressed as absolute and relative frequency. Quantitative variables were expressed as mean±standard deviation from the mean or median, maximum and minimum values. To analyze the quantitative data, we used the GraphPad Prism® 6.0 software and performed an ANOVA of repeated measures and Greenhouse-Geisser curve. Values were considered statistically significant when $p < 0.05$.

RESULTS

Between March 7th, 2020 and May 31st, 2020, a total of 22.718 tests were performed to detect the presence of the SARS-COV-2 virus or for the detection of COVID-19 antibodies in the metropolitan region of São Paulo. A total of 16.297 patients were assessed and the difference between the number of patients and the total number of tests was due to some patients having performed tests on different days or hospitals within this period (table 1). Of the total number of patients assessed, 10.327 (63%) were female and 5.970 (37%) were male (table 2). Among the patients contaminated with COVID-19 in this period, 8.246 were cured, which corresponds to 36%.

Table 1: Total participants assessed and age group (years)

Age group (years)	Quantity
0-5	414
6-20	476
21-40	7.585
41-60	5.635
61 or more	2.187
Total	16.297

Data expressed in absolute values.

Table 2: Total participants by gender and age group.

Female	Quantity
Age group (years)	
0-5	211
6-20	287
21-40	5.161
41-60	3.564
61 or more	1.104
Total	10.327
%	63
Male	
0-5	203
6-20	189
21-40	2.424
41-60	2.071
61 or more	1.083
Total	5.970
%	37

Data expressed in absolute values and relative (%).

Were performed a total of 10,410 RT-PCR tests, 3,027 total antibody serologic tests, 9,281 IGM tests and 8,246 IGG tests. The average time in days to perform the RT-PCR tests was 1.5 days (table 3).

Table 3: Types of tests performed during the period.

Month	RT-PCR	IgM/IgG
March	387	205
April	3.390	3.666
May	6.633	8.437
Total	10.410	12.308

Data expressed in absolute values.

As for the number of cases accumulated per week, it was identified that from the fifth week onwards, the exponential increase in the curve of accumulated cases in general and in the curve of accumulated weekly growth began (figure 1). At the same time, the growth rate and the weekly accumulation of new cases seen at the ABC Medical School's diagnostic service were compared with the official indexes of social isolation in the metropolitan region of São Paulo.

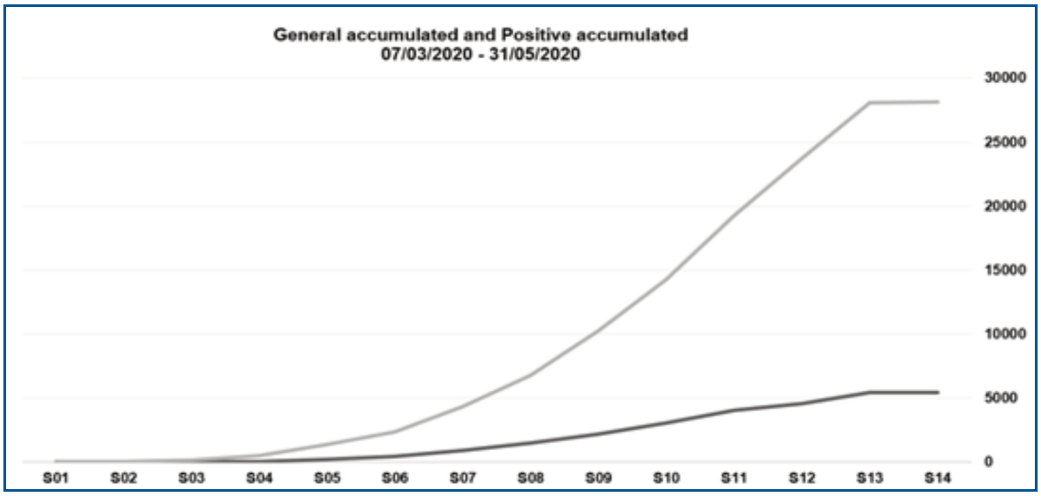

Figure 1: Representative curve of general accumulated cases (light gray line) and positive accumulated cases (dark gray line) in the period from March 7th, 2020 to May 31st, 2020. S= studied weeks

To assess the effect of social isolation in these regions, official data provided by the State Government were evaluated[11]. It was identified that from the first week of quarantine there was better population adherence to these measures. In the first official week of quarantine in the Metropolitan Region there was an adherence of approximately 38%, followed by increasing adherence in the second week (55%), reaching the peak of social isolation in the third week (58%). In the following three weeks, maintenance of these levels was observed, remaining on average at 56%. From the tenth week on, the levels remained below 50%, until reaching 48% in the thirteenth week, the last week of the analyzes in this study (figure 2).

Among the municipalities served by the diagnostic system, it was found that most tests were performed on samples from São Bernardo do Campo, followed by Santo André and São Caetano do Sul. Number of exams during the evaluated period. These results were shown on the map by means of blue circles that identify the municipalities served, and the difference in the size of the circles differentiates the volume of exams per municipality. The number of exams performed in this period was not determined by the total population of the municipalities themselves, but rather by the exams requested by each municipality at that time (figure 3).

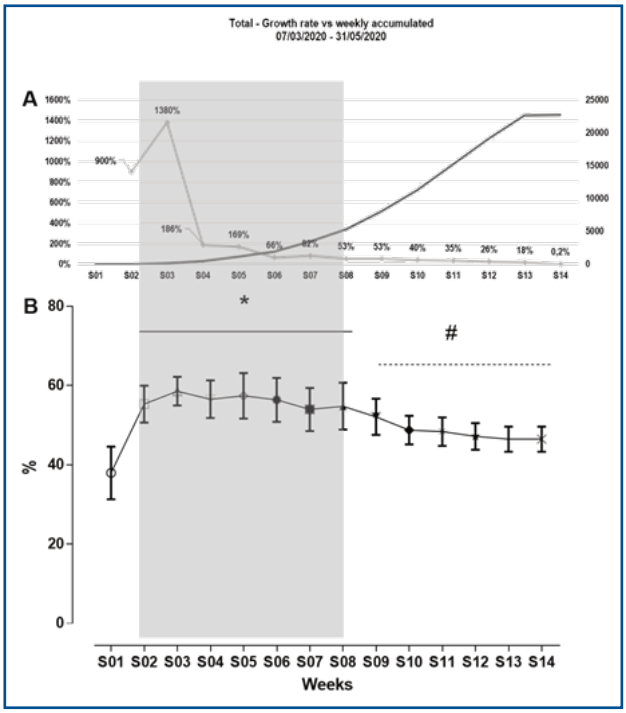

Figure 2: Representative figure of the total accumulated growth rate (dark gray line) versus weekly accumulated cases (light gray) (A). And the percentages of social isolation per week between March and May 2020 in the metropolitan region of São Paulo during the SARS-COV-2 pandemic (B). Values expressed as percentages. One Way ANOVA test (multiple comparisons) with Greenhouse-Geisser correction. *p <0.05 S1 vs. S2, S3, S4, S5. #p <0.05 S5 vs. S9, S10, S11, S12, S13, S14. S=weeks

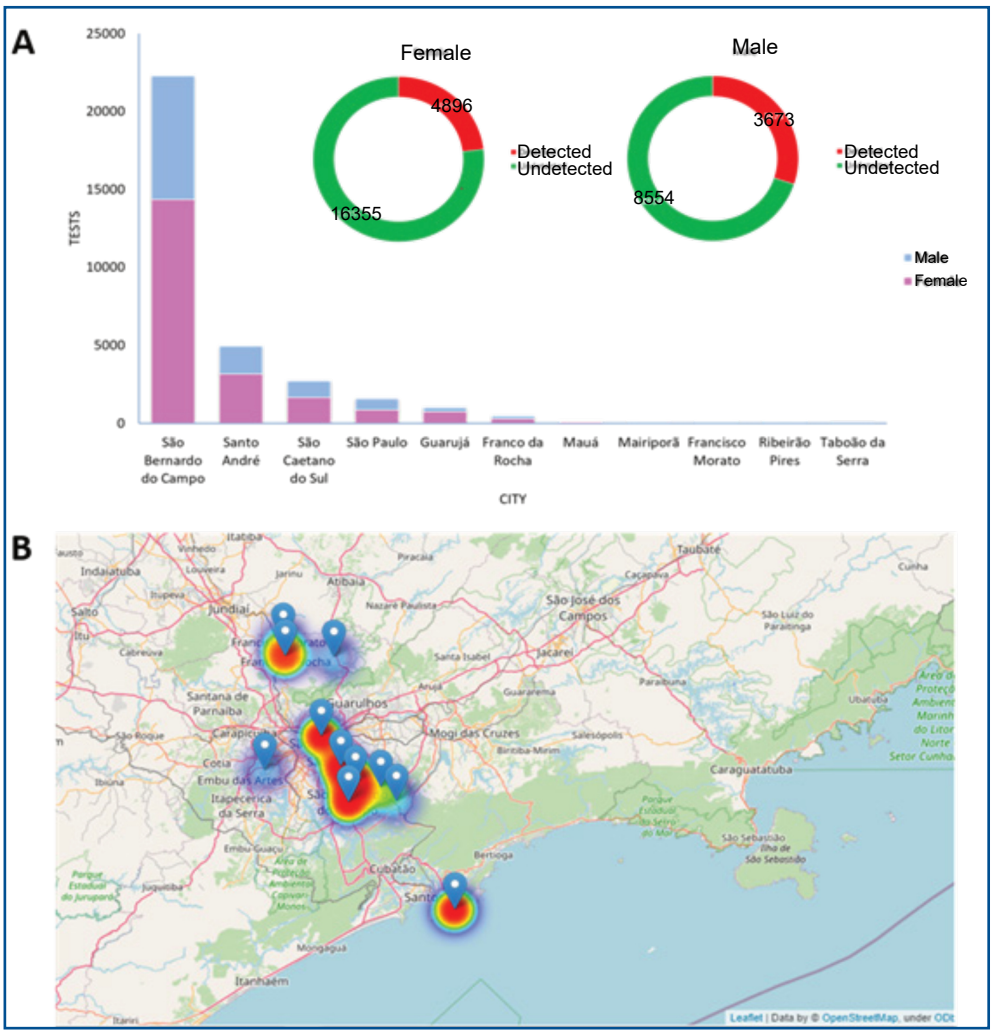

Figure 3: Representative image of the number of tests performed in the metropolitan region of São Paulo in the studied period (3/7/2020 5/31/2020) and the prevalence by sex in this period (A). Geolocation map of cities tested by the Clinical Analysis Laboratory of Centro Universitário FMABC (B). Blue circles identify the serviced cities and the difference in the size of the colored circles differentiates the volume of tests by municipality. Power BI® software

DISCUSSION

This study demonstrated the influence of social isolation on the positivity of the COVID-19 tests in this population. By observing the growth rate curve, parallel to the social isolation curve, it was noted that the growth rate was contained when the population's adherence to social isolation policies increased. While social isolation was above 55%, the growth curve remained stable. Calculations of mobile regression performed by other researchers proved that the restriction to human mobility is effective in promoting the decline in the acceleration of the growth rate from the first week onward, and that from the sixth week of restriction the rates remain stationary, if isolation is maintained12,13, this study corroborate these findings.

Studies of geographic distribution are commonly used in epidemiological studies and represents an important visual tool to understand the density of a disease, or, in the case of this study, the demographic location of the highest concentration of tests requested in

each city[14]. The use of these supplementary indicators to monitoring the spread of the disease is crucial for decision-making regarding the protocols to be followed, besides collaborating to appropriate management of patients in the hospitals and health units[13,15,16].

As for the observed testing, more serological tests (verifying the presence of anti-SARS-CoV-2 antibodies) than molecular tests (RT-PCR) were carried out in the first three months of the pandemic in the Metropolitan Region of São Paulo. It was emphasized that these tests were performed only at the Clinical Analysis Laboratory of the Centro Universitário FMABC, which comprises only one of the diagnostic systems qualified to perform the tests for the detection of COVID-19 in São Paulo. Official data from the government of the state of São Paulo showed that 26 thousand people were tested in March, 108 thousand in April and 361 thousand in May[17]. Thus, we verified that the diagnostic service of this laboratory was responsible for approximately 5% of the total tests carried out in the entire state of São Paulo. We found an average detection of COVID-19 of approximately 25% against 74% of negative tests for this disease. Mass testing is another fundamental tool for controlling the dissemination of COVID-19, and it needs to be expanded in Brazil.

Since the confirmation of the first case of SARS- CoV-2 contamination in Brazil, in the State of São Paulo in February of 2020, the first policies for the containment of the disease were initiated and, concomitantly, measures for social isolation, hand hygiene and wearing masks were stablished. However, a study that evaluated the profile of the people assessed in this area and the impact of social isolation on the positivity of COVID-19 had not been carried out in the Metropolitan region of São Paulo[18,19].

This study observed a higher prevalence of women, with a higher incidence in the age group from 21 to 60 years. The average age was 42 years for women and 45 years for men. The average age was similar to the averages observed in India[20] and Peru[21] and lower than the averages observed in China[22], Europe[23], Argentina[24] and Australia[25]. The age averages are compatible with the age of the economically active population of the assessed municipalities. The population of the Metropolitan Region of São Paulo is composed of young people, mostly, who transit daily between the municipalities using public transportation, due to the conurbation between municipalities. This is an area with a high concentration of companies and jobs, and most people use public transportation to transit, a fact that facilitates the transmission of infectious diseases, such as SARS-CoV-2[10,18]. The difference between the number of men and women is due to the fact that women have a culture of seeking more health services compared to men and several health professionals were tested, which also has a predominance of the female gender[20,26-27].

This study had as a limitation the impossibility of testing all municipalities in the Metropolitan Region of São Paulo. However, the association of social isolation with testing for COVID-19 in the region was demonstrated.

This study is the only one that shows the impact of the restrictive measures adopted in the State of São Paulo on the positivity of SARS-CoV-2 in the Metropolitan Region of the State. This study suggests that social isolation in a large city, such as the assessed region, is a highly effective protection measure against contamination, if followed properly, and associated with social distancing, it is also suggested that testing be expanded in these regions.

CONCLUSION

The data showed that social isolation reflected directly on the positivity of the SARS-CoV-2 tests in the Metropolitan region of São Paulo, in the municipalities covered by the testing service of the Centro Universitário FMABC. We infer that social restriction measures contained the massive spread of COVID-19. Testing in the studied municipalities favored the understanding of the profile of individuals infected in the region in the first three months of the SARS-CoV-2 pandemic.

Author contributions statements

AJN, GLV, JCSP, CGBOR, AVLS: Formal analysis, data curation, writting the main manuscript, preparation of the figures, review and editting. AJN, GLV, CGBOR, MCP, KCG, LIZ, MAS, GRS, AVLS and FLAF: Data collect. VLL, JRSR, BCAA, GLV: Data curation, writting, review and editting. AJN, GLV JCSP, FLAF: data curation, formal analysis, preparation of the figures, review and editting. All authors reviewed the manuscript.

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Data Availability Statement

The data will be available under reasonable request to e-mail glaucia.veiga@fmabc.br (Glaucia Luciano da Veiga, co-author).

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CHAPTER 26

PERFORMANCE OF EARLY LITERACY STUDENTS IN COGNITIVE-LINGUISTIC SKILLS DURING THE PANDEMIC

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Abstract

Introduction: the Covid-19 pandemic made discrepancies between the different educational realities more evident for schoolchildren in the beginning of literacy. **Objective:** to characterize the performance of cognitive-linguistic skills of students in early literacy phases during the pandemic. **Methods:** twenty-two elementary school students participated in this study, distributed in GI 1st year students and 2nd year GII students, submitted to the application of the Cognitive- Linguistic Skills Assessment Protocol for students in the initial stage of literacy. **Results:** students from GI and GII showed average performance for writing the name and writing the alphabet in sequence. The GI presented a refusal response for the subtests of word dictation, pseudoword dictation and picture dictation, word repetition and visual sequential memory of shapes and poor performance for alphabet recognition in random order and average performance for alphabet recognition in sequence. GII showed lower performance for the subtests of word dictation, pseudoword dictation, picture dictation and superior performance for alphabet recognition in random order, alphabet in sequence and visual sequential memory of shapes. **Discussion:** the appropriation of the letter-sound relationship mechanism raises questions, since it evidenced the difficulty of all students in cognitive-linguistic skills necessary for the full development of reading and writing in an alphabetic writing system such as Brazilian Portuguese. **Conclusion:** students in the 1st and 2nd years showed lower performance in cognitive-linguistic skills important for learning reading and writing.

Keywords: Literacy; Pandemic; Learning; Child Development; Education.

Resumo

Introdução: a pandemia do Covid-19 tornou mais evidentes as discrepâncias entre as diferentes realidades educacionais para os escolares em início de alfabetização. **Objetivo:** caracterizar o desempenho de habilidades cognitivo-linguísticas de escolares em fase inicial de alfabetização durante a pandemia. **Método:** participaram deste estudo 22 escolares do Ensino Fundamental I, distribuídos em GI escolares do 1º ano e GII escolares do 2º ano, submetidos a aplicação do Protocolo de Avaliação das Habilidades Cognitivo-Linguísticas para escolares em fase inicial de alfabetização. **Resultados:** os escolares do GI e GII apresentaram desempenho médio para escrita do nome e escrita do alfabeto em sequência. O GI apresentou resposta de recusa para os subtestes de ditado de palavras, ditado de pseudopalavras e ditado de figuras, repetição de palavras e memória sequencial visual de formas e desempenho inferior para reconhecimento do alfabeto em ordem aleatória e desempenho médio para reconhecimento do alfabeto em sequência. O GII

apresentou desempenho inferior para os subtestes de ditado de palavras, ditado de pseudopalavras, ditado de figura e desempenho superior para reconhecimento do alfabeto em ordem aleatória, alfabeto em sequência e memória sequencial visual de formas. **Discussão:** a apropriação do mecanismo de relação letra-som traz questionamentos, uma vez que, evidenciou a dificuldade de todos os escolares em habilidades cognitivo-linguísticas necessarias para o pleno desenvolvimento da leitura e da escrita em um sistema de escrita alfabético como o Português Brasileiro. **Conclusão:** os escolares do 1º e 2º anos apresentaram desempenhos inferiores em habilidades cognitivo-linguística importantes para a aprendizagem da leitura e escrita.

Palavras-chave: Alfabetização; Pandemia; Aprendizagem; Desenvolvimento Infantil; educação.

INTRODUCTION

Covid-19 spread rapidly around the world in 2020 and generated the unprecedented situation of 90% of the student population being isolated worldwide[1]. In this pandemic scenario, social isolation was initiated as a measure of prevention and attenuation of the virus, among these measures, in addition to the closing of many educational institutions, the suspension of in-person classes and remote teaching were implemented[2].

As for remote learning, it was implemented on an emergency basis, that is, they will only return to the face-to-face format once the health crisis has been resolved or controlled, thus providing students with temporary access to educational content in a way that minimizes effects of social isolation on their education and learning[3].

However, the Covid-19 pandemic made the discrepancies between the different realities experienced by young students even more evident, access to virtual classes using more advanced digital tools and teachers trained to practice was not egalitarian or homogeneous between the systems of public and private education[2,3].

Therefore, more than an educational problem, the blocking of access to school reconfigured the education system, society and, consequently, the role of speech therapy in clinical speech therapy.

Based on the above, this study aimed to investigate whether the period of remote access education established during the pandemic compromised the development of cognitive-linguistic skills necessary for the full literacy of students in the initial literacy phase.

Therefore, the aim of this study was to characterize the performance of cognitive-linguistic skills of schoolchildren at an early stage of literacy during the pandemic.

METHODS

Study design

This is a cross-sectional study.

Location and period of study

The evaluation was carried out at the Laboratory for Investigation of Learning Deviations (LIDA) located at CER II - Specialized Center in Rehabilitation of FFC/ UNESP - Marília-SP.

Data collection was carried out during the Covid-19 Pandemic period, and all safety standards determined by the FFC/UNESP-Marília-SP COVID-19 Committee were followed. The protocol was applied individually, in a well- ventilated environment, from July to August 2021.

The procedure of this study was applied in person and followed the guidelines described in the Prope Normative Instruction nº 01 (https://www2.unesp.br/portal#!/covid19/ reorganizacaodastividades/normativas/) in relation to the propagation of the Covid-19 virus, and the recommendations of the World Health Organization (WHO) regarding the correct use of personal protective equipment (PPE) by the researcher, such as: goggles, face shield, surgical mask, waterproof long-sleeved apron and procedure gloves.

As fundamental practices and principles in the prevention of COVID-19, according to the normative document mentioned above, the following were also adopted: frequent hand washing – at least every 2 hours; social distance – individuals must maintain a minimum distance of 1.5m from each other; proper use of a face mask during the entire period you remain on campus, including outdoors; self-assessment for symptoms of COVID-19; the subjects and their guardians only accessed the areas necessary to carry out the research.

Data collection was performed by limited personal contacts through social distancing in a properly ventilated room and distancing, with the availability of a surgical mask and alcohol for all participants.

In addition, all participants had their temperature measured before and after the procedures performed in all collection sessions. The researcher used a triple surgical mask, a disposable apron and a Face Shield. At the end of each individual service, the rooms were completely sanitized by the CER II cleaning team.

Study population and eligibility criteria

A total number of 28 students, with complaints of learning problems, were referred by municipal public schools in the region of Marília-SP, of both genders, aged from 6 years to 7 years and 11 months of the 1st and 2nd year of the Elementary School I, according to the flowchart shown in Figure 1.

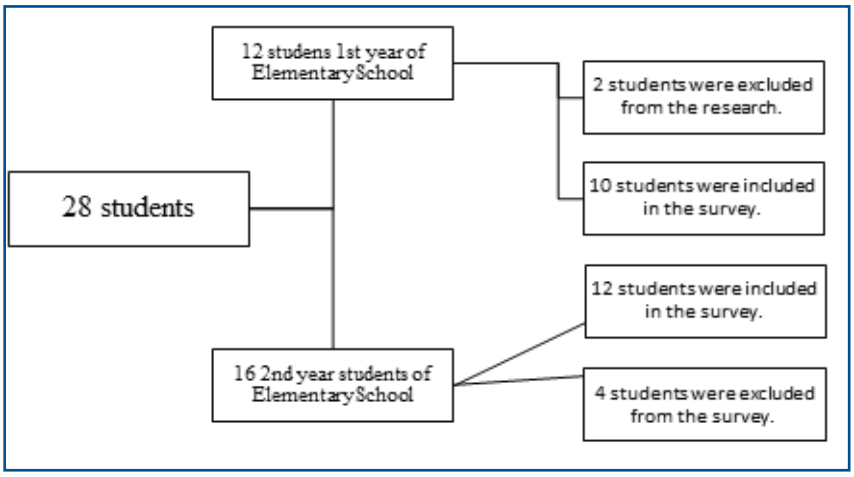

Figure 1: Distribution of the number of subjects with complaints of learning problems referred by municipal public schools in the region of Marília-SP.

From the analysis that 6 students were unable to read and write, the number of participants was redefined to 22 students, of both genders, aged from 6 years to 7 years and 11 months of the 1st and 2nd year of Elementary School I divided into two groups:

- Group I (GI): composed of 10 students from the 1st year of Elementary School I, 50% male and 50% female
- Group II (GII): composed of 12 students from the 2nd year of Elementary School I, 83.33% male and 16.66% female.

The students in this study did not present hearing and visual impairments in their school records at the time of referral, and all parents or guardians signed the Informed Consent Form.

All students were submitted to the application of the collective and individual version of the Cognitive- Linguistic Skills Assessment Protocol for students in the initial phase of literacy[4], consisting of the following tests: Name writing, Alphabet writing in sequence, Copy of forms , Word and pseudo word dictation, Figure dictation, Number dictation, Sequence alphabet recognition, Random alphabet recognition, Word reading, Non-word reading, Rhyme, Alliteration, Syllable segmentation, Sound discrimination, Repetition of words, Repetition of non-words, Repetition of numbers in reverse order, Fast automatic naming of figures, Fast automatic naming of digits, Visual shape memory.

Data analysis

Data analysis was performed using the Statistical Package for Social Sciences, version 25.0. The results were analyzed statistically with a significance level of 5% (0.050).

Ethics Committee Approval

This study was approved by the Research Ethics Committee of the Faculty of Philosophy and Sciences of the Universidade Estadual Paulista “Júlio de Mesquita Filho” - FFC/UNESP - Marília-SP, under number 4.862.668.

RESULTS

In table 1, it was possible to verify that there was a statistically significant difference with the application of the Likelihood Ratio Test in order to verify possible differences between the groups in this study.

Table 1: Frequency distribution of the performance classifications of students from GI and GII in the Cognitive- Linguistic Skills Assessment Protocol. Likelihood Test ($p<0.05$).

Subtests	Classification	Groups				p value
		GI		GII		
		Freq.	Perc.	Freq.	Perc.	
EDN	Refusal	0	0.00%	0	0.00%	0.036*
	Bottom	4	40.00%	1	8.30%	
	Medium	6	60.00%	6	50.00%	
	Higher	0	0.00%	5	41.70%	
CF	Refusal	0	0.00%	0	0.00%	0.015*
	Bottom	4	40.00%	0	0.00%	
	Medium	6	60.00%	12	100.00%	
	Higher	0	0.00%	0	0.00%	
DP	Refusal	7	70.00%	2	16.70%	0.027*
	Bottom	3	30.00%	7	58.30%	

Continuation - Table 1: Frequency distribution of the performance classifications of students from GI and GII in the Cognitive-Linguistic Skills Assessment Protocol. Likelihood Test ($p<0.05$).

Subtests	Classification	Groups				p value
		GI		GII		
		Freq.	Perc.	Freq.	Perc.	
	Medium	0	0.00%	3	25.00%	
	Higher	0	0.00%	0	0.00%	
DPP	Refusal	7	70.00%	2	16.70%	0.036*
	Bottom	3	30.00%	9	75.00%	
	Medium	0	0.00%	1	8.30%	
	Higher	0	0.00%	0	0.00%	
DF	Refusal	8	80.00%	2	16.70%	0.023*
	Bottom	2	20.00%	6	50.00%	
	Medium	0	0.00%	2	16.70%	
	Higher	0	0.00%	2	16.70%	
RAS	Refusal	2	20.00%	0	0.00%	0.002*
	Bottom	3	30.00%	0	0.00%	
	Medium	4	40.00%	1	8.30%	
	Higher	1	10.00%	11	91.70%	
RAOA	Refusal	2	20.00%	0	0.00%	0.006*
	Bottom	4	40.00%	0	0.00%	
	Medium	3	30.00%	3	25.00%	
	Higher	1	10.00%	9	75.00%	
RP	Refusal	5	50.00%	0	0.00%	0.030*
	Bottom	1	10.00%	1	8.30%	
	Medium	3	30.00%	5	41.70%	
	Higher	1	10.00%	6	50.00%	
MSF	Refusal	5	50.00%	0	0.00%	0.031*
	Bottom	2	20.00%	2	16.70%	
	Medium	2	20.00%	5	41.70%	
	Higher	1	10.00%	5	41.70%	

Caption: EDN: name spelling, CF: copying forms, DP: word dictation, DPP: pseudoword dictation, DF: picture dictation, RAS: alphabet sequence recognition, RAOA: alphabet recognition in random order, RP : word repetition, RANF: fast automatic picture naming, RAND: fast automatic digit naming, MSF: sequential visual memory of shapes.

In table 1, it was possible to verify that the students from GI and GII showed average performance for writing the name and writing the alphabet in sequence. The GI presented a refusal response for the subtests of word dictation, pseudoword dictation and picture dictation, word repetition and visual sequential memory of shapes, in addition to lower performance for alphabet recognition in random order and average performance for alphabet recognition in sequence.

GII showed lower performance for the subtests of word dictation, pseudoword dictation, picture dictation, in addition to superior performance for alphabet recognition in random order, alphabet in sequence and visual sequential memory of shapes.

DISCUSSION

All over the world, the pandemic caused substantial changes in the most varied domains and the Education sector was no exception. The unprecedented current situation required a rapid transition from face-to-face teaching-learning to Virtual Education and now to a Hybrid Modality.

The process of developing reading and writing before the pandemic was already questionable and widely discussed due to the fact that current literacy methodologies in Brazil do not focus on the explicit teaching of the alphabetical and orthographic principle of the Portuguese language[5]. Now, in a virtual education system, issues related to the appropriation of knowledge of the letter-sound relationship mechanism bring questions and discussions, since, among the results of this study, it was possible to observe the difficulty of both 1st and 2nd year students in cognitive-linguistic skills necessary for the full development of reading and writing in an alphabetic writing system such as Brazilian Portuguese.

Today, clinical professionals, such as speech therapists, when receiving students with complaints of learning problems, we must consider more than the complaints of parents or teachers, we must consider the context of exposure to teaching-learning situations and the consequences of their deprivation.

With the pandemic, especially in public education, many issues were raised on the agenda, such as the lack of infrastructure in schools, inequality in access to a good internet signal by families, since, according to the IPEA[6], only 40% of students they were not able to take classes via remote learning, nor did they have the support of their parents to carry out activities using remote access. Furthermore, the Brazilian Society of Pediatrics[7] replied that, with the pandemic, there was a significant change in the families' routine, as many parents needed work at home-office and share household chores with work and childcare.

Thus, the repercussions on academic learning of Brazilian students are still invaluable, because the academic learning problems in Brazil are not recent and date back to before the beginning of the COVID-19 pandemic. Overlapping reading and writing difficulties can lead to varied, distinct and perhaps incomparable repercussions.

The beginning of literacy, a phase in which the students in this study are now, is an important period for the acquisition of cognitive-linguistic skills, considered predictors for the learning of reading and writing[8-10] and the delays resulting from an inadequacy of the teaching the alphabetic and spelling principle, that is, teaching the letter-sound conversion mechanism, can trigger difficulties in reading and writing words.

In this study, we found that among the students in the GI group there was a refusal response for the tasks of dictation and repetition of words and visual sequential memory of shapes and lower performance for alphabet recognition in random order, while the students from GII showed lower performance for the dictation tasks, showing that just the knowledge of the sequence of the letters of the alphabet for the two groups was not a guarantee of acquisition for the application of the alphabetic and orthographic principle at the time of writing.

The results of this study indicate that health professionals, including speech therapists, should be prepared to establish an interface between health and education during our clinical diagnostic and interventional reasoning.

This is because, according to UNESCO, the natural drop in learning could expand for more than a decade if public policies that invest in educational improvements are not created[11], which means that it is not enough just to immediately improve distance learning, but it is urgently necessary to think and rethink public policies that represent the planning of academic learning recovery strategies[12].

In addition, the lack of knowledge about the instructional teaching of the alphabetical and orthographic principle of the teacher-literate and the lack of professionals such as the educational speech therapist at the school means that the teaching-learning relationship of students in the initial stage of literacy is at risk , since the lack of a qualified and trained educator, from the early identification of reading and writing problems in the classroom, can contribute to educational planning without the development of necessary

strategies for the acquisition and development of decoding mechanisms and codification of our Portuguese Language Writing System.

The data from this study remind us of the need to think, as clinical and educational speech therapists, that there is still a lot to be done for these students. In a literature review carried out, the authors[13] found 15 scientific articles in 2020 that discussed the impacts of the pandemic on schoolchildren and observed a frequency of psychological and eating disorders and negative emotions in 40% of the articles, anxiety in 33%, depression in 26%; irritability, sedentary lifestyle and sleep disorders were mentioned in 20% of the articles, stress and post-traumatic stress disorder in 6% of the articles.

The data collected in the study mentioned above are alarming, since the referrals to the speech therapy clinic will be carried out by the school and if the educational speech therapist is not able to conduct these referrals well, most of these children will probably be misdiagnosed, however, we should consider that four of the articles in this study reported that the social and educational isolation suffered by the child population made them vulnerable to the occurrence of symptoms of lack of social contact, lack of need for social communication, inattention and hyperactivity, in addition to anxiety, irritability, obsession, hostility and impulsivity that can compromise the formation of memory for learning.

Based on the data found in this study, we conclude this article by highlighting the need for the clinical and/ or educational speech therapist to act as overseers of the acquisition and development of school learning, helping to plan specific actions to promote normal development and detection of deviant processes from the teaching-learning process, thus gaining an important space with teachers and educational staff regarding relevant discussions not only about the importance of cognitive-linguistic skills for the development of academic learning, but also about the milestones of child development and predictors of literacy, so important to ensure the success of reading and writing for these students in the initial stage of literacy and so disregarded or not prioritized during the remote teaching- learning process during the COVID-19 pandemic.

CONCLUSION

First- and second-year literacy students showed lower performance in cognitive-linguistic skills that are important for the development and learning of reading and writing. knowing how to perform the tasks requested because they are probably not literate and do not know how to use the cognitive-linguistic skills necessary to trigger the analysis and synthesis processes necessary for the formation of words for both reading and writing.

Authors' contribution

MTF, NLS, IA and NDB were responsible for collecting and tabulating the data and preparing the manuscript; CG and SAC were responsible for the project and study design and general guidance on the stages of execution and elaboration of the manuscript.

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Confirmations

All authors approved the final version of the manuscript for submission.

Conflict of interest

I declare that there was no conflict of interest

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CHAPTER 27

ANALYSIS OF COVID-19 MORTALITY AND CASE-FATALITY IN A LOW- INCOME REGION: AN ECOLOGICAL TIME-SERIES STUDY IN TOCANTINS, BRAZILIAN AMAZON

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Abstract

Introduction: Inserted in the vulnerable context of the Brazilian Amazon, the state of Tocantins has suffered damages with the dissemination of COVID-19 in its territory; however, little evidence is published from this state. **Objective:** This study aims to analyze the case-fatality, mortality, and incidence of COVID-19 in Tocantins. **Methods:** This is an ecological study, population-based, time- series analysis of COVID-19 cases and deaths in the state of Tocantins from March 2020 to August 2021. **Results:** During the examined period, 219,031 COVID-19 cases, and 3,594 deaths were registered due to disease. Two possible occurrence peaks were characterized in this time- series analysis. Remarkably, the Second Wave had the highest lethality rates (3.02% - April 2021), mortality (39.81 deaths per 100,000 inhabitants – March 2021), and incidence (1,938.88 cases per 100,000 inhabitants – March 2021). At the end of the period, mortality, incidence, and lethality showed flat trends, suggesting a positive outcome of the vaccination program. **Conclusion:** The prevention, surveillance, and control actions of COVID-19 cases in Tocantins State have been directed to mitigate the deleterious effects of the pandemic. Nevertheless, efforts are still needed to decrease lethality, mortality, and incidence trends, and ultimately to achieve control of the COVID-19 pandemic in the region.

Keywords: COVID-19; Case Fatality; Incidence; Mortality; Trends.

Resumo

Introdução: Inserido em vulnerável contexto da Amazônia Brasileira, o estado de Tocantis tem sofrido danos com a disseminação da COVID-19 em seu território; entretanto, escassas evidências têm sido publicadas sobre este estado. **Objetivo:** O objetivo deste estudo é analisar a letalidade, mortalidade e incidência da COVID-19 em Tocantins. **Método:** Este é um estudo ecológico, de base populacional, com análises de séries temporais de casos e óbitos de COVID-19 no estado do Tocantins de março de 2020 a agosto de 2021. **Resultados:** No período examinado, foram registrados 219.031 casos de COVID-19 e 3,594 óbitos devido a

doença. Foram caracterizadas nesta análise de série temporal a formação de duas possíveis ondas. Notavelmente, a segunda onda apresentou as maiores taxas de letalidade (3,02% - abril de 2021), mortalidade (39,81 óbitos por 100.000 habitantes - março de 2021) e incidência (1.938,88 casos por 100.000 habitantes - março de 2021). No final do período, a mortalidade, incidência e letalidade apresentaram tendências estacionárias, sugerindo um resultado positivo do programa de vacinação. **Conclusão:** As ações de prevenção, vigilância e controle dos casos de COVID-19 no Estado do Tocantins têm sido direcionadas para mitigar os efeitos deletérios da pandemia. No entanto, esforços ainda são necessários para diminuir as tendências da letalidade, mortalidade e, em última instância, para alcançar o controle da pandemia de COVID-19 na região.

Palavras-chave: COVID-19; Incidência; Letalidade; Mortalidade; Tendências.

INTRODUCTION

The COVID-19 pandemic has beaten Brazil hardly, ranking second in deaths, behind the United States of America. This South American country has been confronting one of the most complex hospital and health system crises ever[1]. Since its first confirmed COVID-19 case reported on February 26, 2020[2], Brazil has exhibited critical epidemiological circumstances in its enormous territorial dimension, ranging in severity from region to region[3].

These geographical differences in population density, access to health services, age, and socioeconomic factors have accentuated inequities, mainly impacting the country's most impoverished regions, such as the Northern region[4]. This region suffers the imbalances in the failures of social security, and the lack of adequate and integrated control measures aggravate mortality and social vulnerability rates[5].

In the vulnerable context of Northeast Brazil, Tocantins contributes approximately 0.5% to the national gross domestic product, being one of the states that provides the least[6]. Furthermore, 93% of its population depends on the National Health System[7].

Like other states of the Amazonian region, Tocantins is an endemic area for other infectious ailments clinically similar to COVID-19, increasing the arena of differential diagnosis. To illustrate, there is evidence of co- infections of SARS-CoV-2 with dengue[8]. This syndemic context complicates COVID-19 detection and treatment in the region.

The mortality rate is one of the main characteristics differentiating the coronavirus from the Severe Acute Respiratory Syndrome (SARS) and the Middle East Respiratory Syndrome (MERS) outbreaks[9]. Given the fluctuations detected in the incidence and lethality of COVID-19, it is relevant to study and understand regional factors that affect the contagion and spread of this new virus. Besides, time-series studies are helpful to analyze the pandemic behavior curves[10].

The first confirmed case of COVID-19 in Tocantins was reported in the state capital, on March 18, 2020, by a traveler returning from Fortaleza, an urban city in the Northeast[11]. A month later, State authorities reported its first death due to this disease[12]. The situation worsened significantly; more than a year after registering its first COVID-19 case[2]; however, little evidence is published on this state, which is the newest of the Brazilian federative units and concentrates only 0.7% of the country's total population[6].

Therefore, this study analyzed the case-fatality, mortality, and incidence of COVID-19 in Tocantins, Brazil, from March 2020 to August 2021.

METHODS

This is an ecological study of population-based time-series analyzing COVID-19 cases and deaths in the state of Tocantins (figure 1). This study is part of a population-based umbrella project, where each state of Brazil was analyzed separately, following a standard protocol for ecological time-series studies as described by Abreu, Elmusharaf and Siqueira[10] .

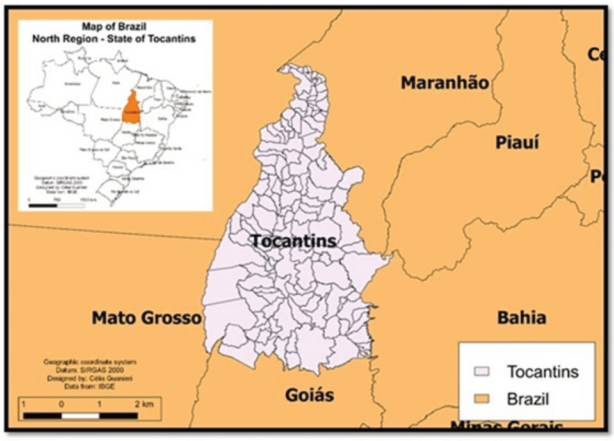

Figure 1: Map of Tocantins and its location in the Brazilian territory.

Data were obtained directly from the COVID-19 Electronic Database of the Health Department of Tocantins. It is a State public database that contains official information on cases and deaths caused by COVID-19 without patient identification[13].

From March 2020 to August 2021, a total of 219,031 accumulated cases and 3,594 deaths were caused by COVID-19. All cases and deaths with laboratory, clinical or epidemiological confirmation of COVID-19 were included in the study. The cases were classified according to test date and death date; those with missing date information were excluded. Two different researchers collected data to avoid collection bias. Then, the extracted information was organized in the Excel spreadsheet software (Microsoft Corp., Redmond-WA, USA, 2021) for further analysis. The database was updated on September 29, 2021.

The incidence (1) and mortality rates (2) by 100,000 inhabitants and the case-fatality (3) (%) were determined with the following equations:

(1) Incidence=(number of cases) ×100.000 population
(2) Mortality=(number of deaths) x 100.000 population
(3) Case-fatality=(number of deaths) x 100 (number of cases)

The population used for calculations was obtained from the Federal Court of Accounts (TCU population). It corresponded to the resident people in Tocantins and was estimated at 1,572,866 inhabitants for 2019[14].

For trends analysis, the period was split into two waves: the First Wave (W1), from March to November 2020, and the Second Wave (W2), from December 2020 to August 2021. Noteworthy, the W1 ended with the lowest mortality rate in November 2020, according to the analysis of the curve shape.

The Prais-Winsten regression model for population mortality rates was used to build a time series as well as to determine incidence, case-fatality and mortality trends15. Probability (p) and Daily Percent Change (DPC) were estimated considering a 95% level significance, according to equations (1), (2), and (3):

(1) DPC=(10^β-1)×100%
(2) (IC95%)ul=(10^ β_max-1)×100%
(3) (IC95%)u=(10^ β_min -1)×100%

In these equations, we considered β as the angular coefficient from the linear regression, the indexes ul as the upper limit, and ll as the lower limit of the confidence level.

Statistical analyses were performed using the STATA 14.0 software (College Station, TX, U.S. 2013). The effective reproductive number (Rt) was estimated using R studio software EpiEstim package16, version 2.2.4, a time-varying reproduction number for epidemics developed by Thompson and colleagues[17]. We used a mean serial interval of

2.97 days with a mean, standard deviation of 3.29 days, as described in previous studies[18,19].

Then, we performed a Spearman correlation analysis between Rt and daily new cases, Rt and daily deaths, and Rt and lethality.

RESULTS

Among the Amazonian states, Tocantins is probably one of the less known in Brazil and the country outside. Table 1 describes some of the sociodemographic characteristics and inherent information of the hospital system infrastructure in Tocantins State.

Table 1: Sociodemographic characteristics of the state of Tocantins, Brazil.

Sociodemographic characteristics	Description
Region*	North
Number of municipalities*	139 municipalities
State's capital*	Palmas
Territorial extension* (2020)	277,423.630 km²
Population**	1,572,866 inhabitants
Demographic density* (according to the latest census, 2010)	4.98 inhabitants /km²
Monthly household income per capita*	1,060 reais
Human Development Index (HDI)*, according to the latest census, 2010	0.699
Average number of people per household+ (2019)	3 people
Number of basic health units#	427 units
Total Hospital Beds## (August 31, 2021)	
Clinical beds - COVID-19 – Public	57 clinical beds
Clinical beds - COVID-19 – Private	14 clinical beds
Number of COVID-19 ICU beds - Public	83 ICU beds
Number of COVID-19 ICU beds - Private	15 ICU beds
Vaccination (number of doses applied)## (August 31, 2021)	1,164,822 doses

Source:
*Brazilian Institute of Geography and Statistics[6].
** Datasus - Estimate of the resident population 2019 - Federal Court of Accounts (TCU population)[14].
+ Sistema IBGE de Recuperação Automática – SIDRA[20].
# Cadastro Nacional de Estabelecimentos de Saude (CNESNet)[21].
Secretary of Health of State of Tocantins[13].

Throughout the period studied, we identified 219,031 cases (Figure 2a) and 3,594 deaths (Figure 2b).

Figure 3 exhibits two possible waves: the first occurred in 2020 from March to November, and the second from December 2020 to August 2021. The highest lethality rate in the period (3.02%) was in April 2021 (Figure 3a), and the highest mortality (39.81 deaths per 100,000 inhabitants) and incidence (1,938.88 cases per 100,000 inhabitants) rates were in March 2021 (Figure 3b and 3c).

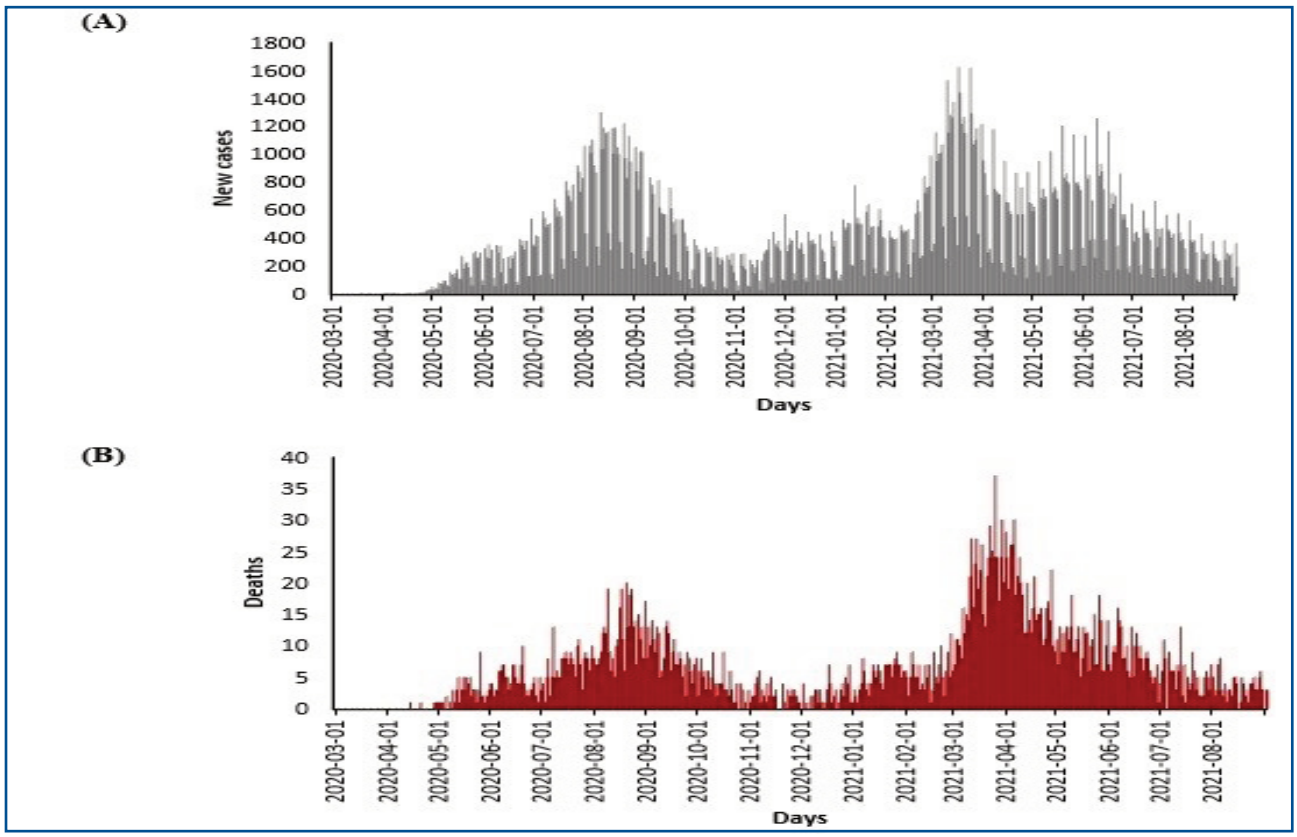

Figure 2: Number of new cases (a) and deaths (b) daily and by COVID-19 in the State of Tocantins from March 2020 to August 2021.

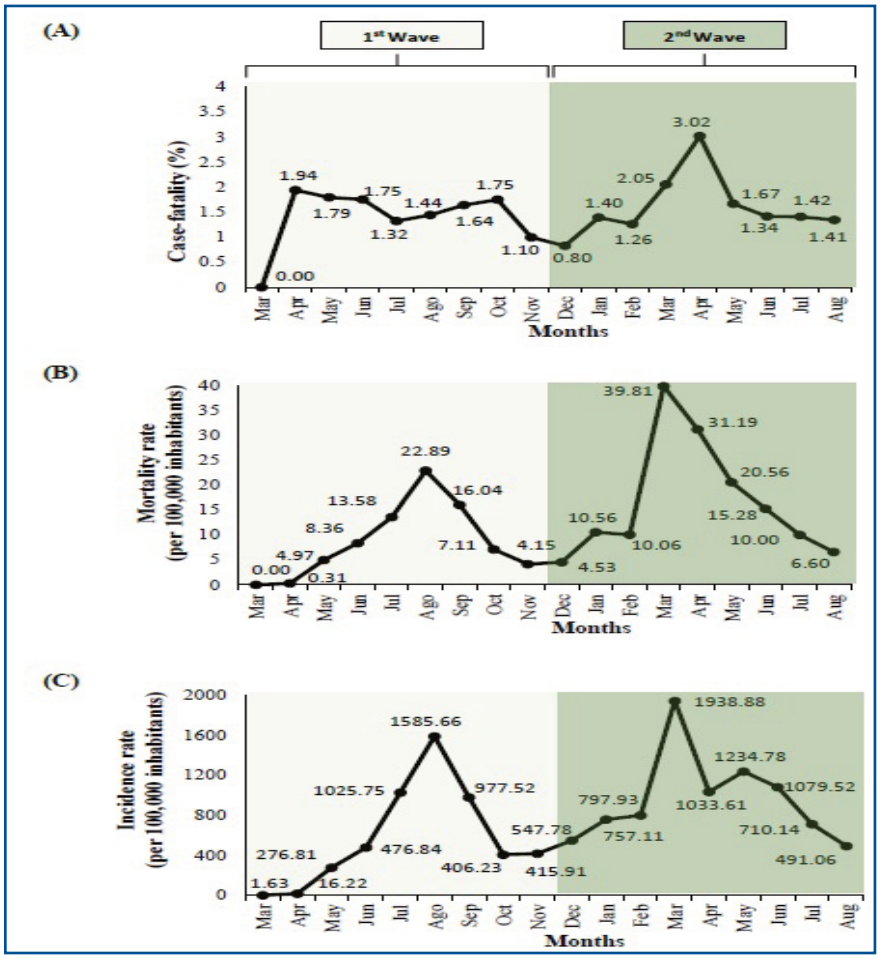

Figure 3: Gross rates of case-fatality percentage (a), mortality (b), and incidence rates (c) by 100,000 inhabitants of COVID-19 in Tocantins state from March 2020 to August 2021.

Furthermore, Table 2 shows stationery trends in mortality and case fatality rates during the W1 although the incidence trend was increased, $p< 0.05$. The trends of all indicators were flat during the W2.

Figure 4 indicates the Rt value, as a function of time for the evaluated period. The estimated Rt value of COVID-19 experienced fluctuations over this period.

There was a significant growth peak between April and May 2020, then a predominance of Rt indexers below one (1) from August 2020, with an increase in viral transmissibility after October 2020. Then, during the W2, a peak is observed in January 2021 with a predominance of Rt above one (1) until June 2021, with a stationary behavior for the remaining months (Rt <01).

Table 2: Prais-Winsten regression estimates and Daily Percent Change (DPC) of case-fatality (%) mortality and incidence rate by 100,000 inhabitants of COVID-19 in the State of Tocantins from March 2020 to August 2021.

	Period	
	March 2020 to November 2020 (1st wave)	**December 2020 to August 2021 (2nd wave)**
DPC (CI 95%) Case-fatality	-0.23 (-0.50:0.05)	0.10 (-0.08:0.27)
p	0.103	0.271
Fatality Trends	Flat	Flat
DPC (CI 95%) Mortality	0.22 (-0.13:0.57)	0.17 (-0.12:0.47)
P3	0.215	0.238
Mortality Trend	Flat	Flat
DPC (CI 95%) Incidence	2.23 (1.39:3.07)	-0.04 (-0.22:0.13)
p	<0.001*	0.647
Incidence Trend	Increase	Flat

DPC – Daily Percent Change (%); CI 95% – Confidence interval 95%; p-value – the probability of statistical significance. *Statistical difference detected by the Prais-Winsten regression test, p<0.05.

Source: Cases, deaths, and population extracted from the Department of Health of State of Tocantins, Brazil13.

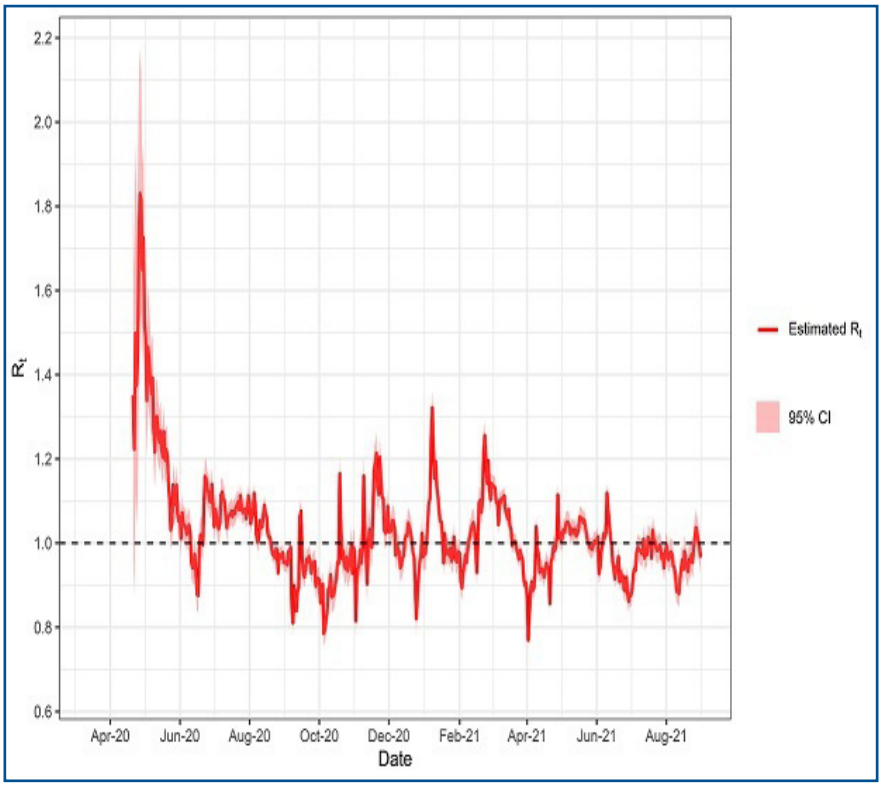

Figure 4: Effective Reproduction Number (Rt) estimated of COVID-19 during April 14, 2020, to August 31, 2021, Tocantins, Brazil.

CI = Confident Interval. Rt = Effective Reproduction Number.

This pattern appears similar to the time series of new cases. Therefore, correlation analyzes were performed between Rt and daily new cases, between Rt and daily deaths, and between Rt and lethality. The results for Spearman's ρ coefficients are shown in Table 3.

In addition, the correlation coefficient between Rt and deaths showed to be significant in Table 3. That is, the behavior of the frequency of deaths is negatively associated with Rt despite the low intensity of the correlation. The expected value for the correlation coefficient between these variables would be ρ ~ 0. Therefore, despite having statistical significance, the value of ρ suggests that Rt is weakly dependent on the number of daily deaths and that Rt has a behavior contrary to this number. There is no significant correlation between Rt and new cases. This result is opposed to what was expected; it is presumed that an increment in Rt implies an increase in the number of new daily cases. However, the correlation coefficient ρ = 0.026 and the p-value = 0.562, which is at least ten times greater than the α significance, revealed these variables are independent. For the correlation be-tween Rt and lethality, ρ = -0.246 with p-value < 0.001 was found, suggesting a significant negative association between Rt and lethality. That is, as the number of infections in-creases, lethality decreases.

Table 3: Study of Spearman's correlation between Rt and lethality, new cases, and deaths.

Analysis	ρ (CI 95%)	Freedom grades	Statistics S	p-Value
Rt x Lethality	-0,246 (-0.334: -0.170)	457	25701472	< 0,001
Rt x New cases	0,026 (-0.061: 0.113)	457	20047628	= 0,562
Rt x Deaths	-0,167 (-0,253: -0,070)	457	24019576	< 0,001

CI: Confidence Interval, p-value: the probability of statistical significance.

Source: Cases, deaths, and population extracted from the Department of Health of State of Tocantins, Brazil[13].

DISCUSSION

From March 2020 to August 2021, Tocantins was affected by 219,031 cases of COVID-19, in which 3,594 of them evolved to death. During this period, there was the formation of two possible waves. The mortality and fatality rates remained flat during the W1, but the incidence had an increasing trend. Prevention initiatives were implemented[22], and social distancing measures were adapted to reduce the risk of transmission. Immediately after confirming the first case, the local authorities declared a state of public calamity, including restrictions on nonessential activities such as commerce and tourism[23]. On the other hand, a process of (re) planning, (re) organization, (re) allocation of human and financial resources must be implemented by the State to have a rapid and effective response during public health emergencies, such as (1) continuity of essential services; (2) well-coordinated implementation of priority actions; (3) clear and accurate internal and external communication; (4) rapid adaptation to increasing demands; (5) effective use of scarce resources; and (6) safe environment for healthcare professionals and patients[24].

The importance of these non-pharmacological actions to prevent the increase in infections was probably not given at the beginning of the pandemic, especially in urban areas, which influenced the increasing number of new cases and benefit the beginning of a new wave at the end of November 2020. However, according to the bulletin from May to June[25], the capital of Tocantins was among the urban cities that adopted more rigorous policies for long periods. It would be possible that the population was not prepared to practice individual and community mask use, distancing, and hand hygiene measures for prolonged periods[26].

The case-fatality rate of 2.38% marked the onset of the pandemic in April 2020, when the first deaths (n=3) of COVID-19 fatal victims were reported. This result matches the COVID-19 case-fatality published by the State Government of Tocantins at the beginning

of the pandemic, with a lethality record of 2.03% in May 2020[27]. However, this fatality is lower than that found in other states such as Piauí (9.09%), Pernambuco (7.35%), and São Paulo (5.97%), during the 13th epidemiological week[28].

According to the COVID-19 Observatory report of Fundação Oswaldo Cruz, on the first six months of the pandemic, Tocantins had one of the highest incidence rates in the country despite its low population. In August 2020 reached the third-highest rate in the Northern region, with trends increasing incidence and mortality rates29. Similar to our findings, peaks of incidence (1,585.66 cases per 100,000 inhabitants) and mortality (22.89 deaths per 100,000 inhabitants) happened in August 2020, during the W1. Despite the high increments in the indicators of incidence and mortality described in August 2020, the W2 presented more distressing circumstances. The alarming rates of incidence and mortality reported in March 2021 (Figures 3b and 3c) almost doubled the number of deaths of the worst month during the W1.

In March 2021, the Fundação Oswaldo Cruz (FIOCRUZ) issued a special bulletin warning on a simultaneous worsening across Brazil of the various indicators, with an increase in the number of cases and deaths of COVID-19, the maintenance of high levels of incidence of SARS, high rates of test positivity and hospital overload. During this period, all states in Northeast Brazil, including Tocantins, had above 80% occupancy rates of COVID-19 ICU beds for adults[30].

The high rates indicate that even after a year of a pandemic, Tocantins and Brazil faced a challenging scenario of catastrophic conditions to control the spread of COVID-19. Several factors may have contributed to this situation, such as typical Brazilian festivities like carnival and the infection with new variants. The high peak of cases and deaths observed during the W2, in March 2021, happened after the carnival holidays. Although the official carnival was canceled[31], still, people gathered in the streets and private parties, which furthered the spread of the virus. Besides, during this period, the P1 (Manaus) variant of SARS-CoV-2 was detected for the first time, presenting greater transmissibility[32]. In this controversial scenario, not enough tests were performed to detect the disease, so there was no factual knowledge regarding asymptomatic patients.

It is possible that the stated factors contributed to Tocantis reaching, in April 2021, the highest case- fatality rate (3.02%) since the beginning of the pandemic; however, in this period, the viral transmissibility rates were predominantly controlled (Rt <1). In this study, a negative correlation was found between Rt and lethality. Still, these results should be interpreted with caution, as many other factors influence the fatal repercussions of COVID-19, such as gender, ethnicity, and risk factors[33,34].

Furthermore, most Brazilian states adopted more restrictive measures to mitigate the spread of SARS-CoV-2, only while experiencing a scenario characterized by a high number of deaths and high hospital bed occupancy rates. In this sense, the Rt would be one of the leading indicators to be considered during government decision-making to contain the spread of the disease and future collapses in health systems.

Monitoring Rt scores is essential to implement strategies for pandemic coping. Relaxation measures to control population mobility should only be adopted when the Rt values are below 1 where the situations can still be handled[35]. The population care can be directed to the primary care services, which is essential to sustain the health systems, protecting against the excessive demands generated by the pandemic.

However, at the end of August 2021, the trend for mortality, fatality, and incidence was flat. Although this fact could have been a positive outcome of the vaccination program, with a predominance of Rt below than one (1), it is noteworthy that the pandemic scenario is always in constant change. Thus, current efforts must be intensified to contain the spread of SARS-CoV-2 in this region and minimize catastrophic consequences in the future. Specific determinants are affecting the pandemic situation in Tocantins, such as its geographical location as a strategical State Road junction. A vast interchange through highways leads to cities in the North, Northeast, and Central-west regions[36], facilitating the spread of the new coronavirus.

The demographic density of Tocantins is 4.98 inhabitants/km[26]. In contrast, the average number of people in the urban area per household is three[20], which affects the

high incidence of infections by COVID-19[37,38]. Besides, people have isolation limitations[39]. These variables primarily impact Palmas, the capital city.

In addition, data from the Tocantins State Health Secretary[40] revealed that 7,886 indigenous people and 6,551 individuals of African descent (Quilombos) communities live on the banks of the rivers in houses where a high number of individuals congregate. The crowded boats through the rivers of the Amazon area[41] are also a risk factor to spread the SARS-CoV-2.

Tocantins was one of the first states to present a contingency plan to face COVID-19. Likewise, they created a crisis committee with authorities representing each power, control and security body, and health authorities and professionals. These initiatives were carried out to debate and seek joint actions and strategies to minimize the impact of the pandemic[42].

However, this state suffers health services constraints at regular times. During the pandemic, the authorities have to deal with a crisis that requires an urgent response mainly because the fatality, mortality, and incidence rates highly rely on poor socioeconomic indexes and local health infrastructure.

The measures were stricter in Palmas, the most populated urban area[43]. The number of beds was increased from 163 to 467 for the exclusive treatment of COVID-19, from April 2020 to April 2021, health professionals were hired, and personal protective equipment was made available[27]. However, the consolidated number of ICU beds (public and private) is approximately 0.9 per 10,000 inhabitants, an indicator that is below 2.2, which is the national average[44].

According to the FIOCRUZ observatory[45], the occupancy rate of intensive care beds in Tocantins has dropped to 75%. Still, this percentage is high, but one of the factors that may have influenced this improvement is the immunization process, with 718,000 people vaccinated. The vaccination plan against COVID-19 has followed the national guidelines, in which the priority groups included indigenous people, afro-descendant communities (Quilombos), and traditional riverine communities[27].

The actions of the leaders of this federative unit to apply prevention, surveillance, and control measures are key elements to minimize the spread of the virus SARS- CoV-2 because Brazil does not have a homogeneous strategy to manage the pandemic of COVID-19. The State governments are accountable for planning and executing non-pharmacological and distancing strategies[46].

The mandatory use of masks and distancing measures must remain to mitigate and restrain the effects of the pandemic in this Brazilian Amazon territory. It is required to monitor mortality, lethality, and incidence indicators and develop further studies comparing those indicators before and after vaccination.

Limitations

It must be considered that the COVID-19 tests were only carried out on people with clinical manifestations of the disease. The deaths related data is counted based on the previous day, but there may be cases of a delay in the notification.

Some Tocantins municipalities with reduced technical staff and access to digital tools have difficulties in the production and systematization of COVID-19 related data[47].

As the pandemic is still in evolution, all the data examined in this research correspond to partial analysis.

CONCLUSION

The W1 showed flat trends in lethality and mortality with an increasing trend in incidence rates, with a Daily Percent Change of 2.23%. The W2 had a more shocking aspect and the highest peaks of mortality, lethality, and incidence occurred in March 2021. However, all indicators showed flat trends at the end of August that may be influenced by the effect of the vaccination.

During the study period, the prevention, surveillance, and control actions of COVID-19 cases in Tocantins were managed to mitigate the effects of the pandemic. However, efforts are still needed to show decreasing trends in lethality, mortality, and incidence.

Author Contributions

Conceptualization, A.E.M.C., B.E.G.D., T.C.M., I.P. and L.C.A.; methodology, A.E.M.C., T.C.M., J.O.E., L.C.J., R.D.R., K.E., C.E.S. and L.C.A.; software, J.O.E., L.C.J.; validation, T.C.M., J.O.E., L.M.R.R., C.E.S. and L.C.A.; data curation, A.E.M.C., T.C.M., L.C.A.; writing- review and editing, all the authors; visualization, all the authors; supervision, K.E., C.E.S. and L.C.A.; project administration, C.E.S. and L.C.A. All authors have read and agreed to the published version of the manuscript.

Data Availability Statement

Data were extracted from a population database in a COVID-19 dashboard, freely accessible on the Health Department of the State of Tocantins website http://integra.saude.to.gov.br/covid19/.

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Conflicts of Interest

The authors declare no conflict of interest.

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CHAPTER 28

EPIDEMIOLOGICAL PROFILE OF COVID-19 IN THE STATE OF ESPÍRITO SANTO, BRAZIL, FROM MARCH 2020 TO JUNE 2021

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Abstract

Introduction: coronavirus 2019 Disease (COVID-19) was quickly declared a pandemic, and Brazil is facing the most significant health and hospital crisis in its history. From March to June 2021 represented 50.8% of all deaths in the State of Espirito Santo. **Objective:** to analyze the lethality and mortality by COVID-19 in the State of Espirito Santo from March 2020 to June 2021. **Methods:** an ecological study was carried out, using a time series of public and official data available on the Health Department of the State of Espirito Santo, Brazil. Were considered information about cases and deaths (from March 2020 to June 2021) of COVID-19. Percentage case-fatality and mortality and incidence rates per 100,000 population were calculated. Time-series analyses were performed using the Prais-Winsten regression model, estimating the Daily Percent Change (DPC), and the trends were classified as flat, increasing, or decreasing. Significant differences were considered when $p<0.05$. **Results:** 524,496 confirmed cases of COVID-19 as of June 30, 2021, and 11,516 progressed to death. The presence of cardiovascular diseases represents more than half of confirmed comorbidities (54.37%) in patients with COVID-19, followed by diabetes (19.95%) and obesity (9.34%). Men had higher mortality and lethality, especially in older age groups, but the incidence was higher among women. A characteristic profile of two waves was observed; the first wave was extended from March to October 2020 and the second complete wave from November 2020 to June 2021. During the second wave, high peaks of incidence, lethality, and mortality were recorded. At the end of the second wave, the incidence rate remained with increasing trends ($p < 0.05$), with a DPC of 2.06%. **Conclusion:** the peak concentration of cases, deaths, and indicators of lethality, mortality evidenced even after one year of pandemic, characterizes the severity of the COVID-19 pandemic, still in entire evolution in the State Espirito Santo and Brazil.

Keywords: Case Fatality; Mortality; COVID-19; SARS-CoV-2.

Resumo

Introdução: a doença do Coronavírus 2019 (COVID-19) foi rapidamente declarada pandemia, e o Brasil está enfrentando a crise hospitalar e de saúde mais significativa de sua história. De março a junho de 2021 representou 50,8% de todas as mortes no Estado do Espírito Santo. **Objetivo:** analisar a letalidade e mortalidade por COVID-19 no Estado do Espírito Santo no período de março de 2020 a junho de 2021. **Método:** foi realizado um estudo ecológico, utilizando uma série histórica de dados públicos e oficiais disponíveis na Secretaria de Saúde do Estado do Espírito Santo, Brasil. Foram consideradas informações sobre casos e óbitos (de março de 2020 a junho de 2021) da COVID-19. Foram calculadas as percentagens de letalidade e mortalidade e taxas de incidência por 100.000 habitantes. As análises de séries temporais foram realizadas usando o modelo de regressão de Prais-Winsten, estimando a variação percentual diária (DPC), e as tendências foram classificadas como estacionaria, crescentes ou decrescentes. Diferenças significativas foram consideradas quando p <0,05. **Resultados:** 524.496 casos confirmados de COVID-19 até 30 de junho de 2021 e 11.516 evoluíram para óbito. A presença de doenças cardiovasculares representa mais da metade das comorbidades confirmadas (54,37%) em pacientes com COVID-19, seguida de diabetes (19,95%) e obesidade (9,34%). Os homens apresentaram maior mortalidade e letalidade, principalmente nas faixas etárias mais velhas, mas a incidência foi maior entre as mulheres. Observou-se um perfil característico de duas ondas; a primeira onda foi estendida de março a outubro de 2020 e a segunda onda completa de novembro de 2020 a junho de 2021. Durante a segunda onda, altos picos de incidência, letalidade e mortalidade foram registrados. Ao final da segunda onda, a taxa de incidência manteve-se com tendência crescente (p <0,05), com DPC de 2,06%. **Conclusão:** o pico de concentração de casos, óbitos e indicadores de letalidade, mortalidade evidenciados mesmo após um ano de pandemia, caracteriza a gravidade da pandemia COVID-19, ainda em evolução total no Estado do Espírito Santo e Brasil.

Palavras-chave: Letalidade; Mortalidade; COVID-19; SARS-CoV-2.

INTRODUCTION

Coronavirus Disease 2019 (COVID-19) was quickly declared a pandemic, causing a global recession in the economic and health systems[1-4]. In Brazil, the fight against the disease resulted in the most significant health and hospital crisis in its history, marked by the lack of government control. It can be evidenced by the number of notifications of more than 19 million cases confirmed of the disease, with 550,502 thousand lives lost until July 26, 2021, 11,826 of them notified by the State of EspíritoSanto[5].

COVID-19 is a respiratory tract infection caused by the Severe Acute Respiratory Syndrome of coronavirus 2 (SARS-CoV-2). While the majority population has mild symptoms, about 20% of patients develop severe complications such as Acute Respiratory Syndrome (SARS), septic shock, and multiple organ failure, with 3-6% achieving mortality. Due to the lack of specific antiviral treatment, the management of this condition remains primarily symptomatic, with intensive support treatment for critically compromised patients[6].

The severity and lethality of COVID-19 have been associated with chronic non-communicable diseases (NCDs) such as high blood pressure, diabetes, respiratory infections, and cardiovascular diseases[7-9]. There is a demographic and epidemiological transition in progress in the Brazilian case, with a high prevalence of NCDs, especially cardiovascular diseases related to obesity and sedentary lifestyle[10-12]. These comorbidity associations make the country's scenario during the pandemic even more problematic from the point of view of Public Health.

For Mesenburg et al.[13], the prevalence of chronic NCD in the country is high. However, people with comorbidities have more severe forms of COVID-19 and a higher prevalence of symptoms. It is highlighted that the transmissibility of the Sars-CoV-2 virus is similar in people with or without these pathologies. Cardiovascular diseases represent 56% of the comorbidities of the COVID-19 confirmed cases, followed by diabetes (20%) and obesity with 8,4%[14].

According to public data from the EspíritoSanto State Health Department[15], there is a more significant number of confirmed cases in females (53%) but a higher frequency of deaths in males (53%). Regarding the age group, there is a predominance of confirmed

cases of Coronavirus disease in an economically active age group, but with the highest frequency in people between 20 and 59 years (74%). The number of deaths is high, especially in the elderly over 60 years of age (69%).

Thus, epidemiological analyses based on the triad person, time, and place generate transformations in the characterizing elements of EspíritoSanto society. The context of the COVID-19 pandemic is complex, and measures to promote the flattening of the epidemiological contamination curve will require multiple analyses and contributions to the knowledge of the pandemic situation and its social repercussions.

According to Malta and collaborators[16], Brazil is the only country globally with more than 200 million inhabitants and has unrestricted access to Unified Health System (SUS-Sistema Único de Saúde). Therefore, it is crucial to understand the dynamics of the pandemic in the most distinct regions of the country, especially the high incidence and mortality caused by the disease. Thus, this study's objective is to analyze the lethality and mortality by COVID-19 in the State of EspíritoSanto from March 2020 to June 2021.

METHODS

Study Design

An ecological study was carried out using a time series of public and official data available on the Health Department of the State of EspíritoSanto, Brazil[15] (2021). This study is part of a population-based umbrella project, where each state of Brazil was analyzed separately, following a standard protocol for ecological time-series studies as described by Abreu, Elmusharaf and Siqueira[17].

Study Location and Period

The State of EspíritoSanto belongs to the southeast region of Brazil; it is formed by 78 municipalities, with Vitória as the capital. The State has a territorial extension of 46,074,447 km², a demographic density of 76.5 inhabitants/km², and an average number of inhabitants per household of 2.8 people. The monthly per capita income is 1,347 reais, the human development index (HDI) is 0.740, and the State has 790 basic health units[18,19]. Furthermore, according to the EspíritoSanto State Health Department[15], until June 13, 2021, the State had 5,013 infirmary beds and 2,560 ICU beds, with 1,300 infirmary beds and 1,611 ICU beds for COVID-19 patients, with an occupancy rate of 62.73% and 42.54% respectively.

The database was updated on July 20, 2021, considering information about cases (from March 2020 to June 2021) and deaths (from April 2020 to June 2021) of COVID-19.

Study Population and Eligibility Criteria

This study included data on 524,496 cases and 11,516 deaths accumulated of COVID-19 reported by EspíritoSanto's municipalities. The cases were classified according to the diagnosis date, while the deaths were classified according to the death date.

All notifications of COVID-19 cases and related deaths were confirmed by clinical, laboratory and/or epidemiological confirmation of disease.

Data Collection

Two researchers independently extracted the data to minimize collection bias and guarantee the quality and reliability of the data obtained. The collected data were organized into spreadsheet software Microsoft® Excel 2016.

Data Analysis

The effective reproduction number (Rt) was estimated using R studio software EpiEstim package[20], version 2.2.4, a previously time-varying reproduction number for epidemics model, developed by Thompson and colleagues[21]. Our model used a mean serial interval of 2.97 days with an average standard deviation of 3.29 days, as described in previous studies[22,23].

The incidence (1) and mortality rates (2) by 100,000 inhabitants and the case-fatality (3) (%) were calculated according to the equations:

(1) Incidence= (number of cases) x 100.000 population
(2) Mortality= (number of deaths) x 100.000 population
(3) Case-fatality= (number of deaths) x 100 (number of cases)

Mortality rates were also calculated and stratified by sex and age for the same period. According to the populational projection of Federation Units for the year 2020, the State of EspíritoSanto had 4,138,657 inhabitants[24]. The distribution of the population by gender and age is described in table 1.

Table 1: Number of inhabitants according to gender and age groups for the State of Espírito Santo.

Age (years old)	Population		
	Male (n)	Female (n)	Total (n)
0 – 19	581,017	561,210	1,142,227
20 – 29	339,254	325,773	665,027
30 – 39	350,542	338,848	689,390
40 – 49	292,310	291,729	584,039
50 – 59	234,227	241,259	475,486
60 – 69	162,788	175,923	338,711
70 – 79	70,821	89,529	160,350
80 or more	32,106	51,321	83,427
Total	2,063,065	2,075,592	4,138,657

Source: DATASUS - Projeção da População das Unidades da Federação por sexo e grupos de idade: 2000-2030.

For trend analysis, the period was divided into the first wave (1st Wave - March to October 2020) and second wave (2nd Wave – November 2020 to June 2021) to define the end of the first wave, the month with the lowest mortality rate was considered, which suggested the end of a first wave in the curve.

The trends were analyzed according to the methodological guidelines byAntunes and Cardoso[25], the Prais-Winsten regression model for population mortality rates was used to build time series, series as well as to determine incidence, case fatality and mortality trends. Were estimated the probability (p), and Daily Percent Change (DPC), considering a 95% level significance, according to equations (1), (2), and (3):

(1) DPC=(10^β-1)×100%
(2) (IC95%)ul=(10^ β_max-1)×100%
(3) (IC95%)u=(10^ β_min -1)×100%

In these equations, we considered β as the angular coefficient from the linear regression, the indexes ul as the upper limit, and ll as the lower limit of the confidence level.

The case-fatality, mortality and incidence trends were classified in increased, decreased, or flat. Flat trends were considered when p value was not significant ($p<0.05$).

Statistical analyses were performed using the STATA 14.0 software (College Station, TX, U.S. 2013).

Ethical and Legal Aspects of the Research

Ethics committee approval was not required because only secondary data available on the internet were used in this study.

RESULTS

There were 524,496 cases and 11,516 deaths accumulated from COVID-19 in EspíritoSanto from March 2020 to June 2021. There was a higher proportion of female individuals in the cases (53.48%) and male (54.71%) in deaths. There was a higher percentage of confirmed cases among people aged 30 to 39 years, while deaths were more prevalent among the elderly (60 to 69 years - 24.85%; 70 to 79 years - 24.85%; and 80 years or more - 23.11%) (table 2).

Table 2: Cases and deaths due to COVID-19 in the State of Espirito Santo, Brazil, from March 2020 to June 2021, distributed according to gender, age, and comorbidities

Description	Cases	Deaths
	n (%)	n (%)
COVID-19 (cases or deaths accumulated)	524,496 (100.00)	11,516 (100.00)
Gender*		
Male	243,938 (46.52)	6300 (54.71)
Female	280,435 (53.48)	5216 (45.29)
Age (years old)**		
0-19	47916 (9.14)	41 (0.36)
20-29	93933 (17.91)	111 (0.96)
30-39	125367 (23.9)	402 (3.49)
40-49	104861 (19.99)	916 (7.96)
50-59	75439 (14.39)	1661 (14.42)
60-69	46068 (8.78)	2862 (24.85)
70-79	20575 (3.92)	2862 (24.85)
80 or more	10321 (1.97)	2661 (23.11)
Total comorbidity notification***	126,981 (100.00)	12324 (100.00)
Lung	11,473 (9.03)	825 (6.69)
Cardiovascular	69,029 (54.37)	6055 (49.13)
Renal	2,151 (1.69)	537 (4.36)
Diabetes	25,337 (19.95)	3228 (26.19)
smoking	7,136 (5.62)	547 (4.44)
Obesity	11,855 (9.34)	1132 (9.19)

* Gender: 524,373 cases described the sex. In 123 cases, this information was ignored. *** Age: A total of 524,480 cases described the age, and 16 cases this information was missed. ***An individual could have 1 or more comorbidities.

It was observed that 126,981 comorbidities reported in cases and 12,324 in deaths from COVID-19. Among the comorbidities reported, cardiovascular comorbidities were the most prevalent in both groups (54.37% cases; 49.13% deaths), followed by diabetes (19.95% - cases; 26.19% - deaths) and obesity (9.34% - cases; 9.19% - deaths) (table 2). The lethality (%), mortality and incidence rates (per 100,000 inhabitants) of COVID-19 in the analyzed State, distributed by sex and age, were illustrated in table 2.

The lethality (%), mortality and incidence rates (per 100,000 inhabitants) of COVID-19 in the analyzed State, distributed by sex and age, were illustrated in table 3.

Table 3: Case-fatality of COVID-19, mortality, and incidence rate per 100,000 inhabitants in the State of Espírito Santo from March 2020 to June 2021, distributed by sex and age group

Age (years old)	Case-fatality (%)			Mortality rate (per 100,000 inhabitants)			Incidence rate (per 100,000 inhabitants)		
	Male	Female	Total	Male	Female	Total	Male	Female	Total
0 – 19	0.08	0.09	0.08	3.10	4.10	3.59	3948.25	4445.04	4194.96
20 – 29	0.12	0.11	0.12	15.62	17.80	16.69	12628.88	15679.32	14124.69
30 – 39	0.37	0.27	0.32	62.47	54.01	58.31	16773.17	19639.19	18185.21
40 – 49	1.06	0.70	0.87	178.92	134.71	156.84	16806.47	19098.20	17954.45
50 – 59	2.72	1.76	2.20	401.32	298.85	349.33	14770.29	16923.31	15865.66
60 – 69	7.45	5.13	6.21	983.49	716.79	844.97	13193.23	13972.59	13600.97
70 – 79	16.57	11.52	13.91	2280.40	1392.84	1784.84	13764.28	12092.17	12831.31
80 or more	30.19	22.50	25.78	4145.64	2591.53	3189.61	13732.63	11519.65	12371.29
Total	2.58	1.86	2.19	305.37	251.30	278.25	11824.06	13511.08	12672.71

The mortality rate of COVID-19, considering the entire period analyzed, was 2.19%, with mortality rates of 278.25 deaths per 100,000 inhabitants and an incidence of 12,672.71 new cases per 100,000 inhabitants. It was observed that the lethality and mortality rates were higher at older ages, in which male individuals aged 80 years or older had the most increased lethality (30.19%) and mortality (4,145.64 deaths per 100,000 population) scores. At the same time, the highest incidence rates were found among females' individuals aged 30 to 39 years (19,639.19 cases per 100,000 inhabitants) and 40 to 49 years old (19,098.20 cases per 100,000 inhabitants) (table 3).

The distribution of cases and deaths per day and the Effective reproduction number (Rt) of COVID-19 in the State of EspíritoSanto were highlighted in figure 1.

There was a significant oscillation in the distribution of new cases and deaths of COVID-19, with maximum peaks of daily cases observed during March 2021 (figure 1A) and fatalities in April 2021 (figure 1B). The Effective reproduction number also suffered large fluctuations; only in July, August, December 2020, and January 2021 did the transmissibility of SARS-COV-2 controlled, with a predominance of Rt with values below one. However, there was an increase in transmissibility during March 2021 (Rt >1), with controlled levels in the subsequent months (figure 1C).

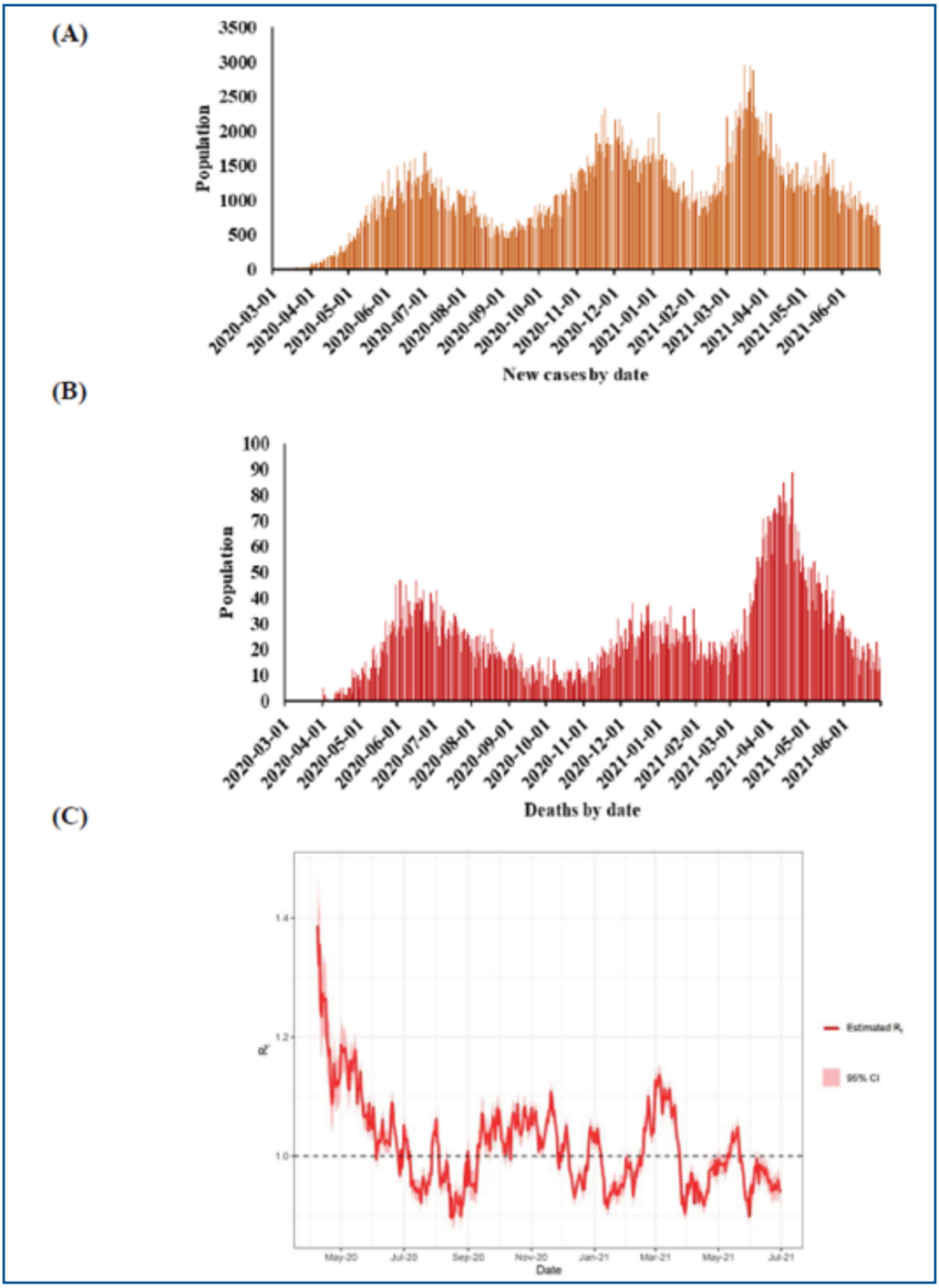

Figure 1: Distribution of daily new cases (A), deaths (B), and effective reproduction number (C) of COVID-19 in the State of Espírito Santo from March 2020 to June 2021. CI = Confident Interval. Effective reproduction Number (Rt), estimated from April 1 to 2021, June 30, 2021.New cases and deaths per day from March 2020 to June 2021.

The indicators of lethality, mortality, and incidence varied according to the months analyzed, presenting a two- wave profile, as illustrated in figure 2. It was evidenced that even after one year of pandemic, the State of EspíritoSanto described higher rates of lethality (4.51%) and mortality (48.90 deaths per 100,000 inhabitants) in April 2021, with a peak incidence in March 2021 (1,618,57 new cases per 100,000 inhabitants) (figure 2).

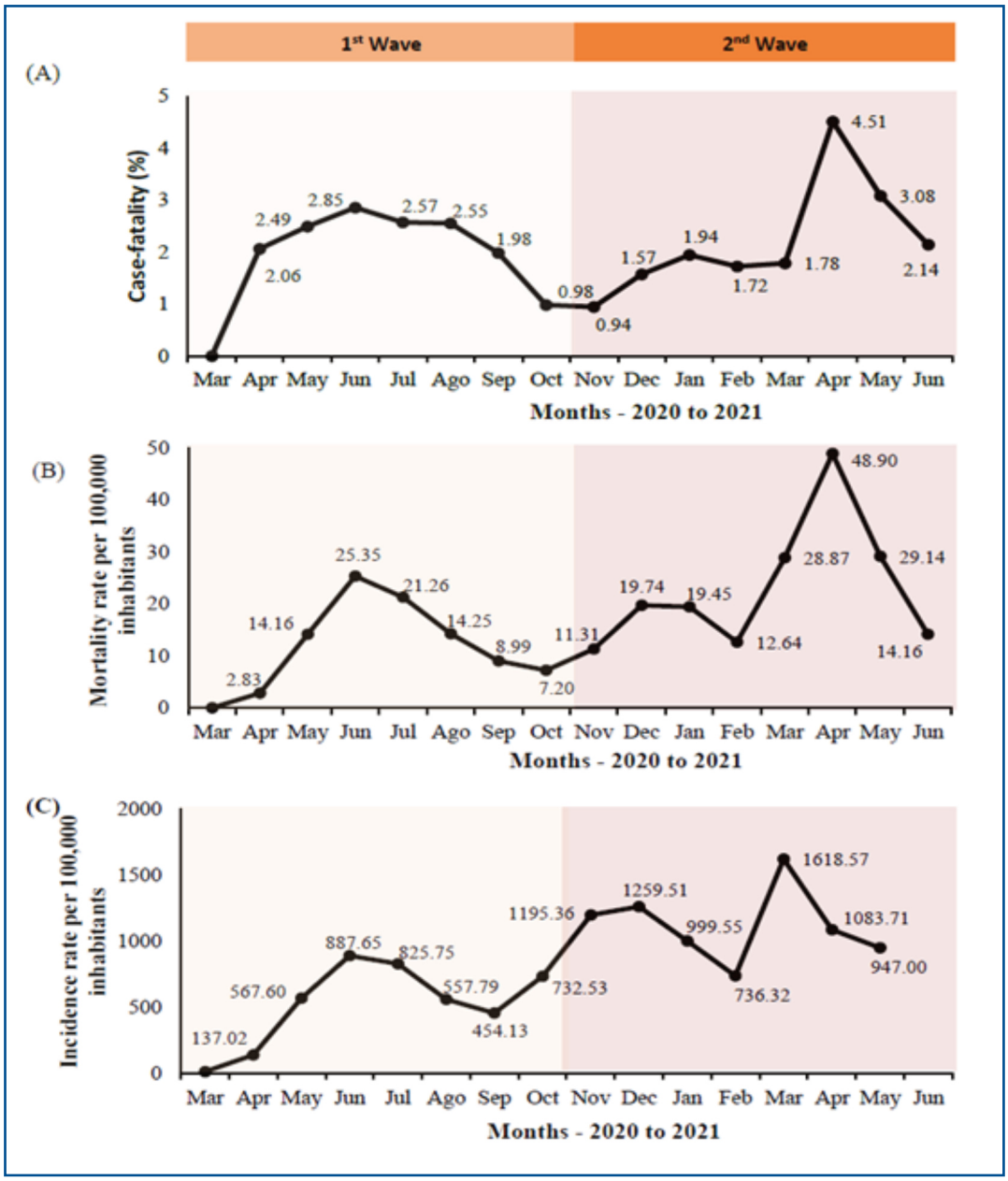

Figure 2: Percentage case-fatality (A), mortality (B), and incidence rate per 100,000 inhabitants (C) due to COVID-19 in the State of Espirito Santo, according to the 1st Wave (March to October 2020) and the 2nd Wave (November 2020 to June 2021).

Prais-Winsten regression estimates and Daily Percent Change (DPC) of the case-fatality (%), mortality (per 100,000 inhabitants), and incidence rates (per 100,000 inhabitants due to COVID-19 in the State of EspíritoSanto according to the first and second wave (table 4). The first wave of COVID-19 in the analyzed region was marked by stationary lethality trends, increasing mortality and incidence trends ($p<0.05$) with respective DPC: 0.36% and 0.78%. In the second wave, despite the incidence growing trends ($p<0.05$), mortality showed stationary trends, with non-significant p-value ($p<0.05$), with lethality with decreasing trends ($p<0.05$) with DPC of -0.33% (table 4).

Table 4: Prais-Winsten regression estimates and Daily Percent Change (DPC) of the case-fatality (%), mortality (per 100,000 inhabitants), and incidence rates (per 100,000 inhabitants due to COVID-19 in the State of Espirito Santo, according to the 1st Wave (March to October 2020) and the 2nd Wave (November 2020 to June 2021).

Período	DPC (CI 95%) Case-fatality	p	Fatality Trends
1st Wave	0.02 (-0.07 : 0.11)	0.685	Flat
2nd Wave	-0.33 (-0.52 : -0.15)	<0.001*	Decreasing
Período	**DPC (CI 95%) Mortality**	**p**	**Mortality Trend**
1st Wave	0.36 (0.21 : 0.52)	<0.001*	Increasing
2nd Wave	0.63 (-0.04 : 1.30)	0.066	Flat
Período	**DPC (IC 95%) Incidence**	**P**	**Incidence Trend**
1st Wave	0.78 (0.25 : 1.31)	0.004*	Increasing
2nd Wave	2.06 (0.72 : 3.42)	0.003*	Increasing

First (1st) Wave (March to October 2020) and the Second (2nd) Wave (November 2020 to June 2021). DPC – Daily Percent Change (%); CI 95% – Confidence interval 95%; p-value – the probability of statistical significance - Prais-Winsten regression test.
Source: Cases, deaths, and population were extracted from the Health Department of the State of Espírito Santo, Brazil.

DISCUSSION

The State of EspíritoSanto, reported 524,496 cases accumulated from COVID-19 up to June 30, 2021, of which 11,516 died from the disease. There were oscillations in viral transmissibility, in the number of cases and deaths, with high peaks in the incidence indicators (March 2021), mortality, and lethality (April 2021) observed even after one year of pandemic. Although lethality rates have decreasing trends at the end of the second wave (November 2020 to June 2021) and mortality is stationary, the incidence remains with increasing trends throughout the analyzed period.

The first case notification of COVID-19 in the State began on February 25, 2020; however, this confirmation was dismissed out by the Central Laboratory of EspíritoSanto. On March 5, 2020, the first case was confirmed, from a resident of the Metropolitan region of Vitória with a history of international travel26. Thus, subsequent cases followed similar behavior in the first half of March 2020, with predominant origin abroad and in the State of São Paulo (Brazil), the epicenter of the disease in Latin America[27,28].

Although the first suspicions of COVID-19 were reported in February 2021, there is evidence that the virus circulated in EspíritoSanto before this date. In a study that analyzed samples of 7,370 patients, without prior suspicion of COVID-19, but who had symptoms compatible with viral infections such as Dengue or Chikungunya, from December 1, 2019, to June 30, 2020, the results illustrated that 210 SARS-CoV-2 positive cases were detected. These hidden cases possibly indicate delays in seeing patients, which may have contributed to the rapid expansion of the COVID-19 outbreak[29].

Community transmission in EspíritoSanto began in March 2020, and cases increased with the first deaths, and the territorial extension of the disease grew, incorporating other neighborhoods and cities. In this initial phase of the disease, there was a predominance of the regions with the highest human development index (HDI) in the State of EspíritoSanto, such as Vitória (MHDI = 0.845) and Vila Velha (MHDI = 0.8)18,27, evidencing the manifestation of the pandemic stratified by social class, sex, and race[30].

Concerning sociodemographic aspects, similar findings were reported by the State Government, with predominant COVID-19 cases in females (53%) but with a higher frequency of deaths in males (53%). There is a predominance of confirmed cases of COVID-19 in populations of economically active age in the age variable. Even with the highest frequency of cases in the 20 to 59 age group (74%), the number of deaths occurs mainly in the elderly population aged 60 and over (70%)[14].

Thus, greater susceptibility to severe conditions of COVID-19 and higher mortality are associated with biological sex and age group. Males have a higher risk of mortality than women; the elderly also have a higher mortality rate than younger individuals[31].

It is noteworthy that comorbidities also represent significant risk factors in addition to gender and age group. According to Wang et al.[32] which evaluated data from 36 patients affected by COVID-19 who required care in the Intensive Care Unit (ICU), illustrated that 72.2% of the individuals had comorbidities. This finding indicates that a history of chronic diseases can lead to the development of complications.

In this context, it is essential to analyze health indicators, especially lethality and mortality rates. Lethality measures the number of deaths about people with active disease and not concerning the total population; that is, it evaluates the percentage of infected people who progress to death, while the mortality rate is used to analyze the impact of a disease or condition on the entire population of a region. These two variables were influenced by associated comorbidities and the immunosuppression presence, especially in elderly patients, with median age above 60 years[33,34]. Moreover, as the pandemic progressed, other elements became risk factors for worsening the situation, such as gender, ethnicity, particularly blacks and Hispanics and comorbidities[35].

The main categories of comorbidities associated with COVID-19 in the State of Espírito Santo, were related to the presence of CVDs, and indicate a higher risk of mortality. The CVDs represented more than half of the morbidities reported (54.37%) by confirmed cases in this State, followed by diabetes (19.95%) and obesity (9.34%). In line with the study by Silva et al.,36 conducted in the state capital of Amapá, Brazil, the authors highlighted those 102 patients with comorbidities and diagnosed with COVID-19 had chronic CVD (38.33%), diabetes (24.16%), and chronic respiratory diseases (13.33%) as the most prevalent risk factors.

Pre-existing conditions impair the body's immune response, such as diabetes mellitus (DM) and obesity, which are potential aggravating factors of the infectious illness generated by SARS-Cov-2, impacting the patient's evolution to death. In a study by Oliveira et al.,[37] the main comorbidities reported in patients with COVID-19 were DM, chronic heart diseases, and hypertension-related to cardiovascular conditions and chronic respiratory diseases. In this case, the comorbidity with the highest record in cases of death was hypertensive disease. Furthermore, several authors highlight systemic arterial hypertension as one of the main aggravating factors for the COVID-19 condition, together with other CVDs, being associated with worse prognoses and high lethality rates[38-40].

Previouscoronavirusoutbreakshavebeenassociated with comorbidities and cardiovascular complications[41]. Increased inflammatory and immunological responses, endothelial damage, microvascular dysfunction or thrombosis due to hypercoagulability, and stress cardiomyopathy are possible pathways of the acute coronary syndrome[42]. A recent systematic review and meta-analysis by Cochrane showed that 20.0% (95% CI 16.1–23.8% with substantial heterogeneity - I2 = 94.9%) of patients hospitalized with COVID-19 had an acute myocardial infarction[43]. For example, a study involving 5,119 Danish patients diagnosed with COVID-19 revealed that the incidence of Acute Myocardial infarction (AMI) was approximately five times higher during the 14 days after infectious diagnosis than the control interval[44]. However, there remains a scarcity of data

regarding the true incidence of acute AMI due to microvascular dysfunction and coronary thrombosis in patients with COVID-19, given the difficulty of outlining such dedicated studies.

About obesity, it has long been known that it is directly associated with poor prognoses and prolonged recovery in cases of viral infections. In the context of COVID-19, other factors related to obesity may be responsible for the higher chances of worsening the clinical picture, which includes deficient respiratory mechanics, low gas exchange rate in the lungs, increased airway resistance, reduced lung strength, and lower lung volume[45].

Among the other most prevalent risk factors, Bornstein et al.,[46] also highlight the direct relationship between DM and the COVID-19 with greater severity of the clinical condition, resulting in a glycemic increase in patients with type 2 DM. In addition, the pre-existence of respiratory diseases was the first and primary risk factor associated with severe conditions of COVID-19[47,48]. Finally, comorbidities such as cerebrovascular diseases, neoplasms, smoking, Alzheimer's disease, pancreatic disease, dengue, alcohol consumption, and puerperal period were also related to the worse prognosis of COVID-19, although to a lesser extent.

Time analysis

After the beginning of community transmission in the State of Espírito Santo in March 202027, the distribution of new cases per day showed a high degree of variation in the distribution of COVID-19 cases throughout 2020, peaking in March 2021, recording an incidence rate of 1,618.57 new cases per 100,000 inhabitants. The estimated Rt is important to understand the changes in the transmissibility of infectious diseases over time. In COVID-19, this parameter has been adopted to evaluate the effects of interventions and support the creation of Public Policies[49]. During the period from March 1, 2020, to June 30, 2021, Rt suffered oscillations and remained higher than one (R>1) for most of the studied period, with higher peaks at the beginning of the pandemic and in March 2021, illustrating a dyscontrol in the transmissibility of SARS- CoV-2 in the analyzed period.

By analyzing the daily percentage variation in lethality, mortality, and incidence rates due to COVID-19, indicating increasing, decreasing, or stationary trend rates, it is possible to understand the dynamics of the pandemic compared to a simple rate analysis.

The highest percentage values of lethality were observed during the first wave in May 2020 (2.85%), and during the second wave and in April (4.51%) and May (3.08%) 2021. In this same period, the highest mortality rates (deaths per 100,000 inhabitants) were also recorded: June 2020 (25.35), April (48.90), and May (29.14) 2021. Despite the peaks of mortality and lethality observed during the second wave, stationary trends for mortality and decreasing for lethality were evidenced. However, the incidence remained increasing, with a DPC of 0.36% during the first wave and 0.78% during the second wave. Trends in lethality, mortality, and incidence rates may change according to the region. The stationary trends in lethality rates found during the first wave followed the global trend of lethality of COVID-19 that remained stationary between December 31, 2019, and August 31, 202050.

Spatial analysis

According to Bernal et al.,[50], the COVID-19 pandemic is still in a global progression phase. In the State of Espírito Santo, this same trend is observed today.

In the analysis of the monitoring of the spread of COVID-19 based on the cartographic analysis of thematic maps on the notifications of confirmed cases, Ferreira et al., (2020)[51] highlight that the first cases occurred in cities with a larger population and have a greater connection with metropolises and medium-sized cities, indicating a possible correlation between the hierarchy of cities in the urban network and the spread of the virus in populations.

Moreover, the spatial propagation of COVID-19 in the State of Espírito Santo territory followed a pattern of combined diffusion, with hierarchical and contagion stages, severely affecting the Metropolitan Region of Greater Vitória (RMGV) at first, but with a tendency to internalization in the State. In the scale of the urban space of the metropolitan agglomeration, there is a process of peripheralization, in which the central neighborhoods have lower lethalities than the peripheral ones[14].

The geographical analysis of the spread of SARS- Cov-2 and the manifestation of COVID-19 shows that population density and mobility are determinants in pandemic control. The mathematical models of transmissibility are supported by the results observed in regions with denser populations that did not implement non-pharmacological contagion prevention measures in their daily lives[52]. These variables contributed to the increase in viral transmissibility and the consequent manifestation of COVID-19, which may increase population lethality and mortality and the impacts already caused by comorbidities and advanced ages associated with more favorable outcomes of death.

Thus, population density/concentration and mobility/flow criteria were determinants for the observed increase in lethality and mortality during the first period of COVID-19 pandemic registration. The population clusters of the RMGV presented the highest viral transmission outcome, and the disease's development was observed in the first cycle of the pandemic analyzed[14,26,27].

Epidemiological analysis

The COVID-19 pandemic has led health systems to collapse worldwide. According to the World Health Organization[53], almost all countries (90%) experienced some interruption in health care at the beginning of the pandemic, with the most considerable number reported in low- and middle-income countries. However, interruptions in essential services are widespread geographically around the world. In Brazil, the dissemination of SARS- CoV-2 presented a complex epidemiological picture, which evidenced the greatness and diversity of the health care network of the unified health system (SUS) public, allowing the maximization of its use and rescue of its classic principles of universality, integrality, and equity.

In each Brazilian State, different strategies were observed by the health authorities to contain the dissemination and spread of the virus. Given the epidemiological picture of COVID-19, there is a need to develop different forms of analysis of outcomes to better understand the aspects of the current pandemic regarding lethality and mortality.

The geographic-temporal distribution of COVID-19 cases in the State of Espírito Santo, in the Southeastern Brazilian Region, was performed from data clusters and divided into two periods: first wave and second wave of COVID-19, with the closing of the analysis on June 30, 2021.

The behavior of the outcome variables lethality and mortality by COVID-19 evidences the difficulties of dealing with transmissibility due to the low testing of individuals in the State of EspíritoSanto. Added to these data clusters is the expectation of the action of herd immunity, which according to Kadkhoda[54] this immunity represents the population's immune protection to cease the chain of transmission of an infectious disease, which can be obtained through infection or vaccination. The adoption of strategies based on herd immunity is implicit in community actions and the feeling of diminishing the severity of the pandemic, mainly due to the absence of education and health actions aimed at disseminating the fundamental aspects of the evolving pandemic in that federative State[28,55].

The profile of the epidemiological manifestation of the pandemic caused by the uncontrolled transmissibility of COVID-19 occurred in municipalities with similar demographic characteristics, high population density, and migration of people within and between cities of the State of Espírito Santo. In the first cycle of the pandemic, characterized by community transmission in the State of Espírito Santo, there was an increase in lethality and mortality evidenced in the records of the March data clusters.

The commemorative date of a great migration of people in this period was the celebration of the largest and most popular Brazilian cultural festival, Carnival.

In the following months, these variables decreased, maintaining this behavior until October 2020. It is noteworthy that non-pharmacological measures of social distancing, as well as the cultural impregnation of the use of masks and local economic incentive to reduce agglomerations, such as the implementation of virtual educational platforms for non-presential (remote) classes at different levels of education (elementary, middle and university education) were adopted in all the municipalities of Espírito Santo.

In the epidemiological phases of the pandemic, three steps stand out. The first phase, consisting of imported cases through infected people in other countries, with March 2020 as the time frame. The second phase is characterized by local transmission when people with no recent international travel history become ill. This phase is characterized by increased lethality and mortality outcomes. It is also noteworthy that it is possible to identify the definitive host (human beings) of the etiological agent (SARS-CoV-2), who are usually relatives or people of close social life. In this way, it is possible to track cases and isolate suspected and confirmed cases. However, this type of intervention for epidemiological control/ surveillance is dependent on testing, which was very low in the State during the first wave of COVID-19 due to the still incipient availability in the national market. Finally, in the third phase, characterized by community transmission, there was an increase in confirmed cases and the number of people who evolved with the disease in the State of EspíritoSanto. It was no longer possible to identify the transmitting source.

In March 2020, during the first cycle of the COVID-19 pandemic, community contamination was already included in the State of EspíritoSanto. Following the epidemiological analysis, considering the lethality and mortality outcomes in the second cycle of the COVID-19 pandemic in the State, the evolution of the 2nd epidemiological wave of the COVID-19 pandemic (November 2020 to June 2021) was characterized by a stationary mortality rate and decreasing lethality rate, with a DPC of - 0.37%. However, it is emphasized that the incidence remains with increasing trends illustrating the possibility of further contamination and subsequent wave formations.

Also, in this period, specifically from March to June 2021, there was a predominance of mortality, with 50.4% of all deaths that occurred since the pandemic in Brazil. In the distribution of mortality due to COVID-19, it was observed that in April, there were 82,401 victims, March with 66,868, May with 58,679, and June with 55,280 deaths per 100,00 inhabitants.

The event of the second wave of COVID-19 in Brazil was more lethal. In the State of EspíritoSanto, there were 586 deaths in June, 1,206 deaths in May, 2,024 deaths in April, which was more aggressive than the first, with a peak of incidence in March, and a rise of mortality and lethality in April 2021. Until July 17, 2021, Brazil was the sixth country with the highest mortality rate, after Peru, Mexico, Afghanistan, Tunisia, and South Africa.

As limitations to this study, it is emphasized that the statistical /epidemiological monitoring of COVID-19 continues to be challenging due to disparities in access to official data and, significantly, in different locations, social groups, as well as divergence of data in the first months on any cumulative indicator of cases. In addition, the use of variables, such as the number of hospitalizations, ICU admissions, and intubations, is restricted in different scenarios, limiting their usefulness for national global analysis. There is quiescence of these indicators in the Brazilian information repository (DATASUS), highlighted as a limitation of the study under discussion.

To our knowledge, this is the first work to comprehensively study the epidemiological profile of the State of EspíritoSanto, evidencing the formation of two possible waves. The findings of this study, such as the increasing trends in the incidence rate even after one year of pandemic, contribute scientifically to a warning that prevention measures such as double facial masking and social distancing are reinforced even after vaccination.

Moreover, due to the limitations arising from incidence rates, which are dependent on the number of tests, the attributes of this study are also associated with the analyses of indicators related to the number of deaths. It is a more reliable indicator to reflect the size

of the pandemic impact; data on fatalities are more comparable and faithful, although not entirely immune to underestimations; this finding characterizes a strong point in data analysis over epidemiological weeks from 2020 to June 2021. Another aspect of the importance of this study is in its state scope, in the sample size and territorial coverage carried out so far, the multidimensional nature of the research.

CONCLUSION

The State of Espirito Santo, during the period from March 2020 to June 2021, presented 524,496 accumulated cases and 11,516 deaths due to COVID-19, with an accumulated lethality of 2.19%, with mortality rates of 278.25 deaths per 100,000 inhabitants and an incidence of 12,672.71 cases per 100,000 inhabitants, with transmissibility suffering large fluctuations during the period.

Notifications of 126,981 comorbidities were recorded between the cases, and 12.324 were mentioned in the reports of deaths. Cardiovascular diseases (69,029 in cases and 6.055 in deaths), followed by diabetes (25,337 in cases and 3,228 in deaths), and obesity (11,855 in cases and 1,132 in deaths) were the most prevalent comorbidities. Moreover, male gender and advanced age have higher lethality and mortality rates, with male individuals aged 80 years or older presenting the highest rates: lethality (30.19%) and mortality (4,145.64 deaths per 100,000 inhabitants).

The epidemiological profile of COVID-19 in the State of Espirito Santo was characterized by the formation of two waves, which evidenced the incidence with increasing trends and a Daily Percent Change of 0.78% during the first wave and 2.06% during the second wave. Although the second wave (November 2020 to June 2021) presented decreasing trends in lethality (DPC = -0.33%) and stationary mortality, this period had the highest rates of all indicators here discussed, and the peak of incidence in March (1,618.57 new cases per 100,000 inhabitants), and lethality (4.51%), and mortality (48.90 deaths per 100,000 inhabitants) in April.

The pandemic is still in evolution in the State of Espirito Santo. Therefore, non-pharmacological measures, such as facial masking use, reduction of agglomerations, hand hygiene with soap and water or gel alcohol, as well as the reduction of movement of people in the State are still necessary measures to combat COVID-19, in addition to the advance of immunization with the Vaccine against SARS-CoV-2.

Author Contributions

Conceptualization, C.D.K.S., B.E.G.D., T.C.M., I.P., M.P.R.C. and L.C.A.; methodology, C.D.K.S., T.C.M., J.O.E., L.C.J., R.D.R., K.E., C.E.S. and L.C.A.; software, J.O.E., L.C.J.; validation, T.C.M., J.O.E., C.E.S. and L.C.A.; data curation, C.D.K.S., T.C.M., L.C.A.; writing- review and editing, all the authors; visualization, all the authors; supervision, K.E., C.E.S. and L.C.A.; project administration, C.E.S. and L.C.A. All authors have read and agreed to the published version of the manuscript.

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Conflicts of Interest

The authors declare no conflict of interest.

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CHAPTER 29

MORTALITY AND CASE FATALITY RATES OF COVID-19 IN THE STATE OF GOIÁS, BRAZIL

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Abstract

Introduction: the initial spread of the pandemic in Brazil was mainly affected by patterns of socioeconomic vulnerability. It should be noted that the Central-West region of Brazil is one of the regions with the lowest number of cases, but the states of this region together have the highest mortality rate of COVID-19 in the country. Goiás was the most affected state of this region, with the highest number of deaths in the area. **Objective:** to assess the incidence of mortality and lethality caused by COVID-19 from March 2020 to June 2021 in the State of Goiás, Brazil. **Methods:** an ecological study, using a series of time series of public and official data of the Department of Health of the State of Goiás, Brazil. Information was collected on cases and deaths from COVID-19 from March 2020 to June 2021. Mortality, case fatality, and incidence rates were calculated. The Prais-Wisten regression model was used to build time series. The daily percent change (DPC) and the effective reproductive number (Rt) were estimated. **Results:** Goiás had a predominance of a greater viral spread during the first and the beginning of the second wave, with Rt higher than 1. The second wave from December 2020 to June 2021 was more lethal and had higher mortality rates than the first wave. It was observed, higher scores of case fatality and mortality belonged to males and the elderly. **Conclusion:** an analysis of mortality and case fatality rates helps understand the COVID-19 pandemic behavior in Goiás. It is essential to monitor epidemiological indicators and strengthen intervention strategies to contain the pandemic in this state.

Keywords: Case Fatality Rate; COVID-19; Epidemiology; Mortality; Trends.

Resumo

Introdução: a propagação inicial da pandemia no Brasil foi afetada principalmente por padrões de vulnerabilidade socioeconômica. Ressalta-se que a região Centro-Oeste do Brasil é uma das regiões com menor número de casos, mas os estados dessa região juntos apresentaram a maior taxa de mortalidade por COVID-19 do país. Goiás foi o estado mais afetado da região, com o maior número de óbitos. **Objetivo:** avaliar a incidência, mortalidade e letalidade por COVID-19 no Estado de Goiás, Brasil, no período de março de 2020 a junho de 2021. **Método:** estudo ecológico, utilizando séries temporais de dados públicos e oficiais da Secretaria de Saúde do Estado de Goiás, Brasil. As informações foram coletadas sobre casos e óbitos de COVID-19 de março de 2020 a junho de 2021. Mortalidade, letalidade e taxas de incidência foram calculadas. O modelo de regressão Prais-Wisten foi usado para construir séries temporais. A mudança percentual diária (DPC) e o número reprodutivo efetivo (Rt) foram estimados. **Resultados:** Goiás teve predomínio de maior

disseminação viral durante a primeira onda e o início da segunda onda, com Rt maior que 1. A segunda onda, dezembro de 2020 a junho de 2021, foi mais letal e apresentou taxas de mortalidade maiores que a primeira onda. Observou-se que os maiores escores de letalidade e mortalidade pertenciam ao sexo masculino e aos idosos. **Conclusão:** uma análise das taxas de mortalidade e letalidade ajuda a entender o comportamento da pandemia do COVID-19 em Goiás. É fundamental monitorar indicadores epidemiológicos e fortalecer estratégias de intervenção para conter a pandemia neste estado.

Palavras-chave: COVID-19; Letalidade; Epidemiologia; Mortalidade; Tendências.

INTRODUCTION

Since the initial outbreak of pneumonia of unknown etiology in Wuhan, China, at the end of 2019, the COVID-19 disease caused by Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2), has become a complex global Public Health problem[1]. According to the Center for Systems Science and Engineering of Johns Hopkins University[2], until July 05, 2021, worldwide, the COVID-19 was responsible for more than 180 million confirmed cases and approximately 4 million deaths. Within this scenario, Brazil accounted for 18,769,808 cases and 524,417 obits, highlighting second place in the ranking of deaths by COVID-19, only behind the United States of America accounting for 605,551 deaths.

It was believed that Brazil, being a country with a population of over 200 million that has a universal, comprehensive health system, would have good tools to mitigate the COVID-19 pandemic. However, Latin America became the pandemic epicenter, mainly due to the high spread of the disease in Brazil[3].

Despite the benefits arising from the Unified Health System in Brazil (SUS), many structural problems hamper the quality of how this system works, including gaps in organization and governance and low public funding. Furthermore, there are numerous regional disparities in access to health services, in which the most impoverished regions and the most disadvantaged socioeconomic population groups are the most impacted[4].

It is noteworthy that the initial spread of the Pandemic in Brazil was mainly affected by patterns of socioeconomic vulnerability; this occasioned a more significant impact than the effects of age and health status. It is known that deaths from COVID-19 are directly associated with socioeconomic vulnerability indices and negatively correlated with the levels of hospital resources. Thus, understanding the dissemination pattern of COVID-19 in a region marked by significant socioeconomic inequalities is essential to containing the spread of the pandemic in the country[5].

Measures to contain the disease are indispensable; the viral dissemination can contribute to the formation of new waves even more lethal, given that the population is tired of the virus and mostly deprived of education on health measures[6].

The country's different regions were impacted with varying intensities; it should be noted that, until mid-2021, the Brazilian Midwest was one with the lowest number of cases (1,910,873). However, it has the highest mortality rate by COVID-19 in the country, with 301 deaths per 100 thousand inhabitants. This average is higher than the gross national mortality (249,9 deaths per 100,000 inhabitants)[7].

Among the states that make up the Midwest, Goiás is the most populous, with an estimated 7.1 million for 2020[8]. Between 2000 and 2017, it had a population growth of 1.75%, above the national average (1.22%). Despite its population growth, the state is below the provision of health services in the Central West and Brazil. Urban sanitary sewerage is still very precarious, and just over half the population benefits[9].

The State of Goiás has significantly been affected by the pandemic. Its first fatal victim from COVID-19 was reported on March 26, 2020, and until early July 2021, it counted almost 20,000 deaths and more than 680,000 cases of COVID-19, the state with the highest number of deaths in the region[7].

Under these circumstances, it is necessary to produce epidemiological studies on COVID-19 in this region. Therefore, this research objective is to evaluate the incidence, mortality, and case-fatality of COVID-19 from March 2020 to June 2021 in Goiás State, Brazil.

METHODS

It is an ecological study, using a time series of public and official data available on the Health Department of the State of Goiás, Brazil[10]. The database was updated on July I7, 2021, including the cases and deaths of COVID-19 from March 2020 to June 2021. Time-series studies are helpful to analyze the pandemic behavior curves[11].

The selected data revealed 694,955 cases and 19,448 deaths of COVID-19 reported by the municipalities of Goiás. The cases were classified according to the date of symptom onset and the deaths according to death date.

All notifications of cases and deaths referred to COVID-19 were considered, using the International Classification of Diseases, 10th edition (ICD-10), of "U07.1 COVID-19, identified virus", or "U07.2 COVID-19, virus not identified"[12] associated with the disease, with clinical, laboratory or epidemiological confirmation of COVID-19.

Two researchers extracted the data independently to minimize collection bias and guarantee the quality and reliability of the data obtained, then the selected data were distributed in an Excel spreadsheet.

The effective reproductive number (Rt) was estimated using R studio software EpiEstim package[13], version 2.2.4, a previously time-varying reproduction number for epidemics model developed by Thompson and colleagues[14]. Our model used a mean serial interval of 2.97 days with a mean, standard deviation of 3.29 days, as described in previous studies[15,16].

Were calculated the incidence (1) and mortality rates (2) expressed per 100,000 inhabitants, and case- fatality (3), expressed as a percentage as the following equations:

$$(1)\ \text{Incidence} = \frac{(\text{number of cases})}{\text{population}} \times 100.000$$

$$(2)\ \text{Mortality} = \frac{(\text{number of deaths})}{\text{population}} \times 100.000$$

$$(3)\ \text{Case-fatality} = \frac{(\text{number of deaths})}{(\text{number of cases})} \times 100$$

Mortality rates in the entire period stratified by sex and age were also calculated. The projection of the Federation Units for the year 2020 indicates a population of 7,017,496 inhabitants for Goiás[17]. Its distribution by sex and age group is described in figure 1.

Age group (years old)	POPULATION OF THE STATE OF GOIAS, BRAZIL		
	Male	Female	Total
0 – 19	1,027,868	983,639	2,011,507
20 – 29	611,614	581,431	1,193,045
30 – 39	595,659	575,586	1,171,245
40 – 49	502,780	511,584	1,014,364
50 – 59	382,447	404,238	786,685
60 – 69	234,885	262,266	497,151
70 – 79	111,520	130,598	242,118
80 or more	44,122	57,259	101,381
Total	3,510,895	3,506,601	7,017,496

Figure 1: Number of inhabitants according to sex and age group for the state of Goiás. Source: DATASUS (2021) - Population Projection of Federation Units by sex and age groups: 2000-203017.

The examined period was divided into first wave (March to November 2020) and second wave (December 2020 to June 2021). To define the end of the first wave, the month with the lowest mortality rate was considered, which suggested the end of a first wave in the curve.

The trend analysis the methodological guidelines by Antunes and Cardoso[18] were adopted. The Prais-Winsten regression model for population mortality rates were used to build time series, as well as to determine incidence, case-fatality and mortality trends.

Probability (p) and Daily Percent Change (DPC) were estimated considering a 95% level significance, according to equations (1), (2), and (3):

(1) DPC=(10^β-1)×100%
(2) (IC95%)ul=(10^ β_max-1)×100%
(3) (IC95%)u=(10^ β_min -1)×100%

In these equations, we considered β as the angular coefficient from the linear regression, the indexes ul as the upper limit, and ll as the lower limit of the confidence level.

The incidence, mortality and case-fatality trends were classified as increased, decreased, or was flat. Was considered flat trends when p>0,05.

Statistical analyzes were performed using the STATA 14.0 software (College Station, TX, U.S. 2013).

RESULTS

Goiás, consists of 246 municipalities and has a territorial extension of 340,242.854 km². It has available 2,290 infirmary beds and 1,058 Intensive Care Unit beds to COVID-19. Table 2 shows a summary of its main sociodemographic characteristics (table 1).

Figure 2, split into two parts (A and B), shows the cases and deaths by COVID-19 in the studied period. From March 2020 to June 2021, 694,955 cases (A) and 19,448 deaths (B) were reported.

Table 1: Sociodemographic characteristics of the state of Goiás, Brazil.

Estate of Goiás	Description
Region*	Midwestern Brazil
Number of municipalities*	246 municipalities
State's capital*	Goiânia
Territorial extension*	340,242.854 km²
Demographic density*	17.65 inhabitants /km²
Total Population (2020)**	7,017,496 inhabitants
Monthly household income per capita*	1,258 reais
Human Development Index (HDI), according last census, 2010)*	0.735
Average number of people per household***(2019)	2.8 people
Number of basic health units#	1297 units
Hospital Beds## (data updated on June 2, 2021)	
Total number of infirmary beds	8,293 infirmary beds
Total number of beds in the Intensive Care Unit (ICU)	1,801 ICU beds
Number of COVID infirmary beds	2,290 COVID infirmary beds
Number of COVID ICU beds	1,058 COVID ICU beds

Source: *Brazilian Institute of Geography and Statistics[8]. **DATASUS - Population projection of Federation Units by sex and age groups: 2000-2030[17]; ***IBGE Automatic Recovery System – SIDRA[19]; #National Register of Health Establishments – CNESNet – Ministry of Health, Brazil[20]; ##State Secretary of Health of the state of Goiás (2021)[10].

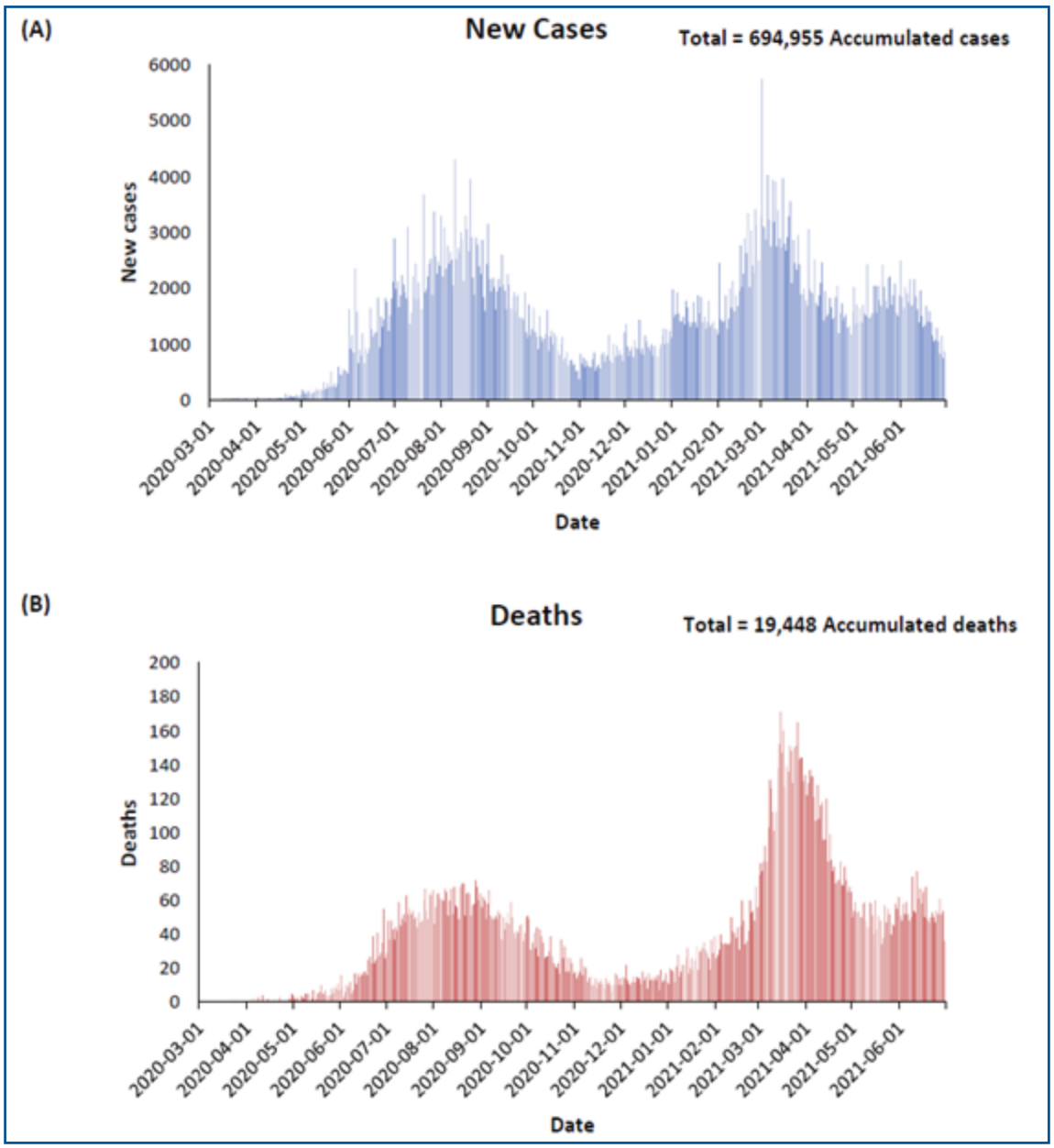


Figure 2: Number of new cases and daily deaths due to COVID-19 in the state of Goiás since the beginning of the Pandemic until the end of June 2021
Source: Cases, deaths and population were extracted from Secretary of Health of the State of Goiás, Brazil10.

The effective reproductive number (Rt) of COVID-19 in the state of Goiás from March 5st 2020 to June 30st 2021, is shown in figure 3.

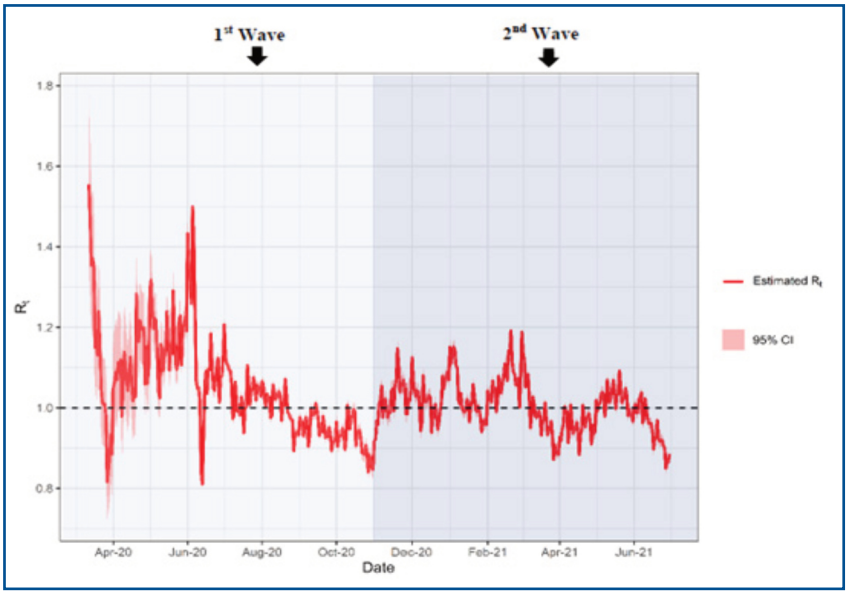
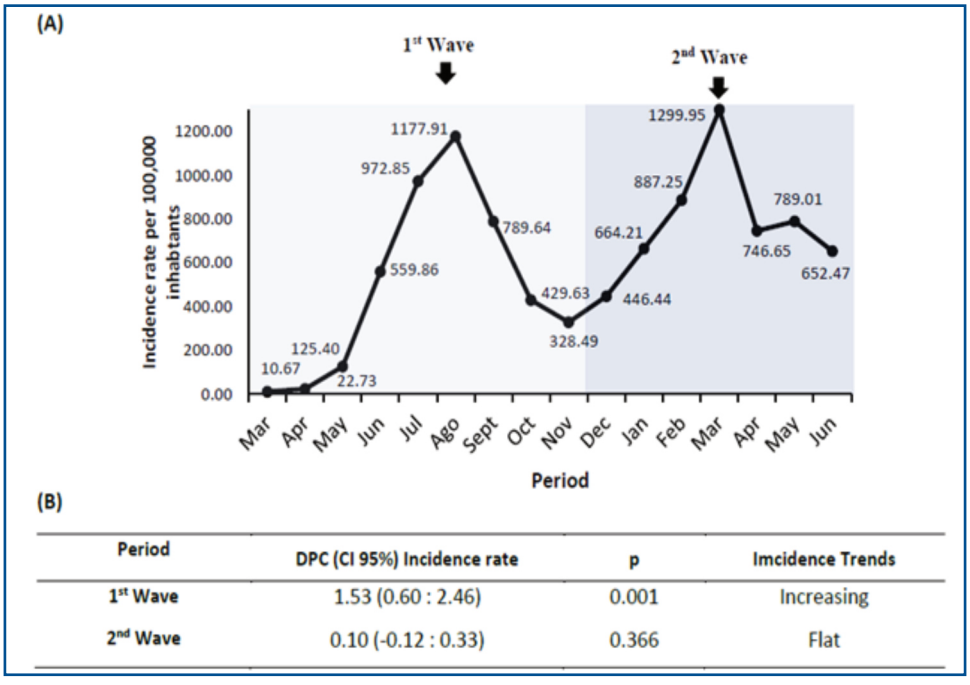


Figure 3: The effective reproductive number (Rt) during 2020, March 5st to 2021, June 30st period to the state of Goiás

CI = Confident Interval. Rt = Effective Reproductive Number.

The onset of the Pandemic in Goiás revealed a vaster viral spread, with Rt higher than 1, especially from March to July 2020. Then, September and October showed a controlled viral spread, with Rt values lower to 1, increasing in later months, with rates indicating a predominance of low viral transmission from Jun 2021 (Rt < 1) (figure 3).

The crude incidence rates of COVID-19 in Goiás, considering the period examined (A) and trend analyses (B), are illustrated in figure 4.



(B)

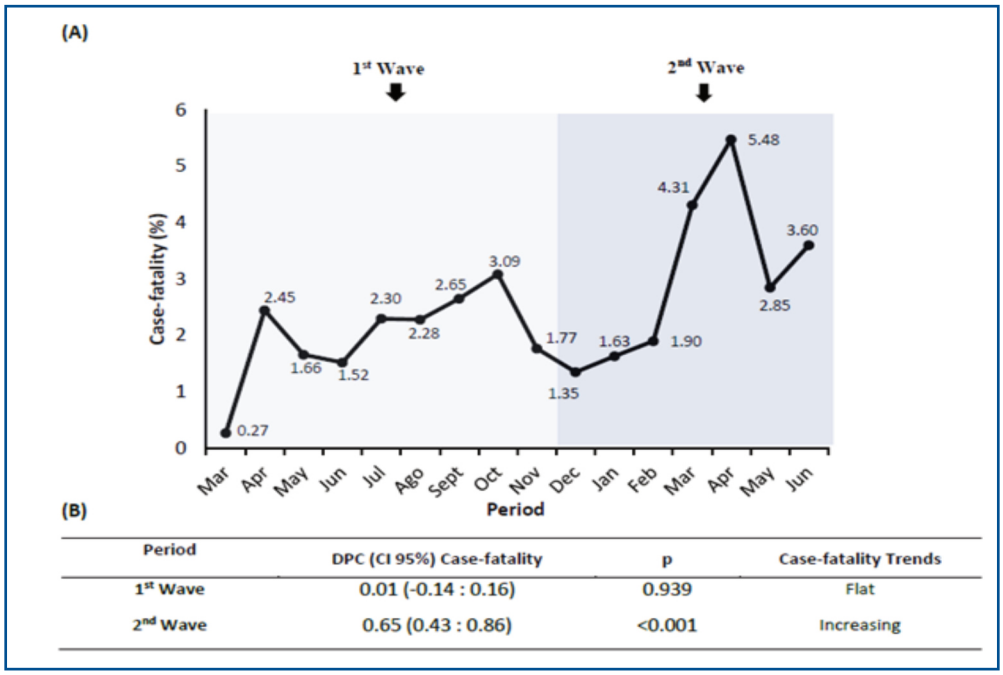
Period	DPC (CI 95%) Incidence rate	p	Imcidence Trends
1st Wave	1.53 (0.60 : 2.46)	0.001	Increasing
2nd Wave	0.10 (-0.12 : 0.33)	0.366	Flat

Figure 4: Incidence rate per 100,000 inhabitants (A) and Prais-Winsten regression estimates and Daily Percent Change (DPC) of incidence rates due to COVID-19 in the State of Goiás, during the 1st wave (March to November 2020) and the 2nd wave (December 2020 to June 2021)

DPC – Daily Percent Change (%); CI 95% – Confidence interval 95%; p value – probability of statistical significance - Prais-Winsten regression test. Source: Cases, deaths and population were extracted from the from Secretary of Health of the State of Goiás, Brazil10.

The state of Goiás had the highest incidence rate in August 2020 (1177.91 new cases per 100,000 inhabitants), indicating the peak of the first wave of the disease in the region. A possible second wave formation from November onwards recorded an incidence peak in March 2021 (1299.95 new cases per 100,000 inhabitants). Distinct trends in the incidence rate were observed during the period, fluctuating from “increasing” during the first wave, with a percentage of daily change (DPC) of 1.53% ($p<0.05$) to “flat” during the second wave ($p>0.05$) (figure 4).

The case fatality percentual of COVID-19 is shown in figure 5.



(B)

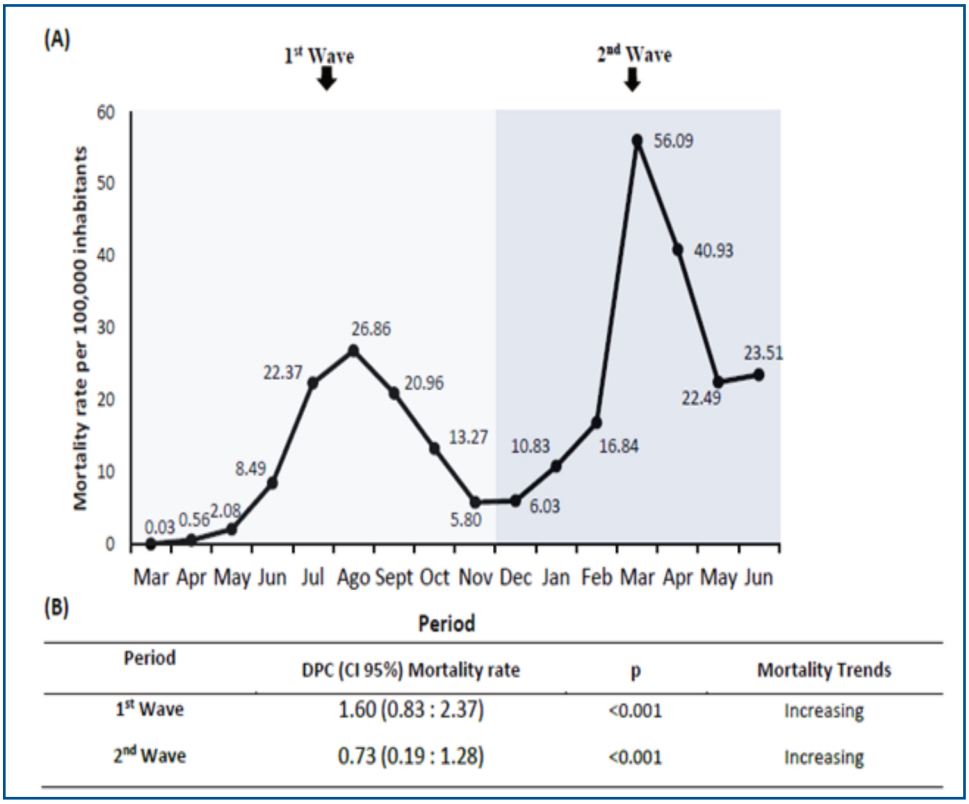
Period	DPC (CI 95%) Case-fatality	p	Case-fatality Trends
1st Wave	0.01 (-0.14 : 0.16)	0.939	Flat
2nd Wave	0.65 (0.43 : 0.86)	<0.001	Increasing

Figure 5: (A) Case-fatality (%) and (B) Prais-Winsten regression estimates and Daily Percent Change (DPC) of case-fatality due to COVID-19 in the State of Goiás, during the 1st wave (March to November 2020) and the 2nd wave (December 2020 to June 2021)

DPC – Daily Percent Change (%); CI 95% – Confidence interval 95%; p value – probability of statistical significance - Prais-Winsten regression test. Source: Cases, deaths and population were extracted from the from Secretary of Health of the State of Goiás, Brazil10.

The second wave was more lethal than the first wave, the highest caste-fatality values were observed in March 2021 (4.31%), April (5,48%) and June (3,60%) with an increasing trend, with a DPC of 0.65% ($p<0.05$) (figure 6).

The mortality rate and Prais-Winsten regression estimates were illustrated in figure 6.



(B)

Period	DPC (CI 95%) Mortality rate	p	Mortality Trends
1st Wave	1.60 (0.83 : 2.37)	<0.001	Increasing
2nd Wave	0.73 (0.19 : 1.28)	<0.001	Increasing

Figure 6: (A) Mortality rate (per 100,000 inhabitants) and (B) Prais-Winsten regression estimates and Daily Percent Change (DPC) of mortality rates due to COVID-19 in the State of Goiás, according to the 1st wave (March to November 2020) and the 2nd wave (December 2020 to June 2021).
DPC – Daily Percent Change (%); CI 95% – Confidence interval 95%; p value – probability of statistical significance - Prais-Winsten regression test. Source: Cases, deaths and population were extracted from the from Secretary of Health of the State of Goiás, Brazil.

The second wave also had the highest mortality rate of the entire period, with a rate of 56.09 deaths per 100,000 inhabitants in March 2021. There was an increasing trend in the mortality rate in both the first wave and the second wave, with respective DPC: 1.60% and 0.73% (figure 6).

Figure 7 illustrates the case-fatality (%) and the mortality rate (per 100,000 inhabitants) by age group and sex.

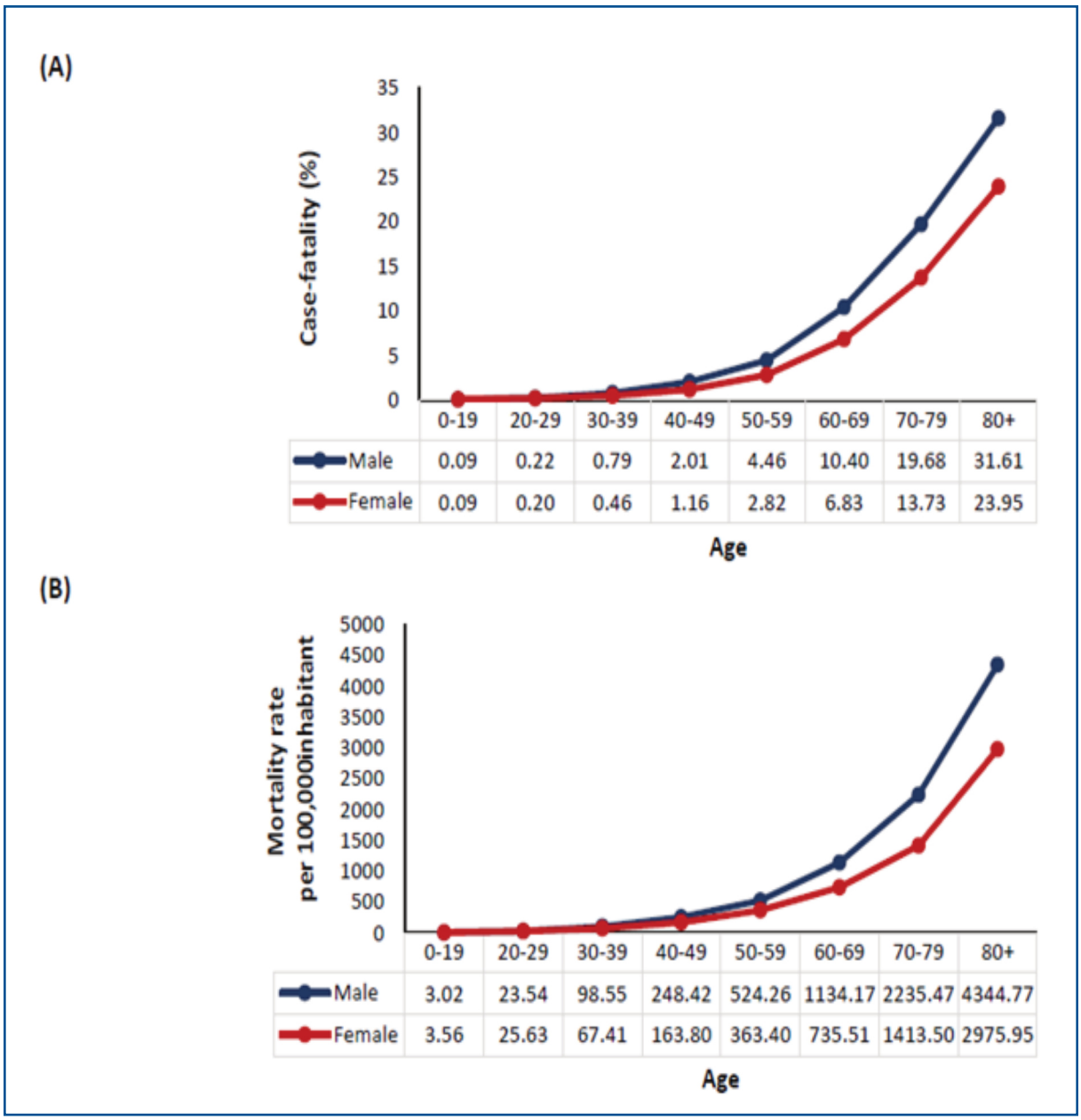


Figure 7: Case-fatality (%) (A) and (B) mortality rate (per 100,000 inhabitants) by sex and age group of COVID 19 in the State of Goiás from March 2020 to June 2021.

DISCUSSION

The state of Goiás has suffered from the pandemic, with 694,955 cases and 19,448 deaths by COVID-19 from March 2020 to June 2021. A more aggravating disease scenario during a possible second wave, from December 2020 to June 2021, increased mortality and case-fatality trends, with maximum peaks observed in March and April 2021, respectively.

The authorities of Goiás adopted measures to contain the spread of COVID-19 and avoid overloading the Health system. Initiatives to provide care throughout the state were implemented, such as commerce closing, social distancing, investment in tracking infected people and their contacts, expansion of RT-PCR testing[21]. However, those efforts were insufficient to contain the virus; the Rt value remains above 1 in most of the period analyzed. A high rise in deaths, mortality, and lethality rates remained during the early months of 2021.

According to the Extraordinary Bulletin of the COVID-19 Observatory of the Oswaldo Cruz Foundation[22], the epidemiological week from March 28 to April 3, 2021, had an acceleration in the spreading of SARS-CoV-2 in Brazil, reaching deaths number records, with continued increment in positive COVID-19 tests and ICU bed occupancy rates. The epidemiological curve of COVID-19 in Goiás, from March 2020 to June 2021, registered the formation of two possible waves. Although the first wave (March to November 2020) exhibited increasing incidence and mortality rates per 100,000 inhabitants, the second wave (December 2020 to June 2021) had a more alarming profile, growing lethality and mortality trends. Besides having a DPC of 0.73% in COVID-19 mortality, the second wave was more lethal, with a DPC of 0,65% for the disease lethality. Furthermore, during the second wave, March 2021 reached the highest mortality rate (56.09 deaths per 100,000 inhabitants) of the entire period and a high score of case-fatality observed in March (4.31%) and April 2021 (5,48%). In that period, the state had a hospital bed occupancy rate above 90%[10].

It is noteworthy that the stationary incidence of COVID-19 observed during the second wave, with the increased mortality and lethality rate, may indicate that the state's number of tests was not enough to keep up with the actual number of new cases in the region. Mainly because Brazil was, for the most part, experiencing an increment in the spread of the virus, reporting records in cases and deaths from COVID-19 during March 2021 compared to previous months[7].

Mortality and lethality observed in the second wave may be due to the impacts caused by the spread of new variants of SARS-CoV-2. In March 2021, the Department of Health of Goiás, through the Center for Strategic Information and Response in Health Surveillance, stated their concern due to the dissemination of new viral variants identified in that region, such as the P.1 variant (strain B.1.1.28.1-Manaus) and VOC 202012/01 (strain B1.1.7- UK) of SARS-CoV223. Furthermore, in June 2021, the State Government24 informed the detection of the delta variant (line B.1,617.2) in a sample of an 18-year-old patient in Goiânia city. The Municipal Health Department of the capital promoted surveillance actions because SARS-CoV-2 underwent numerous mutations over time to improve viral adaptation to environmental factors, climate, and population. It is highlighted that specific viral mutations are not random; this fact indicates that the virus has a vast capacity for change and survival, making it more transmissible and even more aggressive[25].

It is noteworthy that the strains detected in the state of Goiás were responsible for increasing the speed of viral transmission. It caused a sudden jump in the number of cases and deaths, which impacted the sanitary crises. It was similar to what happened with the P1 variant in the state of Amazonas, Brazil; the VOC 202012/01 variant (B.1.1.7) in the United Kingdom[26], and the delta variant (lineage B.1.617.2) in India[27].

The spread of those SARS-CoV-2 variants in the United Kingdom and Brazil[28] and the delta variant in India can also present an escape mechanism to the immune response to Anti-SARS-CoV-2 antibodies, which has important implications for the efforts to contain COVID-19[27,28]. However, it is emphasized that vaccination reduces the risk of developing disease symptoms, especially in fully vaccinated individuals (two doses or a single dose)[27].

The state of Goiás, until early June 2021, received 3,276,290 vaccine doses (1,358.880 CoronaVac, 1,720.850 AstraZeneca, and 196,560 from Pfizer), 1,656,665 were applied throughout the state, and 668,964 people immunized with the two doses[29]. The number of people vaccinated is still tiny, given the estimated size of the population of inhabitants in this state. Efforts must be made to increase the number of vaccines in Goiás to avoid the delta variant's arrival triggering the third wave. Thus, the promotion of vaccination associated with non- pharmacological measures, such as masks and hand hygiene, must be strongly developed to contain the advance of the pandemic[27,30].

Many countries accelerate vaccine coverage and observe reductions in the number of cases and deaths from COVID-19. However, Brazil still lags, and the consequences are measured in human lives, with sociodemographic impacts marked by regional inequalities and losses in significant advances achieved over the years, such as reducing

population longevity. In Goiás, population longevity regressed to values similar to those observed before 2000; that is, the pandemic impacted a setback of approximately 20 years31. In addition, the disease has also caused more significant impacts on older adults and male individuals, as verified in the current study.

The findings of this study reveal higher mortality and lethality rates in older adults and male subjects; these results agree with the scientific literature. According to Goiás Government data, lethality on January 12, 2021, was higher for individuals aged 80 years or older, corresponding to a mortality of 28%, values similar to those found in this study (31.66 % and 24.13% for males and females aged 80 and over, respectively). The group of older people had a higher incidence, severity, mortality, and lethality rate of COVID-19, mainly due to the presence of more comorbidities[32]. Another factor contributing to the increase in COVID-19 rates is hospitalization. The percentage of hospitalization is higher among men. Overall, the lethality rate is relatively high (41.28%) among hospitalized patients, especially the elderly[33].

It is noteworthy that vaccination can contribute to changes in this scenario. During critical months, such as in March 2021, Goiás followed the plan of the National Health Authorities, started vaccination against COVID-19 with the people over 70 years, intending to complete the first vaccine doses in all individuals aged 60 years or older by April 2021[34,35]. Thus, studies at different periods should be carried out to understand the impacts of COVID-19 on the population and protect vulnerable groups. Although men are not considered as priority groups, indeed, they represent vulnerable groups to COVID-19.

A study that evaluated the differences arising from biological sex by age in the mortality of COVID-19 in seven countries found that the fatality rates were higher for men of all age groups. These higher rates in males suggest that sex-related factors affect the natural history of the disease[36].

Similar evidence was also described in a meta- analysis that evaluated 3,111,714 cases of COVID-19 worldwide. The authors reported no difference in the proportion of men and women infected with SARS-CoV-2.

Still, male individuals are approximately three times more likely to need an intensive care unit on admission to the hospital (OR = 2.84) and a greater chance of death (OR = 1.39) than women; the sexual bias observed in COVID-19 is a worldwide phenomenon. Thus, there is a need to analyze the influences of biological sex for the clinical management of the disease and develop strategies to contain the spread of the pandemic[37]. This knowledge can help identify risk factors for COVID-19 and support decision-making for implementing early and appropriate measures to avoid a more aggravating prognosis[33].

It is essential to monitor epidemiological indicators and intervention strategies to contain the pandemic throughout Goiás and across the country until incidence, mortality, and lethality rates show decreasing trends. Therefore, constant surveillance and the development of Public Health strategies are necessary to restrict the advance of COVID-19 and the impacts caused by this pandemic, considering mass testing, detection of variants, and vaccination of the population.

Study limitation

The study is subject to limitations arising from ecological studies and analysis of secondary databases, such as underreporting disease cases and low case testing.

CONCLUSION

In Goiás, Midwest Brazil region, from March 2020 to June 2021, there were 694,955 cases and 19,448 deaths from COVID-19. During the first wave, from March to November 2020, both the incidence and mortality rates showed a growing trend. However, during the 2nd wave, from December to June, a more aggravating scenario was observed, with increasing trends in the mortality rate and case fatality.

Author Contributions

Conceptualization, R.A.T., T.C.M., B.E.G.D., M.P.E. and L.C.A.; methodology, R.A.T., T.C.M., J.O.E., L.C.J., R.D.R., K.E., C.E.S. and L.C.A.; software, J.O.E., L.C.J.; validation, T.C.M., J.O.E., C.E.S. and L.C.A.; data curation, R.A.T., T.C.M., L.C.A.; writing- review and editing, all the authors; visualization, all the authors; supervision, K.E., C.E.S. and L.C.A.; project administration, C.E.S. and L.C.A. All authors have read and agreed to the published version of the manuscript.

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Data Availability Statement

Data were extracted from a population database in a COVID-19 dashboard, freely accessible on the Health Department of the State of Goiás website: https://indicadores.saude.go.gov.br/pentaho/api/repos/:coronavirus:paineis:painel.wcdf/generatedContent.

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Conflicts of Interest

The authors declare no conflict of interest.

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CHAPTER 30

COVID-19 AND ITS RELATIONSHIP WITH KIDNEY DISEASES: A SCOPE REVIEW

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Abstract

Backgroung: COVID-19 is an acute respiratory disease originally from China that emerged in December 2019 and quickly spread around the world, affecting 230,418.415 people, and causing 4,724,876 deaths. Coming from the coronavirus family, SARS-CoV-2 is a new subtype of virus that affects the respiratory tract in different levels and can spread and affect other vital structures in the body. **Objective:** to identify the risk factors that lead patients infected by the new coronavirus to develop kidney disease. **Methods:** this is a systematic review of the Scoping Review type (scope review), according to the method proposed by the Joanna Briggs Institute, with the implementation of a checklist structured by PRISMA-ScR that contains 22 mandatory items. The following descriptors were used: coronavirus infection, acute kidney injury and risk factors in five databases, namely PudMed, Scopus, Embase, Virtual Health Library and Web of Science. **Results:** while reading the studies, it was concluded that Acute Kidney Injury was the main renal finding in patients contaminated by SARS-CoV-2. The risk factors for developing renal worsening in patients with COVID-19 were the extremes of age, race, sex, pre-existing diseases, and the disease evolution. **Conclusion:** it is assumed that renal involvement does not occur only for an exclusive reason, but as a set of factors. It is up to the health team to pay constant attention to the warning signs by monitoring the contaminated patient.

Keywords: Coronavirus Infection; Acute Kidney Injury; Risk Factors.

Resumo

Introdução: COVID-19 é uma doença respiratória aguda original da China que surgiu em dezembro de 2019 e se alastrou rapidamente pelo mundo, atingindo 230.418.415 pessoas e levando 4.724.876 pessoas a óbito. Vindo da família do coronavírus, o SARS-CoV-2 é o novo subtipo de vírus que afeta o trato respiratório em diversos níveis, podendo se alastrar e afetar outras estruturas vitais do corpo. **Objetivo:** identificar os fatores de risco que levam o paciente contaminado pelo SARS-CoV-2 a desenvolver afecções renais. **Método:** trata-se de uma revisão sistemática do tipo Scoping Review (revisão de escopo), de acordo com o método de revisão proposto pelo Joanna Briggs Institute (JBI), com a implementação de um check-list estruturado pelo PRISMA-ScR que contém 22 itens de carácter obrigatórios na revisão. Utilizado os descritores: infecção por coronavírus (coronavírus infection), lesão renal aguda (acute kidney injury) e fatores de risco (risk factors) em cinco bases de dados, sendo elas PudMed, Scopus, Embase, BVS (Biblioteca Virtual em Saúde) e Web of Science. **Resultados:** durante a leitura dos estudos, chegou-se em conclusão de que a Lesão Renal Aguda (LRA) fora o principal achado renal em pacientes contaminados pelo SARS-Cov-2. Os fatores de risco para desenvolver o agravamento renal em pacientes com COVID-19 foi o extremo da idade, raça, sexo, doenças pré-existentes e a evolução da doença. **Conclusão:** supõe-se que o acometimento renal não ocorra apenas por um motivo exclusivo, mas como uma conjuntura de fatores. Cabe a equipe de saúde se atentar de forma constante para os sinais de alerta mediante o acompanhamento do paciente contaminado.

Palavras-chave: Infecção por Coronavírus; Lesão Renal Aguda; Fatores de Risco.

INTRODUCTION

COVID-19 is an acute respiratory disease caused by SARS-CoV-2 that has spread rapidly around the world, originating in Hubei Province, Wuhan, China, in December 2019. This new disease is not the first of its family, but a variation of the coronavirus family that rarely affects humans, being confined only to animals such as bats, cattle, cats, and camels, such as MERS-CoV and SARS-CoV. Although the exact origin of SARS-CoV-2 is not known, it is understood that its viral structure is 96.2% similar to CoV-RaTG13, which mainly affects bats and is 79.5% like SARS-CoV than the other presented forms of the coronavirus family[1-3].

In January 2020, the World Health Organization (WHO) declared the outbreak of COVID-19 as the sixth public health emergency of international attention, in which health workers, governments and the general population in order that the spread of the disease was prevented. As of February 2020, WHO reported 45,171 cases and 1,114 deaths, of which 99% of cases and 99% of deaths were related to COVID-19 in China. The spread of the disease occurred rapidly and exponentially, reaching almost all countries and, even with the attempt to contain the disease, the WHO declared in March 2020, a pandemic caused by SARS-CoV-2[2-4].

SARS-CoV-2 is the virus that causes the COVID-19 disease, which mainly affects the respiratory tract initially with a flu-like condition, with the most common symptoms such as dry cough, runny nose, fever, headache, myalgia, sore throat and, later, anosmia (loss of smell), ageusia (taste alteration), which lead to hyporexia (decreased appetite), with the possibility of progressing to severe pneumonia, with difficulty breathing, dyspnea (shortness of breath), and asthenia (tiredness). Among the symptoms presented by people infected by SARS-CoV-2, many may present gastrointestinal disorders (diarrhea, nausea/vomiting), even though they are not the most common. The transmission of the new virus occurs through the respiratory tract and/or mucous membranes, with dispersion by droplets, respiratory secretions, and direct contact[3,5].

COVID-19 can present itself in 80% of cases in an asymptomatic or oligosymptomatic form (mild symptoms) and, in 20% of cases, it evolves to the severe form of the disease, requiring respiratory support in 5% of cases. Acute respiratory failure syndrome is a complication resulting from COVID-19, which occurs more often in the elderly, immunosuppressed people, or those with other comorbidities, such as hypertension, diabetes, neurological and respiratory diseases. These risk factors, or their accumulation, are the main findings in the emergence of complications and mortality rate[6].

SARS-CoV-2 is found in the respiratory tract secretions, saliva, feces and urine in patients with diarrhea. The onset of symptoms occurs from the 3rd to the 14th day after infection. Its diagnosis is given through laboratory, clinical-imaging, clinical-epidemiological and clinical tests, however, there is no treatment, only vaccines control the disease[4-6].

Renal function is a fundamental part of the functioning of the human body; any injury can harm this cycle and disrupt human metabolism. With acute kidney injury (AKI) as a multifactorial impairment of rapid evolution in renal filtration function, the factors that lead to the development of AKI revolve around preexisting clinical diseases, susceptibility and some therapeutic interventions, however its appearance may vary between stages , such as pre-renal, renal and post-renal, caused by decreased renal perfusion or hypotensive drugs, direct damage to glomerular, tubular or tubulointestinal structures, and obstruction of the flow of urine in renal structures to the urethra, respectively[7-9].

Thus, the study problem is: What are the risk factors that lead the relationship of patients with COVID-19 to develop kidney disease? Thus, the objective of the study is to identify the risk factors that lead the patient contaminated by SARS-CoV-2 to develop kidney diseases.

It is believed that this study becomes relevant, as it makes known the current studies on the subject, defining the reason why so many patients with COVID-19 evolve to some level of renal involvement and enabling the guidance of professionals on the necessary management.

METHODS

This is a systematic review of the Scoping Review type in accordance with the review method proposed by the Joanna Briggs Institute (JBI). The scope review is intended to map, through a transparent and rigorous method, the main concepts of a given area of knowledge, bringing a complete view, to compile and disseminate the data obtained and identify gaps in existing research without evaluating them critically[10].

The research question was made using the PCC acronym (Population, Concept, Context): Population – people affected by COVID-19; Concept – kidney disorders; Context - relationship of COVID-19 with kidney diseases.

The study was based on the Preferred Reporting Items for Systematic Reviews and Meta-Analyses extension for Scoping Review (PRISMA-ScR) Checklist, a guiding script to carry out a scope review built through the guidelines of the Joanna Briggs Institute (JBI). PRISMA- ScR presents 22 separate items according to the mandatory chapters in the review, such as: title, abstract, introduction, method, results, discussions and funding[11].

Thus, the search for relevant studies was carried out through the PudMed, Scopus, Embase, VHL (Virtual Health Library) and Web of Science databases. The bibliographic survey took place from April to July 2021, using the double-checking method.

Descriptors were identified according to the research theme, delimited through MeSh (Medical Subject Headings) and DeCS (Descriptors in Health Sciences). The search strategies were used in English and Portuguese “coronavirus infection AND acute kidney injury AND risk factors”.

To carry out the search in the databases, studies in English and Portuguese were included, in which review studies, case studies, experience reports, editorials, letters, theses, dissertations and course conclusion studies were excluded. The research followed the flow exemplified below (figure 1):

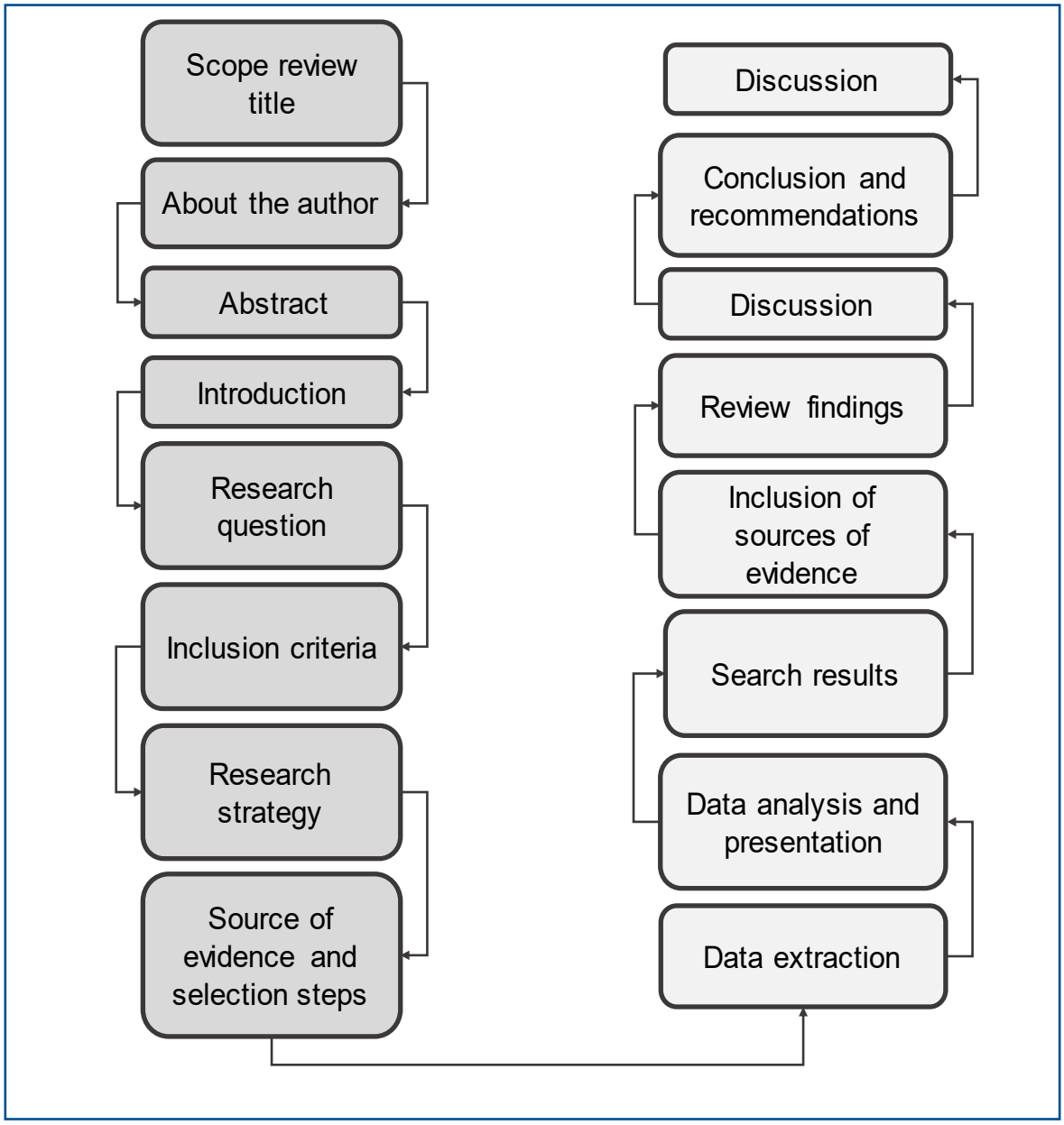

Figure 1: Steps for formulating a Scope Review based on the Joanna Briggs Institute (JBI).

RESULTS

A total of 32 studies were selected, which underwent the process of reading titles, abstracts, application of eligibility criteria and full reading. Initially, 932 studies were identified and 690 of these were excluded by title reading, 51 by abstract reading and 46 by full reading, as shown in the figure below.

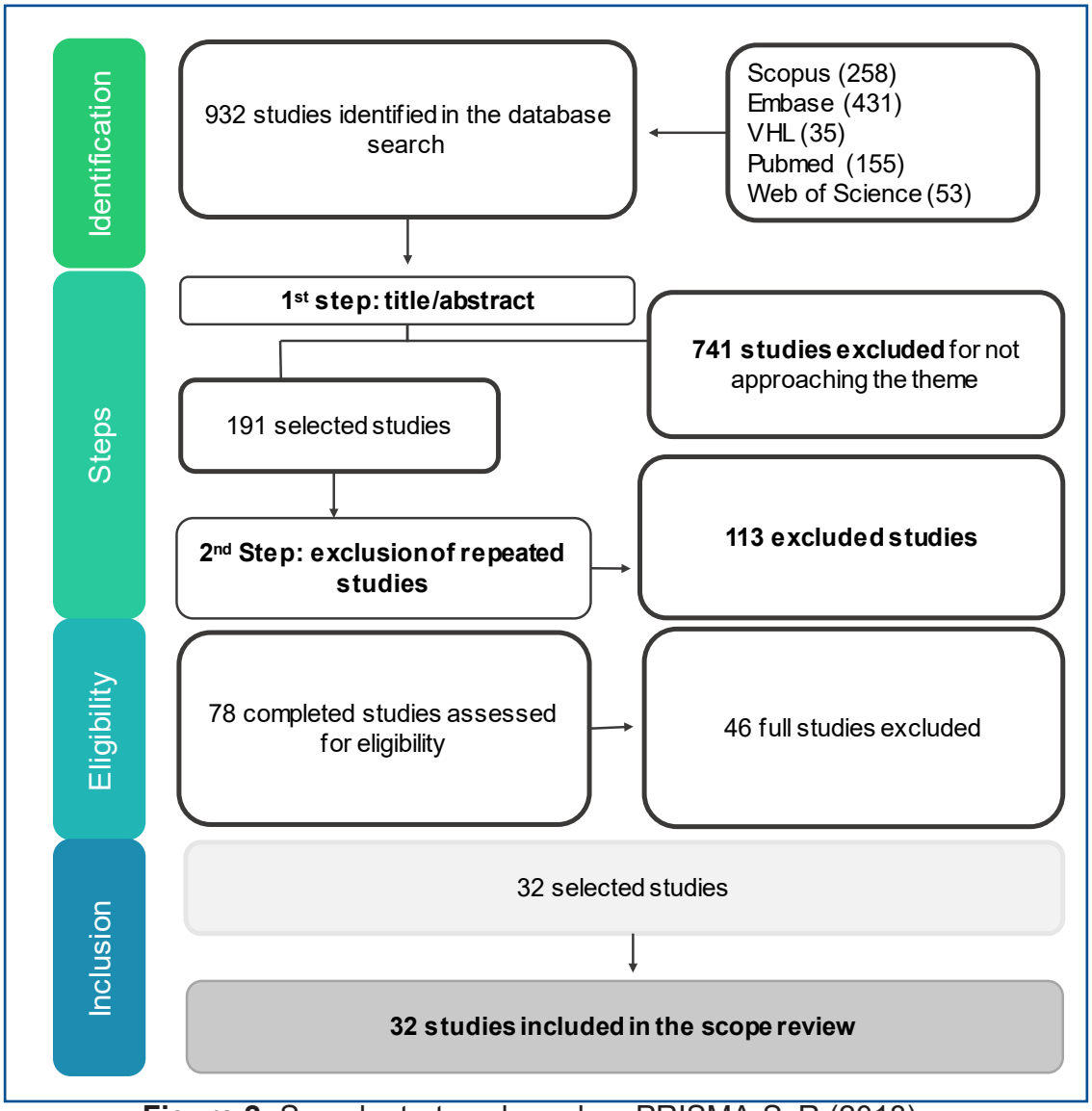

Figure 2: Search strategy based on PRISMA-ScR (2018).

According to the survey in the databases, 32 articles that addressed risk factors related to kidney disease in patients with COVID-19 were part of this review. The first 20 articles were published in 2020, showing the impact of this new disease and the efforts of the scientific community to understand it.

Most articles addressed the disease evolution process in patients affected by COVID-19, as well as the management and identification of the virulent condition, in addition to highlighting possible causes that would lead to the development of Acute Kidney Injury (AKI). The articles also address risk factors for kidney involvement, bringing a discussion focused on possible biomarkers of some degree of kidney injury, such as: laboratory test results, immunological markers, pre-existing diseases, and the individual's biological characteristics.

Thus, for a better organization of this review, it was decided to separate the main findings by topics, following the logic of the individual's trajectory in the disease.

Laboratory findings signaling of kidney injury

Table 1 shows the results that addressed the laboratory analyses. Most authors agreed that the findings represent markers for renal involvement during COVID-19, namely: systemic inflammation markers (serum procalcitonin and blood leukocytes); Estimated Gromerular Filtration Rate (GFR); low serum albumin; lymphopenia; high D-dimer; C-reactive protein (CRP); proteinuria; Soluble urokinase-type plasminogen activator receptor (suPAR); high platelet count; hyperinflammation; tendency to coagulopathy; high lactose dehydrogenase levels; and elevated serum creatinine.

Table 1: the AKI and COVID-19 athwart laboratory findings. Brazil, 2021

Article	Objective	Methods	Main Findings
A[12]	To review data to analyze the incidence of severe AKI, its predictors, and its association with mortality in critically ill patients with COVID-19 in the ICU at the Cleveland Clinic Abu Dhabi.	Retrospective monocenter study including all adult patients (age ≥18 years) admitted to the ICU between March 1 and May 29, 2020, with confirmed SARS-CoV-2 infection.	AKI is not associated with inflammatory processes as identified in tests of IL-6, ferritin and C-reactive protein or thromboembolism markers (D-dimer and fibrinogen).
A[13]	To identify the detailed clinical courses of patients with COVID-19 to identify additional important clues to the pathophysiology of the association of COVID-19 and AKI.	Retrospective observational cohort study that took place between March 1, 2020, and June 3, 2020. Adult patients symptomatic for COVID-19 with positive result who were admitted to any of the 3 hospitals of the Charité – Universitätsmedizin Berlin were included in the survey.	Increased blood levels of systemic inflammation markers (serum procalcitonin and blood leukocytes) emerged as variable risk factors for severe AKI.
A[14]	Identify the clinical characteristics and highlight potential risk factors for ARI related to COVID-19, to facilitate the clinical management of COVID-19.	Retrospective cohort study that took place between March 9 and 17, 2020. Hospital patients with COVID-19 were included.	Estimated glomerular filtration rate (GFR) and procalcitonin can help clinicians identify patients with COVID-19 who have early-stage kidney damage.
A[15]	To share the clinical characteristics and treatment experience of patients with COVID-19 who developed AKI.	Retrospective study that took place from February 17 to March 22, 2020. All patients with COVID-19 who were admitted to this study entered this study.	Among patients with AKI, those who had low serum albumin on admission, among other factors, had a higher incidence of severe AKI.
A[16]	To assess the impact of AKI on mortality and renal prognosis of patients with SARS-CoV-2 infection.	Retrospective single-center study that took place from February 28 to May 4, 2020. Adult patients admitted to the ICU of Hospital Alemão Oswaldo Cruz, Brazil were included in this study.	Lymphopenia, elevated D-dimer, and C-reactive protein (CRP) levels have been associated with an increased risk of developing AKI.
A[17]	To identify involvement prospectively, most especially of proteinuria (quantitative) at baseline and its prognosis in patients with severe or moderate SARS-CoV-2 infection.	Multicenter, prospective observational study from March 15 to April 19, 2020. All patients aged 18 years with proven symptomatic of moderate to severe COVID-19 were included.	Proteinuria is an easily measurable marker to predict outcome and can be used to assess the severity of SARS-CoV-2 infection, in addition to being an independent predictor of length of stay and ICU admission.
A[18]	To characterize the levels of various biomarkers of inflammation and their association with hospital outcomes in patients with COVID-19.	Multinational observational study of adult patients hospitalized for COVID-19.	Glomerular Filtration Rate (GFR) has been independently associated with LRA. Among the biomarkers associated with the emergence of AKI, only suPAR (soluble urokinase-type plasminogen activator receptor) and C-reactive protein were relevant.
A[19]	To analyze the incidence, etiologies and results of AKI in patients contaminated by SARS-CoV-2.	Retrospective single-center study conducted in an ICU assigned to critically ill patients with COVID-19 between February 5th and March 20th, 2020.	Lower lymphocyte level, serum IL-6 level, sepsis, and high platelet count are related to the development of AKI.

Continuation - Table 1: the AKI and COVID-19 athwart laboratory findings. Brazil, 2021.

Article	Objective	Methods	Main Findings
A[20]	To assess the incidence, risk factors and prognosis of AKI in adult patients with COVID-19 at a tertiary university hospital designated for severe cases of COVID-19 by the local government.	Retrospective study performed at Tongji Hospital (Wuhan, China), a hospital designated for the treatment of patients with severe COVID-19.	Lymphopenia, D-dimer, high-sensitivity C-reactive protein, and high lactate dehydrogenase levels were the most common findings in AKI patients, in addition to higher serum creatinine.

Immunological manifestations related to SARS-COV-2 contamination

Table 2 shows the results that addressed immunological markers in patients affected by COVID-19. The main findings are: Elevated levels of IL8, IL10 and IL2R.

Table 2: reaction of the Immune System to COVID-19 and AKI. Brazil, 2021.

Article	Objective	Methods	Main findings
A[21]	To assess the incidence and risk factors of AKI and its impact on hospital and intensive care unit (ICU) hospital mortality.	Retrospective observational study conducted at Tongji Hospital, from January 28 to March 29, 2020. Patients diagnosed with COVID-19 who were admitted to the intensive care unit (ICU) were included in this study.	High levels of IL8, IL10 and IL2R were associated with a high risk of developing severe AKI in critically ill patients with COVID-19.

Pre-existing diseases as a bad prognosis in kidney injury during covid-19

The results that mostly addressed pre-existing diseases of patients who were affected by COVID-19 are shown in table 3. During the data analysis, it was evident that the pre-existing conditions that most cause the development of some type of injury kidney disease in the onset of that disease are: hypertension; diabetes; cardiac insufficiency; peripheral vascular disease; other cardiovascular diseases; Chronic Kidney Disease (CKD); other pre-existing kidney diseases; high body mass index (BMI); hematologic malignancy; immunosuppression in general; and cerebrovascular diseases.

Table 3: risk of pre-existing diseases during the COVID-19. Brazil, 2021.

Article	Objective	Methods	Main findings
A[22]	To examine and to validate the identified risk factors, as well as explore any potential correlation between AKI biomarkers in COVID-19 infection and discuss the possible implications of these findings.	Retrospective analysis of AKI-related biomarkers and comorbidities associated with COVID-19 infections in 632 patients from March 1 to June 10, 2020.	Elevated systolic and diastolic blood pressure is associated with the severity of AKI, supporting the theory that hypertension plays a role in AKI in COVID-19 positive patients, as diabetes, heart failure increases.
A[23]	To characterize the clinical outcomes of critically ill patients with COVID-19 and some preexisting chronic kidney disease and/or Early Suppression and Rapid Response.	Retrospective study in three teaching hospitals which included adult patients (aged ≥18 years) admitted to the ICU with a confirmed diagnosis of COVID-19 in the period between March 10 and July 23, 2020.	Surprisingly, the mortality rates of patients with CKD stages 1-4, and new renal impairment were comparable, although they were more than double the mortality rate seen in patients without renal impairment.

Continuation - Table 3: risk of pre-existing diseases during the COVID-19. Brazil, 2021.

Article	Objective	Methods	Main findings
A[24]	To analyze factors associated with AKI in hospitalized patients to identify factors that can be potentially used for the early identification of patients with COVID-19 who are at high risk of developing AKI.	Retrospective observational single-center study conducted at Hankou Hospital in Wuhan, China. Only patients with confirmed COVID-19 were included in this study.	Pre-existing cardiovascular and renal diseases are potential risk factors for AKI in patients with COVID-19.
A[25]	To examine and validate the identified risk factors, explore any potential correlation between biomarkers and AKI in COVID-19 infection, and discuss the possible implications of these findings.	Retrospective study of data from March 1 to June 10, 2020. All inpatients who tested positive for SARS CoV-2 in polymerase chain reaction (PCR) tests were included.	Diabetes and heart failure increase the risk of AKI in patients with COVID-19 infection. Other additional risk factors were identified in this analysis, such as hypertension, obesity, peripheral vascular disease, and hematologic malignancy.
A[26]	To characterize risk factors for AKI in intensive care patients with Covid-19, their incidence, and patient outcomes.	Single-center cohort study that took place between March 14 and May 12, 2020. All adult patients (>18 years) admitted to the ICU with a confirmed diagnosis of COVID-19 from University Hospital in Southampton (UHS).	Pre-existing diseases that qualify as risk factors for the development of AKI were diabetes mellitus, hypertension, and immunosuppression for any reason.
A[27]	To investigate the incidence and diagnosis of AKI on admission to the ICU in patients with COVID-19, examine the possible association between AKI and hospital mortality with different severities, and generate a nomogram model to predict AKI.	Retrospective study of all patients diagnosed with COVID-19 hospitalized from February 4, 2020, to April 16, 2020.	High BMI (Body Mass Index), cardiovascular and cerebrovascular diseases and CKD are diseases that are at risk for the development of AKI in patients contaminated by SARS-CoV-2.

Biological aspects facing kidney injury at covid-19

Table 4 presents results of biological factors that cause the development of some stage of Acute Kidney Injury (AKI) during the onset of COVID-19. They are elderly, male and African descent.

Table 4: biological aspects, a factor to consider. Brazil, 2021.

Article	Objective	Methods	Main findings
A[28]	To determine the incidence of AKI in patients hospitalized with COVID-19 infection and to assess demographic factors and comorbidities that portend an increased risk of AKI in these patients, in addition to evaluating the association between AKI and mortality in these patients.	Retrospective case study between March 10, 2020, and May 13, 2020.	We found significantly greater odds of AKI with increasing age, among African-Americans, among others.
A[29]	Determine risk factors associated with AKI on admission with confirmed or clinically diagnosed COVID-19.	Single-center retrospective study from January 29 to February 25, 2020. All clinical or confirmed diagnoses of COVID-19 hospital admissions were eligible for inclusion in this study.	Male gender, secondary bacterial infection and use of diuretics were identified as independent risk factors for AKI in patients infected with SARS-CoV-2.

Continuation - Table 4: biological aspects, a factor to consider. Brazil, 2021.

Article	Objective	Methods	Main findings
A[30]	To determine the incidence of in-hospital AKI in patients with COVID-19 and to study the baseline characteristics and laboratory data associated with its development. The secondary objective of the study was the in-hospital mortality associated with AKI in patients with COVID-19.	Retrospective study. All adult patients >18 years of age admitted to Brookdale University Hospital and Medical Center with COVID-19 infection between March 18 and April 23, 2020, were entered into this study.	AKI patients were more likely to be male and older, among other factors.

Trajectory of the patient with covid-19, its evolution and renal impact

According to table 5, the results address the evolution of the disease as a causative factor for kidney injury. It is a fact that AKI is the most recurrent involvement in patients affected by COVID-19. This fact is associated with the use of invasive mechanical ventilation (IMV); vasopressor drugs; nephrotoxic drug; high APACHE II score; diuretics; heart failure; drop in PaO^2/FiO^2; sepsis; and renal replacement therapy (RRT) of some kind, such as dialysis. This direct relationship with the evolution to LRA is indicated.

Another data identified corresponds to the period of hospitalization and diagnosis of AKI in patients positive for COVID-19. Most individuals admitted to the ICU with some degree of renal impairment do not survive after a period of 28 days, in part due to the virulent power of SARS-CoV-2, or due to missed diagnoses. As for the raised histopathological finding, AKI may occur due to acute tubular injury, possibly caused by the direct virulence of SARS-CoV-2 in the proximal tubular epithelium, since virus particles were observed in the tubular epithelium and podocytes.

Table 5: the approach in the management of patients with COVID-19 and the evolution to AKI. Brazil, 2021.

Article	Objective	Methods	Main findings
A[31]	Define the rate of AKI among patients hospitalized with COVID-19 and describe the various aspects of AKI phenomenology in this patient population.	Retrospective observational cohort study of a large New York healthcare system. All adult patients (<18 years) who tested positive in the nasopharyngeal PCR-RT test for COVID-19, hospitalized between March 1 and April 5, 2020, were included.	The need for Renal Replacement Therapy (RRT) and hospital disposition (discharge or death) were the most common outcomes for those who developed AKI. In our analysis, the clearest factors for the development of AKI in severe COVID-19 patients were specifically the need for ventilatory support or treatment with vasopressor drugs.
A[32]	To allow an insight into the clinical impact of AKI associated with SARS-CoV-2.	This is a retrospective cohort study analyzing the electronic medical records of patients with COVID-19 hospitalized in AKI, from March 1st to May 31st, 2020.	Most of the AKI developed in the community were of pre-renal origin, while most of the AKI developed in the hospital were intrinsic. The need for RRT (Renal Replacement Therapy) was significantly more common in intrinsic AKI.
A[33]	To report the incidence, hospital recovery rate, risk factors and mortality of AKI associated with COVID-19 and share our experience in a tertiary hospital in Switzerland.	Retrospective observational cohort study at the University Hospital of Basel. All adult patients hospitalized with a positive polymerase chain reaction (PCR) test for SARS-CoV-2 between February 1 and June 30, 2020, were eligible for this analysis.	AKI is common in patients hospitalized with COVID-19, and is mainly reversible in mild cases, however cases of in-hospital recovery were unsatisfactory in advanced stages of AKI. Severe AKI occurs in critically ill patients with COVID-19 and may also imply that acute tubular injury in the context of multiple organ failure.

Continuation - Table 5: the approach in the management of patients with COVID-19 and the evolution to AKI. Brazil, 2021.

Article	Objective	Methods	Main findings
A[34]	To describe the clinical characteristics, correlates and outcomes of critically ill patients with COVID-19 and AKI complications.	Retrospective, observational, multicenter study conducted at 19 COVID-19 designated hospitals in Wuhan. All adult patients with COVID-19 who were admitted to the ICUs of participating hospitals between January 1 and February 29, 2020, were included if they met the inclusion criteria.	AKI was quite common in severe cases of pneumonia caused by COVID-19, being associated with higher mortality. Most of COVID-19 patients in our study did not survive to day 28, which is worse than the median survival of patients on Continuous Renal Replacement Therapy (CRT) critically ill.
A[35]	To assess the incidence of acute kidney injury (AKI) in hospitalized patients diagnosed with COVID-19 and to identify the risk factors associated with its onset and those associated with its prognosis during the first 90 days of the pandemic in a Brazilian public and tertiary university hospital.	Prospective cohort study of the first 90 days of the pandemic, starting on March 25, 2020. Hospitalized patients diagnosed with COVID-19, confirmed by the PCR-RT molecular test for SARS-CoV-2, in wards and intensive care units (ICUs) of a public and tertiary university hospital in São Paulo, Brazil.	The high APACHE II score is one of the risk factors associated with developing AKI, however, when indicated at the beginning, renal replacement treatment (RRT) may be associated with better patient survival, as it would provide a removal of cytokines or excess fluids.
A[36]	To strictly analyze hospital mortality and renal outcomes among patients with COVID-19 and AKI.	Retrospective observational cohort study of a large New York healthcare system. All adult patients (aged ≥18 years) with positive results for COVID-19 who were hospitalized from March 1, 2020, to April 27, 2020, were eligible.	The development of AKI during hospitalization for COVID-19 was associated with a substantial increase in the risk of death. This risk was amplified when AKI resulted in dialysis. The incidence rate of in-hospital death was higher among patients with stage 3 AKI on dialysis, followed by stages 1-3 AKI and those without AKI.
A[37]	To identify the incidence of AKI in patients with COVID-19 and assess the clinical features of AKI and its impact on patient outcomes.	Retrospective cohort study that ran from February 19 to March 31, 2020. All patients who tested positive for COVID-19 who were admitted to two hospitals in Dongsan were included in this study.	Renal involvement has been associated with poor prognosis, including admission to the ICU, use of MV (Mechanical Ventilation) and hospital mortality.
A[38]	To investigate the incidence and diagnosis of AKI among patients with COVID-19 admitted to the ICU.	Retrospective study that took place from February 4th to April 16th, 2020. All patients admitted to the ICU who had a confirmed diagnosis of COVID-19 were included.	Among all AKI patients, only 54% were recognized by physicians during their ICU stay, and the rate of missed diagnoses was 46%, which may result in a higher mortality rate.

Continuation - Table 5: the approach in the management of patients with COVID-19 and the evolution to AKI. Brazil, 2021.

Article	Objective	Methods	Main findings
A[39]	Describe the incidence, risk factors and impact of AKI and RRT on clinical outcomes in patients with COVID-19 admitted to the ICU.	Retrospective study that took place between March 4 and May 13, 2020. All adult patients (≥18 years of age) with severe acute respiratory syndrome confirmed as COVID-19 infection admitted to the ICU of Hospital Israelita Albert Einstein were included (HIAE), a quaternary private university hospital in Brazil.	The development of AKI was independently associated with the use of diuretics and Invasive Mechanical Ventilation (IMV). AKI develops temporarily after starting VMI.
A[40]	To investigate and compare the clinical features of AKI and their association with overall mortality among different phenotypes.	Retrospective study that took place from January 1 to March 23, 2020. We identified all national electronic medical records of patients with recorded COVID-19 test results.	Findings suggest that AKI may be a sentinel of sequential organ dysfunction or the consequence of multiple organ dysfunction.
A[41]	To assess the incidence, risk factors and prognosis of AKI in critically ill and critically ill patients with Covid-19.	Retrospective study of medical records of patients admitted to the ICU at Wuhan JinYinTan and Guangzhou Medical University Hospitals. All adult patients (>18 years) with laboratory-confirmed Covid-19 who were admitted to the intensive care unit (ICU) between January 23 and April 6, 2020.	The time to hospital admission, diagnosis of AKI, heart failure and drop in PaO^2/FiO^2 is strongly associated with the potential for renal recovery. Stage 3 AKI independently predicted the risk of death within 28 days of admission to the ICU. Sepsis, nephrotoxic drugs and invasive mechanical ventilation, among others, were strongly associated with the development of AKI.
A[42]	To report the experience of renal autopsy findings in patients with severe COVID-19.	Kidney samples were obtained from autopsies of 26 COVID-19 cases with a post-mortem interval ranging from 1 to 6 hours during the period February 18 to March 27, 2020.	Diffuse acute proximal tubular lesion with brush border loss and non-isometric vacuolization, which may be partially caused by direct virulence of SARS-CoV-2, had been observed. Some spherical viral particles characteristic of the coronavirus were found in the proximal tubular epithelium. Virus infection was confirmed by staining using an antibody. Virus particles were also identified in the tubular epithelium and podocytes, known sites for ACE-2 expression.

DISCUSSION

COVID-19 is considered a respiratory disease caused by the SARS-CoV-2 virus, which leads the individual to develop an acute respiratory syndrome. With its spiral shape and the presence of Spike (S) protein around it, SARS-CoV-2 attacks alveolar epithelial cells through the angiotensin-2 converting enzyme (ACE-2) through the protein[43,44].

Although COVID-19 mainly affects the lungs, other organs are affected in the course of the disease, especially the heart, liver, intestine, brain, testicles, and kidneys. The reason why other organs are equally attacked is because of the presence of ACE-2 in cells, such as the continuous circulation of this enzyme in the bloodstream[43].

In the case of kidney disease, according to the data obtained, its identification as Acute Kidney Injury (AKI) was unanimous in the studies analyzed, considering that the kidneys are one of the main organs affected by SARS- CoV-2. For a better understanding of this comorbidity, it is important to mention that the diagnosis of AKI is given by the criteria described in the manual of the organization Kidney Disease Improving Global Outcomes (KDIGO)[45].

AKI is an acute kidney disease that is divided into 3 stages, identified through the quantification of serum creatinine and excreted urine. The stage 1 patient has 1.5- 1.9 times the baseline or ≥0.3mg/dl (≥26.5mmol/l) increase in serum creatinine, and urine quantitation <0.5ml/kg/h between 6-12 hours; stage 2, which presents 2.0-2.9 times the baseline serum creatinine and <0.5ml/kg/h for ≥12 hours of quantified urine; stage 3, for those who present serum creatinine in 3.0 times the baseline or increase in serum creatinine to ≥4.0mg/dl (≥353.6mmol/l) and urine quantification <0.3ml/kg/h for ≥24 hours or anuria for 12 hours[46].

It is noteworthy that patients starting renal replacement therapy or those under 18 years old who show a decrease in GFR to <35ml/min per 1.73m² also fall into stage 3 of AKI[46].

Regarding the importance of laboratory findings for diagnosing acute kidney injury, tests performed for the analysis of some biological materials, such as blood and urine, in order to make a diagnosis or just monitor the functioning of the body[47]. Considering that physiological changes often alter laboratory patterns, with patients affected by COVID-19, it is no different.

According to the results obtained, it is possible to affirm that patients contaminated by SARS-CoV-2 have some laboratory alterations that can serve as indicators of an AKI, namely: serum albumin <3.5g/dl, lymphopenia, thrombocytosis, hyperferritinemia , serum creatinine >1.3mg/dl, proteinuria, gromerular filtration rate (GFR) <60ml/min/ 1.73m², elevated C-reactive protein (CRP) level, D-dimer >0.500µd/ml and lactate dehydrogenase 246 IU/L[15–17,19,20,40].

Still thinking about the laboratory alterations presented by patients with COVID-19, it is known that the soluble urokinase-type plasmogen activator receptor (suPAR) and serum procalcitonin, among others, are also biomarkers associated with the onset of AKI[18,13].

Among the laboratory changes to be observed, it is important to highlight the role of thrombocytosis, fibrinogen and D-dimer in the prognosis of patients affected by COVID-19, as this finding is important when identifying several cases of thromboembolism, which comes as a possible factor for the LRA20,[48]. Still, other studies address the disagreement with the role of ferritin, CRP, D-dimer and fibrinogen in the role of identifiable measurable markers for the detection of AKI[12].

Such findings contribute to the primary signaling of physiological changes in the patient's body, requiring the attention of active health professionals.

Although COVID-19 is a new disease, the way the body behaves is no different. With the activation of the immune system at the first sign of an "invader". The identification of interleukins at an increased level in patients who presented AKI is responsible for the pro-inflammatory action against SARS-CoV-2, presented by IL-6, IL-8, IL- 2R, and later

IL-10, IL- 1β[19,21]. Such identification leads one to believe that these proteins command the immune system and cause a storm of cytokines, which reflects in an exacerbated action of the individual's immune system, causing a protective factor to become harmful, thus interfering with good patient recovery. Cytokine storms, together with other factors such as elevated D-dimer, are related to the formation of blood thrombi, which act as a potential cause of AKI against the complication and evolution of COVID-19 in infected patients[49,50].

Other studies claim that immunobiological identification does not always come as a biological marker signaling the decline in renal function, but only as a clinical finding of the human body's reaction to viral infection[12]. These high levels of protein concentration are important indicators in the follow-up of patients in severe cases of the disease.

It is understood that some chronic diseases already act as a risk factor in infectious diseases in general. In the COVID-19 pandemic, this fact was increasingly discussed, making it clear that care for these people should be redoubled[5]. This relationship happens because patients with chronic diseases have a greater amount of the ACE- 2 enzyme expressed in their body. Thus, due to the great affinity of SARS-CoV-2 with this enzyme, the high risk that carriers have is understandable[51].

Based on the findings during the searches, some pre-existing diseases are a risk during the evolution of COVID-19, such as cardiovascular diseases (heart failure and peripheral vascular disease), hypertension, diabetes mellitus, immunosuppression by any factor, chronic kidney disease, cerebrovascular diseases, and high body mass index (BMI)[22–27]. There are also other conditions that qualify as a risk factor, but which were not identified in the studies evaluated, which are: smoking, pregnancy, asthma, chromosomal diseases in a state of immunological weakness, chronic obstructive pulmonary disease (COPD) and hematological diseases (anemia)[5].

The relationship between pre-existing diseases and COVID-19 is due to the way in which the body responds to contamination by SARS-CoV-2, considering that an individual who has a chronic disease, or factors that compromise full functioning immune system, are more vulnerable to a poor prognosis during contamination and recovery. The fact to be raised is not only about the risk that this individual is predisposed to, but about how the body will respond to the new virus and, consequently, how the disease evolves. The more vulnerable the patient, the more likely he is to develop a more severe condition in COVID-19 and the greater the risk of developing AKI[25,52].

Therefore, it is important to maintain close surveillance for this type of patient, as they are more likely to develop kidney damage from COVID-19.

It is known that biological aspects can influence the onset of AKI in patients infected with SARS-CoV-2. Age, gender and ethnic characteristics may be the characteristics of those who demonstrate a great impact in the search for factors that permeate AKI patients in COVID-19.

According to the data obtained, individuals over 60 years of age and male are the most affected. Being elderly has always been a vulnerability factor, as the body no longer has the same appearance as youth, the physiological course no longer works as it used to and chronic diseases arrive, and by itself the body loses a little more of its defense[53,54]. COVID-19 presents itself more aggressively in older people, its relationship may be linked to a decline in the immune system, as younger patients infected by the virus have a better prognosis and a lower rate of AKI development[55].

The relationship between the prevalence of males in AKI cases in patients contaminated by SARS-CoV-2 is not clear, although studies show that males take care less of their own health, arriving at the health service most of the time with a more advanced disease picture[56].

When related to the fact that people of African descent are more likely to have an increased risk for AKI during COVID-19. This is because the individual is structurally more likely to have hematological diseases, hypertension and diabetes[28,31,56,57]. Also regarding ethnic characteristics, within the samples of selected studies, there was a discrepancy in the percentage of people who developed AKI during COVID-19. Those coming from the West had almost three times more individuals with some degree of AKI

than those from the East. This may be related to the fact that there is a greater expression of the ACE-2 enzyme in the podocytes and proximal tubule of individuals from the West[58].

In general, all factors lead to some pre-existing disease in the infected patient, thus explaining why people with such characteristics are more likely to develop AKI during COVID-19.

AKI does not always start in a hospital setting. There are some acute kidney injuries of pre-renal origin, that is, that developed in a community, either by dehydration or other factors, but which became more significant when combined with COVID-19. Through the study, the equivalence between pre-renal and intrinsic AKI (which originated in a hospital environment) was evident, with an equal risk of mortality for both[32].

Of all stages of AKI, stage 3 is the most dangerous, as it is when there is no possibility of renal capacity returning, unlike stages 1 and 2. Patients who have AKI 3 concomitantly with COVID-19 do not showed improvement in renal function and/or did not survive a period of more than 28 days of hospitalization, with variable outcomes between Continuous Renal Replacement Therapy (TSRC), organ transplantation and death[31,34].

The use of early RRT in patients with developing AKI can bring benefits, as substances harmful to the body will be removed and the amount of excess fluid in that body will decrease[35]. On the other hand, there is a significant increase in the risk of death in patients who underwent dialysis[36].

There are some factors that increase the patient's chance of developing AKI, such as: drop in PaO^2/FiO^2, cardiopulmonary arrest, secondary infections, as well as the necessary approaches during the care of patients affected by COVID-19 that become risk factors for the emergence of AKI, such as: Invasive Mechanical Ventilation (IMV), admission and stay in the ICU, use of diuretics, vasopressor drugs and other nephrotoxic drugs[31,37,41,39]. In contrast, although IMV is a potential risk factor for the development of AKI and, consequently, death, the "delay" in performing the intubation would be the most harmful for these patients[59].

As kidneys have a large amount of the ACE-2 enzyme in their tissue, the histopathological findings of the presence of the virus itself in the proximal tubule are a possible migration of SARS-CoV-2 through the bloodstream, facilitated by the circulating ACE-2[24,42].

It is important that AKI is identified early, in order to intervene and interrupt the progressive worsening trajectory of renal involvement. It is worth considering a worrying factor that provides an increase in the mortality rate: the lack of diagnoses in patients admitted to the ICU who already show signs of acute renal failure. The body demonstrates the signs of AKI and it is up to the professional to investigate and draw a line of care in order to increase the life span of this patient, as well as to preserve as much as possible the renal function of that individual hospitalized for COVID-19[27].

The occurrence of Acute Kidney Injury (AKI) in patients contaminated by SARS-CoV-2 is still not clear, however, it is believed that this pathology will present itself as a sentinel factor signaling a sequential failure of organs, or the consequence itself of a multiple organ failure[40].

Through the analysis of the articles, it was possible to understand that the critical condition of patients with COVID-19 is one of the main factors for renal impairment.

Although some studies address the formation of blood thrombi as one of the main causes of AKI in patients affected by COVID-19, the direct action of the virus on the renal epithelia must be considered. Thus, the need for further studies is clear. It is important to consider the hypothesis that renal impairment does not come from an exclusive reason, but as a combination of factors, such as the drug approach, physiological changes and other factors that harm the renal system.

The healthcare team must be constantly on the lookout for all warning signs for a patient in serious condition due to COVID-19. Early diagnosis can abruptly change the course of the disease and allow the best possible intervention for the individual.

CONCLUSION

It was evidenced that the risk factors that lead the patient contaminated by SARS-CoV-2 to develop kidney diseases were age, male gender, hypertension, diabetes, heart failure, immunosuppression, cerebrovascular diseases, chronic kidney disease, obesity, African descent, use of mechanical ventilation, sepsis and use of diuretics.

Regarding the relationship of patients with COVID-19 and the development of kidney diseases, the age and gender factor of individuals affected by the disease indicate a higher incidence of AKI. This is followed by the observance of pre-existing diseases, such as hypertension and diabetes, which call for attention in monitoring the evolution of the disease. The use of mechanical ventilation and sepsis are also highlighted as preponderant factors in the development of AKI and/or death.

Author Contributions

JSM, Project and manuscript elaboration; MASO, data collection and organization; IMPB, final review of material.

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Conflicts of Interest

No conflicts of interest.

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CHAPTER 31

TRENDS IN COVID-19 MORTALITY AND CASE-FATALITY RATE IN THE STATE OF PARANÁ, SOUTH BRAZIL: SPATIOTEMPORAL ANALYSIS OVER ONE YEAR OF THE PANDEMIC

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Abstract

Introduction: By late 2019, China notified a new disease rising, and with the agent's identification, it was called COVID-19. Despite the efforts of the World Health Organization (WHO) and worldwide countries, the disease spread out of control; on March 11, WHO declared the pandemic state. Brazil is the biggest country in South America, demarcated into 26 states with different economic, cultural, and social aspects. Paraná is one of the Brazilian federative units, it is the sixth more economically important and ranks second in Education. Its first COVID-19 case was confirmed on March 12, 2020, and the first death was on March 27, two weeks after the first death in Brazil. **Objective:** This study objective is to determine the mortality and case-fatality rates of COVID-19 in the State of Paraná, Brazil, from March 1, 2020, to March 31, 2021. **Methods:** It is an ecological time-series study, using all cases (854,326) and deaths (17,229 deaths) of COVID-19 reported in public and official database of the State of Paraná Health Department. Case fatality and mortality rates were stratified by sex and age. For trend analysis, the period was divided into a first "wave" (March to November 2020) and a second "wave" (December 2020 to March 2021). The Prais-Winsten regression model for population mortality and case-fatality rates allowed classifying whether it increased, decreased, or was flat. **Results:** Women were more affected by the number of cases, with 454,056 cases (53.15%) confirmed and 7,257 fatalities (42.12%). A total of 400,270 men (46.85%) were infected and 9,972(57.87%) died. For the first year of COVID-19, in the State of Paraná, the incidence was calculated as 7404.12/100,000 inhabitants, the mortality was 149.32/100,000 inhabitants, and the case-fatality rate was 2.02%. We saw a tendency for decreasing the case-fatality rate (DPC = -0,18; p<0,001). The mortality and incidence showed an increasing trend (DPC=1,13, p<0,001; DPC=1,58, p<0,001, respectively). **Conclusion:** The level and variability of transmission during this first year of pandemic suggest that the disease in the State of Paraná was never under control.

Keywords: COVID-19; Mortality; Case-Fatality; SARS-CoV-2; Epidemiology.

Resumo

Introdução: no final de 2019, a China notificou o surgimento de uma nova doença, com a identificação do agente, passou a chamar-se COVID-19. Apesar dos esforços da Organização Mundial da Saúde (OMS) e de países em todo o mundo, a doença se espalhou fora de controle; em 11 de março, a OMS declarou o estado de pandemia. O Brasil é o maior país da América do Sul, demarcado em 26 estados com diferentes aspectos econômicos, culturais e sociais. O Paraná é uma das unidades federativas brasileiras, é o sexto mais importante economicamente e o segundo em Educação. Seu primeiro caso de COVID-19 foi confirmado em 12 de março de 2020, e o primeiro óbito em 27 de março, duas semanas após o primeiro óbito no Brasil. **Objetivo:** o objetivo deste estudo é determinar as taxas de mortalidade e letalidade da COVID-19 no Estado do Paraná, Brasil, de 1º de março de 2020 a 31 de março de 2021. **Método:** trata-se de um estudo ecológico de série temporal que avaliou todos os casos (854.326) e óbitos (17.229 óbitos) da COVID-19 notificados em banco de dados público e oficial da Secretaria de Saúde do Estado do Paraná. As taxas de letalidade e mortalidade foram estratificadas por sexo e idade. Para análise de tendência, o período foi dividido em uma "primeira onda" (março a novembro de 2020) e uma "segunda onda" (dezembro de 2020 a março de 2021). O modelo de regressão de Prais-Winsten para taxas de mortalidade populacional e letalidade permitiu classificar as tendências em crescentes, decrescentes ou estacionárias. **Resultados:** as mulheres foram as mais afetadas pelo número de casos, com 454.056 casos (53,15%) confirmados e 7.257 óbitos (42,12%). Um total de 400.270 homens (46,85%) foram infectados e 9.972 (57,87%) morreram. Para o primeiro ano da COVID-19, no Estado do Paraná a incidência foi calculada em 7.404,12/100.000 habitantes, a mortalidade foi de 149,32 / 100.000 habitantes e a letalidade foi de 2,02%. Observamos uma tendência de diminuição da taxa de letalidade (DPC= -0,18; p <0,001). A mortalidade e incidência apresentaram tendência crescentes (DPC=1,13, p <0,001; DPC= 1,58, p <0,001, respectivamente). **Conclusão:** o nível e a variabilidade da transmissão durante este primeiro ano de pandemia sugerem que a doença no Estado do Paraná nunca esteve sob controle.

Palavras-chave: COVID-19; Mortalidade; Letalidade; SARS-CoV-2; Epidemiologia.

INTRODUCTION

At the end of 2019, Chinese public health authorities reported a new viral respiratory disease surge to the world. On January 10, 2020, the country identified the etiological agent causing the severe acute respiratory syndrome (SARS), the coronavirus named SARS-CoV-2. Lately, the World Health Organization (WHO) announced the new coronavirus disease 2019 (COVID-19) and declared the pandemic state on March 11, 2020, despite the global efforts to contain the spread of the disease[1].

In Brazil, the first COVID-19 case was confirmed on February 26, 2020. A 61 years old man who had traveled to Italy and returned to his home in São Paulo. The first death was a 57 years old woman from São Paulo, which occurred on March 11, 2020. Since then, COVID-19 has uncontrollably disseminated through all sociodemographic regions of the country, leading to an unprecedented socioeconomic crisis and health system collapse. By July 13, 2021, Brazil had 19.151.993 accumulated cases and 535.838 deaths, with an incidence of 9113.6 new cases by 100,000 inhabitants, mortality of 255.0 deaths by 100,000 inhabitants, and lethality of 2.8%[2] being ranked as the second nation in the global death toll due to COVID-19[3].

Brazil is the largest country in South America, with an estimated population of 210,147,125 inhabitants and an extensive territory (8,510,345,538 km²) divided into 26 states and 1 Federal District. According to economic, cultural, and social aspects, the national territory is demarcated into five geographic regions (North, Northeast, Central-West, Southeast, and South), indicating a situation of disparities and inequalities permanently confronted by consecutive governments[4].

In 1988 Brazil approved a new Constitution, which included a basic definition for health as a universal right and a governmental responsibility. The new Constitution also implemented universal and decentralized health coverage by creating the Unified Health System (Sistema Único de Saúde or SUS), responsible for providing public health care services since 1990[5]. During the past three decades, despite all issues and challenges to cover over 200 million people living in a vast territory and socially unequal country, the SUS is well-known to have a robust primary care provision through the Family Health Strategy (Estratégia de Saúde da Família or ESF) program. Remarkably, the SUS

vaccination program is a worldwide example of success[6]. The COVID-19 pandemic overwhelmed this system, increasing the demand for Intensive Care Unit (ICU) beds and advanced health care services, which evidenced the frailty of the Brazilian preparedness plan in response to public health emergencies[7].

Suppose this sociodemographic condition, by itself, could be a tremendous challenge for the country to fight against a pandemic. In that case, a political situation leaves the country without the federal government's central organization to struggle with the problem. As an example, Brazil changed the Minister of Health four times during the first year of the pandemic.

So, the States had to deal with the pandemic independently, managing their treatment protocols, diagnostic tests, the negotiation of mechanical ventilators, supplies such as personal protective equipment, the training of health workers, and hospital resources like ICU beds. Everything had to be done respecting each state's context. It potentially led to different outcomes and, using the words of WHO's General Director, Mr. Teodros Adhanom Ghebreyesus, "Equity is critical. It applies to information, innovation, essential medical equipment, and supplies, as well as medicines, vaccines, and diagnostic"[8].

Paraná is one of the Brazilian federative units located in the South Region. Together with the Southeast, they are the two more prosperous and developed regions of the country. Paraná is the sixth most crucial Brazilian state in terms of Economy and ranks second in Education. The State shares borders with Paraguay, and the port of Paranaguá, on the coast, is an essential route for international business. The airport of Curitiba, the capital State, is a critical gateway to other countries9. The first COVID-19 case of Paraná was confirmed on March 12, 2020, and the first death on March 27, almost two weeks after the first death in Brazil. As a similarity, all patients aforementioned were linked to recent international travel[10].

To understand the COVID-19 risks and severity to better determine health programs and interventions, it is critical to know indicators like the incidence, mortality, and case-fatality rates. It can also be used to compare the outcomes of different Brazilian States, how they have managed COVID-19, and give insights regarding the expected inequalities that could arise during the fight against the disease.

Under these circumstances, this study objective is to determine the mortality and case-fatality rates of COVID-19 in the State of Paraná, Brazil, from March 1, 2020, to March 31, 2021.

METHODS

Study Design

It is an ecological time-series study, using all the cases and deaths of COVID-19 reported in public and official database of the State of Paraná Health Department, Brazil, available on the website https://www.saude.pr.gov. br/Pagina/Coronavirus-COVID-19. This study is part of a population-based umbrella project, where each state of Brazil was analyzed separately, following a standard protocol for ecological time-series studies as described by Abreu, Elmusharaf and Siqueira[11].

Study Location and Period

The database was updated on June 1, 2021, considering information about cases and deaths of COVID-19 in residents of the state of Paraná, southern Brazil, from March 2020 to March 2021.

Study Population and Eligibility Criteria

Were included in the study all the cases and deaths by COVID-19 that occurred in Paraná and were reported by the municipalities (854,326 cases and 17,229 deaths) from March 2020 to March 2021.

All notifications of cases and deaths referred to COVID-19 were considered, using the International Classification of Diseases, 10th edition (ICD-10) of “U07.1 COVID-19, “identified virus” or “U07.2 COVID-19, virus not identified”12, associated with the diagnosis of the disease, according to with clinical, laboratory or epidemiological confirmation of disease. Cases and deaths were classified according to the date of diagnosis and death, respectively.

Data Collection

Two researchers independently extracted the data to minimize collection bias and guarantee the quality and reliability of the data obtained. The collected data were organized into spreadsheet software Microsoft® Excel 2016.

Population data were obtained using the Projection of the Federation Units Population by gender and age groups for the year 2020[13].

Data from cases and deaths of COVID-19 were collected and stratified by sex (male and female) and age groups (0-19 years, 20-29 years, 30-39 years, 40-49 years, 50-59 years, 60-69 years, 70-79 years, 80 or more years). The variables analyzed were sex (male and female), age groups, date of data de diagnosis, date of death, municipality of residence of the patient, and the number of daily and monthly cases and deaths.

Data Analysis

The effective reproduction number (Rt) was estimated using R studio software EpiEstim package[14], version 2.2.4, a previously time-varying reproduction number for epidemics model, developed by Thompson and colleagues[15]. Our model used a mean serial interval of 2.97 days with an average standard deviation of 3.29 days, as described in previous studies[16,17].

The incidence (1) and mortality rates (2) by 100,000 inhabitants and the case-fatality (3) (%) were calculated according to the equations:

$$(1)\ \text{Incidence} = \frac{(\text{number of cases})}{\text{population}} \times 100.000$$

$$(2)\ \text{Mortality} = \frac{(\text{number of deaths})}{\text{population}} \times 100.000$$

$$(3)\ \text{Case-fatality} = \frac{(\text{number of deaths})}{(\text{number of cases})} \times 100$$

Mortality rates were also calculated and stratified by sex and age for the same period. According to the population projection of Federation Units for the year 2020, the State of Paraná had 11,538,518 inhabitants[13].

For trend analysis, the period was divided into the first wave (1st Wave - March to October 2020) and second wave (2nd Wave – November 2020 to June 2021) to define the end of the first wave, the month with the lowest mortality rate was considered, which suggested the end of a first wave in the curve.

The trends were analyzed according to the methodological guidelines by Antunes and Cardoso18, the Prais-Winsten regression model for population mortality rates was used to build time series, series as well as to determine the incidence, case fatality, and mortality trends. Were estimated the probability (p), and Daily Percent Change (DPC), considering a 95% level significance, according to equations (1), (2), and (3):

$$(1)\ DPC = (10^{\beta} - 1) \times 100\%$$

$$(2)\ (IC95\%)ul = (10^{\beta_max} - 1) \times 100\%$$

$$(3)\ (IC95\%)u = (10^{\beta_min} - 1) \times 100\%$$

In these equations, we considered β as the angular coefficient from the linear regression, the indexes ul as the upper limit, and ll as the lower limit of the confidence level.

The case-fatality, mortality, and incidence trends were classified as increased, decreased, or flat. Flat trends were considered when the p-value was not significant ($p<0.05$).

Statistical analyses were performed using the STATA 14.0 software (College Station, TX, U.S. 2013).

Ethical and Legal Aspects of the Research

It is a secondary data analysis with no identification of the individuals in the database, and therefore no ethics committee approval was necessary.

RESULTS

The population of residents in the State of Paraná was taken from the projection of Federation Units for 2020[13], distributed by age and gender (table 1). Table 2 shows essential sociodemographic characteristics of the State of Paraná. The total population estimated for the State of Paraná in 2020 was 11,538,518 inhabitants.

Table 1: Estimated population of residents in the state of Paraná, distributed according to age and sex.

Age (years old)	Number of inhabitants of State of Paraná, Brazil		Total
	Male	Female	
0 – 19	1,596,030	1,529,193	3,125,223
20 – 29	918,879	898,334	1,817,213
30 – 39	909,586	908,372	1,817,958
40 – 49	792,390	819,364	1,611,754
50 – 59	681,802	738,840	1,420,642
60 – 69	460,619	525,347	985,966
70 – 79	232,176	287,673	519,849
80 or more	97,423	142,490	239,913
Total	5,688,905	5,849,613	11,538,518

Source: Projection of the Federation Units Population by gender and age groups: 2000-2030 - DATASUS, 2021.

Table 2: Sociodemographic characteristics of the state of Paraná, Brazil

Characteristic	Description
Region*	South
Number of municipalities*	399 municipalities
State's capital*	Curitiba
Territorial extension* (2020)	199,298.982 km²
Demographic density* according to the last census, 2010*	52.40 inhabitants/km²
Monthly household income per capita*	1,508 Reais
Human Development Index (HDI), last census, 2010*	0.749
Average number of people per household***(2019)	2.8 people
Number of basic health units****	1,966 units
Total Hospital Beds*****(June 2021)	hospital beds
Number of clinical Beds (SUS) - Adults	6654 clinical beds
Number of clinical Beds (SUS) - Pediatrics	1654 clinical beds
Number of beds in the Intensive Care Unit (SUS)- Adults	938 ICU beds
Number of beds in the Intensive Care Unit (SUS)- Pediatrics	175 ICU beds
Number of clinical COVID beds – Adults	2,842 clinical beds
Number of clinical COVID beds – Pediatric	34 clinical beds
Number of COVID ICU beds – Adults	1980 ICU beds
Number of COVID ICU beds – Pediatric	34 ICU beds

Source: *Brazilian Institute of Geography and Statistics (IBGE, 2021); **DATASUS - Projection of the ederation Units Population by sex and age groups: 2000-2030; ***Sistema IBGE de Recuperação Automática – SIDRA; ****Cadastro Nacional de Estabelecimentos de Saúde (CNESNet); *****State of Paraná Health Department.

According to the official database of the State of Paraná Health Department, from March 1, 2020, to March 31, 2021, there were 854,326 confirmed cases of COVID-19, and 17,229 people died from the disease. The distribution of cases and deaths by municipalities is illustrated in Figure 1.

For the first year of COVID-19 in the State of Paraná, the incidence was calculated as 7404,12/100,000 inhabitants, the mortality was 149,32/100,000 inhabitants, and the case-fatality rate was 2,02%.

Women were more affected by the number of cases, with 454,056 cases (53,15%) confirmed and 7,257 fatalities (42,12%). A total of 400,270 men (46,85%) were infected and 9,972 (57,87%) died. The highest number of confirmed cases was seen in 30-39 years women (99,952), and the deaths were higher in 70-79 years older men (2665) (Table 3).

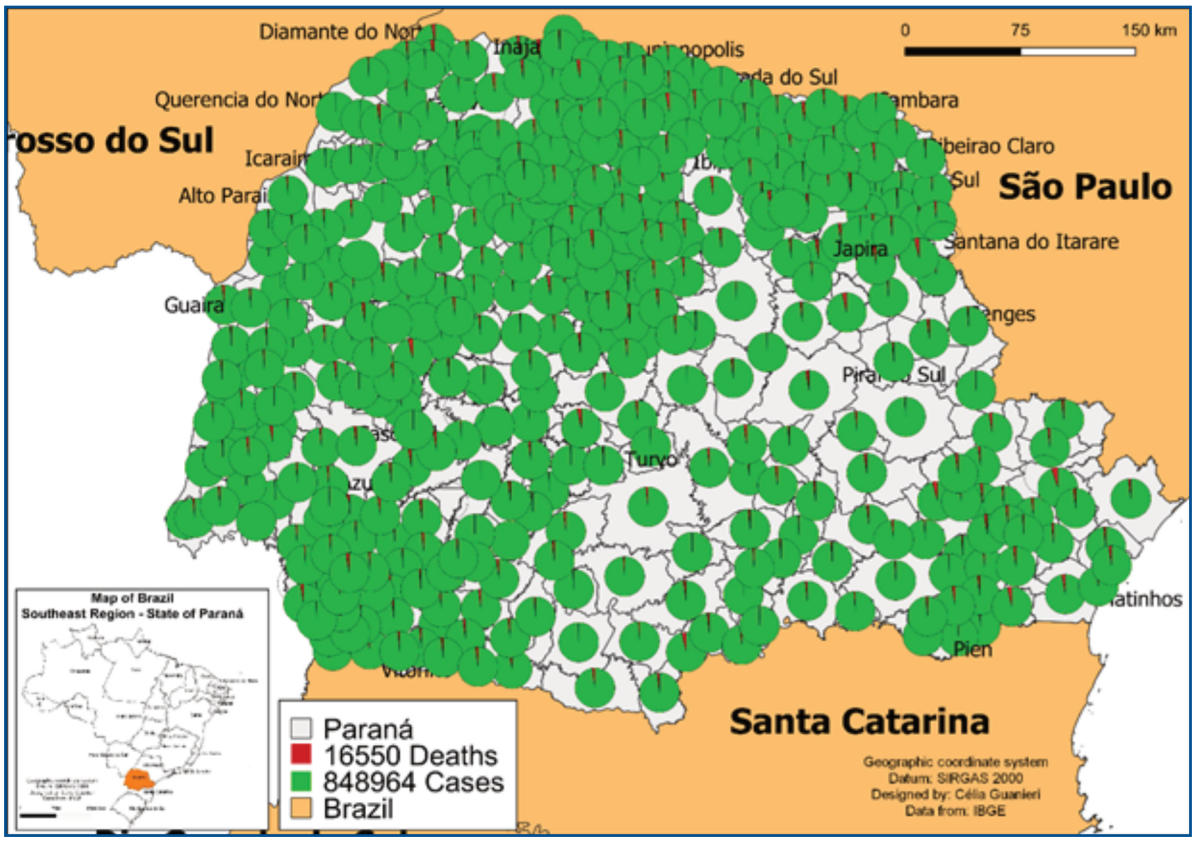

Figure 1: Distribution of COVID-19 cases and deaths among municipalities of the State of Paraná from March 2020 to March 21.

Source: Cases, deaths, and population were obtained from the Secretary of Health of Paraná State, Brazil. (N = 848,964 cases and 16,550 deaths were residents in the state of Paraná, 5,362 cases and 679 deaths notified by the state of Paraná, but residing in another state or information ignored, were excluded).

Table 3: Number of cases and deaths, distributed by age and gender, in Paraná State, from March 2020 to March 2021. Source: State of Paraná Health Department.

Age group (years old)	Cases			Deaths		
	Male	Female	Total	Male	Female	Total
0-19	42321	45941	88262	18	28	46
20-29	83409	94478	177887	103	69	172
30-39	89176	99952	189128	344	208	552
40-49	72865	84965	157830	766	444	1210
50-59	56576	65596	122172	1490	955	2445
60-69	33145	37286	70431	2536	1722	4258
70-79	16148	17383	33531	2665	1937	4602
80-more	6630	8455	15085	2050	1894	3944
Total	400270	454056	854326	9972	7257	17229

The more economically active population, ranging from 20 to 59 years of age, was more infected than the older population (60 or more years) and the youngers (0-19 years), with an incidence of 5,607, 1,031, and 764 per 100,000 inhabitants, respectively. By the other side, mortality and case-fatality rate were higher in people older than 60, compared to the ranges of 20-59 and 0-19 years old (mortality = 110.97; 37.95; 0.40/100,000 inhabitants, and case-fatality = 10.76%; 0.67%; 0.05%, respectively). Figure 2 shows the proportions of cases (A), the proportion of deaths (B), the case-fatality (%) (C), and the mortality rate (per 100,000 inhabitants) of COVID-19 distributed by gender and age in the state of Paraná from March 2020 to March 2021.

According to new cases distributed by day, the effective reproductive number Rt was estimated from March 2020 to March 2021. In the beginning, there was a higher variability, with April having numbers as high as almost 1.7 and low below 0.8. After this, with a few days of variations, from May to August, the Rt was always above 1.0. Only from August to mid-October, a number below 1.0, with a decreasing trend in transmissibility rates, could be seen. After these two and a half months of hope, the levels arose again, with peaks of 1.27 at the beginning of November, 1.16 just after Christmas and New Year's Eve in January, and then 1.22 in the last days of February. Thus, the level and variability of transmission during this first year of pandemic suggest that the disease in the State of Paraná was never under control.

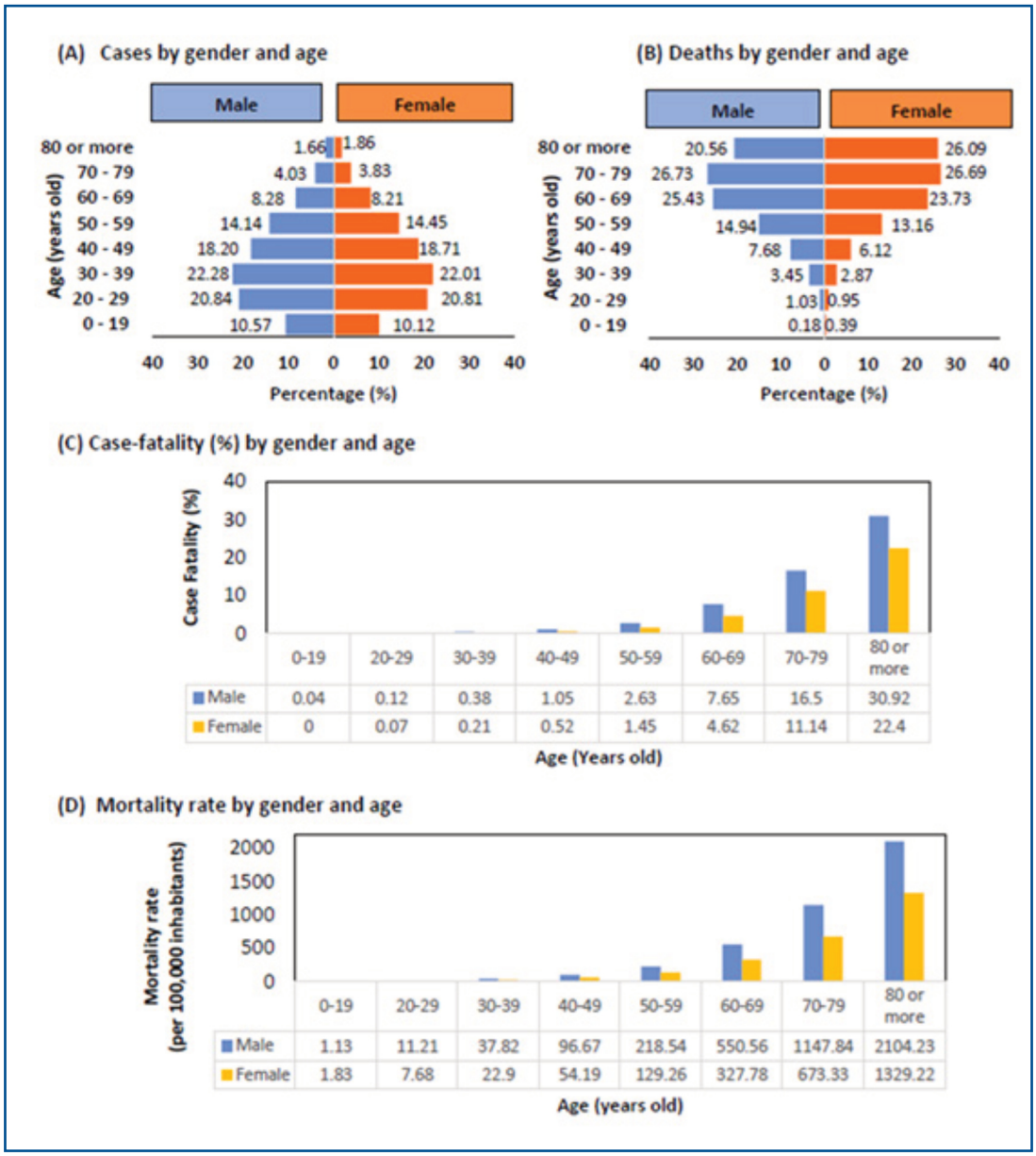

Figure 2: Proportion of cases (A), the proportion of deaths (B), case-fatality (%) (C), and mortality rate (per 100,000 inhabitants) of COVID-19 distributed by gender and age in the state of Paraná from March 2020 to March 2021.
Source: Cases and deaths data were obtained from the Health Department of the State of Paraná, Brazil.

Figure 3 shows the distribution of new cases and the Rt during this period.

To define the periods for trend analysis or "waves," the end of each period must be the one with the lowest level of mortality happening after a peak and then constant dropping in numbers for more than two months. Looking at data, the bottom tier after the first peak descendent was October 2020, with mortality of 7.01/100,000 inhabitants. It gave us a division in the entire period of March 2020 to March 2021 in two waves. The first one was from March 2020 to October 2020, and the second wave was from November 2020 to March 2021 (Figure 4b). We could see mortality as high as 13.63/100,000 inhabitants in August 2020, the peak of the first wave, and much higher mortality, 40.50/100,000 inhabitants, in March 2021.

(A)

(B)

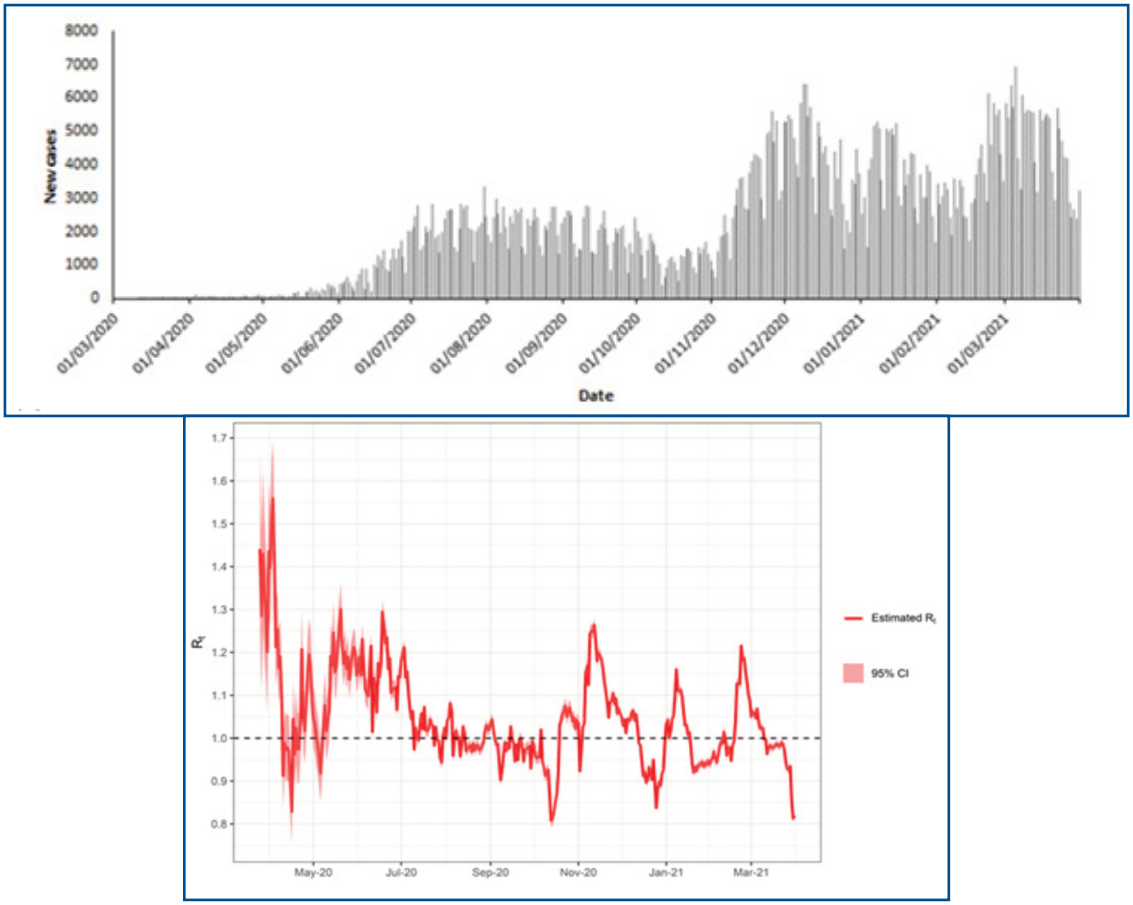

Figure 3: Incidence (per day) (A) and the estimated reproductive number (Rt) (B) of COVID -19 in the state of Paraná in the period from March 2020 to March 2021.
CI = Confidence Interval. Rt estimated during 2020, March 18 to 2021, March 31 period to the state of Paraná.
Source: Cases data were obtained from the Secretary of Health - State of Paraná, Brazil

The case-fatality rate was high in April (4.96%), when there still was a lot of uncertainty about the best way to treat the disease and had the bottom level in November 2020 (1.05%). After this, in March, probably related to the appearance of new variants, the rate rose again to 3.22%.

Figure 4 shows the percentual case-fatality (A), the mortality rate (B), and the incidence rate (C) per 100,000 inhabitants of COVID-19 in the State of Paraná, according to the 1st (March to October 2020) and 2nd (November 2020 to March 2021) waves.

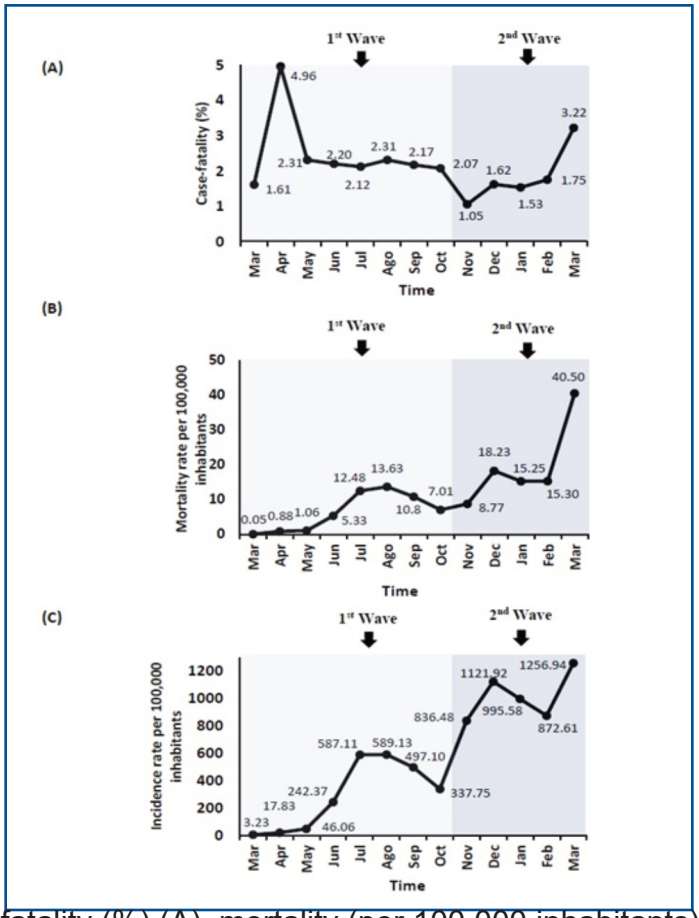

Figure 4: Case-fatality (%) (A), mortality (per 100,000 inhabitants) (B) and incidence (per 100,000 inhabitants) (C) rates of COVID-19 in the State of Paraná, during the 1st (March to October 2020) and the 2nd (November 2020 to March 2021) waves.

The Prais-Winsten regression model for population mortality and case-fatality rates were used to build time series, assessing whether it increased, decreased, or was flat. From March 2020 to March 2021 we saw a tendency for decreasing the case-fatality rate with a daily reduction rate of 0.18% (DPC = -0.18%; $p<0.05$), maybe because of the better knowledge about the disease and how to treat it. However, the mortality and incidence showed an increasing trend ($p<0.001$) (Table 4).

The first wave had a tendency of a decreasing case-fatality (DPC= -0.34; $p<0.001$), and an increasing mortality (DPC= 1.69; $p<0.001$) and incidence (DPC=2.57; $p<0.001$). The second wave, maybe influenced by the explosion of cases and deaths caused by the new variant P1, had an increasing trend of fatalities (DPC= 0.73; $p<0.001$) and mortality (DPC=1.02; $p<0.001$) (Table 4).

Table 4: Prais-Winsten regression estimative and Daily Percent Change (DPC) of case-fatality (%), mortality (per 100,000 inhabitants), and incidence (per 100,000 inhabitants) rates due to COVID-19 in the State of Paraná, during the 1st (March to October 2020) and the 2nd (November 2020 to March 2021) waves.

Period	DPC (CI 95%) Fatality	p	Fatality Trends
total	-0.18 (-0.27 : -0.08)	<0.001*	Decreasing
1° wave	-0.34 (-0.51 : -0.18)	<0.001*	Decreasing
2°wave	0.73 (0.49 : 0.97)	<0.001*	Increasing
Period	**DPC (CI 95%) Mortality**	**p**	**Mortality Trend**
total	1.13 (0.88 : 1.37)	<0.001	Increasing
1° wave	1.69 (1.20 : 2.19)	<0.001	Increasing
2° wave	1.02 (0.70 : 1.34)	<0.001	Increasing
Period	**DPC (IC 95%) Incidence**	**p**	**Incidence Trends**
total	1.58 (1.13 : 2.03)	<0.001*	Increasing
1°wave	2.57 (1.80 : 3.35)	<0.001*	Increasing
2°wave	0.30 (-0.02 : 0.61)	0.063	Flat

Source: cases and deaths were obtained from the Health Department of the State of Paraná, Brazil.
DPC-Daily Percent Change (%); CI 95%-Confidence Interval 95%; p-value – probability of statistical significance - *p<0,05 – Prais-Winsten regression test; Total – Period from march 2020 to march 2021; 1°W – First Wave: Period from March to October 2020; 2°W – Second Wave: Period from November 2020 to March 2021.

DISCUSSION

The first year of the COVID-19 pandemic in the State of Paraná, Brazil, had an incidence of 7404.12 new cases by 100,000 inhabitants, the mortality was 149.32 deaths by 100,000 inhabitants, and the case-fatality rate was 2.02%.

In our results, women are more affected by the disease than men, although men died more than women. The range of 30 to 39 years old had more confirmed cases, both in men and women. However, the number of deaths was higher in 70 to 79 years old, both in men and women. In a wide range of ages, the more economically active population, between 20 to 59 years, had the higher incidence of the disease. The more elderly, with 60 or more, had a higher case-fatality rate. These results could be explained by the more economically active population having to work to earn their money for the family. Even with the risk of being infected, they are more prominent not to follow public health advisory of social distancing or lockdowns. It is especially true in low-income countries. Regarding age, since the beginning of the pandemic and mainly when Italy was brutally hit by it, older adults (60> or older) were identified as a significant risk factor for COVID-19 severity, which may be related to their higher frequency of comorbidities compared to the general population.

COVID-19 transmissibility in Paraná, during the first year of the pandemic, looks out of control most of the time. The estimated Rt was higher than 1.0, with peaks in April, the second month of the pandemic in Brazil, and the months of November, early days of January, and the end of February, possibly related to the Christmas and New Year's Eve and the appearance, in the city of Manaus, of the P1 variant, more contagious and aggressive19. Except for some slight days variation, from mid-August to mid- October was the only period when the estimated Rt was below 1.0. It could be explained by the results of the measures taken by states and municipalities to control the transmission (social distancing measures, obligatory use of masks, borders control, closure of schools, bars, restaurants, and stores). Maybe, after this short period, without political support, the population, tired of being at home and needed to restart working, did not see more periods of the low transmission rate.

Following the periods defined for trend analysis or waves, the first wave (March to October 2020) showed a peak of incidence and mortality in August (589.13 and 13.63/100,000 inhabitants, respectively), and the end of the curve at the lowest level showed an incidence of 337.75/100,000 inhabitants and mortality of 7.01/100,000 inhabitants. Because of the reasons mentioned above, the case-fatality rate had a peak in April (4.96%) and the lowest level in November (1.05%). The second wave (October 2020 to March 2021) has not ended by the data collection date. We established our study's scope as the first year of the pandemic, so further studies are needed to know the curve's behavior. The incidence, mortality, and case-fatality were rising at the end of March (1256.94/100,000 inhabitants, 40.56/100,000 inhabitants, and 3.22%, respectively).

This was a critical period, the pandemic caused by the COVID-19 has battered the healthcare infrastructure all around the globe, reverberating in the health care workers' tiredness as a reason, and expect that mass vaccination reduces these numbers[20]. The vaccination program started in Brazil on January 2021[21].

The Prais-Winsten regression estimates showed a statistically significant tendency ($p<0.001$) of an overall increasing incidence and mortality, indicating that the pandemic was still out of control. The decreasing trend in the fatality-case rate during the first wave and during the entire period could be explained by better knowledge and treatment protocols, and the increasing tendency during the second wave could be influenced by the appearance of new variants, problems with supplies like oxygen and the tiredness of health workers. These factors must be better studied. The lack of diagnostics and underreporting can influence the results of the incidence in the second wave.

Looking at the results around the world, Brazil is still not going well[7]. Besides the fact that it is difficult to compare the effects of countries and regions with different sociodemographic characteristics, health systems capacities, and amount of diagnostic tests done, by July 27, 2021, the country was the second in the number of deaths (550,586) and the third in cumulative cases (19,707,662), only behind the USA (611,010) and the USA and India (34,536,402 and 31,440,951), respectively[22]. During the first year, the incidence of COVID-19 in Brazil was 5974,41/100,000 inhabitants, the mortality was 150.67/100,000 inhabitants, and the case-fatality rate was 2.52%.

The State of Paraná had a similar result. Nevertheless, compared to the other two states from South Region, Santa Catarina, and the Rio Grande do Sul, with very similar sociodemographic characteristics, Paraná had the worst indicators[23]. The study of Marinho et al.,[24], using another source of database (COVID-19 Data Hub project - https://covid19datahub.io/) and looking for the rates of mortality and lethality in Brazil until October 2020, showed a slight variation in lethality (2.89%) but drew the attention to the fact that these indicators had potentially bias because the low number of reliable diagnostic tests. They also ranked among the ten worst Brazilian states according to the severity of the disease, although Paraná was not.

There are a lot of factors that are important to be accessed in a respiratory tract viral pandemic. The agent, the host, the environment, the health workforce, Primary Health Care (PHC) programs and hospital structures and supplies, the political situation, and leadership. In their review article, Lippi, Sanchis-Gomar, and Henry[25] used the expression "the perfect storm" to define the Covid-19 pandemic. They pointed that SARS-CoV-2 structure and peculiar biology of infection, high risk of inter-human transmission, long incubation time combined with early and sustained viral load, the existence of asymptomatic or mildly-symptomatic carriers, viral shedding for days after symptom relief, unfavorable progression towards respiratory distress and death in up to 5–10% of patients thus causing dramatic healthcare challenges, as well as environmental contamination", were factors that contribute to the magnitude of the pandemic.

We found that more men died in Paraná, and the elderly are more at risk too. Analyzes of the mortality risk factors in Brazil, using the SIVEP-Gripe, Brazilian Ministry of Health database of 162,045 patients (March to August 2020), showed that elder age,

male gender with comorbidities are at higher risk of death[26]. The same result was found in the first 500 patients hospitalized in a major tertiary hospital in São Paulo. Age (older than 60 years old, gender (male), pulmonary CT scan findings, and troponin are variables that influence the outcome of death[27].

Sociodemographic aspects and their relationship with the incidence and mortality of COVID-19 were analyzed in a prospective geospatial study between February and July 2020. The authors suggested that the incidence was influenced by houses where two or more people sleep in the same room and cities where the index of social vulnerability (SVI) and the municipality human development index (MHDI) were low. Mortality was also affected by low numbers in both indexes[28].

Paraná is the 6th most populated state in the country, and besides this higher demographic density (52.4 inhab./km2), it is ranked five in the Human Development Index (HDI)[9]. Paraná also has a good health infrastructure. In January 2020, the number of ICU beds was 6559 in the South region, representing an average of 2.2/10,000 inhabitants. The area with the best index is the Southeast with 2.7/10,000 inhabitants, and the worst is the North with 0.9/10,000 inhabitants. The recommended number by the Brazilian Ministry of Health and WHO is 1 to 3/10,000 inhabitants29. On March 31, 2021, there was a higher occupation of 95% of ICU beds[10]. Whether there were cases of patients who died waiting for a bed or without assistance requires further investigations.

Our study did not evaluate the transmissibility of the virus, influenced by environmental factors such as the weather or season[30,31]. Paraná is part of the South region of Brazil, with subtropical weather and temperatures with a mean approximate of 19ºC. Curitiba is the coldest state capital of Brazil[32]. The estimated Rt found in our study, during the winter in Paraná, was the lowest of the entire period, and the mortality also was in a descending curve. According to another study made in Pará, a North region State, where the spread of the virus didn't give up even in a tropical climate and much higher temperatures[33].

The transmissibility and, consequently, the incidence are also influenced by social isolation or distancing measures[34]. Chen and colleagues[35] examined coronavirus transmission and associated factors in six countries (China, Korea, Japan, Italy, the USA, and Brazil). In a qualitative analysis, they compared mitigation measures like border control, isolation and lockdowns, tracking of contaminated patients and their contacts, and the disease severity, measured by the number of cases and deaths. They concluded that China and Korea had taken high mitigation measures and had low severity of the disease. The USA and Brazil had insufficient mitigation and high severity. Another analytic, comparative study tried to see the correlation between social isolation in the states of Paraná and Santa Catarina and mortality. The level of social isolation in Paraná was never above 54%, with a mean of 37%, and the author saw no correlation between this factor and the variability of cases and deaths[36].

We still need to investigate more about the consequences of Brazilian political leaders' influence on the disease behavior in the country. According to Ortega and Orsini[37] Paraná is governed by a federal government ally who has been criticized for defending the Economy at the expense of health. Denemark[38] in his article covering the historical perspective of past pandemics like the Spanish Flu and the Black Death, pointed that the best way to control a pandemic is to attack the problem as a public health challenge, and more than the type of government, authoritarian or democratic, is the leader positioning taking rapid scientific, informed decisions that will have the trust of the citizens and reach the best results. He also emphasized the low number of deaths in 12 countries led by women and needs further investigation.

"This pandemic reminds us that we have a shared destiny.
None of us, our health systems, and our economies operate in a vacuum.
We are interdependent. We cannot win without solidarity.
As long as COVID-19 persists in one country, it is a threat to all of us."
Mr. Teodros Adhanom Ghebreyesus – WHO's General Director (WHO, 2020).

Limitations

The current study used a secondary database. Although the database is from an official government department and collected on a large scale, secondary data will always have the limitation of reliability of data. In this particular case, the underreporting of COVID-19 in Brazil is recognized as a significant problem. The number of tests is deficient in the country. It directly impacts the case-fatality rate since many non-fatal cases have not been tested.

Another limitation is that the pandemic has not ended in Paraná, Brazil. The study comprised only the first year period. Otherwise, the number of cases and deaths revealed a continuous increase by March 2021. So, it was not possible to analyze until the end of the second established wave. It will be necessary to continuously investigate the numbers after the pandemic ends to have the final mortality and case-fatality rate results in the state.

CONCLUSION

During the first year of the COVID-19 pandemic in Paraná, Brazil, there were 854,326 confirmed cases of COVID-19, and 17,229 people died from the disease.

Even more than a year after the start of the Pandemic, Paraná registered a high concentration of new cases and deaths from COVID-19, factors that contributed to the second wave representing a more alarming scenario, with increasing trends in lethality (DPC= - 0.73 %) and mortality (DPC = 1.02%).

Author Contributions

Conceptualization, D.S.J., T.C.M., IP, M.P.E.C; B.E.G.D. and L.C.A.; methodology, D.S.J., T.C.M., L.C.J., R.D.R., K.E., C.E.S., and L.C.A.; software, T.C.M. L.C.J.; validation, L.C.J.; T.C.M., C.E.S., and L.C.A.; data curation, D.S.J., T.C.M., L.C.A.; writing- review and editing, all the authors; visualization, all the authors; supervision, K.E., C.E.S.; project administration, C.E.S., and L.C.A. All authors have read and agreed to the published version of the manuscript.

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Conflicts of Interest

The author declares that there is no conflict of interests related to this study.

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CHAPTER 32

COVID-19 IN RIO DE JANEIRO, BRAZIL: A PERSPECTIVE ON EPIDEMIOLOGICAL EVENTS

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Abstract

Introduction: the progression of SARS-CoV-2 highlighted the Americas region for the number of COVID-19 cases and deaths. In Brazil, the Southeast region was one of the most affected, especially the state of Rio de Janeiro, due to its cosmopolitan characteristics. **Objective:** to analyze temporal variations in the incidence, mortality and lethality of COVID-19 in the state of Rio de Janeiro from January 2020 to December 2022. **Methods:** ecological time-series study with publicly available data on COVID-19 cases and deaths. Crude incidence, mortality, and fatality rates, and estimates of percent daily change (DPC) were analyzed using Prais-Winsten linear regression. With calculation of crude rates were performed using Microsoft Excel 2019, and DPC estimates were performed using STATA MP 17.0 software. **Results:** 2.5 million cases and 76 thousand COVID-19 deaths were confirmed in the state of Rio de Janeiro from 2020 to 2022, with lethality declining from 4.89% to 0.60%. The highest lethality occurred in May 2020 (11.59%), October 2021 (9.13%) and March 2022 (6.78%), showing a stationary trend. In 2020, incidence and mortality rates peaked in December (797.76 per 100,000 inhabitants) and May (43.96 per 100,000 inhabitants), respectively, followed by subsequent declines. Incidence trend was increasing in 2020 and stationary in 2022, while mortality decreased in 2021 and 2022 after stability in 2020. **Conclusion:** The incidence of COVID-19 peaked in 2020 and subsequently declined, suggesting partial transmission control. Mortality stabilized after 2020, indicating evolution in health care. Lethality showed a stationary trend, indicating an improvement in hospital capacity. The divergent behavior of the epidemiological indicators reflected the complex dynamics of the pandemic in the analyzed state. There were 790 thousand deaths from COVID-19 in the State of Rio de Janeiro in the period from 2020 to 2022.

Keywords: COVID-19; Mortality; Lethality; Incidence; Tendency.

Resumo

Introdução: a progressão do SARS-CoV-2 destacou a região das Américas pelo número de casos e óbitos de COVID-19. No Brasil, a região Sudeste foi uma das mais afetadas, em especial o estado do Rio de Janeiro, devido suas características cosmopolitas. **Objetivo:** analisar as variações temporais da incidência, mortalidade e letalidade da COVID-19 no estado do Rio de Janeiro no período de janeiro de 2020 a dezembro de 2022. **Método:** estudo ecológico de séries temporais com dados de acesso público de casos e óbitos de COVID-19.

Analisou-se as taxas brutas de incidência, mortalidade e letalidade, e estimativas das taxas de variação percentual diária (DPC) utilizando a regressão linear de Prais-Winsten. Para o cálculo das taxas brutas usou-se o aplicativo Microsoft Excel 2019, e na estimativa da DPC o software STATA MP 17.0. **Resultados:** foram confirmados 2,5 milhões de casos e 76 mil óbitos por COVID-19 no estado do Rio de Janeiro, no período de 2020 a 2022, com letalidade declinando de 4,89% para 0,60%. A maior letalidade ocorreu em maio de 2020 (11,59%), outubro de 2021 (9,13%) e março de 2022 (6,78%), com tendência estacionária no período. Em 2020, as taxas de incidência e mortalidade, atingiu pico em dezembro (797,76/100 mil hab.), com posterior declínio e em maio (43,96/100 mil hab.), também com posterior queda, respectivamente. A tendência de incidência foi crescente em 2020 e estacionária em 2022, a mortalidade decresceu em 2021 e 2022, após estabilidade em 2020. **Conclusão:** a incidência de COVID-19 atingiu pico em 2020 e decresceu posteriormente, sugerindo controle parcial da transmissão. A mortalidade se estabilizou após 2020, indicando evolução da assistência à saúde. A letalidade apresentou tendência estacionária no período, sinalizando melhoria da capacidade hospitalar. O comportamento divergente dos indicadores epidemiológicos refletiu a complexa dinâmica da pandemia no estado do Rio de Janeiro. Houve 790 mil óbitos por COVID-19 no Estado do Rio de Janeiro no período de 2020 a 2022.

Palavras-chave: COVID-19; Mortalidade; Letalidade; Incidência e Tendência.

INTRODUCTION

The new coronavirus (SARS-CoV-2) was identified in Wuhan, China at the end of 2019 and demonstrated high severity and great power to spread across continents, overcoming social and economic problems, becoming a global health disaster[1]. The World Health Organization (WHO) declared COVID-19 a pandemic on March 11, 2020[2] and it was recognized in Brazil through Ordinance No. 454/2020 of March 2020[3,4].

Sanitary measures were already being established and the Chamber of Deputies approved Decree No. 6/2020, which recognizes the state of public calamity in the country, reflecting the expansion of expenses to face the pandemic[5]. Given this scenario, the Unified Health System (SUS) assisted as a health service for about 200 million inhabitants, however with its large territorial extension and different sociodemographic and geographic characteristics, the epidemiological behavior of the virus was strongly influenced by unequal access to health services[6].

In Brazil, the southeast region was the most affected with 14,996,985 cases and 338,854 confirmed deaths 7 and the state of Rio de Janeiro stood out in the region for having the highest mortality rate in Brazil with 447.1 cases per 100,000 inhabitants . In addition, it was widely affected by the virus due to socioeconomic issues, such as type of housing, access to basic sanitation, means of transport and, mainly, the population contingent[7-9].

Even with the declaration of the end of the Public Health Emergency of International Concern regarding COVID-19 on May 5, 2023, this is still a topic that has been studied and discussed in the most varied contexts and associations, and knowing the profile of the mortality and lethality due to COVID-19 should be priorities, considering that the disease evolves unfavorably in vulnerable and infected patients. In view of the above, the present study aims to analyze temporal variations in the incidence, lethality and mortality rates due to COVID-19 in the state of Rio de Janeiro during the period from January 2020 to December 2022.

METHODS

Study Design

This is an ecological study of population-based time series of public access available on the website of the Secretary of Health of the State of Rio de Janeiro. This study is part of an umbrella project in which each state in Brazil was analyzed separately, following a standard protocol[10].

Study Place and Period

Research carried out from January 2020 to December 2022 in the conglomerates of the 92 municipalities that make up the state of Rio de Janeiro, one of the Federation Units located in the Southeast Region of Brazil.

Study Population and Eligibility Criteria

The population of the state of Rio de Janeiro was used and all confirmed cases and deaths related to COVID-19 using the International Classification of Diseases, 10th edition (ICD-10), of “B34.2, Coronavirus infection of unspecified location” and “U07.1 COVID-19, identified virus” or “U07.2 COVID-19, unidentified virus”, considering clinical and/or epidemiological criteria of the disease.

Data collect

Confirmed COVID-19 cases and deaths were extracted from the Rio de Janeiro Health Secretariat 11 on February 8, 2023. Data on the population of the state of Rio de Janeiro were extracted from the Brazilian population projection base of the Units of the Federation by sex and year for the period 2000-2030 from the Brazilian Institute of Geography and Statistics (IBGE) available in the database of the Department of Informatics of the Unified Health System (DATASUS), and for the years between 2020 and 2022 16,946,541, 17,014,734 and 17,078,778 inhabitants were considered, consecutively[12].

Data Analysis

The study variables were organized into independent (time) and dependent (confirmed cases, confirmed deaths, lethality rate, mortality rate and incidence rate). The incidence, mortality, and gross lethality rates were calculated using the direct method, with incidence and mortality expressed per 100,000 inhabitants, and lethality expressed as a percentage.

For trend analysis, the methods proposed byAntunes and Cardoso 13 were used . Time series construction rates were calculated using the statistical technique of generalized linear regression by the Prais-Winsten method, which allowed first order autocorrelation corrections in the analysis of the values of the organized time series.

Thus, the following values were estimated: angular coefficient (β) and its respective probability (p), considering a significance level of 95% (CI95%) and the percentage variation of daily change (Daily Percent Change – DPC) . This procedure made it possible to determine the rates as increasing, decreasing or stationary and to quantify the percentage variation in the daily rates of incidence, mortality and lethality. Data tabulation and calculation of raw rates were performed using the Microsoft Excel 2019 application and estimates of annual percentage change rates were performed using the statistical software STATA MP 17.0[14].

Ethical and Legal Aspects of Research

This research used data from the public domain and open access, available in the Health Information base of the Health Department of Rio de Janeiro, without needing to be assessed by the National Research Ethics Committee (CONEP) and analysis of the Research Ethics Committee system (ZIP CODE).

RESULTS

In the state of Rio de Janeiro, the Health Department notified, from January 2020 to December 2022, 2,457,510 cases and 76,368 confirmed deaths of COVID-19. Table 1 details the distribution of the number and proportion of confirmed COVID-19 cases and deaths by month and year in the state of Rio de Janeiro, from 2020 to 2022. The first cases occurred in January (0.08%) and February (0.02%) of 2020. The highest frequencies were concentrated in November of 2020 (17.00%) and December of 2020 (21.24%). In 2021, March (15.72%) and in January 2022 (56.51%). As for deaths, March 2020 (0.39%) obtained the first records, the peak being in May 2020 (23.92%), followed by April 2021 (19.64%), January 2022 (28.20 %) and February 2022 (28.62%).

Table 1: Distribution of the number and proportion of confirmed COVID-19 cases and deaths by month and year in the state of Rio de Janeiro. Brazil, 2020 – 2022.

Year	Month	Confirmed cases		confirmed deaths	
		n	%	n	%
2020	January	489	0.08	0	0.00
	February	108	0.02	0	0.00
	March	8,639	1.36	122	0.39
	April	53,947	8.48	3,487	11.2
	May	64,261	10.10	7,449	23.92
	June	57,613	9.05	3,596	11.55
	July	60,017	9.43	2,388	7.67
	August	51,629	8.11	2,182	7.01
	September	47,958	7.53	2,193	7.04
	October	48,425	7.61	1,899	6.10
	November	108,224	17.00	2,537	8.15
	December	135,193	21.24	5,289	16.98
Total		636,503	100.00	31,142	100.00
2021	January	90,287	11.33	4,259	10.89
	February	50,053	6.28	2,346	6.00
	March	125,206	15.72	5,101	13.04
	April	104,007	13.06	7,682	19.64
	May	106,556	13.38	5,724	14.64
	June	69,297	8.70	3,575	9.14
	July	73,292	9.20	2,521	6.45
	August	100,354	12.6	3,306	8.45
	September	39,160	4.92	2,833	7.24
	October	12,676	1.59	1,157	2.96
	November	8,802	1.11	388	0.99
	December	16,853	2.12	216	0.55
Total		796,543	100.00	39,108	100.00

Table 1: Distribution of the number and proportion of confirmed COVID-19 cases and deaths by month and year in the state of Rio de Janeiro. Brazil, 2020 – 2022.

Year	Month	Confirmed cases		confirmed deaths	
		n	%	n	%
2022	January	578,975	56.51	1,725	28.20
	February	37,998	3.71	1,751	28.62
	March	5,087	0.50	345	5.64
	April	4,731	0.46	102	1.67
	May	44,241	4.32	91	1.49
	June	155,421	15.17	596	9.74
	July	39,782	3.88	587	9.59
	August	4,964	0.48	182	2.97
	September	2,237	0.22	60	0.98
	October	7,345	0.72	51	0.83
	November	117,718	11.49	332	5.43
	December	25,965	2.53	296	4.84
Total		1,024,464	100.00	6,118	100.00
Grand total	2,457,510		76,368		

Source: Confirmed cases and deaths extracted from SES/RJ on February 8, 2023, available at: http://sistemas.saude.rj.gov.br/tabnetbd/dhx.exe?covid19/esus_sivep.def

Figures 1-3 demonstrate and compare the time series of the incidence, mortality and lethality rates of COVID-19 by month and year in the state of Rio de Janeiro, between 2020 and 2022. The graphical analysis by month and year was inconclusive as to the existence of a trend. Statistical analyzes of daily percentage change rates (DPC) will be presented in Table 2, estimates by the linear regression technique using the Prais-Winsten method.

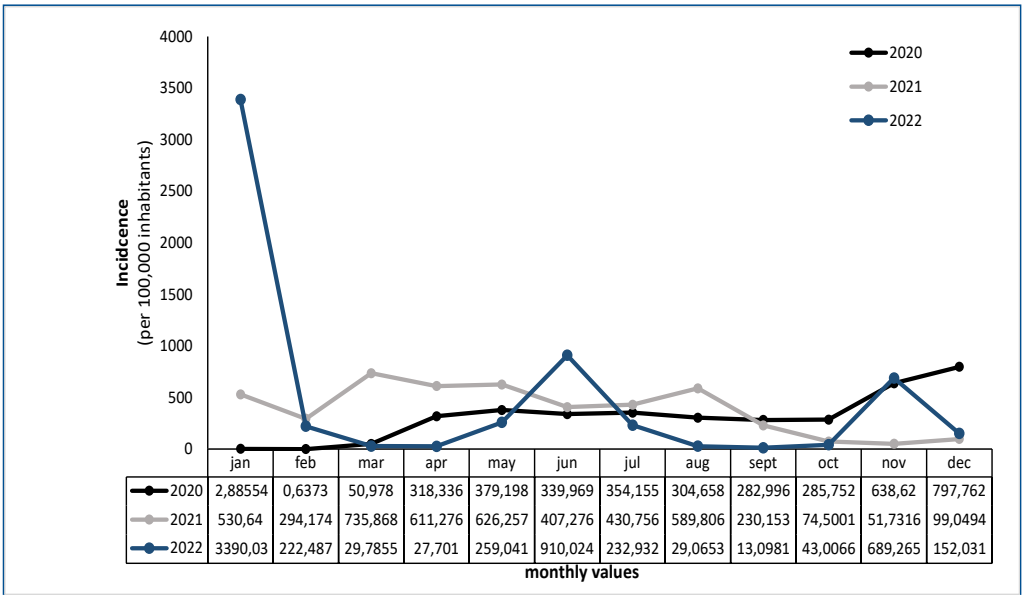
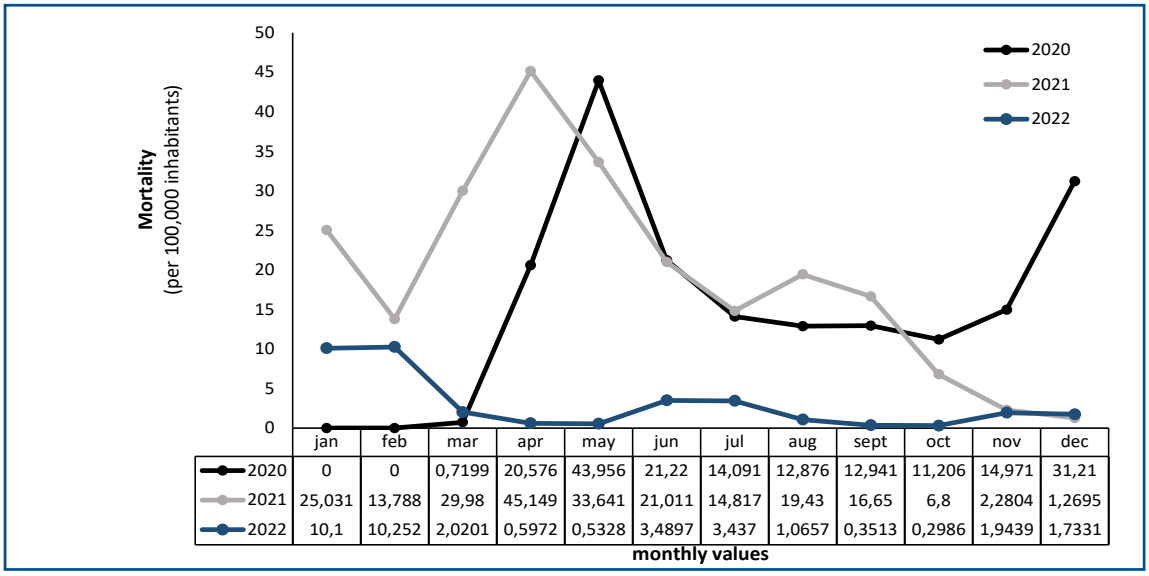


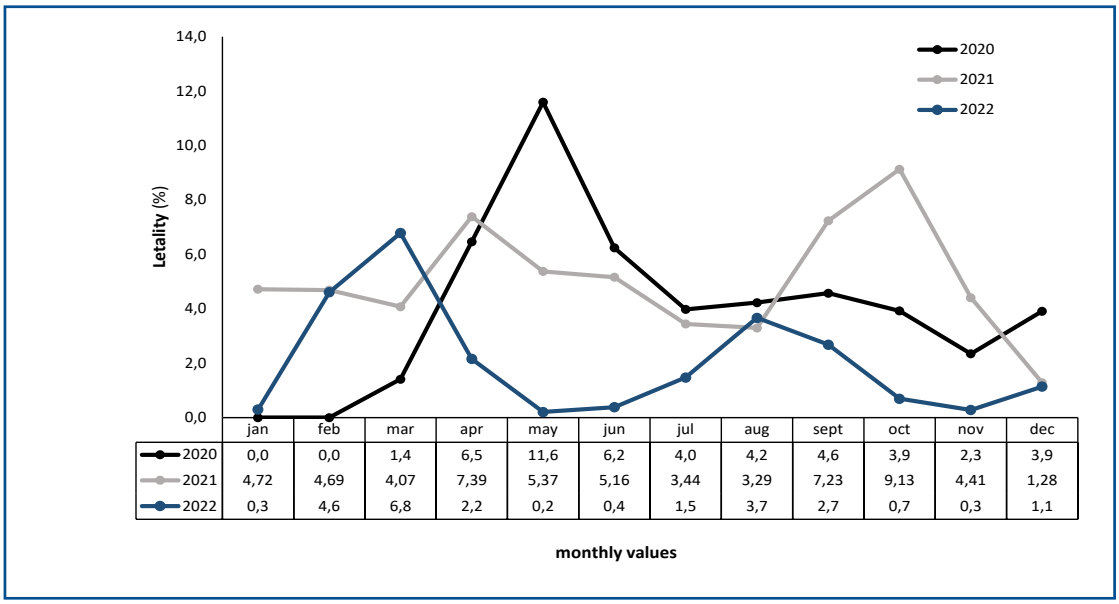
Figure 1: Monthly time series of the incidence of COVID-19 in the state of Rio de Janeiro. Brazil, 2020-2021.

No seasonal pattern or cyclical fluctuations that tend to repeat themselves at certain times of the year were observed. Random or unpredictable fluctuations occurred over time, without following a consistent pattern, determining important irregular peaks and valleys, however, the points are dispersed non-uniformly.



	jan	feb	mar	apr	may	jun	jul	aug	sept	oct	nov	dec
2020	0	0	0,7199	20,576	43,956	21,22	14,091	12,876	12,941	11,206	14,971	31,21
2021	25,031	13,788	29,98	45,149	33,641	21,011	14,817	19,43	16,65	6,8	2,2804	1,2695
2022	10,1	10,252	2,0201	0,5972	0,5328	3,4897	3,437	1,0657	0,3513	0,2986	1,9439	1,7331

Figure 2: Monthly time series of COVID-19 mortality in the state of Rio de Janeiro. Brazil, 2020-2021.



	jan	feb	mar	apr	may	jun	jul	aug	sept	oct	nov	dec
2020	0,0	0,0	1,4	6,5	11,6	6,2	4,0	4,2	4,6	3,9	2,3	3,9
2021	4,72	4,69	4,07	7,39	5,37	5,16	3,44	3,29	7,23	9,13	4,41	1,28
2022	0,3	4,6	6,8	2,2	0,2	0,4	1,5	3,7	2,7	0,7	0,3	1,1

Figure 3: Monthly time series of COVID-19 lethality in the state of Rio de Janeiro. Brazil, 2020-2021.

Table 2 presents the daily variation estimates obtained by Prais-Winsten linear regression to assess the trend in incidence, mortality and lethality rates due to COVID-19 in the state of Rio de Janeiro between 2020 and 2022. The incidence of COVID-19 19 in Rio de Janeiro peaked in 2020, with a trend towards significant growth (DPC = 2.03%) this year, followed by a deceleration in the following years. In the same year, mortality remained stable, but subsequently declined from 2021 onwards, with a CPD of -0.82% ($p<0.001$) in 2021 and -0.52% ($p=0.009$) in 2022. For lethality , the estimates indicate the absence of a significant trend throughout the analyzed period, characterizing stationarity.

Table 2: Estimates from the Prais-Winsten regression and daily change variation (DPC) of the death rate, lethality and incidence of COVID-19 in the state of Rio de Janeiro. Brazil, 2020 – 2022.

RATE/YEAR	LINEAR REGRESSION				
	β	CPD	(CI95%)	P	Trend
INCIDENCE					
2020	0.0087457	2.03	1.13; 2.94	<0.001	Growing
2021	-0.002439	-0.56	-0.91; -0.21	0.002	Descending
2022	-0.003361	-0.77	-2.04; 0.51	0.237	stationary
MORTALITY					
2020	0.0045185	1.05	-0.04; 2.14	0.058	stationary
2021	-0.003558	-0.82	-1.15; -0.48	<0.001	Descending
2022	-0.002272	-0.52	-0.91; -0.13	0.009	Descending
LETHALITY					
2020	-0.000526	-0.12	-0.35; 0.11	0.300	stationary
2021	-0.000654	-0.15	-0.32; 0.02	0.084	stationary
2022	0.000631	0.15	-0.38; 0.67	0.584	stationary

β – regression coefficient; P – p-value; DPC – daily percent change; 95%CI - 95% confidence interval.

DISCUSSION

This study analyzed the temporal variations of the lethality, mortality and incidence rates of COVID-19 in the state of Rio de Janeiro. The initial records of COVID-19 occurred in January 2020 and presented a percentage of 0.08% in the analyzed year. Cumulative data of confirmed cases, from January 1, 2020 to December 31, 2022, recorded the highest incidence in the year 2020 with a daily growth of 2.03%. In 2021 and 2022, there was a change in behavior, which is decreasing (-0.56%) and stationary (-0.77%).

With regard to deaths, the month of May 2020 and 2021 maintained similar behaviors and the highest frequency occurred in 2020 with 23.92%. In the same year, a stationary trend for mortality was observed and in subsequent years the serial correlation remained decreasing, -0.82% and -0.52%, respectively. The fatality rate of 11.6% was the highest of all the years analyzed and the trend of this epidemiological measure remained stationary during the three pandemic years.

Other researchers demonstrated that the studied health indicators presented similar serial correlation parameters in other Brazilian states[15,16]. Some years of mortality, lethality and incidence indicators did not show statistical significance during the analysis of the temporal trend, however the values presented are important for planning at the state level to propose measures to reduce or stabilize the number of cases and deaths. This result corroborates the findings of a study conducted in the state of Piauí[17].

The first cases of COVID-19 started on March 6, 2020 and Rio de Janeiro was the second state in the country to report confirmed cases[18-20]. At the beginning of the pandemic, there was a variation in the number of cases and deaths per day in the state, as well as in the country. Because it is a new disease and the biological behavior of the virus is still unknown, health services had to organize themselves regarding the implementation of the distribution network for diagnostic tests[21,22].

However, the late adoption of non-pharmacological intervention measures highlighted the most critical phase of the pandemic, which was marked by the collapse of the health system and the occurrence of localized health crises, combining a lack of equipment, supplies for the ICU and exhaustion of the ICU workforce. health[23,24].

The intensification of the measures raised would postpone the collapse of health services, reducing the infection rate and the number of deaths[23,24]. Such evidence could be observed in other states and countries, especially in China, which was successful in using non- pharmacological sanitary measures to mitigate the impact of COVID-19 in the country and these measures have a direct impact on the lethality rate[17,25,26].

A stationary phase of cases was observed between April and August 2020[27] . On the other hand, the incidence showed a significant increasing behavior in the year 2020, mainly in the months of November and December. According to Santos et al [28] , the same upward trend was observed, especially in December 2020, with 562.56 cases per 100,000 inhabitants. Other disease peaks were observed in this research in March 2021 and January 2022.

It should be noted that carelessness with health policies, reduction in levels of social distancing, isolation, quarantine, relaxation of mobility restriction measures, especially in the months of November and December 2020, associated with holidays and some important national events, such such as elections, year-end celebrations, including Christmas and New Year, and even Carnival possibly resulted in a new increase in cases in these periods[27,29].

Between March and June 2021, there was an abrupt increase in the number of cases and deaths in the state of Rio de Janeiro. In March 2021, peaks in cases and deaths were correlated with crowds celebrating Carnival festivities, even though the event was canceled[9,16].

The ratification of measures capable of reducing the spread of the virus was the responsibility of city halls[30]. However, stricter measures had to be implemented and, through Decree No. 48,500, of February 4, 2021, specific rules were established aimed at protecting the health of the population, aiming to reduce the speed of contagion by COVID-19 with the prohibition of carnival and similar events[31]. Brito et al.[32], corroborate the findings and observed the same movement in other Brazilian states.

In the most intensified moments of the pandemic, massive informal events outside health safety standards were reported. And additional inspection actions could have contributed for the established norms to be complied with[18]. It was in this context that the rapid growth and predominance of new Variants of Interest (VOIs) occurred, reaching its peak in April 2021, with high values of cases and deaths from March to June of the same year[33]. The Southeast region, in turn, was fundamental for the emergence and rapid dissemination of Sars-CoV-2 VOIs in the country[27].

Rio de Janeiro is one of the states that make up this region and, as it is a national metropolis, it is considered an important entry point for international travelers due to its tourist attractions known worldwide, which may have contributed to the insertion of the virus in the territory[34, 35].

Ribeiro et al.,[9], corroborate the findings and point out that air flows contributed to the importation of the virus into the state of Rio de Janeiro, just as the road flow also played an important role in the spread of COVID-19 throughout the state of Rio de Janeiro. This fact was due to the state's high connectivity with other urban centers[34,35].

During the pandemic period, Rio de Janeiro had an accumulated 449.93 deaths per 100,000 inhabitants. These data are similar to those presented by the Brazilian Ministry of Health for the period from February 26, 2020 to December 31, 2022, in which the rate was 440.6 deaths per 100,000 inhabitants, which is the highest in the country for the region of this study[36].

When stratifying the research data, it was observed that the mortality rate was lower in March 2020 and February 2021, and higher in May and December 2020. In a study carried out in the city of Rio de Janeiro, The mortality rate in the state was lower in March 2020 (0.70 deaths/100,000 inhab.) and February 2021 (7.98 deaths/100,000 inhab.) and higher in May (41.62 deaths/100,000 inhab.) 100,000 inhab.) and December 2020 (24.48 deaths/100,000 inhab.)[28].

Deaths were concentrated between April and June 2020 and 2021, respectively. The year 2022 did not follow this same pattern, with a higher concentration between January and February. An uncontrolled dissemination is observed, a behavior that was related to the pandemic response model[18]. And it can be justified by access to health care, socioeconomic and demographic conditions, and factors intrinsic to the population, such as age, lifestyle, comorbidities, among others[15].

The highest lethality rates (8.3%) were described in Rio de Janeiro[37] and the presented data validate the findings of this research. The high values of this indicator express important flaws in the health system, which may suggest lower diagnostic capacity of the

local health network, slowness in identifying the disease in vulnerable groups, limited access to more complex services and care, political scenario, targeted testing to the most severe cases and with more deaths[30,38].

There is no evidence that the COVID-19 pandemic is fully under control in the state of Rio de Janeiro, since the new coronavirus has not spread homogeneously and simultaneously in the state. It was possible to observe high averages of confirmed cases in most months and years compared during the analyzed period.

However, the divergent pattern between incidence and mortality suggests that, despite the continuity of viral transmission, there has been progress in the care and treatment of critically ill patients, resulting in a decrease in mortality. The stabilization of lethality indicates an improvement in the capacity for hospital care and therapeutic procedures over the period.

The national response to the COVID-19 pandemic maintained a close relationship between policy and public health with ups and downs in a continuous learning curve process. Rio de Janeiro decreed social isolation and voluntary quarantine, there was an early easing of sanitary measures, favoring a further increase in cases.

The rigidity and duration of health interventions, as well as the actions of leaders to apply measures for the prevention, surveillance and control of COVID-19 must be continuous and are fundamental in the pandemic. In addition, an effective and balanced approach is important to mitigate the impacts caused on the health, economy and well-being of the population.

The study has inherent limitations to the information analyzed due to records in the information system and even considering underreporting, these are the best data available for the formulation of public health policies and that define strategies to deal with and control the COVID-19 pandemic.

Furthermore, the method and the analysis applied in the study cannot infer causality, in addition to the individual variables not being considered, thus limiting the research conclusions. The time series regression model used in this work made it possible to quantify the percentage variation in the daily change in incidence, lethality and mortality rates, ensuring the assessment of daily changes in the dynamics of the pandemic in the state of Rio de Janeiro.

CONCLUSION

Based on the divergent trends observed through the daily temporal variations for the incidence, mortality and lethality of COVID-19 in Rio de Janeiro between 2020 and 2022, it can be concluded, from an epidemiological point of view, the transmission of the coronavirus (measured by the incidence) had an initial peak in 2020, with subsequent partial control resulting in a deceleration in the following years. Health care measures were able to keep mortality under control after the initial peak of 2020, despite subsequent waves of infection. The capacity for hospital care and adequate treatment has evolved, resulting in stabilization/reduction of lethality in the years analyzed.

The divergent behavior of the indicators suggests a combination of factors that influenced the epidemiological dynamics in a complex way over the period, and may have impacted the health indicators that were not homogeneous and showed different behaviors in the three years analyzed. The pandemic is not yet over in Rio de Janeiro and surveillance, prevention and assistance measures are still necessary.

Author Contributions

All authors contributed to the manuscript. Edna do Nascimento Moratti: Participated in the study design, data collection phase and revision of the text. Gabriella Lima Santos: Participated in the study design, data collection phase, data analysis, statistical analysis, construction of the construct and final version of the text. João Batista Francalino da Rocha:

Participated in the study design, data analysis, statistical analysis, discussion of results and final version of the text. Leonardo Gomes da Silva: Participated in data collection, data analysis, statistical analysis and final version of the text. Luiz Carlos de Abreu: Participated in the general orientation of the research, definition of the study design, statistical analysis, discussion of results and final version of the text. Sidnei Anastacio Sampaio: Participated in data collection, data analysis, statistical analysis and writing of the text. Tassiane Cristina Morais: Participated in the general orientation of the research, definition of the study design and final revision of the text.

Conflicts of Interest

The authors report no conflict of interest.

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CHAPTER 33

COMPARATIVE ANALYSIS OF EPIDEMIOLOGICAL OUTCOME OF INCIDENCE, MORTALITY AND LETHALITY BY COVID-19 BETWEEN THE STATES OF ESPÍRITO SANTO AND MINAS GERAIS, BRAZIL

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Abstract

At the beginning of December 2019, a new type of coronavirus emerged, SARS-CoV-2. This virus causes COVID-19, a highly contagious disease that can initially present asymptomatically and can also lead to death. Our ecological study goal was to evaluate the incidence, mortality, and lethality rates for COVID-19 between the states of Espírito Santo and Minas Gerais, with time series analysis using secondary and public databases on COVID-19 from January 2020 to December 2022. Prais–Winsten linear regression was used for trend analyses. In 2020, the rate in Espírito Santo was 2.19 times greater than in Minas Gerais. This trend continued in 2021, with Espírito Santo's rate being 1.29 times greater. In 2022, Espírito Santo's rate remained 2.65 times higher than Minas Gerais. Furthermore, Espírito Santo had the highest mortality, with the exception of 2021. In turn, Minas Gerais had the highest fatality rate throughout the analyzed pandemic period. The state of Espírito Santo had a higher incidence of COVID-19, as well as higher mortality when compared to the state of Minas Gerais. Furthermore, both states showed similar trends for mortality, lethality, and incidence in the years 2020 and 2021.

Keywords: Coronavirus; COVID-19; Mortality; Incidence; Lethality.

Resumo

No início de dezembro de 2019, surgiu um novo tipo de coronavírus, o SARS-CoV-2. Esse vírus causa a COVID-19, uma doença altamente contagiosa que pode inicialmente se apresentar de forma assintomática e também pode levar ao óbito. O objetivo do nosso estudo ecológico foi avaliar as taxas de incidência, mortalidade e letalidade da COVID-19 entre os estados do Espírito Santo e de Minas Gerais, por meio de análise de séries temporais utilizando bases de dados secundárias e públicas sobre a COVID-19, no período de janeiro de 2020 a dezembro de 2022. A regressão linear de Prais–Winsten foi utilizada para as análises de tendência. Em 2020, a taxa no Espírito Santo foi 2,19 vezes maior do que em Minas Gerais. Essa tendência se manteve em 2021, com a taxa do Espírito Santo sendo 1,29 vez maior. Em 2022, a taxa do Espírito Santo permaneceu 2,65 vezes superior à de Minas Gerais. Além disso, o Espírito Santo apresentou a maior mortalidade, com exceção do ano de 2021. Por sua vez, Minas Gerais apresentou a maior taxa de letalidade ao longo de todo o período pandêmico analisado. O estado do Espírito Santo apresentou maior incidência de COVID-19, bem como maior mortalidade, quando comparado ao estado de Minas Gerais. Ademais, ambos os estados apresentaram tendências semelhantes de mortalidade, letalidade e incidência nos anos de 2020 e 2021.

Palavras-chave: Coronavírus; COVID-19; Mortalidade; Incidência; Letalidade.

INTRODUCTION

The narrative commences in December 2019, precisely within the confines of Wuhan, China, where a novel strain of coronavirus, SARS-CoV-2, was first detected and efforts have been made to counteract the virus responsible for the pandemic. It is worth noting that this newfound strain of coronavirus has given rise to the emergence of COVID-19, a swiftly spreading ailment with transmission modes that are challenging to manage[1].

Regarding the impacts caused in the economic sphere, jurisdictional tax measures and exemptions were adopted in response to combating COVID-19. Such measures were taken in order to encourage acceptance by the population. Regarding social impacts, it also reveals that there were changes in lifestyle, limitations on travel, and bans on meetings, among others[2].

Currently, data provided through the World Health Organization (WHO) Coronavirus (COVID-19) Dashboard shows that by the month of August 2023, globally, 770,085,713 confirmed cases of COVID-19 infection have been recorded. In addition, 6,956,173 deaths have been confirmed due to the disease. Among these records, Europe is the continent with the highest cumulative number of confirmed cases[3].

According to data highlighted in the weekly epidemiological update on COVID-19 made available by the World Health Organization (2023)[4], there was a global increase in the number of new cases and deaths due to COVID-19 until mid-January 2023, which is why they included it in the new document updates on the variants and subvariants of concern, as well as records on the increase in the number of hospitalizations in several countries, including in the Intensive Care Unit (ICU).

However, in the last update of the global document made available by the WHO (2023)[5], which concerns the month of August 2023, there is information on the decrease in the number of deaths (50%), despite the increase (38%) in the number of confirmed cases, in addition to the decrease in the number of ICU admissions.

Having been considered a new disease, the virus in question behaves similarly to viruses that cause pandemics, which results in similar adoption of measures to contain transmission. This transmission is classified as community transmission, given that SARS- CoV-2 remains stable on surfaces such as plastic and stainless steel for up to three days, in addition to being transmissible in aerosol form for hours when outside the human body[6].

In this aspect, a study has indicated a potential relationship between the incidence of COVID-19 and temperature, considering that temperature affects human behavior and interaction with the environment, thereby influencing the dynamics of disease transmission. Additionally, it has been demonstrated that between 17 °C and 24 °C, the transmission of COVID-19 is reduced, as it directly impacts the potential for virus aerosolization through particles in the environment[7].

Furthermore, Li et al.[8] describe that infection with SARS-CoV-2 can initially be asymptomatic and can progress seriously and even lead to death, and can affect all ages. In this sense, Zhang et al.[9] point out that SARS-CoV-2 variants represent a great threat to the prevention and control of COVID-19 transmission, given the ability of new strains to be imported between different countries.

In this context, Abate et al.[10] point out in research on admissions to Intensive Care Units that the mortality rate reached 39% of patients infected with the new coronavirus admitted to this sector. Furthermore, it points out that around 66% of patients admitted to the ICU had associated comorbidities, which in turn, through regression analysis, detected that the comorbidity increased the risk of death by 39%.

However, in May 2023, the end of the Public Health Emergency of International Importance regarding COVID-19 was declared, following statements about the decreasing trend in deaths due to COVID-19, a decrease in hospitalizations and ICU admissions as well as an increase in the population's level of immunity to SARS-CoV-2[11].

Despite the declaration, in terms of comparison between countries, Brazil is currently in 6th position in the ranking of cumulative cases, totaling 37,717,062 confirmed cases, be- hind countries such as the United States of America, China, India, France, and Germany[3]. In turn, considering the southeastern region of Brazil, more specifically the

states Espírito Santo (ES) and Minas Gerais (MG), 1,339,629 confirmed cases and 15,110 deaths from COVID-19 were registered in ES, while MG recorded 4,209,719 cases and 65,740 deaths, until the beginning of September 2023, as published by the coronavirus panel[12]. Given this scenario, the question arises: what are the incidence, mortality, and lethality rates for COVID-19 in the states of Espírito Santo and Minas Gerais between 2020 and 2022? The study is justified by the emerging need to carry out research in order to understand the profile of infected people in terms of incidence, mortality, and lethality rates due to infection by the new coronavirus in the states of Espírito Santo and Minas Gerais. In this way, deepening this theme may contribute to better coping with the disease by policymakers, through robust and specific evidence, in order to contribute to the development and implementation of local interventions, thus making coping with the pandemic in the states more efficient.

Therefore, the objective of the present study is to evaluate the incidence, mortality, and lethality rates for COVID-19 between the states of Espírito Santo and Minas Gerais, Brazil, from 2020 to 2022.

MATERIALS AND METHODS

Study Design

This is a quantitative ecological study where time series analyses were conducted using a public database on COVID-19 provided by the Brazilian Ministry of Health through the website https://covid.saude.gov.br/ (accessed on 8 February 2023).

Time series analyses help organize quantitative information over time, allowing for the prediction of potential future scenarios of the disease within the population[13,14].

Location and Period of Research

The states Espírito Santo and Minas Gerais were selected to carry out this research, considering that both are part of the Southeast region of Brazil (Figure 1) and border each other, where Espírito Santo has 23 cities bordering Minas Gerais[15–17].

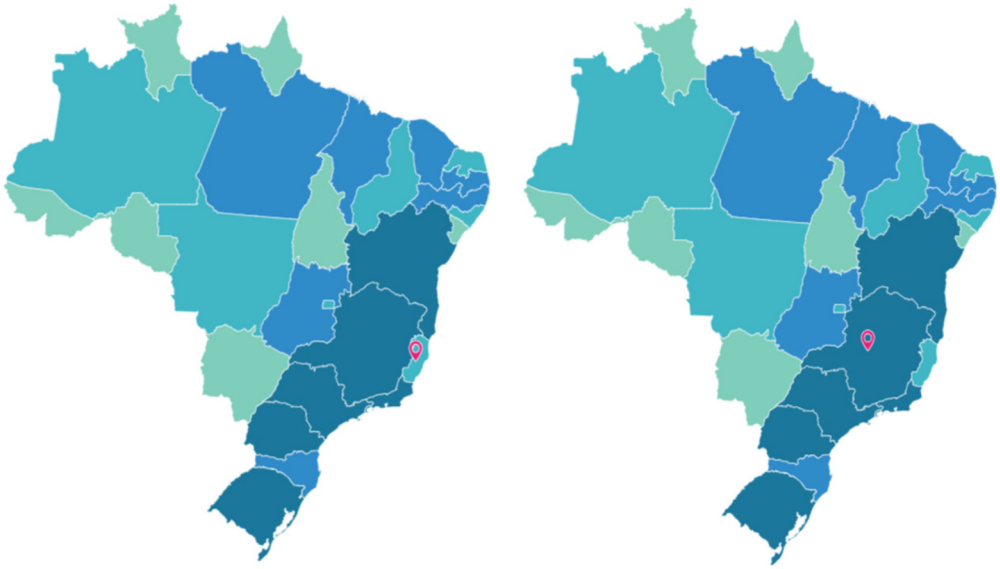

Figure 1. Map of Brazil with representation of the states Espírito Santo (left) and Minas Gerais (right). Source: IBGE (2023).

According to the last census carried out by the Brazilian Institute of Geography and Statistics (IBGE)[15] in the year 2022, the state of Espírito Santo (Figure 2) had a total population of 3,833,486 people. The state has a total territorial area of 46,074.448 km2, with a Human Development Index (HDI) in 2021 of 0.771, occupying 5th position in the national ranking and per capita income of R$1723.

In turn, the state of Minas Gerais (Figure 2), in 2022, presented in the census the equivalent of 20,538,718 people, in a total territorial area of 586,513,983 km2. The state presented a Human Development Index (HDI) in 2021 of 0.774, occupying 4th position in the national ranking and nominal monthly income per capita of R$1529[16].

Comparing the two states, it is noticeable that the state of Minas Gerais is approximately 12 times larger than the state of Espírito Santo, as well as having a larger population, roughly five times, and a higher HDI as well.

The data collected pertained to the period spanning from January 2020 to December 2022.

Figure 2. Map of the states of Espírito Santo (left) and Minas Gerais (right). Source: IBGE (2023).

Study Population and Eligibility Criteria

The population of the states of Espírito Santo and Minas Gerais was used, and all confirmed cases and deaths related to COVID-19 were included in the study using the International Classification of Diseases, 10th edition (ICD-10), of “B34.2, Coronavirus infection of unspecified location” and “U07.1 COVID-19, identified virus” or “U07.2 COVID- 19, unidentified virus”. It should be noted that all cases and deaths included in the research are confirmed.

Data that did not provide complete information regarding the state were excluded from collection, making identification unfeasible.

Data Collection

The data on confirmed cases and confirmed deaths were extracted from the Coronavirus Panel, available on the website https://covid.saude.gov.br/, on 8 February 2023. This panel was created by the Brazilian Ministry of Health and designed to be the official and public vehicle for communication about the epidemiological situation of COVID-19 in the country, registered by the State and Municipal Health Secretariats. Data on the resident population of the states of Espírito Santo and Minas Gerais were

extracted from the projection base of the population of Brazil of the Federation Units by sex and year for the period 2000–2030 from the Brazilian Institute of Geography and Statistics (IBGE)[15,16] available in the database of the Department of Informatics of the Unified Health System (DATASUS)[18], on the website https://datasus.saude.gov.br/informacoes-de-saude-tabnet/(accessed on 8 February 2023).

DATASUS provides information that can serve to support objective analyses of the health situation, evidence-based decision making, and the development of health action programs. It is important to highlight that data collection was conducted by two independent researchers, and the data were organized into Microsoft Excel spreadsheets. A comparison of the collected data and totals of each variable was performed to mitigate collection bias.

Study Variables

Dependent (outcome): confirmed cases, confirmed deaths, fatality rate, mortality and incidence.

Independent (explains the outcome): years 2020, 2021 and 2022.

Data Analysis

The data were tabulated in a Microsoft Excel 365 spreadsheet, version 2019, to ensure the organization of absolute frequencies, taken from the public platform, by variable, with the independent and dependent variables. Thus, the relative frequency was calculated, obtaining data on the number of cases and deaths confirmed by COVID-19 in the month and/or year and divided by the total number of the period evaluated and multiplied by 100, expressed as a percentage (%).

The incidence rate relies crucially on the recording of new cases of a disease, serving as a measure of events and can be used as an estimate of the risk of falling ill, as it uses in its denominator the population at risk of developing the disease. Meanwhile, the mortality rate serves as a measure of disease severity and the risk of death from the disease, as its denominator includes the entire population, both sick and not sick. Conversely, the case fatality rate is not a rate but is expressed as a percentage and its denominator is limited to the sick population. Therefore, the incidence and mortality rates were expressed per 100,000 inhabitants, and lethality was expressed as a percentage (%), following the formulas, respectively:

$$\text{Incidence} = \frac{\text{number of confirmed cases}}{\text{population}} \times 100{,}000 \text{inhabitants}$$

$$\text{Mortality} = \frac{\text{number of confirmed deaths}}{\text{population}} \times 100{,}000 \text{inhabitants}$$

$$\text{Lethality} = \frac{\text{number of confirmed deaths}}{\text{number of confirmed cases}} \times 100\%$$

For trend analyses, the methods proposed by Antunes and Cardoso[13] were used, where time series construction rates were calculated using the Prais–Winsten regression model, which allowed first-order autocorrelation corrections to be performed. In values, organized by time. Thus, the following values were estimated: angular coefficient (β) and respective probability (p), considering a significance level of 95% confidence interval (95% CI).

The data modeling process included transformation rates (dependent variable = Y value) into a base 10 logarithmic function. The independent variable (X value) was the days or months of the historical series. The Durbin–Watson test was also used to measure the existence of first-order autocorrelation of the time series composed of daily coefficients and to verify whether the correlation was compatible with the hypothesis of random distribution regression residuals.

The results of the logarithmic rates (β) of the Prais–Winsten regression made it possible to estimate the percentage variation in daily change (Daily Percent Change—DPC) in each state, with the respective confidence intervals (95% CI), expressed by the following formulas:

$$DPC = (10^{\hat{}}\beta - 1) \times 100\%$$

$$IC95\% = [-1 + 10^{\hat{}}\beta min] \times 100\%; [-1 + 10^{\hat{}}\beta max] \times 100\%$$

In this way, it was possible to determine the rates as increasing, decreasing, or stationary and quantify the percentage variation in daily incidence, mortality, and lethality rates. The trend was considered stationary when the coefficient was not significantly different from zero ($p > 0.05$). When the coefficient value was statistically significant ($p < 0.05$), the trends were classified as increasing or decreasing according to the β value. To facilitate visualization of lethality trends, random variation in the graph was reduced using the five-order moving average technique. All statistical analyses were performed using STATA 17.0 statistical software[19].

Legal and Ethical Aspects

By using only aggregated secondary data from the public domain, the work meets the ethical considerations set out in Resolution of the National Health Council (CNS) No. 466, of 12 December 2012 and in Resolution 510, of 7 April 2016, and is exempt from evaluation by the Research Ethics Committee and the National Commission for Ethics in Research on Human Beings.

RESULTS

In the state of Espírito Santo, from January 2020 to December 2022, a total of 1,313,710 cases and 15,400 deaths confirmed by COVID-19 were recorded. Table 1 shows the monthly distribution of cases and deaths confirmed by COVID-19 in Espírito Santo over time (2020 to 2022).

Table 1. Monthly distribution of cases and deaths confirmed by COVID-19 in the state of Espírito Santo, Brazil, from January 2020 to December 2022.

Year	Month	Confirmed Cases		Confirmed Deaths	
		Frequency Absolute (*n*)	Frequency Relative (%)	Frequency Absolute (*n*)	Frequency Relative (%)
2020	January	0	0.00	0	0.00
	February	1	0.00	0	0.00
	March	151	0.01	0	0.00
	April	4101	0.31	116	0.75
	May	17,704	1.35	591	3.84
	June	35,880	2.73	1060	6.88
	July	37,305	2.84	904	5.87
	August	25,285	1.92	609	3.95
	September	19,108	1.45	397	2.58
	October	28,160	2.14	328	2.13
	November	46,414	3.53	505	3.28
	December	54,659	4.16	861	5.59
	Total	268,768	20.46	5371	34.88

Table 1. Cont.

Year	Month	Confirmed Cases		Confirmed Deaths	
		Frequency Absolute (*n*)	Frequency Relative (%)	Frequency Absolute (*n*)	Frequency Relative (%)
2021	January	44,897	3.42	851	5.53
	February	30,527	2.32	568	3.69
	March	65,900	5.02	1274	8.27
	April	50,456	3.84	2112	13.71
	May	42,498	3.23	1273	8.27
	June	31,201	2.38	626	4.06
	July	21,211	1.61	377	2.45
	August	19,037	1.45	239	1.55
	September	24,322	1.85	266	1.73
	October	18,278	1.39	334	2.17
	November	13,116	1.00	215	1.40
	December	9852	0.75	122	0.79
	Total	371,295	28.26	8257	53.62
2022	January	255,645	19.46	298	1.94
	February	137,628	10.48	619	4.02
	March	12,073	0.92	171	1.11
	April	2394	0.18	29	0.19
	May	7262	0.55	21	0.14
	June	75,481	5.75	108	0.70
	July	77,148	5.87	231	1.50
	August	7938	0.60	85	0.55
	September	1372	0.10	19	0.12
	October	1202	0.09	6	0.04
	November	33,716	2.57	39	0.25
	December	61,788	4.70	146	0.95
	Total	673,647	51.28	1772	11.51
	Total	1,313,710	100.00	15,400	100.00

Source: Information extracted by the author from the Coronavirus Panel, (2023).

In the state, the first confirmed case of COVID-19 was registered in February 2020, corresponding to 0.0001% of the total cases throughout the analyzed period. As for deaths, the first records appeared in Aprilof the same year, corresponding to a relative frequency of 0.75% of total deaths.

In 2020, in Espírito Santo, 268,768 cases and 5371 confirmed deaths from COVID-19 were recorded, with a monthly average of 22,397 and 448 respectively. The months with the highest number of confirmed COVID-19 cases were July (2.84%), November (3.53%) and December (4.16%). In relation to deaths confirmed by COVID-19, the months that stood out were June (6.88%), July (5.87%) and December (5.59%).

Continuing the pandemic period, in 2021, 371,295 cases and 8257 confirmed deaths from COVID-19 were recorded, with an average of 30,941 and 688, respectively. Here, the months of January, March, and April stand out for confirmed cases, being 3.42%, 5.02%, and 3.84%, respectively, in relation to the total period. However, for deaths, the months with the highest number of records were March (8.27%), April (13.71%), and May (8.27%).

In turn, in 2022, 673,647 cases and 1772 deaths from COVID-19 were recorded, with an average number of cases and deaths of 56,137 and 148, respectively. The month of January stands out, corresponding to 19.46% of the total cases, followed by the month of February, with 10.48% of cases, and July, with 5.87%. For all the months mentioned above, the relative frequencies of deaths also behaved as the highest, equivalent to 1.94%, 4.02%, and 1.50% respectively. It was noted that, in the annual comparison for the state of Espírito Santo, in 2022 there was a greater number of case records, with a lower number of deaths.

In turn, in the state of Minas Gerais, between January 2020 and December 2022, a total of 3,430,099 cases and 64,498 deaths confirmed by COVID-19 were recorded. In the state, the first confirmed cases of COVID-19 were registered in January 2020, corresponding to 0.004% of the total cases throughout the analyzed period and one death, in the same month.

The monthly distribution of cases and deaths confirmed by COVID-19 in Minas Gerais can be seen in Table 2.

Table 2. Monthly distribution of cases and deaths confirmed by COVID-19 in the state of Minas Gerais, Brazil, from January 2020 to December 2022.

Year	Month	Confirmed Cases		Confirmed Deaths	
		Frequency Absolute (*n*)	Frequency relative (%)	Frequency Absolute (*n*)	Frequency Relative (%)
2020	January	139	0.00	1	0.00
	February	38	0.00	0	0.00
	March	1090	0.03	10	0.02
	April	3261	0.10	100	0.16
	May	13,596	0.40	305	0.47
	June	55,809	1.63	1035	1.60
	July	98,548	2.87	2360	3.66
	August	87,196	2.54	2365	3.67
	September	77,405	2.26	1941	3.01
	October	58,327	1.70	1499	2.32
	November	85,455	2.49	1160	1.80
	December	153,817	4.48	2560	3.97
	Total	634,681	18.50	13,336	20.68
2021	January	174,870	5.10	3730	5.78
	February	127,810	3.73	3329	5.16
	March	266,414	7.77	8483	13.15
	April	195,856	5.71	9262	14.36
	May	205,034	5.98	6220	9.64
	June	197,379	5.75	5100	7.91
	July	122,518	3.57	3243	5.03
	August	82,423	2.40	2006	3.11
	September	49,316	1.44	1143	1.77
	October	30,301	0.88	807	1.25
	November	17,368	0.51	388	0.60
	December	20,915	0.61	183	0.28
	Total	1,490,204	43.44	43,894	68.05

Table 2. Cont.

Year	Month	Confirmed Cases		Confirmed Deaths	
		Frequency Absolute (*n*)	Frequency relative (%)	Frequency Absolute (*n*)	Frequency Relative (%)
2022	January	568,480	16.57	1348	2.09
	February	302,803	8.83	2275	3.53
	March	49,652	1.45	739	1.15
	April	13,956	0.41	127	0.20
	May	63,177	1.84	157	0.24
	June	182,948	5.33	619	0.96
	July	116,177	3.39	829	1.29
	August	2792	0.08	345	0.53
	September	792	0.02	93	0.14
	October	381	0.01	45	0.07
	November	1253	0.04	111	0.17
	December	2803	0.08	580	0.90
	Total	1,305,214	38.05	7268	11.27
	Total	3,430,099	100.00	64,498	100.00

Source: Information extracted by the author from the Coronavirus Panel, (2023).

In 2020, in the state of Minas Gerais, the average number of cases and deaths confirmed by COVID-19 was 52,890 and 1111, totaling 634,681 and 13,336, respectively. The months with the highest number of confirmed COVID-19 cases were July (2.87%), Au- gust (2.54%), and December (4.48%). In relation to deaths confirmed by COVID-19, the months mentioned above were also highlighted, corresponding in sequence to 3.76%, 3.77%, and 4.07%.

In 2021, the average number of cases was 124,184 and the number of deaths confirmed by COVID-19 was 3658. Here, the months of March, May, and June stand out for confirmed cases, being 7.77%, 5.98%, and 5.75%, respectively, in relation to the total period. However, for deaths, the months with the highest number of records were March (13.15%), April (14.36%) and May (9.64%). That year, 1,490,204 cases and 43,894 deaths were recorded. It is noteworthy that this year stands out among those analyzed for presenting the highest number of cases, as well as deaths.

In 2022, the total number of cases was 1,305,214, with a monthly averag of 108,768, with the months of January (16.57%), February (8.83%) and June (5.33) standing out. As for death records, there is a total of 7268, with a monthly average of 606, highlighting the months of January, February, and July, with rates of 2.09%, 3.53%, and 1.29%, respectively.

When comparing the incidences of COVID-19 between states, Espírito Santo (ES) stands out compared to the state of Minas Gerais (MG), presenting the highest rates, as in 2020 (Figure 3A), where the rate was higher in 2, 19 times and in 2021 (Figure 3B), in which the rate was 1.29 times higher than the other state. In the year 2022 (Figure 3C), the highest incidence rate for COVID-19 continued to be in Espírito Santo, with a total of 15,979.12/100,000 inhabitants, compared to a rate of 6029.64/100,000 inhabitants in the state of Minas General, which corresponds to 2.65 times higher.

To better visualize the data, see Figure 3 below, with comparative graphs between the states, year by year.

Now, when comparing the lethality rates between the states of Minas Gerais and Espírito Santo, it was noted that during the period analyzed, the total rate remained higher in the state of Minas Gerais, with the months of April/2020 being highlighted (Figure 4A) with 3.07, April/2021 (Figure 4B) with 4.73 and December/2022 (Figure 4C) with 20.69.

Below is Figure 4, which concerns the comparison of lethality between states.

Although lethality in Minas Gerais was higher throughout the analyzed period, mortality was higher than in the state of Espírito Santo only in the year 2021 (Figure 5B), reaching a rate of 203.67/100,000 inhabitants. For the years 2020 (Figure 5A) and 2022 (Figure 5C), the state of Espírito Santo recorded a mortality rate of 2.09 and 1.25 times higher than the state of Minas Gerais, respectively, as shown in Figure 5.

In addition, an analysis of trends in mortality, lethality, and incidence rates of COVID-19 in the states of Espírito Santo and Minas Gerais was carried out, which can be seen in Table 3.

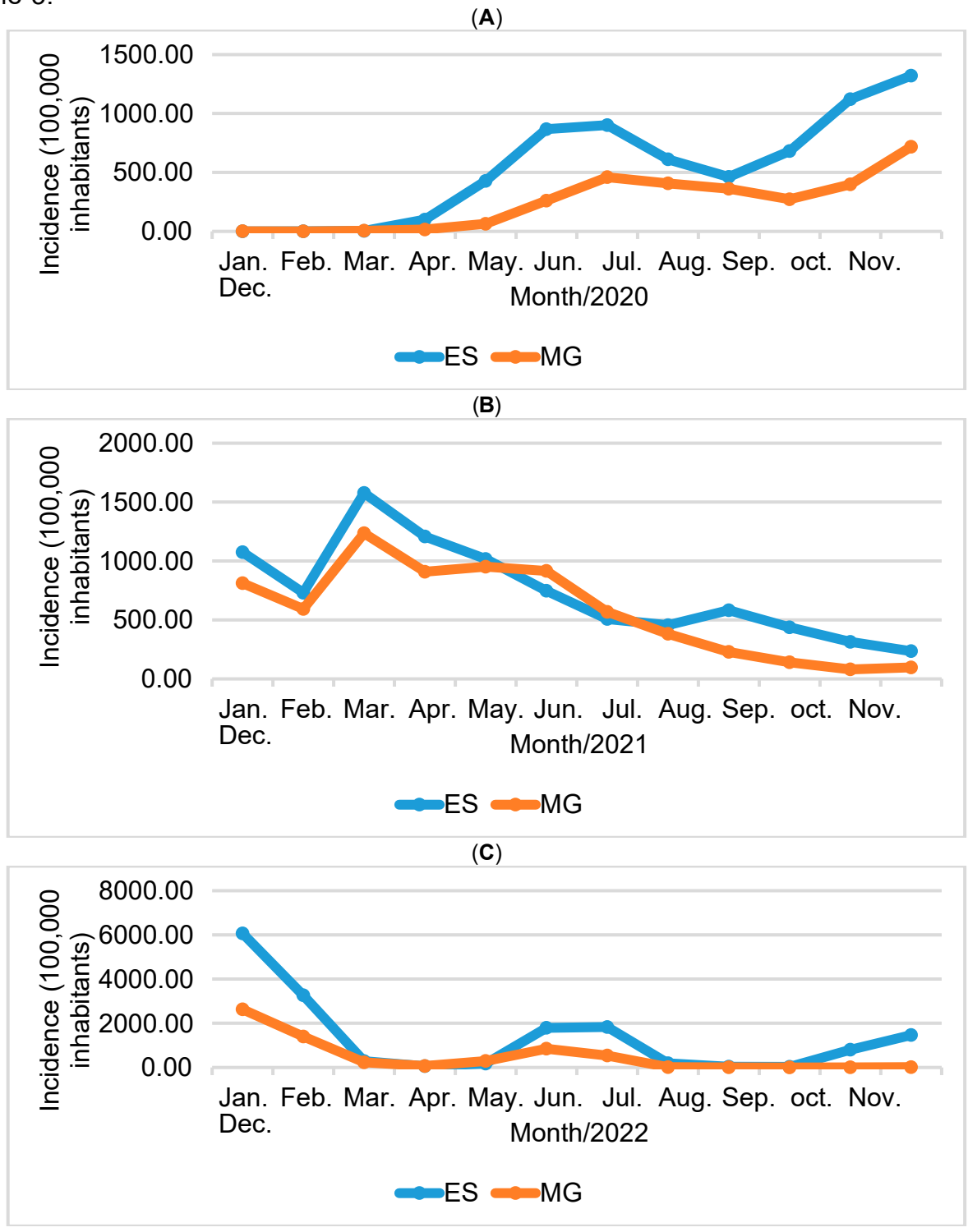

Figure 3. Comparative incidence graph (100,000 inhabitants) for the states Espírito Santo (ES) and Minas Gerais (MG) for the years 2020 (A), 2021 (B), and 2022 (C). Source: Prepared by the author (2023).

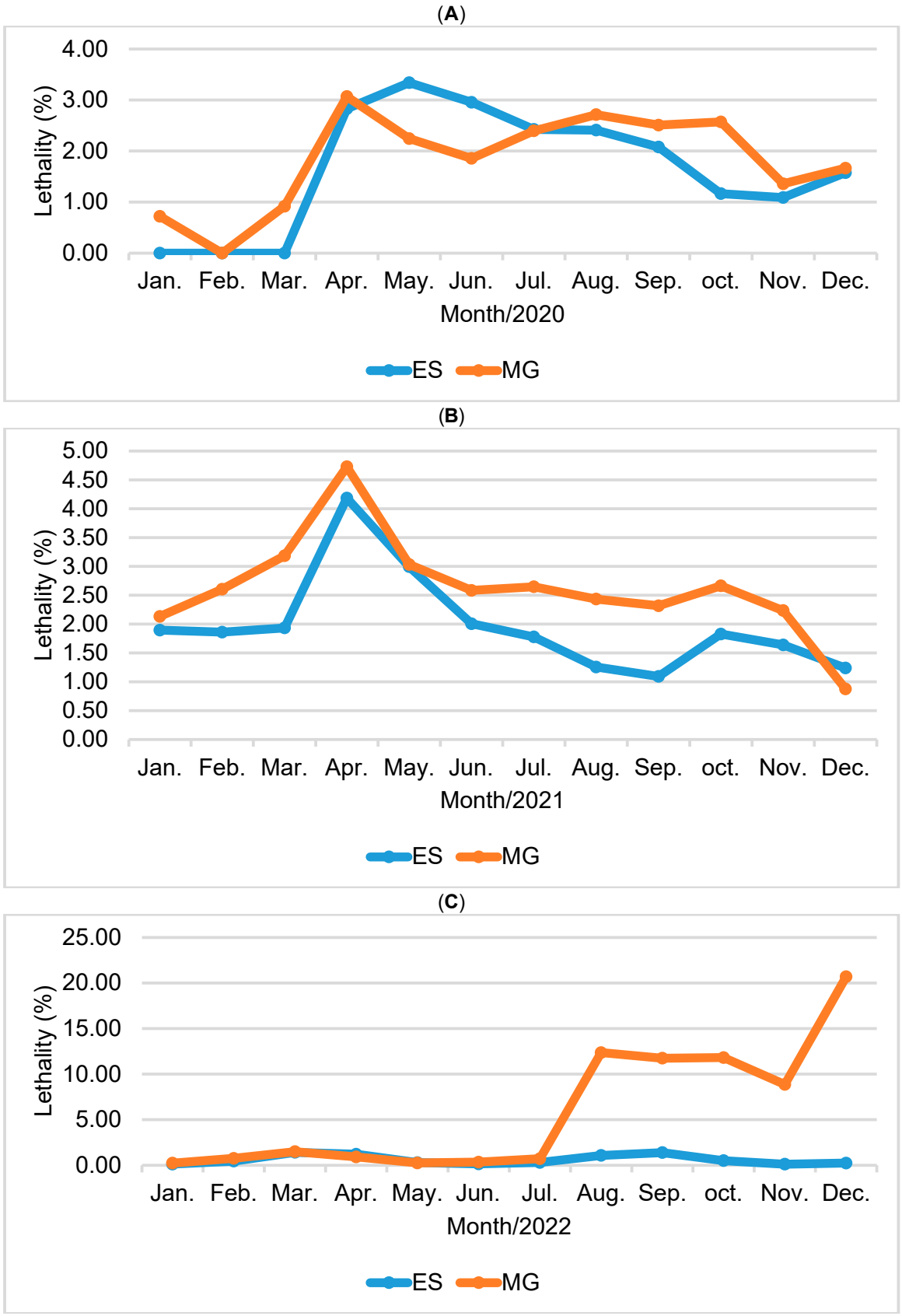

Figure 4. Comparative graph of lethality (%) for the states of Espírito Santo (ES) and Minas Gerais (MG) for the years 2020 (A), 2021 (B), and 2022 (C). Source: prepared by the author (2023).

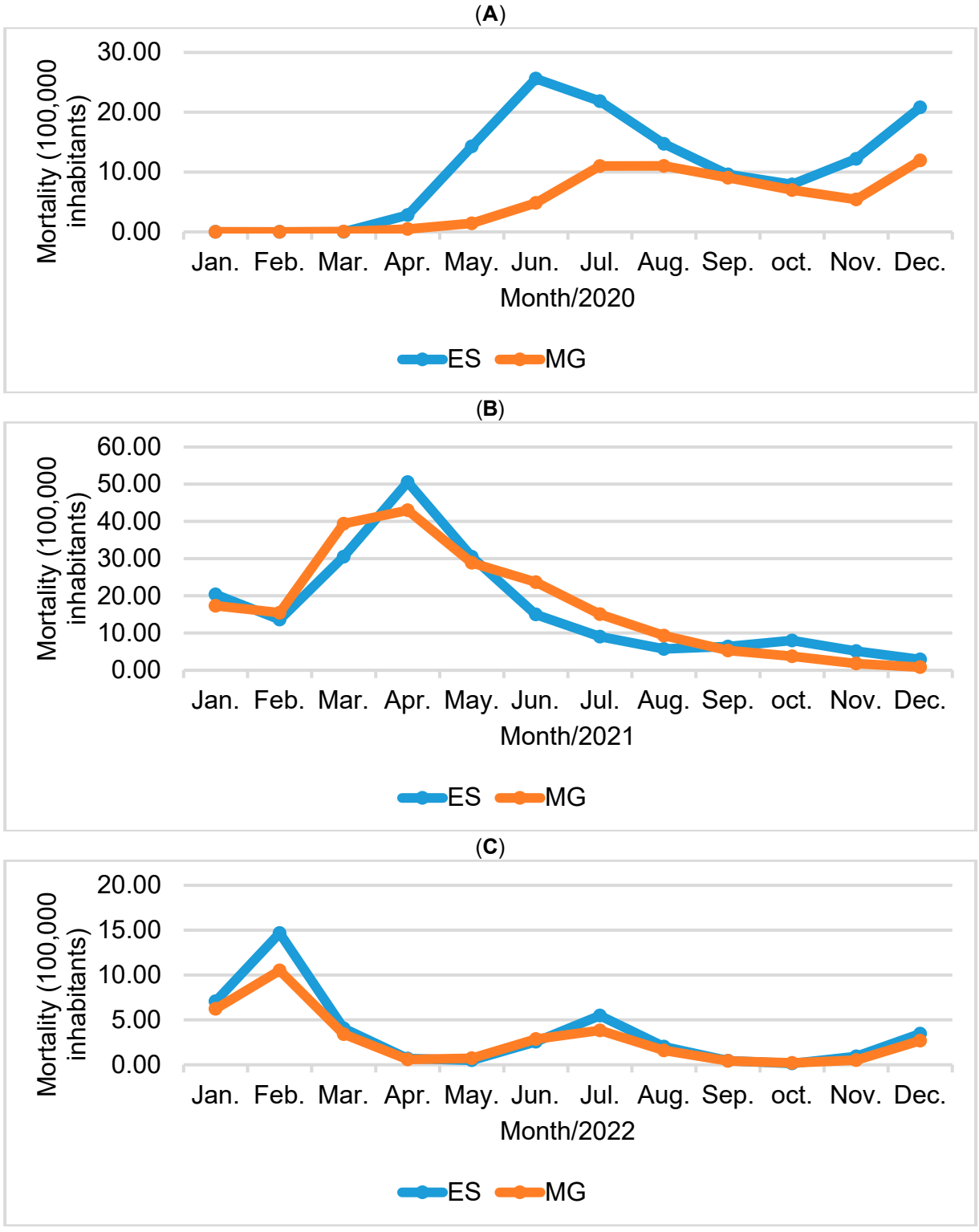

Figure 5. Comparative mortality graph (100,000 inhabitants) for the states Espírito Santo (ES) and Minas Gerais (MG) for the years 2020 (A), 2021 (B), and 2022 (C). Source: prepared by the author (2023).

Table 3. Prais–Winsten regression estimates and daily change variation (DPC) of mortality, lethality, and incidence rates of COVID-19 in the states of Espírito Santo and Minas Gerais, Brazil, from January 2020 to December 2022.

Rate/Year	β	DPC (IC95%)	p	Trend
		Espírito Santo		
Mortality				
2020	0.0023056	0.53 (0.16:0.90)	0.005 *	Growing
2021	− 0.002948	− 0.68 (− 0.80:− 0.55)	<0.001 *	Descending
2022	− 0.0011957	− 0.27 (− 0.58:0.03)	0.076	Stationary
Lethality				
2020	− 0.0019347	− 0.44 (− 0.57:− 0.32)	<0.001 *	Descending
2021	− 0.0008737	− 0.20 (− 0.29:− 0.11)	<0.001 *	Descending
2022	− 0.0000461	− 0.01 (− 0.39:0.37)	0.957	Stationary
Incidence				
2020	0.0084347	1.96 (1.26:2.67)	<0.001 *	Growing
2021	− 0.0020619	− 0.47 (− 0.56:− 0.38)	<0.001 *	Descending
2022	− 0.0020398	− 0.47 (− 1.20:0.27)	0.209	Stationary
		Minas Gerais		
Mortality				
2020	0.0063002	1.46 (1.03:1.90)	<0.001 *	Growing
2021	− 0.0041913	− 0.96 (− 1.25:− 0.67)	<0.001 *	Descending
2022	− 0.002702	− 0.62 (− 1.07:− 0.16)	0.008 *	Descending
Lethality				
2020	− 0.0008331	− 0.19 (− 0.31:− 0.07)	0.002 *	Descending
2021	− 0.0008216	− 0.19 (− 0.29:− 0.09)	<0.001 *	Descending
2022	0.0059761	1.39 (1.11:1.66)	<0.001 *	Growing
Incidence				
2020	0.0122493	2.86 (2.26:3.46)	<0.001 *	Growing
2021	− 0.0034395	− 0.79 (− 0.93:− 0.65)	<0.001 *	Descending
2022	− 0.0078885	− 1.80 (− 2.35:− 1.25)	<0.001 *	Descending

β—regression coefficient; p—p-value; DPC—daily percentage change; 95% CI—95% confidence interval. (*) Statistical difference detected by the Prais–Winsten regression test, p < 0.05. Source: prepared by the au- thor (2023).

After conducting the analyses, the variables considered statistically significant based on the p-value (p < 0.05) were subjected to the calculation of the daily percent change (DPC). This calculation reveals the percentage of daily change, indicating whether the variable increased or decreased during the period.

Thus, it was observed that for the years 2020 and 2021, the trends in both states were the same for mortality, lethality, and incidence. However, in 2022, there will be different behaviors between states for each variable analyzed. In the state of Espírito Santo, that year, for the variables mortality, lethality, and incidence, there was a stationary trend. In turn, Minas Gerais presents decreasing mortality (− 0.62%/day), increasing lethality (+1.39%/day), and decreasing incidence (− 1.80%/day).

DISCUSSION

After analyzing the individual totals of confirmed COVID-19 cases and deaths in the states of Espírito Santo (ES) and Minas Gerais (MG), in the period from 2020 to 2022, it is clear that for the year 2021, the state of Minas Gerais recorded a higher number of cases, as well as deaths. For the state of Espírito Santo, the highest number of cases recorded during the pandemic period occurred in 2022; however, a lower number of deaths was already recorded.

When comparing the states, it is clear that, in proportion, ES had the highest incidence and mortality rates, while MG had the highest fatality rate.

Furthermore, in detail, there is a certain similarity with regard to the months that stood out due to the relative frequency in the distribution of cases and deaths for both states, with the vast majority being months at the beginning, middle, and end of the years. analyzed, such as January, February, June, July, November, and December. Another similar factor between states is the behavior of the increase in the number of deaths occurring in the current month or subsequent to the increase in the number of cases.

Nevertheless, the estimates demonstrated a stationary trend for incidence, mortality, and lethality in Espírito Santo in the year 2022, while in the state of Minas Gerais, there is a decreasing trend for incidence and mortality and an increasing trend for lethality in the same period. The daily increase in lethality is 1.39% (95%CI 1.11: 1.66).

Regarding the increase in the number of cases and deaths in months with specific holidays, a study carried out by Ren and Hwang[20] corroborates this research, which shows that approximately six to eight days after a holiday, there was an increase of 1.30 to 1.41 times the incidence rate.This expected time is directly related to the period of manifestation of symptoms and/or the results of the exam performed. Another study, carried out by Hadianfar et al.[21] also agrees with the results found, where an approximate increase of up to 1872 new cases was observed after holidays ($p < 0.001$).

A study conducted in the United States revealed that the period significantly impacting the number of confirmed cases corresponds to holidays such as New Year's Day, Martin Luther King Day, Good Friday, Independence Day, Memorial Day, Labor Day, Christmas, elections, vacations, among others [20]. In this regard, it aligns with the data found in our research, considering that these months also have similar holidays in Brazil, such as Christmas, New Year's, elections, and vacation periods, leading to an increase in the number of people circulating, as well as group gatherings.

In this context, the results of the present study demonstrate an increase in incidence, mortality, and lethality in November and December 2022. During this period, a major event that may have favored this increase in cases and deaths was the election. There were two rounds of presidential elections, where for both the state of Espírito Santo and the state of Minas Gerais, approximately 80% of eligible electorates in each state turned out to vote[22].

Other factors may also be associated with the increase in the number of cases and, consequently, the number of deaths. For Wu et al.[23], information on demographic density, average family income, percentage of the population in poverty, education, etc., provides support for a better understanding of the disease's behavior. In this aspect, the state of Espírito Santo has a demographic density 2.38 times greater than the state of Minas Gerais, with 83.20 inhabitants/km2 against 35.02 inhabitants/km2[15,16].

Demographic density is important in influencing the impacts of an epidemic, considering its population groups and their vulnerabilities, assuming that the greater the population density, the greater the difficulty of distancing, given that distancing is related to human behavior and is challenging, contributing to reducing or increasing the damage caused by virus transmission[24].

In this sense, it may be a factor that justifies the state of Espírito Santo presenting higher incidence and mortality rates when compared to the other states. On the other hand, a study carried out by Sutton et al.[25] revealed that mortality from COVID-19 was higher in regions with lower population density, linking this to two factors: rural regions and a higher proportion of elderly people in these regions. It is noteworthy that these specificities end up being important, as they point out that these standards contribute information for the implementation of specific health policies for these areas and populations.

With regard to intervention measures, Wong and Li[24] report that implementations can occur according to population density, thus considering more stringent policies in high-density areas, compared to those with lower density, which would result in optional measures.

As measures, many countries have implemented different types of blockades, some as compulsory, others with penalties applied to non-compliance. Among the measures, blockades in transport areas were adopted, such as stations, airports, and highways, in order to reduce population movement. Thus, Tsuboi, Fujiwara, and Itoh[26] state that blo-

ckades, information, and changes in the population's behavior to the detriment of the pandemic contribute to reducing the risk of infection.

However, in order to effectively control the spread of the virus and consequently the disease, early implementation of measures is necessary. Among the measures, social distancing is influential in reducing daily cases of COVID-19, and for every day of delay in its implementation, there is a 2.41-day delay in containing the pandemic[21,27]. Corroborating this idea, Remuzzi and Remuzzi[28] argue that the exponential increase in mortality in the population may be linked to the late implementation of control measures.

A study carried out in different countries such as Spain, China, the United States, Japan, and Sweden, demonstrated that in 2021, compared to 2020, people reacted with less sensitivity to the suggested measures, arguing that in the first year of the pandemic, the measures were more effective[26].

When evaluating the results of our research, a discrepancy was noted compared to the previously mentioned study, as they advocate for greater adherence to the measures adopted, which contributed to the decrease in rates. However, in the states of Espírito Santo and Minas Gerais, there was an increase in the number of cases and deaths during the first year of the pandemic.

A study conducted in Curitiba, Brazil, spanning from 2020 to mid-2022, resulted in finding that in the year 2022, the incidence of COVID-19 was twice as high compared to previous years. However, lethality was already declining, being the lowest recorded during the pandemic period for this city[29].

Furthermore, with the emergence of new variants, especially Omicron, it was noted that in previously infected or vaccinated people in the United States, cases were classified as mild, which made it possible to reopen gathering spaces[30]. However, it appears that although there was a risk of an increase in the number of cases, the scenario did not increase lethality[31]. In view of this, Adamoski et al.[29] reinforce that, although it is milder, the increase in number can lead to an overload of the health service.

Also, the behavior of COVID-19 demonstrates a combination of several factors that influence its epidemiological dynamics, and the lingering effects of COVID-19 will continue to impact our communities, requiring sustained initiatives and interventions to provide comprehensive care to the population and promote overall well-being[32–35].

In this aspect, the process of understanding the course of the disease, as well as its trend throughout the pandemic period in the states of Espírito Santo and Minas Gerais, is understood as important, considering that the robustness of information is capable of bring- ing greater understanding about the disease, as well as on the interventions implemented over the years studied.

Such information, in addition to contributing to the present time, assuming that there are still records of new cases of COVID-19 in both states and that specific measures continue to be adopted, can support the process of evaluating the interventions carried out, as well as, new measures to be implemented in future epidemics, especially actions to promote, prevent, monitor and control the disease.

Given the stationary trend in most rates in 2022, it is suggested that the measures were important, from their first implementations to their revocations and/or changes, for maintaining a controlled state in a pandemic period, which reinforces the need for new studies to further understand the profile of the disease, thus ensuring that there are specific measures and better control of COVID-19.

The present study stands out for bringing a comparative analysis of epidemiological outcomes between two states in the period from 2020 to 2022; however, it presents aspects of limitations regarding the information analyzed, considering that the process of updating information in municipalities, states, and at the federal level it is dynamic and complex, where data undergoes changes every day. Furthermore, it is worth noting that this database may reflect numbers lower than the actual figures, given the possibility of underreporting in the number of COVID-19 cases and deaths.

CONCLUSIONS

There were 15,400 deaths in the state of Espírito Santo and 64,498 deaths in the state of Minas Gerais confirmed by COVID-19 in the period from January 2020 to December 2022.

When comparing the rates studied during this period, it was possible to observe that the state of Espírito Santo had a higher incidence of COVID-19, as well as higher mortality, when compared to the state of Minas Gerais. In turn, with regard to lethality, Minas Gerais stood out throughout the period of analysis, presenting the highest rate. Although divergent, both states had higher records in similar months, with specific months of greater festivities.

Furthermore, it was observed that both states showed equal trends for mortality, lethality, and incidence in the years 2020 and 2021. For the year 2022, Minas Gerais presents decreasing mortality and incidence and increasing lethality, while the state of Espírito Santo presents a stationary trend for all variables.

Author Contributions

Conceptualization, L.G.d.S., I.M.P.B., G.L.S. and L.C.d.A.; methodology, L.G.d.S., I.M.P.B. and L.C.d.A.; software, L.G.d.S., G.L.S.; validation, L.G.d.S., I.M.P.B., G.L.S. and L.C.d.A.; formal analysis, L.G.d.S. and G.L.S.; investigation, L.G.d.S., I.M.P.B. and L.C.d.A.; resources, L.G.d.S., I.M.P.B. and L.C.d.A.; data curation, L.G.d.S., G.L.S.; writing—original draft preparation, L.G.d.S.; writing—review and editing, L.G.d.S., I.M.P.B. and L.C.d.A.; visualization, L.G.d.S., I.M.P.B., G.L.S. and L.C.d.A.; supervision, I.M.P.B. and L.C.d.A.; project administration, L.G.d.S., I.M.P.B. and L.C.d.A.; funding acquisition, L.G.d.S. All authors have read and agreed to the published version of the manuscript.

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Data Availability Statement

Data supporting reported results can be found in the URL: https://docs.google.com/spreadsheets/d/1u7naOWd4O3YtDzP8j89LykfXqJyBWXFn/edit? usp=drive_link&ouid=104493025969896953886&rtpof=true&sd=true (accessed on 26 May 2024).

Conflicts of Interest

The authors declare no conflicts of interest.

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CHAPTER 34

EVOLUTION OF COVID-19 IN THE STATE OF SÃO PAULO: ANALYSIS OF INCIDENCE, MORTALITY AND LETHALITY FROM 2020 TO 2023

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Abstract

Introduction: COVID-19 is a respiratory disease caused by the SARS-CoV-2 virus, which belongs to the coronavirus family. SARS-CoV-2 is related to other viruses that cause severe acute respiratory syndrome. The emergence of cases of pneumonia of unknown origin triggered the largest viral pandemic in modern times, presenting major challenges to global public health. Objective: To analyze the evolution of the COVID-19 pandemic in the state of São Paulo from 2020 to 2023, focusing on trends in incidence, mortality, and lethality. Methods: Ecological study of time series of incidence, mortality and lethality by COVID-19 in the state of São Paulo using Prais-Winsten regression considering the Weekly Percentage Change (WPC) and probability values (p), considering a significance level of 95% (95% CI). To ensure the reliability of the entered data, double-blind typing was performed by different researchers in the same database extracted from the 2024 Ministry of Health Coronavirus dashboard. Results: From February 2020 and the end of December 2023, 6,763,310 accumulated cases and 182,254 deaths were recorded. Stationary trends were observed for the year 2022, with a reduction in incidence and mortality in the year 2023. However, the epidemiological variable lethality showed a stationary trend. Conclusion: The analysis of the trends in incidence, mortality, and lethality revealed variable dynamics over time, with emphasis on the significant reduction of these indicators in 2023.

Keywords: COVID-19; Coronavirus; Time Series Studies; Epidemiology.

Resumo

Introdução: A COVID-19 é uma doença respiratória causada pelo vírus SARS-CoV-2, pertencente à família dos coronavírus. O SARS-CoV-2 está relacionado a outros vírus responsáveis pela síndrome respiratória aguda grave. O surgimento de casos de pneumonia de origem desconhecida desencadeou a maior pandemia viral dos tempos modernos, impondo grandes desafios à saúde pública global. Objetivo: Analisar a evolução da pandemia de COVID-19 no estado de São Paulo no período de 2020 a 2023, com foco nas tendências de incidência, mortalidade e letalidade. Métodos: Estudo ecológico de séries temporais da incidência, mortalidade e letalidade por COVID-19 no estado de São Paulo, utilizando regressão de Prais-Winsten, considerando a Variação Percentual Semanal (VPS) e os valores de probabilidade (p), com nível de significância de 95% (IC95%). Para

garantir a confiabilidade dos dados inseridos, foi realizada digitação duplo-cega por diferentes pesquisadores na mesma base de dados, extraída do painel do Coronavírus do Ministério da Saúde (2024). Resultados: Entre fevereiro de 2020 e o final de dezembro de 2023, foram registrados 6.763.310 casos acumulados e 182.254 óbitos. Observou-se tendência estacionária no ano de 2022, com redução da incidência e da mortalidade em 2023. Entretanto, a variável epidemiológica letalidade apresentou tendência estacionária. Conclusão: A análise das tendências de incidência, mortalidade e letalidade evidenciou dinâmicas variáveis ao longo do tempo, com destaque para a redução significativa desses indicadores em 2023.

Palavras-chave: COVID-19; Coronavírus; Estudos de Séries Temporais; Epidemiologia.

INTRODUCTION

In December 2019, cases of pneumonia of unknown origin were described in the city of Wuhan, China. Weeks later, Chinese authorities identified a novel coronavirus as the cause of the disease[1]. The International Committee on Taxonomy of Viruses named the virus SARS-CoV-2[2], and the World Health Organization (WHO) designated the disease COVID-19[3].

With the progressive increase in confirmed cases, on 30 January 2020, the WHO declared the viral epidemic a public health emergency of international concern[1]. Called COVID-19, the viral disease was characterized by symptoms of dyspnea, fever, cough, fatigue, and muscle pain[4,5], with the possibility of worsening to Severe Acute Respiratory Syndrome (SARS) and death[6]. Aggravated by viral proliferation, COVID-19 has shown a high prevalence rate due to high transmissibility and high lethality among those infected[7]. As of 30 June 2024, approximately 776 million cases of COVID-19 had been recorded worldwide, resulting in 7.1 million deaths.

In terms of fatalities, the Americas were the most affected region, totaling 3,023,053 deaths[8]. These numbers highlight the severity of the pandemic and the contin- ued need for surveillance and adoption of control measures. The high mortality rates across the globe underscored the importance of implementing effective public health strategies and vaccination programs to attenuate the impacts of COVID-19.

One of the main challenges in combating the pandemic was the rise of new variants of SARS-CoV-2, considering that the accumulation of mutations resulting from viral replication is a natural phenomenon. Although most of the mutations have no noticeable impact, some of them have given rise to new variants with greater infectivity and virulence[6,9].

The high mutability of SARS-CoV-2 has come to require continuous updating of treatments and booster doses of vaccines, as mutations alter the effectiveness of the vaccines developed. The development and continuous updating of newly developed vaccines have become necessary to contain the damage caused by the pandemic, both in the economic sphere and in the daily social activities[10,11]. Several non-pharmacological strategies have been proposed to try to contain the transmissibility of SARS-CoV-2, with emphasis on hand hygiene and maintaining social distancing, however, they were not enough to prevent the spread of the agent on a pandemic scale, aggravating the syndemic behavior of COVID-19 around the world[10,11].

In Brazil, since the beginning of the pandemic in January 2020 until mid-July 2024, 38,840,012 cases were registered with the Ministry of Health, of which more than 712 thousand resulted in death[12,13]. The mortality rate of 339.08 per 100,000 inhabitants[14] reveals the severity of the challenges faced by the health system, highlighting the severity of the complications caused by COVID-19. In addition, the incidence rate of 18,482.30 per 100,000 inhabitants[12] highlights the spread of the virus throughout the country, impacting urban and rural communities, large centers and even more remote regions.

The Southeast Brazilian region reported a total of 15,511,185 confirmed cases and 343,520 deaths. The State of São Paulo (SP) alone had around 6 million cases and more than 183 thousand deaths, demonstrating the severity of the health scenario. As the epicenter of the pandemic in the country, SP faced the challenges of exhaustion of hospital capacity, distribution of medical resources, in addition to efforts to contain the virus's spread.

The high incidence of cases and deaths, combined with the state's population density, high mobility rates, and the complexity of public health management, underscores the critical

importance of studying the pandemic's impact. SP as Brazil's most densely populated state, presents a unique case for examining the evolution of COVID-19. This temporal series study examined the progression of the COVID-19 pandemic in the state from February 2020 to December 2023, focusing on trends in incidence, mortality, and lethality.

MATERIALS AND METHODS

Outline of the Study

This is a population-based ecological study of the time series of incidence and lethality rates of COVID-19 that occurred in the State of SP based on reported data extracted from the Brazilian Ministry of Health CORONAVIRUSPANEL for the year 2024, accessed through the link: https://covid.saude.gov.br, extracted on 31 January 2024[15]. The information excluded personal identifiers and included confirmed COVID-19 cases and deaths recorded from February 2020 to December 2023[15].

Criterion of Inclusion and Exclusion and Collect of Data

The inclusion criteria for the cases considered included deaths of individuals with a laboratory diagnosis of COVID-19, cases reported in the CORONAVIRUS PANEL system based on the International Classification of Diseases, 10th edition (ICD-10), specifically as "U07.1 COVID-19, virus identified" or "U07.2 COVID-19, virus not identified", or COVID-19 "U02.2", virus not identified[15].

To ensure data accuracy, cases and deaths according to the date of notification were classified independently by two different researchers, whose results are present in the research results section. The original data are kept by the main author of this study in case they are needed for future analysis or verification.

Data Analysis

The data were tabulated to calculate the relative frequency, by dividing the number of confirmed cases and deaths from COVID-19 in the month and/or year by the total period evaluated and multiplying by 100, expressed as a percentage (%).

The incidence and mortality rates for COVID-19 per 100,000 inhabitants were calculated. For both indicators, monthly measurements of cases (48 months) and deaths (48 months) were used. To calculate the monthly rates, the intercensal estimates carried out by the Fundação Sistema Estadual de Análise de Dados (SEADE) for the period between 2019 and 2023 were considered, and the population data were considered on the reference date of the collection[16]. The night of 31 July to 1 August. Next, population projections were made for the calendar months of the years 2020 to 2023, with the aim of ensuring greater reliability for the analyses[12].

The incidence and mortality rates were standardized for 100,000 inhabitants and the Lethality Rate, expressed as a percentage, demonstrating the proportion of people who died among those diagnosed with COVID-19. This approach expresses the impact of COVID-19 on a standardized scale, facilitating comparison between different populations and periods. The mathematical Equations (1)–(3) indicate the calculations performed:

$$DPC = (10^{\beta} - 1) \times 100\% \quad (1)$$

$$(CI95\%) = (10^{\beta MAX} - 1) \times 100\% \quad (2)$$

$$(CI95\%) = (10^{\beta MIN} - 1) \times 100\% \quad (3)$$

In calculating incidence and mortality, the population was obtained from the "Population Projection of the Federation Units by Sex and Age Group: 2000–2030" for 2020 (46,289,333 inhabitants), 2021 (46,649,132 inhabitants), 2022 (46,997,428 inhabitants) and 2023 (47,333,328)[12]. In our study, we sought to analyze how COVID-19 indicators change in 4 segments:

1- 2020 (from February to December),
2- 2021 (from January to December),
3- 2022 (from January to December) and
4- 2023 (from January to December).

The approach made it possible to observe the evolution of events in each specific time interval, favoring the accurate trend analysis according to the recommendations of Antunes and Cardoso[17]. From then on, the Prais-Winsten regression model was used to consider the influence of first-order autocorrelation in the analysis of time series data. The data modeling process included the transformation of the rates (dependent variable = Y value) into a base 10 logarithmic function, and the results of the logarithmic rates (β) allowed the estimation of the Weekly Percentage Change (WPC) and its respective confidence intervals with 95% significance. The probability (p) and DVP values were calculated using Equations (1)–(3), where β is the slope of the linear regression, the indices ul represent the upper limit and ll the lower limit of the confidence level[17,18]. Allowing the categorization of incidence, mortality and lethality trends as increasing (p-value < 0.05 and positive beta), decreasing (p-value < 0.05 and negative beta) or stable or stationary (p-value ≥ 0.05)[17].

Statistical analyses were performed using STATA 14.0 software College Station, TX, USA, 2013. As stated in an opinion dated 21 January 2021, by the Research Ethics Committee of the MultiVIX Faculty in Cachoeiro do Itapemirim, ES, Brazil (02.213.188/0002-62), this work does not require approval from the Research Ethics Committee.

RESULTS

The State of SP has a population of 44,411,238 inhabitants and a density of 178.92 inhabitants per km2. It has a Human Development Index (HDI) of 0.806, which reflects the standard of living of the population at the time of this study[13,16].

During the study period, 6,763,310 reported cases and 182,254 deaths were recorded, represented in Table 1 with the respective incidences and monthly relative frequencies of cases and deaths. The first two cases were recorded in February 2020, representing less than 0.001% of cases, while in the month of the first death in March 2020, 136 deaths were found (0.07%).

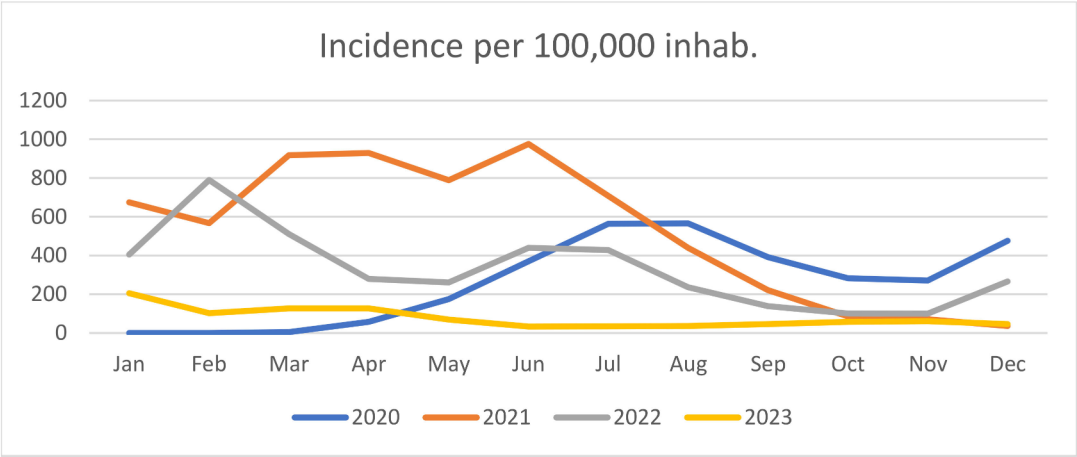
The monthly analysis of the first year showed that July and August had the highest incidence of cases with 260,924 (3.85%) and 262,038 (3.87%) respectively. Regarding mor- tality, July was marked by 8234 deaths, representing 4.51% of deaths for the entire period. In 2021, it was observed that June had the highest incidence, with 455,305 (6.73%) cases recorded, and April led the number of deaths, with 21,539 fatalities.

April 2021 stands out as the month with the highest relative frequency (11.81%) of deaths in a single month. In 2022, February reported the highest number of cases and deaths, with 371,347 (5.49%) and 6678 (3.66%) registered respectively. In 2023, January had the highest number of cases and deaths, with 97,174 (1.43%) and 1064 (0.58%) recorded, respectively.

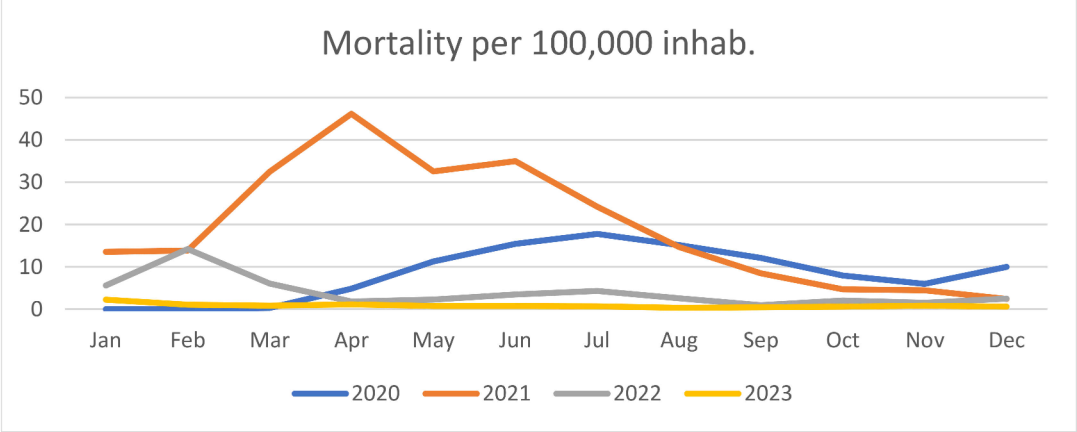
Table 1. Distribution from the frequency absolute and relative of cases and Deaths put COVID-19 by month and year in São Paulo state, Brazil, 2020–2023.

Year	Month	Cases		Deaths	
		No.	%	No.	%
2020	Jan	0	0	0	0
	Feb	2	<0.01	0	0
	Sea	2337	0.03	136	0.07
	Apr	26,359	0.38	2239	1.22
	May	81,000	1.19	5240	2.87
	June	171,682	2.53	7148	3.92
	Jul	260,924	3.85	8234	4.51
	Aug	262,038	3.87	7017	3.85
	Set	181,286	2.68	5608	3.07
	Out	130,499	1.92	3689	2.02
	Nov	125,526	1.85	2784	1.52
	Ten	220,644	3.26	4622	2.53
2021	Jan	315.071	4.65	6317	3.46
	Feb	264,260	3.90	6459	3.54
	Sea	428.221	6.33	15,159	8.31
	Apr	433,860	6.41	21,539	11.81
	May	368,334	5.44	15,183	8.33
	June	455.305	6.73	16,307	8.94
	Jul	330,520	4.88	11,315	6.20
	Aug	204,816	3.02	6840	3.75
	Set	103,448	1.52	3974	2.18
	Out	39,945	0.59	2192	1.20
	Nov	33,028	0.48	2075	1.13
	Ten	17.003	0.25	1128	0.61
2022	Jan	189,998	2.80	2649	1.45
	Feb	371,347	5.49	6678	3.66
	Sea	240,240	3.55	2842	1.55
	Apr	131,652	1.94	849	0.46
	May	122,594	1.81	1061	0.58
	June	206,553	3.05	1623	0.89
	Jul	200,954	2.97	2037	1.11
	Aug	111.100	1.64	1215	0.66
	Set	65,566	0.96	445	0.24
	Out	47,437	0.70	950	0.52
	Nov	46,970	0.69	695	0.38
	Ten	124,814	1.84	1162	0.63
2023	Jan	97,174	1.43	1064	0.58
	Feb	48,658	0.71	518	0.28
	Sea	60.381	0.89	395	0.21
	Apr	59,912	0.88	528	0.28
	May	32,610	0.48	351	0.19
	June	15,807	0.23	345	0.18
	Jul	16,095	0.23	327	0.17
	Aug	16,855	0.24	155	0.08
	Set	22,069	0.32	200	0.10
	Out	27,559	0.40	290	0.15
	Nov	28,912	0.42	392	0.21
	Ten	21,945	0.32	278	0.15
	Total	6,763,310	100.00	182,254	100.00

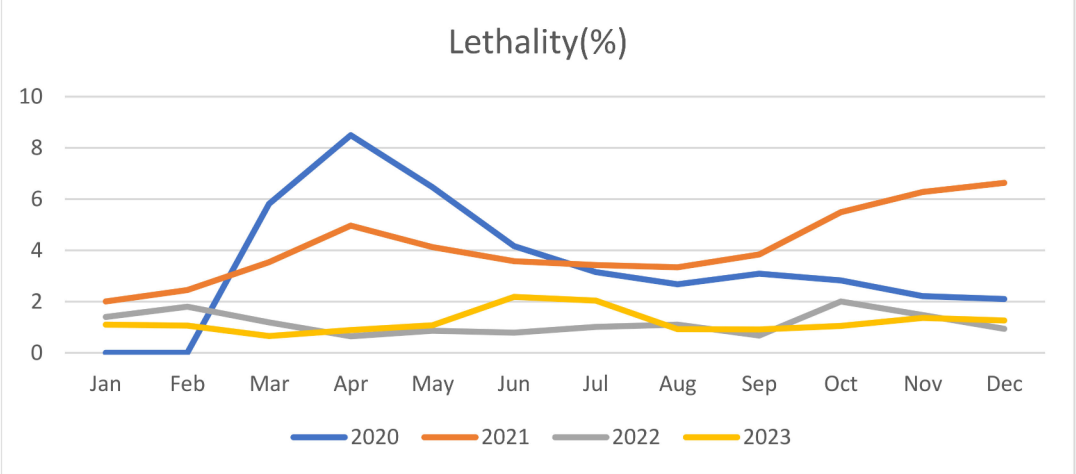
The highest incidence rate was observed during 2021 with peak values recorded from March (917.15 per 100,000 inhabitants) to July (976.02 per 100,000 inhabitants). High numbers were also noted in August 2020 (566.08 per 100,000 inhabitants) until the end of the year (476.66 per 100,000 inhabitants), while the lowest incidences rates occurred in 2023, with emphasis in June, recorded at 33.39 per 100,000 inhabitants. (Figure 1a).



(a)



(b)



(c)

Figure 1. Incidence, rates of mortality and Lethality from the COVID-19 in the state of SP from Jan- uary 2020 to December 2023. Temporal analyses were illustrated as described as follows: (a) incidence, (b) mortality, and (c) lethality of COVID-19 cases.

Regarding mortality rates, the year 2021 presents the highest values, particularly from February (13.84 per 100,000 inhabitants) to August (14.66 per 100,000 inhabitants). Similarly, from August (15.15 per 100,000 inhabitants) to December (9.98 per 100,000 inhabitants) of 2020 mortality rates remained higher compared to other years. Differently, 2023 remained stable and represents the lowest rates throughout the analyzed period, with August reporting the lowest mortality rate observed during the four years (0.32 per 100,000 inhabitants), as illustrated in Figure 1b.

Regarding lethality, the graph illustrates a different pattern in relation to the other observed rates, with 2020 showing the highest peaks. Lethality rates were highest in March (5.81%) and June (4.16%), followed by an increase from July 2021 (3.42%) to December (6.63%). The lethality rates were at their minimum between 2022 and 2023, with the low- est values in 2023 occurring in January (1.09%), March (0.65%), August (0.91%), Octo- ber (1.05%), and November (1.35%). In 2022, the lowest rates were recorded in April (0.64%), July (1.01%), September (0.67%), and December (0.93%) (Figure 1c)

The COVID-19 pandemic showed distinct patterns of incidence, mortality and lethality trends (Table 2) providing a comprehensive assessment of how the pandemic progressed during the analyzed period in SP until the end of 2023. The monthly distribution of COVID-19 cases and deaths in the state totaled approximately 6 million cases and 182,000 deaths. The first deaths were recorded in March 2020, with a total of 136 deaths that month. In 2020, the highest number of deaths occurred in August and July. In 2021, June recorded the highest number of deaths, followed by April, which also had the highest relative frequency. In 2022, February saw the highest number of cases and deaths, while in 2023, January reported the highest figures for both.

Table 2. Prais–Winsten regression estimates and Weekly percentage change (WPC) of incidence, mortality and Lethality of COVID-19 node state of They are Paul, Brazil, of January of 2020 the December of 2023.

Indicators	Year	Beta	WPC	Linear Regression (IC 95%)	*p*	Trend
Incidence	2020	0.0980708	25.33	7.19:46.54	0.006	Growing
	2021	− 0.029841	− 6.64	− 9.55:− 3.64	<0.001	Descending
	2022	− 0.008616	− 1.96	− 4.21:0.33	0.092	Stationary
	2023	− 0.01105	− 2.51	− 4.43:− 0.56	0.013	Descending
Mortality	2020	0.0436532	10.57	0.56:21.59	0.039	Growing
	2021	-2.15×10^{-2}	− 4.84	− 9.18:− 0.29	0.038	Descending
	2022	-8.33×10^{-3}	− 1.90	− 4.59:0.87	0.172	Stationary
	2023	-8.67×10^{-3}	− 1.98	− 3.21:− 0.73	0.003	Descending
Lethality	2020	− 0.013166	− 2.99	− 4.04:− 1.92	<0.001	Descending
	2021	0.0104584	2.44	1.15:3.74	<0.001	Growing
	2022	-7.07×10^{-5}	− 0.02	− 1.34:1.32	0.98	Stationary
	2023	0.002399	0.55	− 0.76:1.88	0.402	Stationary

The incidence showed an increasing trend for 2020 (WPC = 25.33%, $p < 0.05$) with a decrease in 2021 (WPC = − 6.64%, $p < 0.05$), remaining stationaryin 2022 (WPC = − 1.96, $p > 0.05$) and a new decrease in 2023 (WPC = − 2.51%, $p < 0.05$). For mortality, the trend remained increasing (WPC = 10.57%, $p < 0.05$) in 2020, decreasing for 2021 (WPC = − 4.84%, $p < 0.05$); remaining stationary in 2022 (WPC = − 1.90%, $p > 0.05$), and decreasing in 2023 (WPC = − 1.98%, $p < 0.05$). Lethality had a decreasing trend in 2020 (WPC = − 2.99%, $p < 0.05$), while in 2021 it was increasing (WPC = 2.44%, $p < 0.05$), being stationary in 2022 (WPC = − 0.02%, $p > 0.05$) until 2023 (WPC = 0.55%, $p > 0.05$). Despite the mostly stationary trends observed in 2022, there is a decreasing behavior in incidence (WPC = − 2.51%, $p < 0.05$) and mortality (WPC = − 1.98%, $p < 0.05$). In 2023, however, this behavior is not observed for lethality, which presented a stationary trend (WPC = 0.55%, $p > 0.05$).

DISCUSSION

The trajectory of the COVID-19 pandemic in the state of SP was marked by intense dynamics, with the number of deaths showing considerable variations throughout the analyzed period. The epidemic curve, with its peaks and valleys, reflected the complexity of interactions between the SARS-CoV-2 virus and society. These dynamics were influenced by various factors including the emergence of new viral variants[19,20], the implementation of control measures[21,22] and the demographic and socioeconomic characteristics of the populations affected[23,24].

Throughout the period analyzed, the highest incidence and mortality rates were recorded in 2021. Conversely, the lowest rates were observed in 2023, which can be considered the year when epidemic behavior significantly subsided, with incidence rates reaching their lowest values compared to previous years. Regarding lethality, 2020 stands out as the year with the highest rates, differing from the trends observed for incidence and mortality specific to COVID-19.

Older adults and individuals with comorbidities, such as hypertension, diabetes and cardiovascular diseases, were disproportionately vulnerable to worsening COVID-19 and deaths arising from the illness. Those groups presented a bigger risk of severe complications due to the compromise of their immune systems and the presence of pre-existing conditions that make recovery difficult[25,26]. Furthermore, social inequalities exacerbated the impact of the pandemic. People with less access to health care and living in precarious conditions face additional challenges, such as a lack of adequate medical resources and the inability to follow effective prevention measures, such as social distancing and proper hygiene. These disparities exacerbated health inequalities, making certain groups' populations yet more vulnerable to the effects from the COVID-19[23,24].

Consistent with the findings of this study, which revealed a decrease in the incidence rate of COVID-19 in the state of São Paulo in 2023, an additional ecological analysis highlighted that the federative units with the highest incidence rates between 2020 and 2021 were Amapá, Rio Grande do Sul, Rondônia, and Roraima. These states, located in the North and Northeast of Brazil, face significant challenges due to structural deficiencies in their health systems. In contrast, the state of São Paulo which reported a lower incidence rate, benefits from a more robust infrastructure within the Unified Health System (SUS)[27,28] Overall, Brazil faces profound inequalities and inequities in the distribution of goods, services, and wealth, resulting from a historical accumulation unequally divided across generations. In the field of health, these inequalities are evident in variations in access to technological advancements and differences in opportunities for exposure to health determinants, disease, and mortality. As a result, the number of COVID-19 cases and related deaths increased rapidly in urban peripheries and gradually expanded to inland areas, intensifying regional and socioeconomic disparities in health[29–31].

The reduction in the incidence rate in the State of São Paulo suggests that mitigation and control strategies have been effective, contributing to a significant decrease in the spread of the disease compared to previous years. Similar trends were observed in other Brazilian regions and highlight the importance of continuing vaccination and epidemiological surveillance efforts to maintain control over the pandemic[32–35].

Similar to the trends in incidence, the lowest mortality rates in the state of São Paulo were observed in the final year of analysis, 2023. The start of vaccination against COVID-19 in Brazil provoked significant changes in the profiles of hospitalizations and Deaths associates the disease. An increased risk of hospitalization and mortality was observed among younger individuals who did not receive the vaccine, while the mortality rate among vaccinated elderly individuals was substantially reduced. In addition, there was an overall decrease in both hospitalization and death rates, highlighting the effectiveness of vaccination campaigns in protecting vulnerable populations and mitigating the severe impacts of the pandemic[36].

In agreement with the findings of Sobczak and Pawliczak, 2022[37], a crucial factor in reducing COVID-19 mortality is an adequate health system combined with an accurate restriction policy. The reduction of mortality and Lethality by COVID-19 in the state of SP in 2023 can be attributed to a combination of strict preventive measures and an effective

vaccination campaign.

As seen in several European countries that implemented strict restrictions and promoted awareness of the importance of hygiene, SP authorities also adopted measures such as mandatory use of masks, social distancing and campaigns of vaccination in mass. These actions collaborated to control the dissemination of the virus and protect the vulnerable population. In addition, the ready response of the government and the increased hospital capacity contributed to a decrease in hospitalizations and deaths[38–40].

However, regarding the incidence of COVID-19, globally, the incidence rate in the third year of the pandemic remained high[41]. The persistence of a high incidence rate can be attributed to several factors, including the continuous circulation of new variants of virus, inequalities in access to the vaccines, resistance to adherence to prevention measures and variations in public health policies between countries[42].

The vaccination evidenced to be the most effective measure to reduce the mortality related the COVID-19. It significantly reduced mortality rates among patients. In some countries, as Bulgaria, Latvia, Lithuania and Romania, the number of people fully vaccinated was positively correlated with the mortality rate. In contrast, in Hungary, Romania and Slovakia, the increase in the number of vaccine doses and boosters was also associated with an increase in COVID-19 mortality[37].

A study analyzed the relationship between the incidence rate of COVID-19 in the population of different countries and the types of vaccines used against SARS-CoV-2, considering demographic and immunobiological factors. In the Asia Eastern, the highest incidence of COVID-19 was observed in South Korea, what used predominantly messenger RNA vacci-nes, while the smallest incidence proportion was found in China, which used mainly inactivated virus vaccines[42].

In Europe, countries with a predominance of mRNA vaccines, such as France and Portugal, had an 18% to 45% higher incidence rate of COVID-19 than the United Kingdom, which had a balanced mix of vaccine types and superior testing coverage. This suggests that the number of COVID-19 cases depends not only on testing and vaccination coverage but also on the types of vaccines used. Countries that predominantly used vector and inactivated virus vaccines showed a significantly lower incidence rate than those that predominantly used mRNA vaccines[42].

In Brazil, nine types of vaccines have been used to combat the coronavirus. The most widely used vaccines in adults were ChAdOx1-S/nCoV-19 [recombinant] (AstraZeneca), CoronaVac (Butantan), Bnt162b2 (BioNTech/Pfizer) and Ad.26.COV2.S (Janssen Pharma)[43]. The effectiveness and the scope of the vaccines against new variants were sufficient to significantly reduce the incidence of severe acute respiratory syndrome and decrease the number of deaths and hospitalizations associated with SARS-CoV-2[43].

Vaccination against COVID-19 in Brazilian states presents heterogeneous coverage, reflecting the country's socioeconomic and structural disparities. Evidence revealed that states with a lower HDI, limited primary care coverage and fewer public health facilities have lower rates of primary and booster vaccination coverage[44,45].

Spatial and temporal analysis of vaccination reveals that the North and Northeast regions have lower vaccination rates compared to the Southeast and South, which concentrate most of the vaccines administered[46,47]. Furthermore, the pandemic has exacerbated existing inequalities, with indigenous and quilombola populations having the lowest vaccination rates[46,47].

However, despite of continuous efforts in vaccination campaigns and improvement of vaccine formulations, ideal prevention against virus transmission has not yet been achieved[48]. This challenge is markedly evident in the context of new variants, which present mutations capable of reducing the effectiveness of existing vaccines, highlighting the need for continuous adaptations and updates in immunizers to effectively face the evolution of the virus[48,49].

The findings of this study reveal significant variations over the analyzed period, highlighting peaks and valleys in the COVID-19 epidemic curve. These fluctuations reflect the complex interaction between the virus SARS-CoV-2, society, and the emergence of new variants. The data indicate that the pandemic in São Paulo was marked by different phases,

with timelines of high transmission and mortality, followed by periods of relative stabilization. The evolution of incidence, mortality and lethality rates over time highlights the importance of continuous epidemiological surveillance strategies, vaccination and effective communication with the population to face future challenges and mitigate the impacts of new variants.

This study has some limitations: firstly, the use of secondary data extracted from the DATASUS database may lead to issues related to data quality and integrity. Another limitation is related to the generalization of the results, since the analysis was restricted to the population of SP, it is not possible to extend the conclusions to other regions of the country or to Brazil as a whole. Furthermore, external factors, such as changes in the population health or behavioral policies may influence the trends observed throughout the period analyzed, which could impact the interpretation of the results.

Despite these limitations, this study has strong points and demonstrates its significant importance. The use of a time series method provides a robust approach to examine the temporal variations of health indicators over the period, which allows identifying possible changes in trends over time, providing important information for understanding the evolution of COVID-19. In addition, the use of data coming from DATASUSallows a comprehensive and representative analysis of the epidemiological situation of COVID-19 in the state of SP. Understanding the trends and factors associated with the pandemic is crucial to guiding effective interventions of health public.

Therefore, this study contributes to the scientific knowledge about the epidemiology of COVID-19 in SP and offers essential information for the formulation of health policies and programs aimed at preventing and controlling disease, adapting to the specific needs of the population and developing improvements in response to new variants of the virus.

CONCLUSIONS

The analysis of incidence, mortality, and lethality trends revealed variable dynamics over time, with a notable reduction in these indicators in 2023. However, the persistence of high global incidence rates and the emergence of new variants highlight the continued need for epidemiological surveillance and the development of effective public health strategies. This study provides valuable insights into the temporal trends of COVID-19 in SP, contributing to the broader understanding of the pandemic's progression. The findings offer critical information to guide the formulation of public health measures, for managing and responding to future public health crises.

Author Contributions

Conceptualization, L.J.M.J. and F.A.M.d.S.F.; methodology, G.d.A.V.P. and L.J.M.J.; software, M.P.E.C.; validation, R.L.M.A.; formal analysis, M.P.E.C.; investigation, Y.E.B.; resources, R.L.M.A.; data curation, F.A.M.d.S.F.; writing—original draft preparation, L.J.M.J.; writing— review and editing, L.J.M.J., M.P.E.C., G.d.A.V.P., F.A.M.d.S.F., Y.E.B. and L.C.d.A.; visualization, H.M.J.; supervision, L.C.d.A.; project administration, L.C.d.A. All authors have read and agreed to the published version of the manuscript.

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Data Availability Statement

The data presented in this study are available in https://covid.saude.gov.br, (Accessed on 31 January 2024). These data were derived from the following resources available in the public domain: CORONAVIRUSPANEL.

Conflicts of Interest

The authors declare no conflicts of interest.

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