

ORIGINAL ARTICLE

Space-temporal analysis of the incidence, mortality and case fatality of COVID-19 in the State of Rio Grande do Norte, in the period from 2020 to 2022, in the Northeast of Brazil

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Abstract

Introduction: the COVID-19 pandemic, caused by the SARS-CoV-2 coronavirus, has had a great impact on the state of Rio Grande do Norte, as well as around the world, constituting a relevant challenge for public health. Since its emergence, the disease has spread widely, causing a significant number of confirmed cases and deaths in the state.

Objective: to analyze the trend of incidence, mortality and case fatality of COVID-19 in the state of Rio Grande do Norte, located in the Northeast region of Brazil, between 2020 and 2022.

Methods: consists of an ecological analysis of time series of retrospective secondary data in population level. Incidence and mortality rates per 100,000 inhabitants were estimated, as well as case fatality and daily percentage variation, both expressed in percentages. The daily percentage variation was calculated using the generalized linear regression technique using the Prais-Winsten method, and served to classify the trend as increasing, decreasing or stationary, considering a significance level of 95%.

Results: data analysis showed the registration of 582,618 cases and 8,689 deaths from COVID-19 in the state of Rio Grande do Norte, during the period from March 2020 to December 2022. There was an initial increase in the incidence rate in 2020, followed by a significant reduction in 2021 and 2022. Mortality showed a decreasing trend in 2021 and a stationary trend in 2022, without notable variation in 2020. The case fatality rate decreased in 2020, but did not show significant trends in the following years.

Conclusion: the epidemiological analysis of COVID-19 in the state of Rio Grande do Norte revealed variations in incidence, mortality and case fatality over the study period. The daily percentage change over the total period of the incidence time series was stationary, while mortality and case fatality were decreasing.

Keywords: COVID-19, pandemic, epidemiology, incidence, mortality, case fatality.

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Authors summary

Why was this study done?

This type of study can have significant implications both in the academic and epidemiological areas. Because it provides important information about the dynamics of COVID-19 in the state of Rio Grande do Norte, and can help in the planning of interventions and health policies, regional and temporal comparisons, and in the evaluation of the effectiveness of the implemented control measures, as well as boosting advance scientific knowledge and help make informed decisions in fighting the pandemic and future public health emergencies. Thus, monitoring the patterns of the time series of incidence, mortality and case fatality of COVID-19 is essential to develop adequate mitigation and management strategies, taking into account the specificities of the federative units, regions and the country.

What did the researchers do and find?

An analytical epidemiological study of time series of incidence, mortality and case fatality of COVID-19, of the population-based ecological type, was carried out in the state of Rio Grande do Norte, located in the Northeast region of Brazil, in the period from 2020 to 2022. findings suggest that the incidence of COVID-19 presented monthly variations over the period analyzed, with a progressive increase in cases from March 2020, reaching a peak in June 2021, followed by a reduction in subsequent months. There was a significant increase in deaths from COVID-19 from April 2020, with a peak in June 2021. Subsequently, the numbers decreased, but there were still variations over the months. Case fatality showed a significant decrease in 2020, however, a significant trend was not observed in 2021 nor in 2022.

What do these findings mean?

The monthly variation in the incidence of the disease over the analyzed period indicates the dynamics of virus transmission, with periods of increase and decrease in cases. The significant increase in deaths from April 2020 and the peak observed in June 2021 reflect the severity of COVID-19 and highlight the need for effective interventions to reduce mortality. The subsequent decrease in deaths can be attributed to more effective control measures, such as the advancement of vaccination and the adoption of social distancing and personal hygiene measures. The reduction in case fatality in 2020 indicates a possible improvement in the ability to diagnose, treat and manage the disease. However, the absence of a significant trend in 2021 and 2022 suggests that case fatality has remained relatively stable over these years, requiring continued attention to the proper care of severe and critical cases.

Highlights

Between March 2020 and December 2022, Rio Grande do Norte registered a total of 582,618 confirmed cases and 8,689 deaths due to COVID-19.

The year 2021 had the highest incidence and mortality rates, with 7, 419.56 and 126.24 per 100,000 inhabitants, respectively.

The case fatality rates was highest in Rio Grande do Norte in 2020 (2.53%), but registered a decrease in the following years.

It becomes evident that certain months, such as June and July 2020, as well as May and June 2021, saw higher numbers of cases and deaths, indicating potential peaks in transmission during these specific periods.

INTRODUCTION

The COVID-19 pandemic, caused by the SARS-CoV-2 coronavirus, has represented one of the greatest challenges for global public health in recent years¹. Since its emergence in late 2019, the disease has spread rapidly around the world, resulting in millions of confirmed cases and a worrying number of deaths².

The rapid spread of the virus and the high number of cases have overwhelmed health systems in many countries, creating a shortage of hospital beds, personal protective equipment and adequate medical resources, which has been challenging, both for health professionals and for the health system as a whole^{1,3}.

The way in which the virus spreads has been driven by factors such as rapid urbanization, high levels of informal work, resource-limited health systems, among others³⁻⁵. These challenges have contributed to the increase in the disease burden and mortality related to COVID-19 in Latin American countries^{6,7}.

Government authorities in several nations have adopted containment measures, such as social distancing, confinement, wearing masks and limiting travel, in order to contain the spread of the virus. These measures are considered legitimate only when there is a substantial threat to public health⁸.

The scientific community has dedicated efforts to the study of COVID-19, conducting research in several areas, including epidemiology, virology, treatment and vaccine development. The global collaboration between scientists, government institutions and organizations has

played a crucial role in advancing knowledge and in the search for solutions to face the pandemic^{1,4}.

On the American continent, COVID-19 has become an important public health problem, especially in Latin America, where high population densities and socioeconomic inequalities have impacted the spread and control of the disease^{9,10}.

In Brazil, due to its diversity and continental dimensions, COVID-19 presented heterogeneous patterns of dissemination and impact in different regions¹¹. The Northeast region of Brazil, with its socioeconomic and demographic particularities, faced additional setbacks during the pandemic^{11,12}.

It is noteworthy that the population concentration in densely populated urban areas, limited health infrastructure and regional inequalities in access to medical care amplify the effects of COVID-19¹¹. In addition, socioeconomic factors, such as low income, limited access to basic sanitation and difficulties in social distancing, can contribute to the spread of the virus in vulnerable communities¹².

The constant evolution of the SARS-CoV-2 pandemic dynamics, and the new evidence that may emerge as the pandemic continues to be studied and confronted² are aspects that justify this study in the state of Rio Grande do Norte, located in the Northeast region of Brazil.

The state of Rio Grande do Norte has socioeconomic characteristics that play a relevant role in the dynamics of the COVID-19 pandemic. These characteristics can influence both the spread of the virus and the State's ability

to respond to the challenges posed by the disease^{5,13-15}.

In this way, the presence of socioeconomic inequalities is reinforced¹³. Given that a significant part of the Potiguar population lives in conditions of social and economic vulnerability, which directly impacts their ability to adopt preventive measures, such as social distancing and proper hygiene^{16,17}.

Socioeconomic inequalities can affect access to health services and resources needed to face the pandemic, increasing disparities in the fight against the disease^{4,18,19}. The state's socioeconomic indices, such as per capita income and access to basic services, can also influence the response to the pandemic²⁰.

Populations with lower purchasing power may face difficulties in acquiring essential resources, such as masks, hand sanitizer and hygiene products, which are essential to prevent the spread of the virus. The lack of access to primary services, such as adequate basic sanitation, also contributes to the spread of the disease in vulnerable communities⁴.

Health infrastructure is another factor to consider. The state of Rio Grande do Norte has a limited health network in certain regions, which may hinder the provision of hospital beds, medical equipment and adequate resources for the treatment of COVID-19¹⁴. This limitation of health infrastructure overloads local health systems, jeopardizing the ability to provide adequate care to patients affected by the disease²⁰.

The interaction between socioeconomic aspects and public health constitutes additional adversity for state authorities in coping with COVID-19¹⁷. In this way, understanding the temporal evolution of the incidence, mortality and case fatality of this disease is essential and contributes to the monitoring, evaluation of the effectiveness of implemented interventions and identification of possible gaps in the response to the pandemic²¹.

Therefore, the present study aimed to analyze the temporal evolution of the incidence, mortality and case fatality of COVID-19 in the state of Rio Grande do Norte, located in the Northeast region of Brazil, during the period between 2020 and 2022.

METHODS

Study design and location

It is a study ecological time series based on the protocol developed by Abreu, Elmusharaf and Siqueira (2021)²². Time series are necessary to make valid inferences from the data, accounting for the correlation between repeated observations over time²³.

Official secondary data from government public disclosure of cases and deaths from COVID-19 notified to the Ministry of Health (MS) of Brazil for the state of Rio Grande do Norte were used (<https://www.saude.pr.gov.br/Page/Coronavirus-COVID-19>).

The sociodemographic characteristics of Rio Grande do Norte are shown in table 1.

Table 1 - Sociodemographic characteristics of Rio Grande do Sul and Paraná, southern Brazil

Sociodemographic characteristics	Rio Grande do Norte
Region*	Northeast
Counties*	167
State's capital*	Christmas
Territorial area*	52,809.599 km ²
Estimated population (2022)*	3,302,406 people
Population density (2022)*	62.53 inhab/km ²
Urban household situation (2010)*	2,464,991 people
Rural household situation (2010)*	703,036 people
Nominal monthly household income per capita (2022)*	1,267 BRL
Human Development Index (HDI) (2021)*	0.728
Number of Basic Health Units of the Unified Health System (SUS) (2009)*	1932 establishments
outpatient SUS*	1372 establishments
SUS dialysis*	14 establishments
SUS emergency*	106 establishments
SUS admission*	161 establishments
US ICU*	26 establishments
Number of beds for hospitalization in health facilities (2009)*	6,851 beds
Public*	3,706 beds
Private*	3,145 beds

*Source: IBGE.

Sample and Eligibility Criteria

All cases and deaths due to COVID-19 from March 2020 to December 2022 were included. The occurrences were confirmed by laboratory diagnosis, clinical and epidemiological clinical. The disease COVID-19 has been classified according to the International Classification of Diseases, 10th edition (ICD-10) as “U07.1 COVID-19, identified virus” or “U07.2 COVID-19, unidentified virus”, respectively²⁴.

According to the last day of care, we classified deaths and cases by the onset of symptoms. Then, a second author checked the extracted data and a third researcher did a final review to check for discrepancies. Finally, the information was written in an Excel spreadsheet (Microsoft Corporation, Redmond, WA, USA)²⁵ for analysis of incidence, mortality and case fatality.

Data analysis and statistics

The number of COVID-19 cases and deaths were illustrated by absolute (n) and relative (%) frequency. For each state, the incidence rate (number of cases per 100,000 inhabitants), mortality (number of deaths per 100,000 inhabitants) and case fatality (%) were calculated, as described below:

- (1) Incidence
(number of cases)/population×100.000
- (2) Mortality
(number of deths)/population×100.000
- (3) Case fatality
(number of cases)/population×100

The estimated population for the year 2020 (3,598,288 inhabitants), 2021 (3,627,158 inhabitants) and 2022 (3,655,233 inhabitants) was used²⁶.

To analyze the trend, the protocol by Antunes and Cardoso (2015)²⁷ was used. Time series were constructed applying the Prais-Winsten regression model. It allowed first-order autocorrelation to analyze time series values

and facilitate the evaluation and classification of incidence, mortality and case fatality in increasing, decreasing or stationary. Trends were classified as stationary when the p-value was not significant ($p > 0.05$).

The probability (p) and daily percentage variation (DPV) values, considering a 95% significance level, were calculated using the equations below (4 - 6), where β is the linear regression angular coefficient, the indices ul mean the upper bound, and ll is the lower bound of the confidence level.

$$DPC=(10\beta-1)\times 100\% \quad (4)$$

$$(CI95\%)_{ul}=(10\beta_{max}-1)\times 100\% \quad (5)$$

$$(IC95\%)_{ll}=(10\beta_{min}-1)\times 100\% \quad (6)$$

To compare proportions, the two-tailed z test was used, considering differences with p-value < 0.05 as significant.

Statistical analyzes were performed using STATA 14.0 software (College Station, Texas, USA, 2013)²⁸.

Ethical aspects

The data obtained from the information systems maintained by the Ministry of Health are reliable, enabling its use as a feasible tool for analyzing the epidemiological indicators of COVID-19. As these are public and widely accessible data, it is not necessary to enter the Scientific Research Ethics Committee (CEP) in order to obtain study approval.

RESULTS

In the initial period of COVID-19 infections, between March 2020 and December 2022, in the state of Rio Grande do Norte, a total of 582,618 cases and 8689 confirmed deaths were registered.

In table 2, it is possible to observe the monthly distribution of cases and deaths confirmed by COVID-19 in the state of Rio Grande do Norte in the total period analyzed.

Table 2: Distribution of absolute and relative frequency of cases and deaths from COVID-19, according to month and year, in the state of Rio Grande do Norte. Brazil, 2020-2022

Year	months	Confirmed Cases		Confirmed Deaths	
		Absolute frequency	Frequency relative	Frequency absolute	Frequency relative
		n	%	n	%
2020	March	82	0.01	1	0.01
	April	1,095	0.19	55	0.63
	May	6,225	1.07	249	2.87
	June	22,885	3.93	729	8.39
	July	20,129	3.45	743	8.55
	August	11,332	1.95	479	5.51
	September	7,685	1.32	137	1.58
	October	11,743	2.02	184	2.12
	November	13,947	2.39	111	1.28
	December	22,960	3.94	305	3.51

Continuação - Table 2: Distribution of absolute and relative frequency of cases and deaths from COVID-19, according to month and year, in the state of Rio Grande do Norte. Brazil, 2020-2022

Year	months	Confirmed Cases		Confirmed Deaths	
		Absolute frequency	Frequency relative	Frequency absolute	Frequency relative
		n	%	n	%
2021	January	22,500	3.86	292	3.36
	February	26,312	4.52	300	3.45
	March	29,366	5.04	922	10.61
	April	26,714	4.59	953	10.97
	May	45,451	7.80	656	7.55
	June	71,739	12.31	652	7.50
	July	19,500	3.35	325	3.74
	August	5368	0.92	174	2.00
	September	3586	0.62	70	0.81
	October	5065	0.87	60	0.69
	November	8019	1.38	99	1.14
	December	5499	0.94	76	0.87
2022	January	38,664	6.64	133	1.53
	February	51,806	8.89	345	3.97
	March	19,567	3.36	71	0.82
	April	6173	1.06	54	0.62
	May	3162	0.54	27	0.31
	June	19,905	3.42	65	0.75
	July	20,233	3.47	128	1.47
	August	4991	0.86	49	0.56
	September	5122	0.88	25	0.29
	October	692	0.12	14	0.16
	November	6987	1.20	13	0.15
	December	18,114	3.11	193	2.22
Total		582,618	100.00	8,689	100.00

Source: Information extracted from the Coronavirus Panel on January 12, 2023, available at: <https://covid.saude.gov.br/>.

When analyzing the absolute and relative frequency data of cases and deaths, we observed that the first case occurred in March 2020, which corresponds to 0.01% of the total cases in the total period analyzed. In addition, the first death from COVID-19 occurred in the same month, corresponding to a relative frequency of 0.01% of the total deaths analyzed.

In the first year analyzed (2020), the state of Rio Grande do Norte had 118,083 (20.26%) total cases and 2993 (34.44%) deaths from COVID-19. The highest proportions of cases in the year 2020 were in June (3.93%) and December (3.94%) while that of deaths was in July (8.55%) and June (8.39%).

Moving on to the second year (2021), the highest

proportion was observed in relation to the entire period, both for cases and deaths, with a total of 269,119 cases (46.19%) and 4579 deaths (52.69%). The most affected months with numbers of confirmed cases and deaths were June (12.31%) and April (10.56%) respectively.

When analyzing the table of relative and absolute frequencies (table 2) for the year 2022, a total of 195,416 (33.54%) cases and 1117 (12.85%) confirmed deaths were verified. The month of February had the highest number of cases and deaths this year, with a total of 51,806 (8.89%) cases and 345 (3.97%) deaths.

In table 3, we can see the incidence, mortality and case fatality rates of COVID-19 for the state of Rio Grande do Norte in the 3 years analyzed.

Table 3: Monthly distribution of incidence and mortality rates and the proportion of case fatality of COVID-19 in the state of Rio Grande do Norte, from January 2020 to December 2022

months	Incidence (100,000 inhab.)	Mortality (100,000 inhab.)	Case fatality (%)
Year		2020	
Jan	0	0	0
Feb	0	0	0
Sea	2.28	0.03	1.22
may	30.43	1.53	5.02
June	173.00	6.92	4.00
June	636.00	20.26	3.19
Jul	559.40	20.65	3.69
Aug	314.93	13.31	4.23
set	213.57	3.81	1.78
Out	326.35	5.11	1.57
Nov	387.60	3.08	0.80
Ten	638.60	8.48	1.33
Total*	3281.64	83.18	2.53
Year		2021	
Jan	620.32	8.05	1.30
Feb	725.42	8.27	1.14
Sea	809.61	25.42	3.14
April	736.50	26.27	3.57
May	1253.07	18.09	1.44
June	1977.83	17.98	0.91
Jul	537.61	8.96	1.67
Aug	147.99	4.80	3.24
set	98.87	1.93	1.95
Out	139.64	1.65	1.18
Nov	221.08	2.73	1.23
Ten	151.61	2.10	1.38
Total*	7419.56	126.24	1.70
Year	2022		
Jan	1057.77	3.64	0.34
Feb	1417.31	9.44	0.67
Sea	535.31	1.94	0.36
apr	168.88	1.48	0.87
may	86.51	0.74	0.85
June	544.56	1.78	0.33
Jul	553.54	3.50	0.63
Aug	136.54	1.34	0.98
set	140.13	0.68	0.49
Out	18.93	0.38	2.02
Nov	191.15	0.36	0.19
Ten	495.56	5.28	1.07
Total*	5346.20	30.56	0.57

When analyzing the values of incidence, mortality, and case fatality by COVID-19 for the state of Rio Grande do Norte, it was observed that the year 2021 had the highest incidence and mortality rate per 100,000 inhabitants with 7419.56 and 126.24 respectively, case fatality was higher in 2020 (2.53%).

In 2020, the most impacted months in terms of incidence, mortality and case fatality were June (636.00 per 100,000 inhab.) and December (638.08 per 100,000 inhab.) with similar incidence values, whereas for mortality the months of June (20.26 per 100,000 inhab.) and July (20.65 per 100,000 inhab.) were the most significant, while for case fatality the month of April (5.02%) was the most affected.

In the following year (2021), the month of April was marked with the highest values of mortality (26.27 per

100,000 inhab.) and case fatality (3.57%), while the month of June had the highest incidence rate of the year (1977.83 per 100,000 inhab.).

At the end of the analyzed period (2022), it was found that the highest incidence rates (1417.31 per 100,000 inhabitants) and mortality (9.44 per 100,000 inhabitants) were in the month of February, while the highest proportion of case fatality was presented in the month of October (2.02%).

Trends in incidence rates, mortality and the proportion of case fatality of COVID-19 in the state of Rio Grande do Norte can be seen in Table 4. For analyzes considered statistically significant ($p < 0.005$), the Daily Percentage Variation (DPV) reveals the percentage of daily variation, showing the increase or decrease for the variables.

Table 4: Estimates of the Prais-Winsten regression and daily percentage change (DPV) of the rates of incidence, mortality and case fatality ratio of COVID-19 in the state of Rio Grande do Norte, Brazil, from January 2020 to December 2020 2022

Rate/year	Linear regression				
	β	CPD	(CI95%)	P	Trend
MORTALITY					
2020	-0.00019	-0.04	-0.37 : 0.28	0.794	stationary
2021	-0.00302	-0.69	-0.86: -0.52	<0.001*	Descending
2022	-0.00085	-0.19	-0.40: 0.02	0.069	stationary
CASE FATALITY					
2020	-0.00339	-0.78	-0.96: -0.59	<0.001*	Descending
2021	-0.00015	-0.03	-0.18 : 0.11	0.656	stationary
2022	0.00057	0.13	-0.14: 0.41	0.345	stationary
INCIDENCE					
2020	0.00471	1.09	0.75: 1.43	<0.001*	Growing
2021	-0.00294	-0.68	-0.85: -0.50	<0.001*	Descending
2022	-0.00161	-0.37	-0.72: -0.02	0.037*	Descending

β – regression coefficient; P – p-value; DPC – daily percent change; 95%CI - 95% confidence interval.

* Statistical difference detected by the Prais-Winsten regression test, $p < 0.05$.

The incidence rate showed an increasing trend in 2020, followed by a reduction in subsequent years. Regarding the mortality rate, there was a downward trend in 2021, while in the years 2020 and 2022 it remained stable. As for case fatality, there was a decrease in 2020, followed by stability in the following years.

For a better visualization at a graphic level, we can observe in figures 1, 2 and 3 the projections of the incidence rates, mortality and the proportion of case fatality, respectively, in the total period analyzed.

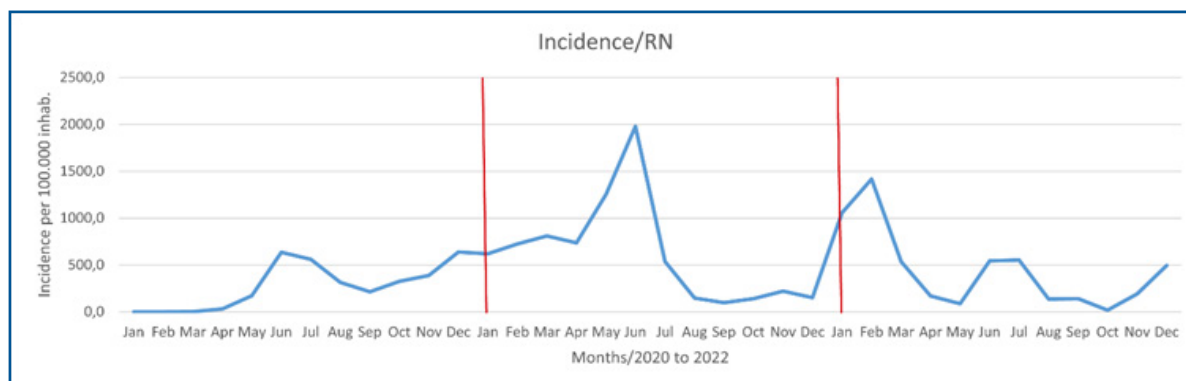


Figure 1: Trend analysis of the incidence rates of COVID-19 in the state of Rio Grande do Norte, Brazil, from January 2020 to December 2022



Figure 2: Trend analysis of COVID-19 Mortality rates in the state of Rio Grande do Norte, Brazil, from January 2020 to December 2022

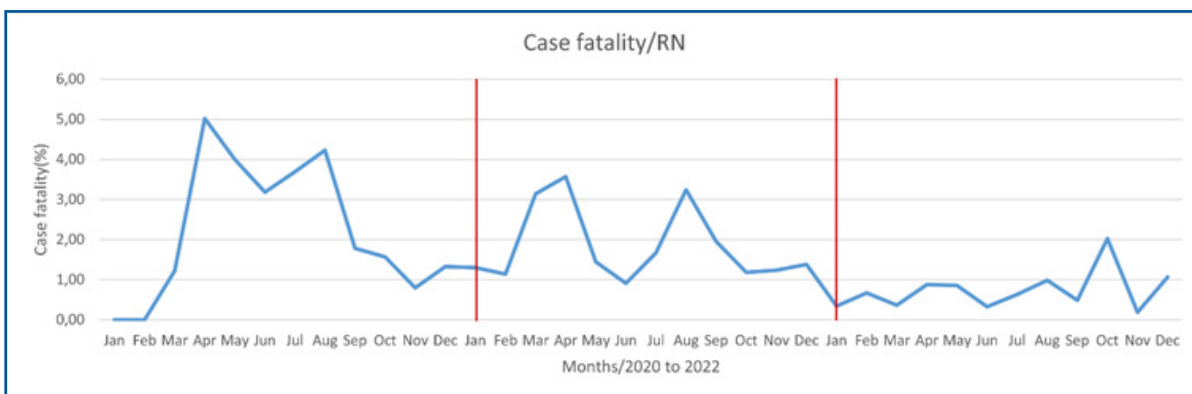


Figure 3: Trend analysis of the case fatality proportions of COVID-19 in the state of Rio Grande do Norte, Brazil, from January 2020 to December 2022

In the years 2021 and 2022, the state of Rio Grande do Norte presented a decreasing trend in the incidence of COVID-19, contrary to the pattern observed in 2020, which was marked by an increase. It is important to point out that both in 2020 and in 2022, there was an increasing trend in the incidence of COVID -19 between the months of October and December (figure 1), showing a similarity between these two periods.

Throughout the analyzed period, there were variations in the increase and decrease in the incidence, which may have been influenced by several factors such as protection measures and vaccination. It is noteworthy that, in these three years, the month of May presented similar characteristics, of increased incidence, as observed in the graph (figure 1). On the other hand, the months in which there was the most reduction in this rate were September in the years 2020 and 2021 and between October and November in 2022.

Figure 2 represents the mortality rate due to COVID-19 in the state of Rio Grande do Norte between the years 2020 and 2022. Like the incidence, mortality also showed increasing and decreasing variations over these three years. The period of greatest increase in mortality occurred between February and May 2021.

In the three years studied, the highest case fatality rate was found between March and May 2020. On the other hand, the lowest rates were observed in June 2022. This fact may be related to the lack of understanding of viral behavior, the overload of health systems, lack of specific treatments and immunization against COVID-19.

DISCUSSION

Over the analyzed period, significant variations were identified in the time series of cases and deaths from COVID-19, indicating changes in the incidence, mortality and case fatality of this disease in the state of Rio Grande do Norte. It is important to highlight that seasonal discrepancies were observed in the monthly values, evidencing the occurrence of higher numbers of cases and deaths in the months of June and July 2020, as well as May and June 2021. These patterns suggest a possible increase in the transmission of COVID -19 during these specific periods.

The increase in cases was progressive from March 2020, starting from 82 cases and reaching its peak in June 2021, with 71,739 cases registered. Then, there was a gradual decrease in the subsequent months, reaching 18,114 cases in December 2022. This reduction presents or the lowest value in the month of October, with 692 cases . However, in February 2022, a further increase in the number of cases was observed, with a total of 51,806 cases.

These variations underscore the continued importance of monitoring the epidemiological situation and adopting disease control measures. It is critical to recognize that the initial reduction in cases and deaths does not necessarily imply a steady and sustainable decline in COVID-19 incidence and mortality. Thus, a vigilant and proactive approach is needed to address potential relapses and ensure public health protection at all times. The observed results of seasonal patterns reinforce the need for

a continuous and flexible response to effectively face the evolution of the pandemic^{18,29}.

In Rio Grande do Norte, the differences in the relationship between confirmed cases and deaths from COVID-19 are notable. During the period from March to April 2021, there was a significant increase in deaths, while there was no corresponding increase in the frequency of confirmed cases of the disease. It is important to highlight that in June and July 2020, as well as in March and April 2022, a relatively high proportion of deaths was recorded in relation to cases, which suggests a greater severity of the disease.

Regarding the number of deaths from COVID-19, a significant increase was found from April 2020, reaching 743 deaths in July of the same year. As of April 2021, significant increases were recorded, with 953 deaths.

The high numbers of deaths and the variations identified indicate a critical period between 2020 and 2022, in relation to the impact of the disease in the state of Rio Grande do Norte. This highlights the importance of implementing effective interventions with the aim of reducing morbidity and mortality associated with the disease.

Reinforcing this hypothesis, after April 2021, the state of Rio Grande do Norte showed a gradual reduction in the number of deaths. This scenario can be attributed to the adoption of more effective control measures, such as the wide distribution of vaccines, awareness and adherence to social distancing, in addition to the emphasis on hygiene care. These strategies played a key role in containing the disease and protecting the population^{30,31}.

In the analyzed period, distinct patterns were observed in the COVID-19 time series in the state of Rio Grande do Norte. In 2020, mortality showed a stationary trend, case fatality showed a decreasing trend and, on the other hand, the incidence was increasing. In 2021, the incidence and mortality assumed a downward trend, and case fatality, stationary, indicating a worsening of the situation. In the year 2022, incidence and case fatality decreased, and mortality remained stationary, which suggests better management of the disease and its spread.

However, throughout the study period, while the incidence of the disease remained stationary, that is, with limited variation over time, both mortality and case fatality showed a decreasing trend, indicating an improvement in response to treatment and in control measures.

The stability of the incidence over the years underscores the need to maintain constant attention in the implementation of appropriate measures to contain the disease and deaths. This highlights the importance of a continuous and careful approach to dealing with COVID-19.

The occurrence of variations in incidence, mortality and case fatality over time frequently occurs in different countries and regions, as was also observed in this study. These patterns are widely observed and have been studied in different contexts^{29,32}.

For Matos (2018)³³, it is essential to carry out constant monitoring of patterns of cyclical variation, taking into account the experience gained with influenza pandemics. Although there is considerable uncertainty, it

is extremely important to seek some predictability from studies already carried out in order to face future pandemic situations.

It is important to emphasize the distinct characteristics of each region, and that the variations in the time series of cases and deaths from COVID-19 differ between locations, not showing a uniform pattern of behavior. In this way, each region and/or country has its own epidemiological characteristics and based on these, specific response measures are developed and adopted^{4,29,32,34}.

According to the findings of a comparative study carried out by Fiocruz Pernambuco, in the North and Northeast regions of Brazil, a significant increase in the incidence rates of COVID-19 was evidenced during two different periods: until mid-April and until mid-May 2020. The rate of acceleration of incidence rates in these regions was considerably higher compared to the rest of the country³⁵.

In this way, the analysis reveals or a displacement of higher incidence of COVID-19 between the Brazilian states of the North and Northeast regions. This change indicates a possible influence of government absences and vulnerability in less favored regions of Brazil³⁵.

The COVID-19 pandemic unequally impacts the most vulnerable populations, including those with the least access to adequate health care, appropriate housing and safe working conditions. Socioeconomic factors and poor living conditions contribute to the spread and increase in cases of the disease^{35,36}.

Therefore, in the context of the state of Rio Grande do Norte, it is relevant to consider socioeconomic factors and precarious living conditions as fundamental explanatory variables³⁷. This approach enables better planning for the implementation of effective disease control and prevention measures, as well as for reducing the impact of the pandemic in this location and in other locations that resemble socioeconomic and epidemiological characteristics^{17,36,37}.

According to the study by Horton (2022)³⁸, the government's approach to dealing with the pandemic is largely based on scientific perspectives and epidemiological data. In this way, the author recommends that health authorities and public authorities develop strategies for the prevention, control and mitigation of COVID-19 guided by the perspective of the pandemic.

This concept encompasses the complex interaction between biological, social, economic and cultural factors that influence the spread and impact of COVID-19. In addition to recognizing that control measures must go beyond just containing the transmission of the virus, but also considering social inequalities and vulnerability, socioeconomic conditions and structural determinants¹⁶.

Social and contextual aspects play a crucial role in the unfolding and behavior of the disease³⁸. It is a context that requires a comprehensive integrated response of public policies, social protection strategies and specific interventions aimed at the most vulnerable populations, such as the populations of the North and Northeast of Brazil^{17,36,37}.

Research on COVID-19 in Brazil and around the world, involving time series analyses, have highlighted the importance of socioeconomic conditions as vulnerability factors^{18,19}, which influence the epidemiological profile of this disease, and have a positive linear correlation with cases and deaths³⁹⁻⁴², corroborating the proposition of Horton et al. (2022)³⁸.

The epidemiological study by Baggio et al. (2021)⁴², on the spatial dynamics of COVID-19 and its relationship with living conditions in the state of Amapá, northern region of Brazil, highlights the highest incidence rates in municipalities with lower HDI and in those with greater social vulnerability. This provides relevant insights to understand the situation of the COVID-19 pandemic in the North and Northeast, and in other locations with unfavorable socioeconomic conditions.

However, the increase in COVID-19 cases in the state of Rio Grande do Norte was lower compared to other Brazilian states located in the North and Northeast regions, which experienced growth in case rates per million inhabitants higher than the national average, during the period from 2020 to 2021. In two of them the increase was almost 50 times in May: Tocantins (49.8) and Sergipe (47.8)²⁹.

Among the states in the North and Northeast regions, case rates per million inhabitants in Alagoas, Pará and Paraíba increased by more than 20 times. Meanwhile, in Roraima, Piauí, Acre, Maranhão, Amazonas and Amapá, there was an increase of more than 10 times, and in Bahia, Roraima, Ceará and Pernambuco, the increase was 9 times. On average, the country has seen a 7-fold increase in case rates per million population. Rio Grande do Norte was the only state below the national value, with 6.6^{32,43,44}.

In addition, Rio Grande do Norte had average mortality and case fatality rates below the regional and national averages. On the other hand, the findings of the multidimensional vulnerability study by the Superintendence of Northeast Development (Sudene) pointed out that the Fortaleza/CE-Mossoró/Rio Grande do Norte axis would be one of the regions most affected by the pandemic in the Northeast⁴⁴.

In the context of the Northeast region of Brazil, the most affected states, in terms of reported cases and mortality per million inhabitants in May 2020, were Ceará, Sergipe and Rio Grande do Norte³⁷. As for the spatial distribution of incidence and mortality, it is observed that the North and Northeast regions have the highest rates⁴⁵. These regions have municipalities with incidence rates 2 to 10 times higher than the Midwest, South and Southeast regions⁴⁴.

The heterogeneity of the disease reinforces the hypothesis that the incidence and mortality from COVID-19 are associated with a combination of geographic, economic, social and cultural factors that reflect the way of life of the population¹⁹. The Northeast, one of the most socioeconomically disadvantaged regions in the country, represents 27% of the Brazilian population and has about a third of all cases (34%) and deaths (32%) of COVID-19. This reinforces the hypothesis that the high mortality rate is related to these conditions⁴⁴.

In Mascarello *et al.*, (2021)¹⁹, 2021, the need for

a comprehensive approach that takes into account social, cultural and geographic determinants when analyzing the incidence and mortality of COVID-19 is highlighted. Understanding and considering these aspects is extremely important to guide the implementation of effective interventions, public policies and social protection strategies, with the aim of mitigating the impact of the disease on vulnerable populations.

It's important to highlight the limitations arising from the study design, which, as it is an ecological study of time series analysis, its focus is restricted to the space-time analysis of time series patterns of incidence, mortality and case fatality of COVID-19 in the state from Rio Grande do Norte, not analyzing the multifactorial context or determining factors of higher or lower mortality and case fatality.

The analysis of secondary data may be limited by the incompleteness or/and lack of detail in the dataset used. We highlight the fact that individual variables such as age, sex and race were not considered, which may restrict the study's conclusions. Furthermore, the number of cases may be greater than that entered in the database, as the number of specific tests for the disease was limited over the three years of the pandemic. However, this study allows a portrait of the three years of evolution of the pandemic in the state of Rio Grande do Norte.

The reduction in the incidence observed in the study does not mean a decrease in the circulation of the SARS-CoV virus, but that its manifestations in the form of the disease COVID-19 are lighter and its symptoms more similar to the flu present in the daily life of the population.

On the other hand, case fatality and mortality are decreasing over the three years of the COVID-19 pandemic and very possibly due to the action of the pharmacological barrier of mass vaccination that occurred in Brazil in the years 2022 and 2023.

At the beginning of the COVID-19 pandemic, in 2020, fighting the pandemic was restricted to non-pharmacological measures. However, these measures were not enough for the health system to adequately care for patients who developed the most severe form of the disease and required hospitalization.

The mass vaccination measures that took place in Brazil in the last two years of the COVID-19 pandemic were the determining factor for reducing case fatality and mortality in the general population, especially in the state of Rio Grande do Norte.

Limitations

One of the limitations is linked to the method used. Because it is an ecological study, it has an ecological fallacy bias. Being a regional study with data inherent to the state of Acre, we cannot make causal inferences outside the analyzed region, including the approach of individual variables.

Another limitation of the work is the underreporting in the database, due to the development of means for identifying the virus, especially at the beginning of the pandemic. In patients affected by COVID-19, there may be errors related to the time of virus identification, which can generate altered values in the confirmed virus status,

resulting in direct changes in the number of cases and, consequently, in the calculated incidence.

CONCLUSION

The COVID-19 pandemic is a major public health problem in the Northeast region of Brazil, more specifically in Rio Grande do Norte. During the three years analyzed, there were significant variations in incidence, mortality and fatality rate.

In addition, an initial increase in the incidence rate was observed in 2020, followed by a significant reduction in 2021 and 2022. Regarding mortality, a downward trend was observed in 2021 and a stationary trend in 2022, with

no notable variation in 2020. As for the case fatality rate, there was a decrease in 2020, with no identification of significant trends in subsequent years.

It is essential to emphasize the importance of continuous monitoring of the pandemic, especially in relation to the development of COVID-19 in later stages based in on epidemiological and scientific data, which remains a major challenge for public health managers.

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Resumo

Introdução: a pandemia de COVID-19, causada pelo coronavírus SARS-CoV-2, tem exercido grande impacto sobre o estado do Rio Grande do Norte, bem como em todo o mundo, constituindo-se um desafio relevante para a saúde pública. Desde sua emergência, a doença propagou-se amplamente, ocasionando uma quantidade expressiva de casos confirmados e óbitos no Estado.

Objetivo: analisar a tendência da incidência, mortalidade e letalidade da COVID-19 no estado do Rio Grande do Norte, situado na região Nordeste do Brasil, entre 2020 e 2022.

Método: consiste em uma análise ecológica de séries temporais de dados secundários retrospectivos em nível populacional. Foram estimadas as taxas de incidência e mortalidade por 100.000 habitantes, assim como a letalidade e a variação percentual diária, ambas expressas em porcentagem. A variação percentual diária foi calculada por meio da técnica de regressão linear generalizada utilizando o método de Prais-Winsten, e serviu para classificar a tendência em crescente, decrescente ou estacionária, considerando um nível de significância de 95%.

Resultados: a análise dos dados mostrou o registro de 582.618 casos e 8.689 óbitos de COVID-19 no estado do Rio Grande do Norte, durante o período de março de 2020 a dezembro de 2022. Houve um aumento inicial na taxa de incidência em 2020, seguido por uma redução significativa em 2021 e 2022. A mortalidade apresentou uma tendência decrescente em 2021 e uma tendência estacionária em 2022, sem variação notável em 2020. A taxa de letalidade diminuiu em 2020, mas não mostrou tendências significativas nos anos seguintes.

Conclusão: a análise epidemiológica da COVID-19 no estado do Rio Grande do Norte revelou variações na incidência, mortalidade e letalidade ao longo do período de estudo. A variação percentual diária no período total da série temporal de incidência foi de movimento estacionário, enquanto da mortalidade e letalidade foram decrescente.

Palavras-chave: COVID-19, pandemia, epidemiologia, incidência, mortalidade, letalidade

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