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ORIGINAL ARTICLE

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.

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Authors summary

Why was this study done?
This study was carried out due to gaps in the scientific literature about the evolution of COVID-19 in the state of Tocantis, northern Brazil, in addition to the need for constant monitoring of epidemiological indicators of incidence, mortality and lethality of COVID-19 in areas inserted in a context of vulnerability as is the case of territory belonging to the Brazilian Legal Amazon.

What did the researchers do and find?
The researchers conducted an ecological study with temporal analysis of the incidence, mortality and lethality rates of COVID-19 in Tocantins from March 2020 to August 2021. The researchers found the formation characteristic of two possible waves of COVID-19 in Tocantins; it was during the second wave that the state recorded the highest rates of incidence, lethality and mortality. However, at the end of August 2021 the incidence, mortality and lethality rates showed flat trends suggesting a positive outcome of the vaccination program.

What do these findings mean?
Efforts are still needed to decrease lethality, mortality, and incidence trends in order to reach the control of the COVID-19 pandemic in the Tocantins.

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]

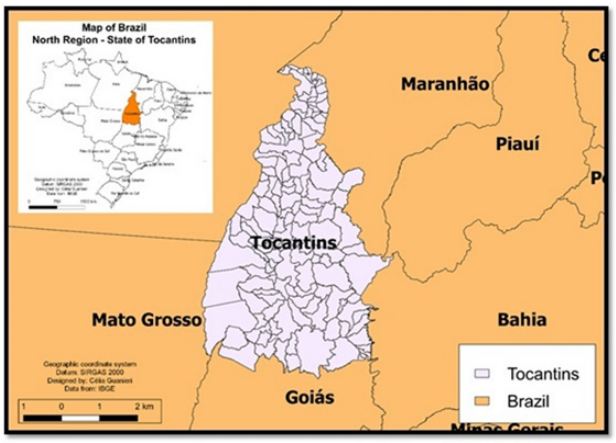

Figure 1: Map of Tocantins and its location in the Brazilian territory.

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:

$$(1)\ \text{Incidence} = \frac{\text{(number of cases)}}{\text{population}} \times 100.000$$

$$(2)\ \text{Mortality} = \frac{\text{(number of deaths)}}{\text{population}} \times 100.000$$

$$(3)\ \text{Case-fatality} = \frac{\text{(number of deaths)}}{\text{(number of cases)}} \times 100$$

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 trends[15]. Probability (p) and Daily Percent Change (DPC) were estimated 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.

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 package[16], 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).

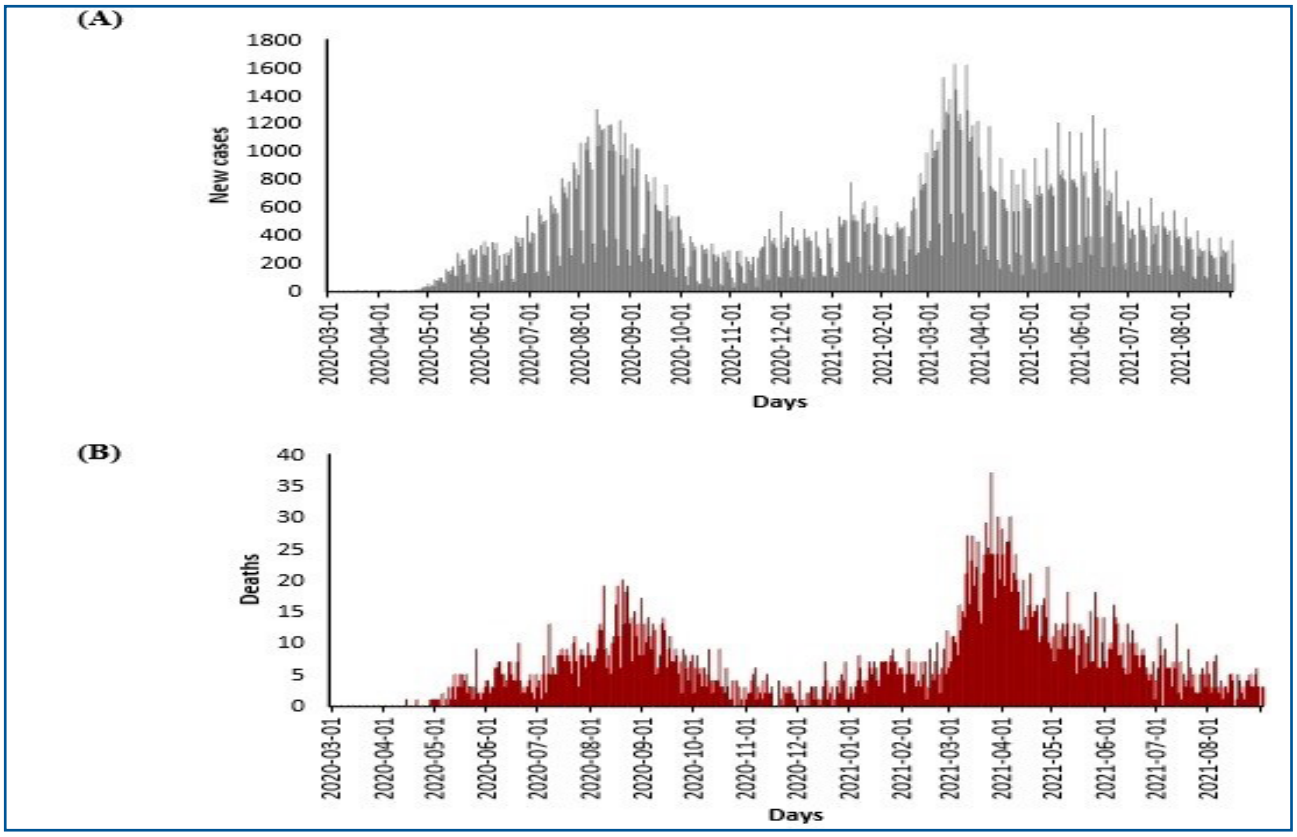

Figure 2: Number of new cases (a) and deaths (b) daily and by COVID-19 in the State of Tocan-tins from March 2020 to August 2021.

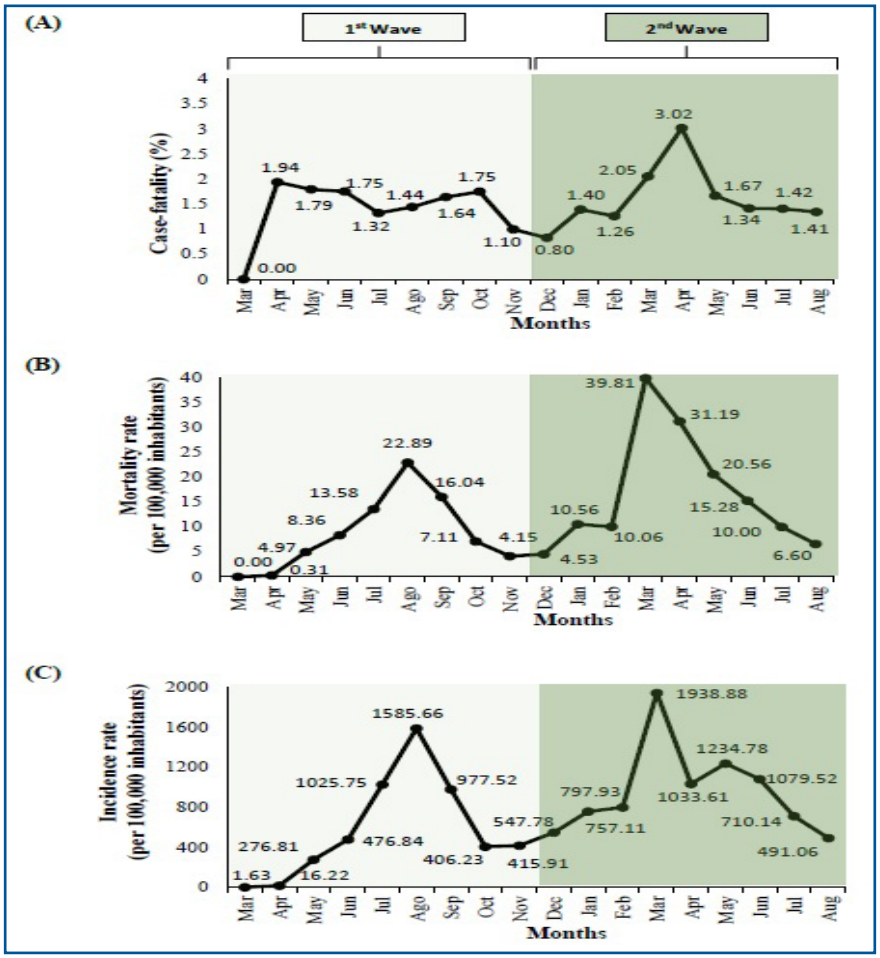

Figure 3: Gross rates of case-fatality percentage (a), mortality (b), and incidence rates (c) by 100,000 inhabitants of COVID-19 in Tocantins state from March 2020 to August 2021.

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.

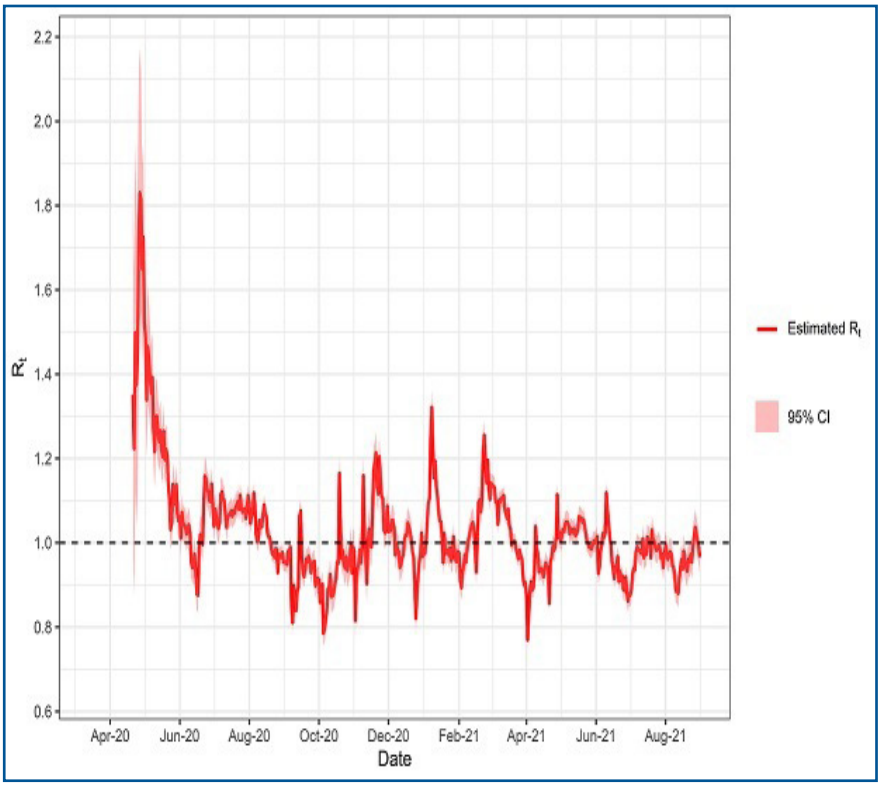

Figure 4: Effective Reproduction Number (Rt) estimated of COVID-19 during April 14, 2020, to August 31, 2021, Tocantins, Brazil.

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 $\rho \cong 0$. 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 $\rho = 0.026$ 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, $\rho = -0.246$ 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 non-essential 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 rates[29]. 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/km2[6]. 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.

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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 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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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.