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ORIGINAL ARTICLE

Deaths due to COVID-19 in a state of northeastern Brazil: spatiotemporal distribution, sociodemographic and clinical and operational characteristics

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Background: The detection of spatiotemporal clusters of deaths by coronavirus disease 2019 (COVID-19) is essential for health systems and services, as it contributes to the allocation of resources and helps in effective decision making aimed at disease control and surveillance. Thus we aim to analyse the spatiotemporal distribution and describe sociodemographic and clinical and operational characteristics of COVID-19-related deaths in a Brazilian state.
Methods: A descriptive and ecological study was carried out in the state of Maranhão. The study population consisted of deaths by COVID-19 in the period from 29 March to 31 July 2020. The detection of spatiotemporal clusters was performed by spatiotemporal scan analysis.
Results: A total of 3001 deaths were analysed with an average age of 69 y, predominantly in males, of brown ethnicity, with arterial hypertension and diabetes, diagnosed mainly by reverse transcription polymerase chain reaction in public laboratories. The crude mortality rates the municipalities ranged from 0.00 to 102.24 deaths per 100 000 inhabitants and three spatiotemporal clusters of high relative risk were detected, with a mortality rate ranging from 20.25 to 91.49 deaths per 100 000 inhabitants per month. The headquarters was the metropolitan region of São Luís and municipalities with better socio-economic and health development.
Conclusions: The heterogeneous spatiotemporal distribution and the sociodemographic and clinical and operational characteristics of deaths by COVID-19 point to the need for interventions.

Keywords: coronavirus infections, COVID-19, epidemiology, mortality, spatiotemporal analysis

Introduction

The public health emergency caused by coronavirus disease 2019 (COVID-19) led the World Health Organization (WHO) to declare a pandemic situation on 11 March 2020.[1,2] Information released by the WHO on 10 January 2021 reported 88 828 387 confirmed cases of COVID-19 and 1 926 625 deaths worldwide.[3]

The first case of COVID-19 in Brazil was registered on 26 February 2020, and the first death was confirmed on 12 March 2020, in the city of São Paulo. After more than 10 months of the declared pandemic, Brazil ranked third in the number of cases (7 716 405), behind the USA (20 426 184) and India (10 323 965) and remains in second place for the absolute number of deaths, with 195 725, while the USA and India registered 350 186 and 149 435 deaths, respectively.[4]

Due to the extensive continental area and the economic, social and cultural diversity of Brazil, the impacts of COVID-19 in terms of morbidity and mortality may have a heterogeneous distribution.[5] The challenges may be even greater for the Brazilian public health system, considering the lack of knowledge about the transmissibility of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). Also, the great social inequality, problems related to housing and sanitation and the large

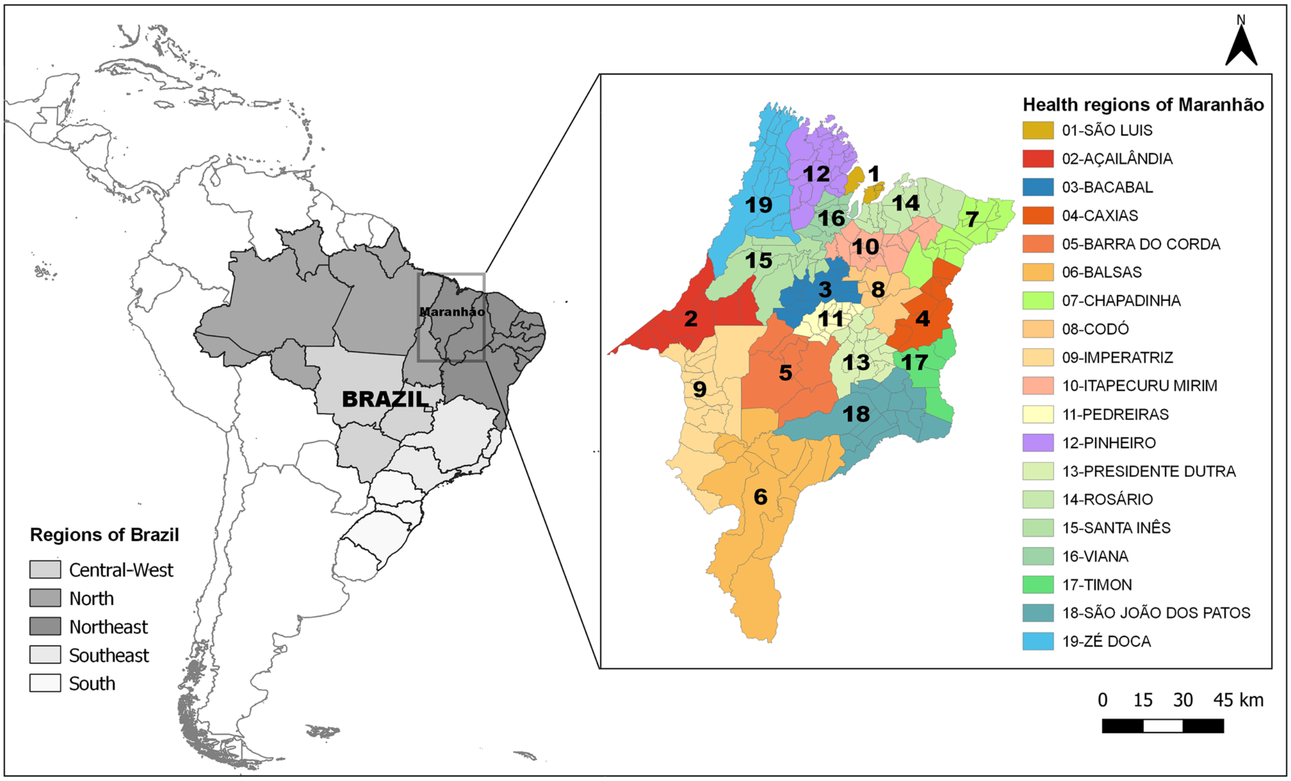

Figure 1. Map of the state of Maranhão, Brazil, highlighting the health regions. Source: Adapted from geographical databases.[14]

number of people living in crowded households make it even more difficult to control COVID-19 cases and deaths.[6]

In Brazil, at the beginning of the pandemic, of the 10 states with the highest mortality rates, 6 were from the Northeast Region, including Maranhão (6.10%).[5] In order to reduce the impacts and prevent the collapse of health services, Maranhão adopted measures to contain SARS-CoV-2, including the lockdown of all non-essential activities.[7] Measures like this proved to be effective in four Brazilian capitals, including São Luís (capital of Maranhão), where lockdown led to a 37.85% reduction in daily deaths due to COVID-19.[8] Despite this, Maranhão remained prominent among the other federal units, with an increase in COVID-19 morbidity and mortality indicators.[9]

Faced with this challenging pandemic scenario of high transmissibility, and potential aggravating complications and deaths due to COVID-19, geoprocessing is an alternative for analysing the spatiotemporal distribution of deaths from diseases, contributing to the development of strategies to control SARS-CoV-2 and future health crises.[10] Spatiotemporal analysis through scanning studies, also known as scan statistics, has aided in the identification of spatial and temporal clusters of events and health problems.[11]

Studies aimed at detecting COVID-19 spatiotemporal death clusters are essential for health systems and services since their findings can contribute to a better allocation of resources and assist in the implementation of effective decisions aimed at disease control and surveillance.[12] From this perspective, there is a need for investigations that can be used to support strategies against COVID-19,[13] especially considering the scarcity of studies with spatiotemporal analysis of deaths related to this disease in Brazil.

Thus our aim was to analyse the spatiotemporal distribution and describe sociodemographic and clinical and operational characteristics of COVID-19-related deaths in the state of Maranhão, Brazil.

Methods

Study design and location

A descriptive and ecological study was carried out in the state of Maranhão (Figure 1), which has 217 municipalities distributed in 19 health regions (Table 1). It occupies an area of 329 642 182 km^2, with an estimated population of 7 114 598 for the year 2020 and borders the Atlantic Ocean to the north, the state of Piauí to the east, the state of Tocantins to the south and southwest and the state of Pará to the west.[14]

Study population and data collection

The study population consisted of COVID-19-related deaths in Maranhão from 29 March 2020 (date of the first death caused by the disease in the state) to 31 July 2020. Records of patients living in Maranhão who died due to COVID-19 were included, while

Table 1. Distribution of municipalities by health regions, Maranhão, Brazil. Source: Department of Health of the State of Maranhão – Health Regions Coordination

Health region	Code-municipality
01-São Luis	M1-Alcântara, M2-Paço do Lumiar, M3-Raposa, M4-São José de Ribamar, M5-São Luís
02-Açailandia	M6-Açailândia, M7-Bom Jesus das Selvas, M8-Buriticupu, M9-Cidelândia, M10-Itinga do Maranhão, M11-São Francisco do Brejão, M12-São Pedro da Água Branca, M13-Vila Nova dos Martírios
03-Bacabal	M14-Altamira do Maranhão, M15-Bacabal, M16-Bom Lugar, M17-Brejo de Areia, M18-Conceição do Lago-Açu, M19-Lago Verde, M20-Marajá do Sena, M21-Olho d'Água das Cunhãs, M22-Paulo Ramos, M23-São Luís Gonzaga do Maranhão, M24-Vitorino Freire
04-Caxias	M25-Afonso Cunha, M26-Aldeias Altas, M27-Buriti, M28-Caxias, M29-Coelho Neto, M30-Duque Bacelar, M31-São João do Soter
05-Barra Do Corda	M32-Arame, M33-Barra do Corda, M34-Fernando Falcão, M35-Grajaú, M36-Itaipava do Grajaú, M37-Jenipapo dos Vieiras
06-Balsas	M38-Alto Parnaíba, M39-Balsas, M40-Feira Nova do Maranhão, M41-Formosa da Serra Negra, M42-Fortaleza dos Nogueiras, M43-Loreto, M44-Nova Colinas, M45-Riachão, M46-Sambaíba, M47-São Félix de Balsas, M48-São Pedro dos Crentes, M49-São Raimundo das Mangabeiras, M50-Tasso Fragoso
07-Chapadinha	M51-Água Doce do Maranhão, M52-Anapurus, M53-Araioses, M54-Brejo, M55-Chapadinha, M56-Magalhães de Almeida, M57-Mata Roma, M58-Milagres do Maranhão, M59-Paulino Neves, M60-Santa Quitéria do Maranhão, M61-Santana do Maranhão, M62-São Bernardo, M63-Tutóia
08-Codo	M64-Alto Alegre do Maranhão, M65-Codó, M66-Coroatá, M67-Peritoró, M68-São Mateus do Maranhão, M69-Timbiras
09-Imperatriz	M70-Amarante do Maranhão, M71-Buritirana, M72-Campestre do Maranhão, M73-Davinópolis, M74-Estreito, M75-Governador Edison Lobão, M76-Imperatriz, M77-João Lisboa, M78-Lajeado Novo, M79-Montes Altos, M80-Porto Franco, M81-Ribamar Fiquene, M82-São João do Paraíso, M83-Senador La Rocque, M84-Sítio Novo, M85-Carolina
10-Itapecuru Mirim	M86-Anajatuba, M87-Arari, M88-Belágua, M89-Cantanhede, M90-Itapecuru Mirim, M91-Matões do Norte, M92-Miranda do Norte, M93-Nina Rodrigues, M94-Pirapemas, M95-Presidente Vargas, M96-São Benedito do Rio Preto, M97-Urbano Santos, M98-Vargem Grande, M99-Vitória do Mearim
11-Pedreiras	M100-Bernardo do Mearim, M101-Esperantinópolis, M102-Igarapé Grande, M103-Lago da Pedra, M104-Lago do Junco, M105-Lago dos Rodrigues, M106-Lagoa Grande do Maranhão, M107-Lima Campos, M108-Pedreiras, M109-Poção de Pedras, M110-São Raimundo do Doca Bezerra, M111-São Roberto, M112-Trizidela do Vale
12-Pinheiro	M113-Apicum-Açu, M114-Bacuri, M115-Bequimão, M116-Cedral, M117-Central do Maranhão, M118-Cururupu, M119-Guimarães, M120-Mirinzal, M121-Pedro do Rosário, M122-Peri Mirim, M123-Pinheiro, M124-Porto Rico do Maranhão, M125-Presidente Sarney, M126-Santa Helena, M127-Serrano do Maranhão, M128-Turiaçu, M129-Turilândia
13-Presidente Dutra	M130-Capinzal do Norte, M131-Dom Pedro, M132-Fortuna, M133-Gonçalves Dias, M134-Governador Archer, M135-Governador Eugênio Barros, M136-Governador Luiz Rocha, M137-Graça Aranha, M138-Joselândia, M139-Presidente Dutra, M140-Santa Filomena do Maranhão, M141-Santo Antônio dos Lopes, M142-São Domingos do Maranhão, M143-São José dos Basílios, M144-Senador Alexandre Costa, M145-Tuntum
14-Rosário	M146-Axixá, M147-Bacabeira, M148-Barreirinhas, M149-Cachoeira Grande, M150-Humberto de Campos, M151-Icatu, M152-Morros, M153-Presidente Juscelino, M154-Primeira Cruz, M155-Rosário, M156-Santa Rita, M157-Santo Amaro do Maranhão
15-Santa Ines	M158-Alto Alegre do Pindaré, M159-Bela Vista do Maranhão, M160-Bom Jardim, M161-Governador Newton Bello, M162-Igarapé do Meio, M163-Monção, M164-Pindaré-Mirim, M165-Pio XII, M166-Santa Inês, M167-Santa Luzia, M168-São João do Carú, M169-Satubinha, M170-Tufilândia
16-Viana	M171-Bacurituba, M172-Cajapió, M173-Cajari, M174-Matinha, M175-Olinda Nova do Maranhão, M176-Palmeirândia, M177-Penalva, M178-São Bento, M179-São João Batista, M180-São Vicente Ferrer, M181-Viana
17-Timon	M182-Matões, M183-Parnarama, M184-São Francisco do Maranhão, M185-Timon
18-São Joao Dos Patos	M186-Barão de Grajaú, M187-Benedito Leite, M188-Buriti Bravo, M189-Colinas, M190-Jatobá, M191-Lagoa do Mato, M192-Mirador, M193-Nova Iorque, M194-Paraibano, M195-Passagem Franca, M196-Pastos Bons, M197-São Domingos do Azeitão, M198-São João dos Patos, M199-Sucupira do Norte, M200-Sucupira do Riachão
19-Ze Doca	M201-Amapá do Maranhão, M202-Araguanã, M203-Boa Vista do Gurupi, M204-Cândido Mendes, M205-Carutapera, M206-Centro do Guilherme, M207-Centro Novo do Maranhão, M208-Godofredo Viana, M209-Governador Nunes Freire, M210-Junco do Maranhão, M211-Luís Domingues, M212-Maracaçumé, M213-Maranhãozinho, M214-Nova Olinda do Maranhão, M215-Presidente Médici, M216-Santa Luzia do Paruá, M217-Zé Doca

those with incomplete information (such as date of notification) and registers of deaths outside the study period were excluded.

The data referring to deaths due to COVID-19 were obtained from the website of the State Department of Health of Maranhão (SES/MA) through an open data spreadsheet accessed on 5 August 2020.[9]

Study protocol and data analysis

The sociodemographic and clinical and operational variables of interest included the date of notification, municipality of occurrence, age, gender, ethnicity, institution of occurrence, type of diagnostic test performed, laboratory that performed the test and comorbidities. Continuous variables were analysed descriptively (minimum and maximum, median, mean and standard deviation [SD]) and categorized into age groups (0–19, 20–59 and ≥60 y). Also, absolute and relative values of the categorical variables were calculated.

A spatial analysis by area was performed, using the municipalities of the state of Maranhão as an ecological analysis unit to obtain the crude mortality rates due to COVID-19 at each municipality in the analysed period. Thus the occurrence of total deaths in each municipality was considered, divided by the estimated population and multiplied by the constant 100 000.[15]

For the detection of spatiotemporal clusters of deaths by COVID-19, the municipalities of the state of Maranhão were used as spatial units of representation and ecological analysis. For that, a spatial scan analysis was performed (scan statistics)[16] using SaTScan 9.4 software (https://www.satscan.org/). In this analysis, a single point is established within the polygon, called the centroid, to which the information of a given area is associated, aiming to identify the relative risk (RR) calculated for each statistically significant cluster identified.[17] The null hypothesis (H0) established was the absence of death clusters by COVID-19 in the municipalities of Maranhão, while the alternative hypothesis (H1) was that region Z would be a death cluster for COVID-19.

The Poisson model was used, which requires specific conditions, such as the non-geographical overlap of clusters, the maximum size of the temporal cluster equal to 50% of the study period, accuracy of time (day, month and year), the period between 29 March 2020 and 31 July 2020 and 999 replications. Furthermore, the spatiotemporal scan was performed by controlling for the occurrence of deaths by the municipalities' population size, age distribution and gender to detect clusters of high and low RR.

The detection of statistically significant clusters ($p<0.005$) was based on the comparison between the likelihood ratio test statistics against a null distribution, according to the Monte Carlo method.[16] A retrospective method of analysis was used, thus allowing the identification of conglomerates that persisted not only until the end of the period, but also those that ceased to exist before the end of the period.

The crude mortality rate due to COVID-19 of the identified spatiotemporal clusters was determined for every 100 000 inhabitants, considering all reported deaths by the population of each cluster and detection period, according to population data from the Brazilian Institute of Geography and Statistics.[18] All thematic maps were constructed using the ArcGIS 10.5 program (Esri, Redlands, CA, USA).

Results

In the period between 29 March and 31 July 2020, 3032 deaths caused by COVID-19 were registered in Maranhão, of which 20 were excluded due to incomplete information (such as date of notification) and 11 because they were outside the study period, for a total of 3001 deaths. In 35 of the 217 municipalities of Maranhão, no deaths related to COVID-19 were recorded, and São Luís and Imperatriz had the highest number of deaths (1128 and 225, respectively) in the investigation period.

The mortality rates due to COVID-19 ranged from 0.00 to 102.24 deaths per 100 000 inhabitants, denoting a heterogeneous spatial distribution of the event under investigation, with higher rates dispersed among the municipalities linked to the health regions of Açailândia, Bacabal, Caxias, Chapadinha, Imperatriz, Pedreiras, Pinheiros, Santa Inês, São João dos Patos, São Luís, Timon and Zé Doca (Figure 2).

The average age of individuals who died was 69 y (SD 15) and the median was 71 y. Deaths were recorded in individuals from 1 to 112 y of age.

Table 2 describes the sociodemographic and clinical and operational characteristics of individuals who died due to COVID-19 in the municipalities studied. Most deaths occurred in male individuals (1843 [61.41%]), ≥60 y of age (2354 [78.45%]) and of brown ethnicity (1487 [49.55%]). Regarding the clinical and operational characteristics, it was observed that most were recorded in public institutions (2339 [77.94%]).

Regarding the diagnosis of COVID-19 infection, most cases were diagnosed using reverse transcription polymerase chain reaction (RT-PCR; 1667 [55.55%]) followed by the rapid test (1332 [44%]). Most of the tests conducted to confirm COVID-19 were carried out in public institutions (2778 [92.57%]). As for comorbidities, systemic arterial hypertension (1670 [55.65%]) and diabetes mellitus (1159 [38.62%]) were most common, while 466 (15.53%) patients who died did not have comorbidities. It is also important to note that a number of deaths occurred in subjects having other conditions, such as smokers (91 [3.03%]), and the high number (697 [23.22%]) without ethnicity data.

As for the spatiotemporal scan analysis, three statistically significant clusters ($p<0.001$) of deaths due to COVID-19 were detected, controlled for age, gender and population size in each municipality of Maranhão. Characteristics such as detection period, number of municipalities, number of deaths, population, RR and 95% confidence interval (CI), mortality rate (deaths per 100 000 inhabitants per month) and municipalities in the observed spatiotemporal clusters are shown in Table 3. It was also observed that the spatiotemporal clusters had mortality rates ranging from 20.25 to 91.49 deaths per 100 000 inhabitants per month.

Regarding the spatiotemporal death clusters identified, the lowest RR (2.15) was observed in cluster 1, detected between 1 June 2020 and 30 July 2020, involving three municipalities in the Timon and Caxias regions.

Cluster 2, detected between 1 May 2020 and 30 June 2020, comprised 28 municipalities of the Imperatriz, Açailândia, Bacabal, Barra do Corda, Tufilândia and Zé Doca regions (RR 2.93). Cluster 3, detected between 1 April 2020 and 31 May 2020, with four municipalities belonging to the health region of São Luís, had 1198 deaths (RR 8.89) (Figure 3).

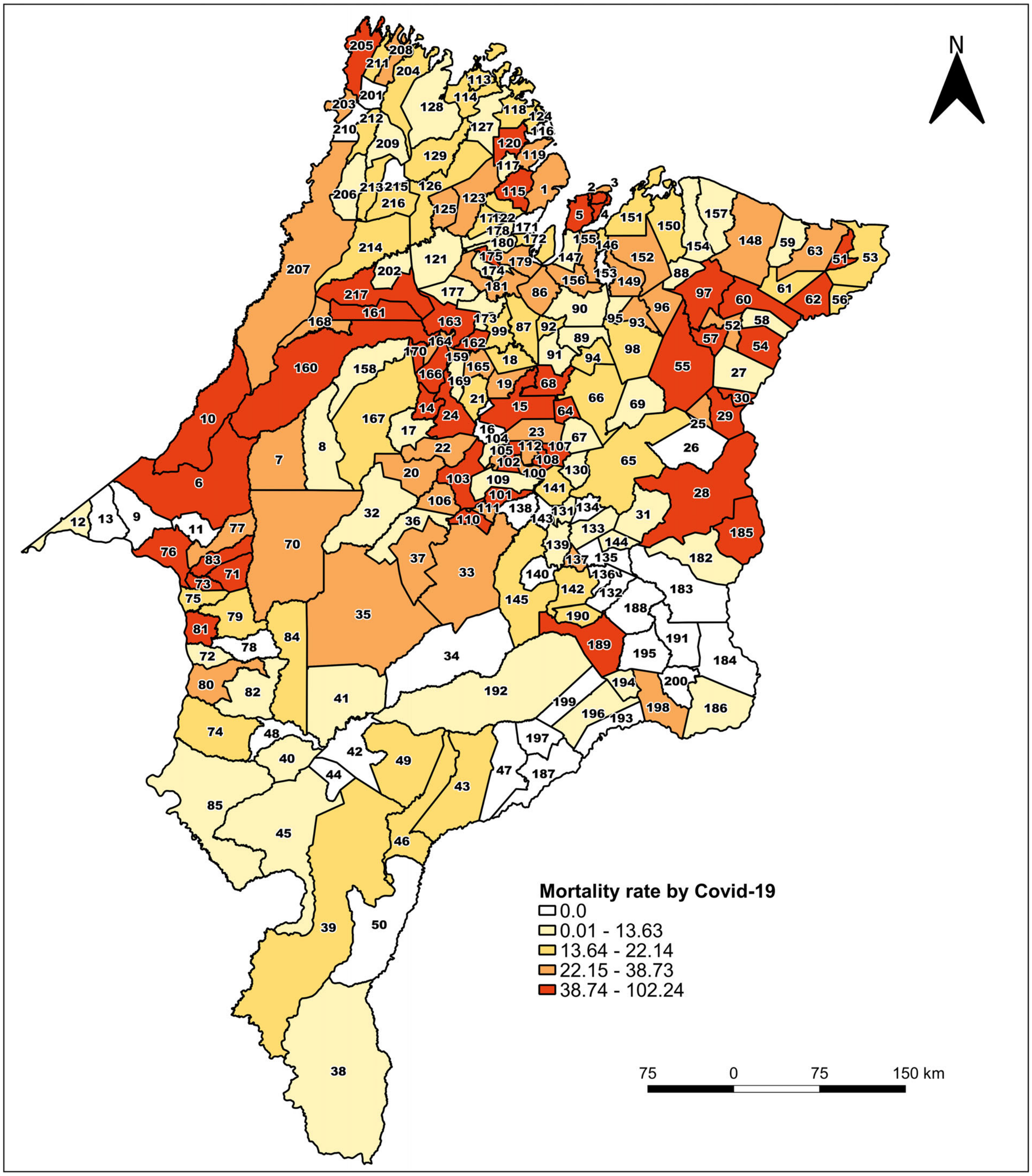

Figure 2. Spatial distribution of crude mortality rates due to COVID-19 by municipalities in Maranhão, Brazil, 29 March–31 July 2020.

The clusters occurred in different regions of the state, with emphasis on cluster 2, which was the largest in number of municipalities, located in the west of Maranhão, where Imperatriz is located, the city with the highest number of deaths. Cluster 3 was in the north of the state and included the city of São Luís, the capital of the state, while cluster 1 was in the east of the state.

Discussion

The Geographic Information System (GIS) can be used to map diseases using various parameters, including demographic data, propagation patterns and intensity.[19] In this study, the GIS was used to understand the behaviour of COVID-19, particularly concerning deaths, and to analyse the spatiotemporal

Table 2. Sociodemographic and clinical and operational characteristics of deaths due to COVID-19 in Maranhão, Brazil, 29 March–31 July 2020

Variables	n (%)
Age (years)	
0–19	31 (1.03)
20–59	616 (20.52)
≥60	2354 (78.45)
Gender	
Male	1843 (61.41)
Female	1158 (38.59)
Ethnicity	
Brown	1487 (49.55)
White	367 (12.23)
Yellow	240 (8.00)
Black	199 (6.63)
Indigenous	11 (0.37)
Unknown	697 (23.22)
Institution of death occurrence	
Public	2339 (77.94)
Private	328 (10.93)
Unknown	334 (11.13)
Diagnostic test type	
RT-PCR	1667 (55.55)
Rapid test	1332 (44.38)
Serology	2 (0.07)
Laboratory conducting the test	
Public	2778 (92.57)
Private	220 (7.33)
Unknown	3 (0.10)
Comorbidity[a]	
Systemic arterial hypertension	1670 (55.65)
Diabetes mellitus	1159 (38.62)
Cardiac diseases	374 (12.46)
Urologic diseases	190 (6.33)
Kidney diseases	174 (5.80)
Respiratory diseases	143 (4.77)
Obesity	129 (4.30)
Oncologic diseases	114 (3.80)
Other	301 (10.03)
No comorbidities	466 (15.53)
Other conditions	
Smoking	91 (3.03)
Psychiatric disorders	16 (0.53)
Postpartum	11 (0.37)
Pregnancy	4 (0.13)
Total	3001 (100.00)

[a]The same patient may have had more than one comorbidity.

distribution of these deaths. Furthermore, this study investigated the sociodemographic and clinical and operational characteristics of COVID-19-related deaths, including factors such as age, comorbidities and lifestyle, which are known to influence lethality.[20]

The results showed that the average age of the analysed death cases was 69 y, with a predominance of males and brown ethnicity. Arterial hypertension and diabetes mellitus were the most common comorbidities, while smoking was the most common risk factor observed. These data were similar to those of a study on the epidemiological profile of SARS-CoV-2 notifications, which also found a predominance of males, age ≥60 y and comorbidities.[13]

A study carried out in China suggests that male gender is a risk factor that contributes to more severe cases and mortality due to COVID-19, regardless of age. The authors reiterate that this fact is not restricted to COVID-19 and applies to many other diseases, which may be correlated with demographic issues and the lower life expectancy of men compared with women.[21] This finding may also be related to sociocultural issues, since men are less likely than women to seek medical care when they are ill and are usually less concerned with hygiene and thus tend to become more critically ill from diseases (especially chronic ones).[22]

It should be noted that associated morbidities contribute significantly to the increase in severe COVID-19 cases and mortality, especially when added to another risk factor, such as advanced age. A study conducted in Brazil found that the accumulated incidence and mortality in the elderly population are related to demographic issues, such as age, ethnicity and income, highlighting the indispensability of care and the specific monitoring of elderly persons. The authors also pointed out that immunosenescence increases the vulnerability to infectious diseases and makes the prognosis of chronic degenerative diseases significantly worse.[23]

In this investigation, deaths were predominant in people of brown ethnicity, a socio-economic determinant that reflects inequalities in health conditions. This ethnic group has been vulnerable to COVID-19 in Brazil, representing more than half of the Brazilian population. Also, this group is predominant among the urban periphery residents, homeless individuals, subjects with specific morbidities like diabetes and hypertension and people with less access to health services.[23,24]

Advanced age, male gender, brown ethnicity and comorbidities, especially diabetes and hypertension, identified in the state of Maranhão are also the main risk factors pointed out in other studies as indicators of COVID-19 severity.[20,22,25] Although not investigated in this series, such conditions, associated with fear of SARS-CoV-2 infection at the beginning of the pandemic, may have led people at greater risk to stop seeking medical attention, increasing health risks in the face of the symptoms of the disease.

As for the clinical and operational characteristics, it was observed that 77.94% of deaths due to COVID-19 in Maranhão occurred in public institutions. In Brazil, about 75% of the population depends exclusively on the public health system.[26] Consequently, during the COVID-19 pandemic, these institutions received more patients than usual and had a higher number of deaths than private institutions.

As for laboratory tests, RT-PCR and rapid tests were the most used to assist in diagnosis, mostly performed in public laboratories used by the Ministry of Health to detect cases of COVID-19 in Brazil.

The RT-PCR test is considered the gold standard for the diagnosis of SARS-CoV-2 in patients with clinical symptoms and in the acute phase of the disease. In contrast, the rapid test identifies

Table 3. Characterization of spatiotemporal clusters of deaths due to COVID-19 adjusted for the municipalities' population and by gender and age distribution, Maranhão, Brazil, 29 March–31 July 2020

Spatiotemporal clusters and detection period	Cities (n)	Deaths (n)	Population (inhabitants)	RR (95% CI)	Mortality rate (deaths per 100 000 inhabitants per month)	p-Value	Municipalities
1 (1 June 2020–30 July 2020)	3	87	429 544	2.15 (1.01 to 3.17)	20.25	<0.001	Timon[a], M28 and M29
2 (1 May 2020–30 June 2020)	28	544	1 199 601	2.93 (1.12 to 4.99)	45.34	<0.001	Imperatriz[a], M6, M7, M8, M10, M11, M14, M17, M20, M22, M24, M32, M35, M70, 71, M73, M75, M77, M81, M83, M158, M160, M161, M166, M167, M168M M170 and M217
3 (1 April 2020–31 May 2020)	4	1198	1 309 330	8.89 (4.12 to 11.34)	91.49	<0.001	São Luís[a], M2, M3 and M4

[a]Municipality with the highest number of deaths in the cluster.

the presence of antibodies and, in general, plays an important role when used in hospitalized individuals from day 7 of symptom onset. It is worth noting that the barriers encountered, both due to the lack of tests and the delay in processing these tests, may have contributed to the increase in disease transmission, making early diagnosis and disease control difficult.[27] Regarding the spatial scan analysis, the identified clusters presented a heterogeneous distribution of deaths from the disease in the municipalities of Maranhão, with an increased risk of death due to COVID-19. Such findings are consistent with other studies regarding the heterogeneity of the impact of COVID-19 in Brazil.[5,28]

The results of this study revealed mortality rates due to COVID-19 distributed in a heterogeneous, non-random manner, ranging from 0.00 to 102.24 deaths per 100 000 inhabitants in the municipalities of Maranhão. Such variation may be associated with socio-economic inequalities, given that poverty results in the worsening of respiratory diseases, especially due to the difficulty of access to health services during the pandemic.[29]

Compared with other states in the north and northeast of the country, the mortality rates found in the different municipalities of Maranhão become even more worrying, considering the uncertainty surrounding virus transmission in a context of social and demographic inequalities, with populations living in precarious conditions of sanitation and housing, restricted access to water, agglomerated and with a high prevalence of chronic diseases.[30] Therefore interventions aimed at the social protection of low-income individuals through income preservation policies that support social isolation and expanding the number of beds in the public health system are needed.[29]

This study showed that the spatiotemporal distribution of deaths involved municipalities in the north, east, west and centre of Maranhão. Two of the clusters identified, although located in different regions of Maranhão, had in common the fact that they bordered on other states, which could be indicative of an area with increased risk for COVID-19, as issues related to the increased flow of people and vehicles can influence the spread of SARS-CoV-2.[31]

The municipality of Imperatriz, as well as São Luís, the capital of Maranhão, may have the highest number of deaths due to COVID-19 among the municipalities in cluster 2 because of the economic growth that, in recent years, has been driving new activities, attracting more industries and people to these cities.[32] Cluster 1 included the municipality of Timon, located in a region close to the city of Teresina (capital of Piauí), with which it has a strong social and economic relationship.[14]

Cluster 3, with the highest risk of death, located in the north of the state, included the municipalities of São Luís, São José de Ribamar, Paço do Lumiar and Raposa. The capital, São Luís, which has ports, airports, highways and railways, accounts for an important flow of people entering and leaving the state. Furthermore, it was observed that cluster 3 accounted for the largest number of deaths due to COVID-19. Similar results were presented in a study carried out in Maranhão at the beginning of the pandemic, in which the municipality of São Luís had the highest mortality for the period (81 deaths).[13]

The municipalities that presented the highest mortality rates due to COVID-19 are composed of municipalities linked to industrial and commercial activities and concentrations of road junctions, characteristics of regions where the risk of contamination is increased.[28] Also, cities with $\geq$100 000 inhabitants (like some of the detected clusters) are usually characterized by large sociospatial discrepancies and high demographic densities that, in addition to verticalization, transport networks, the growth of favelas and absent or precarious water and sewage networks, make them fertile ground for the dissemination of COVID-19.[17]

Besides the factors presented above, these cities have referral hospitals and are considered macroregions of the healthcare

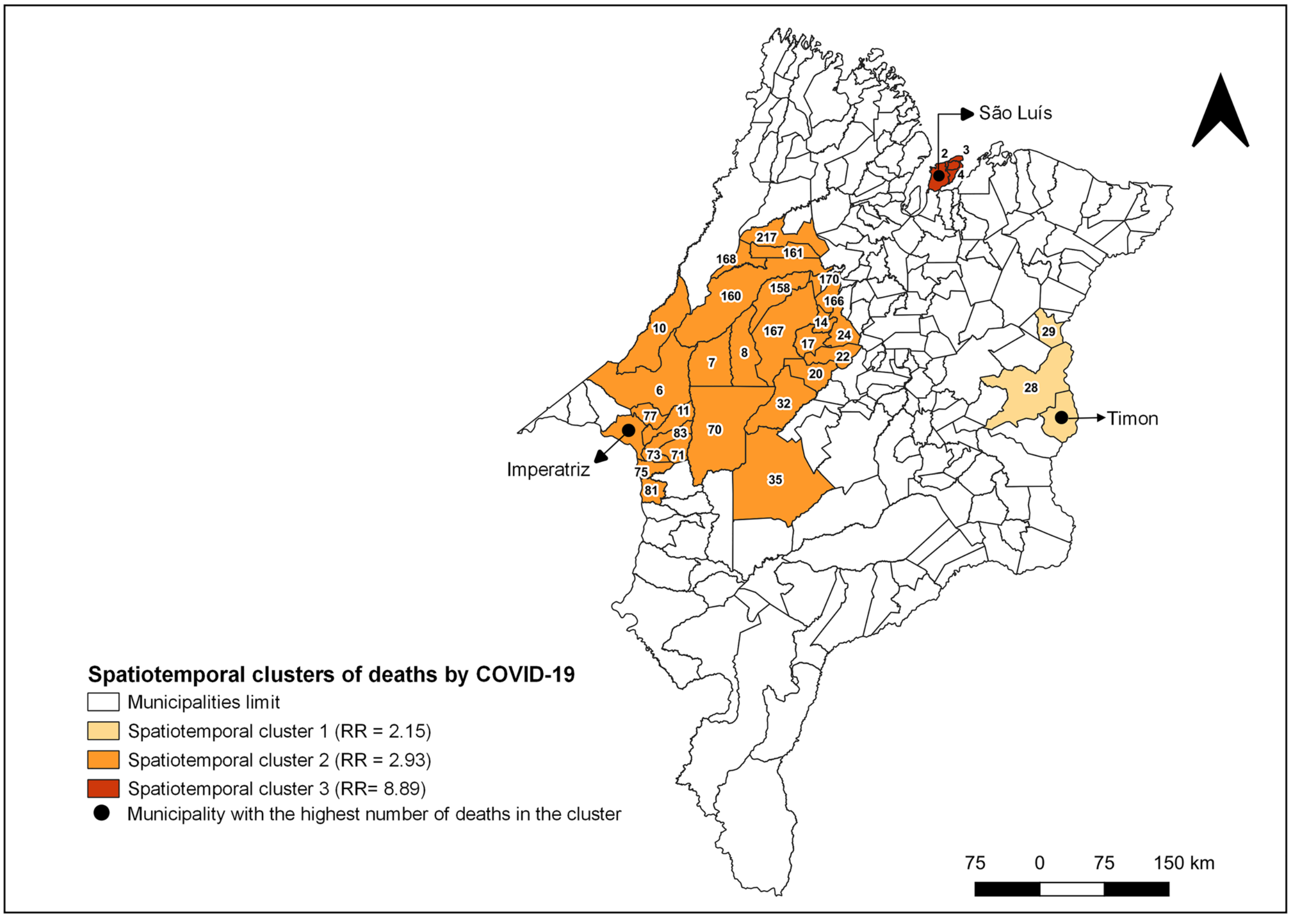

Figure 3. Spatiotemporal clusters of deaths due to COVID-19, adjusted for the populations of the municipalities and their distribution by sex and age, Maranhão, Brazil, 29 March–31 July 2020.

system. Therefore, the increased risk of contamination in such cities, along with the burden on hospitals, may have contributed to higher mortality rates in these regions. One study points out that the health regions with the highest mortality rates are located in places where there is a shortage of intensive care unit beds and ventilators, especially in the northeast of Brazil and Maranhão, including the city of São Luís.[33]

It is also worth mentioning that Maranhão had an increase in the mortality rate from the beginning of the pandemic until 7 July 2020, from 8.48 to 323.10 per million inhabitants—an increase of 28.68%.[34]

Regarding the spatiotemporal clusters of mortality, the highest rate was found in cluster 3 (91.49 per 100 000 inhabitants) in São Luís (metropolitan region), from 1 April to 31 May 2020, the first months of the pandemic. These findings corroborate those of another study showing that metropolitan areas in the USA had incidence and mortalities rates greater than those of smaller and non-metropolitan areas.[35]

Similarly, a study carried out in Brazil identified higher mortality rates due to COVID-19 in the capitals of the Brazilian states compared with other municipalities,[36] pointing to a greater risk of illness and death in groups living in metropolitan regions.[24] Another study evaluated the distribution of deaths due to COVID-19 in the period from March to April 2020 and has also found that the city of São Luís had the highest number of deaths.[13]

The spatiotemporal distribution of mortality also reflects the so-called COVID-19 interiorization process, since clusters 1 and 2, represented by Timon and Imperatriz Timon, occurred from May to June 2020 and June to July 2020, respectively. Therefore it followed the diffusion process in Brazil, which occurred primarily in the capitals and areas of greatest development and with the greatest flow of people.[37]

The spatial dissemination of COVID-19 to municipalities in the countryside has become a problem, as these regions are deprived of better social and health conditions. Factors such as a tendency to reduce social isolation, demand for clinical beds and few intensive care beds may have contributed to a high mortality rate in these periods and regions.[37]

This study has the limitations of using secondary data provided by SES/MA. The absence of some information in the registries was observed, such as the date of notification and the possibility of underreporting due to low testing of the state's population in the period investigated. Regarding ecological studies, the 'ecological fallacy' is observed, a limitation that occurs when it is not possible to consider statements at a more aggregated level to be valid at a disaggregated level.[15]

Although the results presented about deaths due to COVID-19 in the initial periods of the pandemic in this region of Brazil are preliminary, such findings can effectively contribute to the identification of areas and spatiotemporal clusters vulnerable to the occurrence of the event. These findings are important and can also support decision-making by health managers and services that provide subsidies for health surveillance in the establishment of more efficient preventive and control measures against the disease.

This study also highlights the need for further studies, both clinico-epidemiological and operational, in the scenarios pointed out in this investigation that had the highest mortality rates and RRs in space and time, considering smaller ecological units such as census sectors, neighbourhoods, health districts or even group quarters. Local, social and demographic characteristics of these smaller ecological units should be considered in future research in order to provide a better understanding of the occurrence of these events, in addition to unveiling whether health services are organized and whether they are sensitive to the realities of their communities.

Conclusions

The spatiotemporal distribution of deaths due to COVID-19 was considered heterogeneous, with the detection of mortality rates ranging from 0.00 to 102.24 deaths per 100 000 inhabitants in the different municipalities of the state and three clusters of statistically significant high risk and mortality rates ranging from 20.25 to 91.49 deaths per 100 000 inhabitants per month. The metropolitan region of São Luís had the highest mortality rate and the highest RR among the clusters.

São Luís and Imperatriz were the cities with the highest number of deaths in the investigated period. The average age of individuals who died was 69 y, with a predominance of males and people of brown ethnicity. The diagnoses occurred mostly through RT-PCR and rapid tests, performed in large part in public institutions. The most prevalent comorbidities were systemic arterial hypertension and diabetes mellitus.

Such findings will aid in the planning and evaluation of public health actions in the state of Maranhão aimed at fighting SARS-CoV-2. Sociodemographic and clinico-epidemiological information can assist managers and health professionals in the identification and evaluation of clusters with increased risk of death due to COVID-19, in addition to directing healthcare, given the impacts of the disease on vulnerable groups.

Authors' contributions: WMS and PBS conceived the study. MSN provided supervision for the study development. All authors were involved in the implementation of the study. LFSS, JCS, FSS and ALFP extracted data from the information system. GGSS, VMF, LMP and LHS performed the statistical analysis. IGF, JSML and ACPJC analysed the data. WMS, PBS and MSN wrote the initial draft of the manuscript. All authors reviewed and edited the draft manuscript and reviewed and approved the final version of the article to be published.

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References

1. World Health Organization. WHO Director-General's statement on IHR Emergency Committee on Novel Coronavirus (2019-nCoV). Geneva: World Health Organization; 2021. Available from: https://www.who.int/director-general/speeches/detail/who-director-general-s-statement-on-ihr-emergency-committee-on-novel-coronavirus-(2019-ncov) [accessed 6 January 2021].
2. World Health Organization. WHO Director-General's opening remarks at the media briefing on COVID-19. Geneva: World Health Organization; 2021. Available from: https://www.who.int/dg/speeches/detail/who-director-general-s-remarks-at-the-media-briefing-on-2019-ncov-on-11-february-2020 [accessed 6 January 2021].
3. World Health Organization. WHO coronavirus disease (COVID-19) dashboard. Geneva: World Health Organization; 2021. Available from: https://COVID19.who.int/ [accessed 11 January 2021].
4. Ministério da Saúde. Secretaria de Vigilância em Saúde. Boletim Epidemiológico Especial 44. Doença pelo Coronavírus COVID-19. Semana Epidemiológica 53 (27/12/2020 a 02/01/2021). Brasília: Ministério da Saúde; 2021. Available from: https://www.gov.br/saude/pt-br/media/pdf/2021/janeiro/07/boletim_epidemiologico_covid_44.pdf [accessed 11 January 2021].
5. Souza CD, Paiva JP, Leal TC, et al. Evolução espaçotemporal da letalidade por COVID-19 no Brasil, 2020. J Bras Pneumol. 2020;46(4):e20200208.
6. Werneck GL, Carvalho MS. A pandemia de COVID-19 no Brasil: crônica de uma crise sanitária anunciada. Cad Saude Publica. 2020;36(5):e00068820.
7. Maranhão. Tribunal de Justiça do Estado do. Ação Civil Pública - processo n° 0813507-41.2020.8.10.0001. São Luís, 30 de abril de 2020. Available from: https://pje.tjma.jus.br/pje/ConsultaPublica/DetalheProcessoConsultaPublica/listView.seam?ca=805477f513645fad184d8d7f0b6a41c24eb86999373711c1# [accessed 11 January 2021].
8. Silva L, Figueiredo Filho D, Fernandes A. The effect of lockdown on the COVID-19 epidemic in Brazil: evidence from an interrupted time series design. Cad Saude Publica. 2020;36(10):e00213920.
9. Maranhão. Secretaria de Estado da Saúde do Maranhão (SES/MA). Boletins- COVID-19, atualizado em 1 de agosto de 2020. Maranhão: SES/MA; 2020. Available from: https://www.saude.ma.gov.br/boletins-COVID-19/ [accessed 6 January 2021].
10. Guimarães RB, Catão RC, Martinuci OS, et al. O raciocínio geográfico e as chaves de leitura da COVID-19 no território brasileiro. Estud Avançados. 2020;34(99):119–40.

11. Ibiapina E, Bernardes A. O mapa da saúde e o regime de visibilidade contemporâneo. Saúde Soc. 2019;28(1):322–36.
12. Desjardins MR, Hohl A, Delmelle EM. Rapid surveillance of COVID-19 in the United States using a prospective space-time scan statistic: detecting and evaluating emerging clusters. Appl Geogr. 2020;118:102202.
13. Almeida JD, Cardoso JA, Cordeiro EC, et al. Epidemiological characterization of COVID-19 cases in Maranhão: a brief analysis. Rev Prev Infec Saúde. 2020;6:10477. Available from: https://revistas.ufpi.br/index.php/nupcis/article/view/10477 [accessed 6 January 2021].
14. Instituto Brasileiro de Geografia e Estatística. Geociências. Organização do Território. Malhas territoriais. Malha municipal. Brasília: Instituto Brasileiro de Geografia e Estatística; 2019. Available from: https://www.ibge.gov.br/geociencias/organizacao-do-territorio/malhas-territoriais/15774-malhas.html?=&t=acesso-ao-produto [accessed 6 January 2021].
15. Rouquayrol MZ, Silva MG. Rouquayrol epidemiologia & saúde. 8. ed. Rio de Janeiro: MedBook; 2018.
16. Kulldorff M, Nagarwalla N. Spatial disease clusters: detection and inference. Stat Med. 1995;14(8):799–810.
17. Barrozo LV, Serafim MB, Moraes SL, et al. Monitoramento espaço-temporal das áreas de alto risco de COVID-19 nos municípios do Brasil. Hygeia Rev Bras Geogr Méd Saúde. 2020;6:417–25. Available from: http://www.seer.ufu.br/index.php/hygeia/article/view/54547 [accessed 6 January 2021].
18. Instituto Brasileiro de Geografia e Estatística. Brasil/Maranhão. Panorama 2010. Brasília: Instituto Brasileiro de Geografia e Estatística; 2020. Available from: https://cidades.ibge.gov.br/brasil/ma/panorama [accessed 6 January 2021].
19. Al-Kindi KM, Alkharusi A, Alshukaili D, et al. Spatiotemporal assessment of COVID-19 spread over Oman using GIS techniques. Earth Syst Environ. 2020;4:797–11.
20. Feng Y, Ling Y, Bai T, et al. COVID-19 with different severities: a multicenter study of clinical features. Am J Respir Crit Care Med. 2020;201(11):1380–8.
21. Jin JM, Bai P, He W, et al. Gender differences in patients with COVID-19: focus on severity and mortality. Front Public Health. 2020;8:152.
22. Conceição AM. O que pode explicar a predominância de mortes causadas pela COVID-19 em homens? Sanar Saúde. 2020. Available from: https://www.sanarmed.com/o-que-explica-a-predominancia-da-morte-de-homens-pela-COVID-19 [accessed 6 January 2021].
23. Barbosa IR, Galvão MH, Souza TA, et al. Incidência e mortalidade por COVID-19 na população idosa brasileira e sua relação com indicadores contextuais: um estudo ecológico. Rev Bras Geriatr Gerontol. 2020;23(1):200171.
24. Gomes DS, Andrade LA, Ribeiro CJ, et al. Risk clusters of COVID-19 transmission in northeastern Brazil: prospective space-time modeling. Epidemiol Infect. 2020;148:e188.
25. Niquini RP, Lana RM, Pacheco AG, et al. SRAG por COVID-19 no Brasil: descrição e comparação de características demográficas e comorbidades com SRAG por influenza e com a população geral. Cad Saude Publica. 2020;36(7):e00149420.
26. Bufrem LS. A pandemia da COVID-19 no Brasil. P2P Inovação. 2020;7:101–20. Available from: https://doi.org/10.21721/p2p.2020v7n1.p101-120 [accessed 6 January 2021].
27. Oliveira RF, Bastos-Filho CJ, Medeiros AC, et al. Machine learning applied in SARS-CoV-2 COVID 19 screening using clinical analysis parameters. IEEE Latin Am Trans. 2021;19(6):978–85. Available from: https://latamt.ieeer9.org/index.php/transactions/article/view/4368 [accessed 6 January 2021].
28. Cavalcante JR, Abreu AJ. COVID-19 no município do Rio de Janeiro: análise espacial da ocorrência dos primeiros casos e óbitos confirmados. Epidemiol Serv Saude. 2020;29(3):e2020204.
29. Aquino EML, Silveira IH, Pescarini JM, et al. Social distancing measures to control the COVID-19 pandemic: potential impacts and challenges in Brazil. Cien Saude Colet. 2020;25(suppl 1):2423–46. doi:10.1590/1413-81232020256.1.10502020.
30. Barreto ML, Barros AJD, Carvalho MS, et al. O que é urgente e necessário para subsidiar as políticas de enfrentamento da pandemia de COVID-19 no Brasil? Rev Bras Epidemiol. 2020;23:e200032.
31. Giraldi Cocco R, Collishonn E, Meurer M. Relações entre a distribuição espacial da COVID-19 e a dinâmica das interações espaciais no estado do Rio Grande do Sul. Hygeia Rev Bras Geogr Méd Saúde. 2020;183–92. Available from: https://doi.org/10.14393/Hygeia0054406 [accessed 6 January 2021].
32. Souza JR, Pietrafesa PA. A nova indústria do sudoeste maranhense: impactos socioeconômicos na cidade de Imperatriz – MA. Desenvolv Reg em Debate. 2019;9(9):143–55.
33. Moreira RS. COVID-19: unidades de terapia intensiva, ventiladores mecânicos e perfis latentes de mortalidade associados à letalidade no Brasil. Cad Saude Publica. 2020;36(5):e00080020.
34. Demenech LM, Dumith SC, Vieira ME, et al. Desigualdade econômica e risco de infecção e morte por COVID-19 no Brasil. Rev Bras Epidemiol. 2020;23:e200095.
35. Zhang CH, Schwartz GG. Spatial disparities in coronavirus incidence and mortality in the united states: an ecological analysis as of May 2020. J Rural Health. 2020;36(3):433–45.
36. Silva GA, Jardim BC, Santos CV. Excess mortality in Brazil in times of COVID-19. Cienc Saude Coletiva. 2020;25(9):3345–54.
37. Faria R, Erthal DB, Costa IT, et al. Difusão da COVID-19 nas grandes estruturas territoriais do estado do Rio Grande do Sul, Brasil. Hygeia Rev Bras Geogr Médica e da Saúde. 2020;426–35.