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Research Article

Spatial clusters, social determinants of health and risk of maternal mortality by COVID-19 in Brazil: a national population-based ecological study



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ABSTRACT

Background: Detailed information on how socio-economic characteristics are related to COVID-19 incident cases and maternal deaths is needed. We investigated the spatial distribution of COVID-19 cases and maternal deaths in Brazil and their association with social determinants of health.

Methods: This was a population-based ecological study with a spatial analysis of all cases and deaths of COVID-19 in the obstetric population. Data on COVID-19 cases and deaths in the obstetric population, social vulnerability, health inequities, and health system capacity at the municipal level were obtained from several publicly sources in Brazil. A Bayesian empirical local model was used to identify fluctuations of the indicators. Spatial statistic tests were used to identity the spatial clusters and measure the municipalities' risk of COVID-19 in the obstetric population. Beta regression was used to characterise the association between socio-economic indicators and the burden of COVID-19.

Findings: A total of 13,858 cases and 1,396 deaths due to COVID-19 were recorded in Brazil from March 2020 to June 2021. There was a variation in the number of cases per municipality, with 105 municipalities with rates from 2,210 to 3,884 cases and 45 municipalities with rates from 3,884 to 7,418 cases per 100,000 live births. The maternal mortality ratio also varied widely across municipalities. There was a spatial dependence on smoothed maternal mortality rates (I Moran 0.10; P = 0.010), and 15 municipalities had higher risk of maternal deaths. Municipalities characterized by lower health resources and higher socioeconomic inequalities presented the highest rates of incidence and maternal mortality by COVID-19.

Interpretation: In Brazil, COVID-19 cases and deaths in the obstetric population had a heterogeneous geographical distribution, with well-defined spatial clusters mostly located in the countryside. Municipalities with a high degree of socioeconomic dissimilarities showed higher maternal mortality rates than areas with better social and infrastructure indicators.

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Research in context

Evidence before this study

Preliminary evidence has demonstrated that pregnant and postpartum women with some outstanding comorbidities have a higher risk of death by COVID-19. However, there is little information on how maternal deaths due to COVID-19 are related to social and economic characteristics. We searched PubMed, Scopus, Web of Science, Embase, medRxiv and bioRxiv on 28 June 2021 for published studies without language restriction, that described the spatial distribution of maternal deaths by COVID-19 and their association to social vulnerability. We used the search terms "COVID-19", "maternal mortality", "spatial distribution" and "social vulnerability" and related synonyms. One study conducted in New York, USA on social determinants in health and pregnancy was identified, but none on maternal deaths and social vulnerability in low- and middle-income countries.

Added value of this study

We describe the spatial distribution of all COVID-19 cases and deaths in the obstetric population and their association with socioeconomic characteristics in Brazil from March 2020 to June 2021. The data provides evidence of the effects of geographic and regional inequities, health disparities and poverty on the outcomes of pregnant and postpartum women affected by COVID-19 in a low- and middle-income country.

Implications of all the available evidence

COVID-19 cases and maternal deaths were heterogeneously distributed across the Brazilian regions, with clusters mostly located in areas with a high degree of social vulnerability. Identifying the geographical areas at highest risk of exposure to adverse maternal outcomes could be used to target interventions for mass testing, isolation of cases to mitigate the spread of the disease, as well as allocating the necessary health resources to prevent maternal deaths. Furthermore, our data corroborate that pregnant and postpartum woman constitute a priority group to receive COVID-19 vaccines.

1. Introduction

Coronavirus disease-19 (COVID-19), an infectious disease caused by Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2), which emerged in China in December 2019 and rapidly spread worldwide, has caused social, economic and health system disruption in several countries. COVID-19 presents a wide clinical spectrum, and the most severe cases and deaths have been associated with underlying comorbidities [1] and social and health inequalities. [2,3]

COVID-19 has disproportionately impacted several population groups, [4–6] including the obstetric population. [7–9] Pregnant women with COVID-19 are more likely to have adverse outcomes compared to pregnant women without COVID-19. [7–10] SARS-CoV-2 infection at the time of birth is associated with higher rates of foetal death, preterm birth, preeclampsia, and emergency caesarean delivery compared to pregnant women without SARS-CoV-2 infection. [8] Further, a higher risk of maternal death among SARS-CoV-2 infected pregnant women with some comorbidity [11] and certain socio-demographic characteristics, such as black ethnicity, living in a peri-urban area and also distant from the referral hospital. [8,11,12] Notwithstanding, information on how COVID-19 maternal deaths are related to social determinants of health (SDH) is

still scarce, [13] particularly from low- and middle-income countries

Brazil is a country of continental dimensions with marked social inequalities where millions of people live in precarious living conditions. Thus, we conducted a comprehensive analysis to investigate the spatial distribution of COVID-19-related maternal deaths in Brazil and their association with SDH, including social vulnerability index (SVI), between 26 March 2020 and 26 June 2021.

2. Methods

2.1. Study design

This was a population-based ecological study with a spatial analysis of all cases and deaths of COVID-19 (confirmed by real time reverse transcription [RT-PCR]) among pregnant and postpartum women in Brazil from March 2020 to 26 June 2021. The units of analysis were the 5,570 Brazilian municipalities. We examined the relationship between municipalities' incidence, case fatality and maternal mortality rates due to COVID-19 and the municipallevel indicators for socioeconomic characteristics and availability of health care resources. All analyses were performed considering women's residence data.

2.2. Study area

Brazil has an area of \sim 8.5 million square kilometres, which is equivalent to 50% of the South American territory and has a population of approximately 210 million people. Brazil comprises 26 states and one federal administrative district and is subdivided into 5,570 municipalities. The current human development index (HDI) is 0.765. Brazil has an illiteracy rate in persons aged \geq 15 years of 6.6%, infant mortality of 12.4 deaths per 1,000 live births (LB) and an overall maternal mortality of 60/100,000 LB. [14]

2.3. Data source and measures

The data for the study was obtained from a variety of data sources. The number of cases and deaths by COVID-19 among pregnant and postpartum women was obtained from the SIVEP-Gripe dataset (Influenza Epidemiological Surveillance Information System) and the number of LB from the National Live Birth System. SIVEP-Gripe is a nationwide database established by Brazilian Ministry of Health in 2009 for the surveillance of acute respiratory distress syndromes (ARDS). With the emergence of the COVID-19 pandemic in Brazil. SIVEP-Gripe was redesigned in March 2020, allowing the notification of ARDS cases due to COVID-19 from both private and public hospitals. COVID-19 case notification is mandatory, and records are stored in the computerized SIVEP-Gripe database. [15,16] Detailed information on the filters used in SIVEP-Gripe is available in the appendix (p 1). Data were obtained for each of the Brazilian municipalities, and they were used to estimate the incidence and maternal mortality rates due to COVID-19 per 100,000 LB. The number of live births is the traditional denominator for calculating maternal mortality as well as for estimating incidence of any disease in the obstetric population. [17] COVID-19 case fatality rate (CFR) was calculated by dividing the number of maternal deaths by the number of COVID-19 cases among pregnant and postpartum women.

Social, demographic and economic data were extracted from the 2010 National Census, available at the Brazilian Institute of Geography and Statistics (IBGE; https://www.ibge.gov.br). We obtained the following socio-economic indicators at the municipal level: Gini index, unemployment rate (%), percentage of illiterate people (%), percentage of the population living in households with inadequate water supply, sewage or rubbish collection services (%),

and the percentage of households with a per capita income below half the Brazilian minimum salary (%). Gini index is an instrument to measure the degree of concentration of income in a given group and it shows the difference between the income of the poorest and the richest. Numerically, it varies from 0 to 1. Values closer to 1 indicate greater income concentration.

To assess pre-existing hospital services at the municipal level, we used Ministry of Health's National Registry of Health Establishments (CNES, acronym in Portuguese) to quantify the number of public and private intensive care units (ICU) beds. From this database, we also obtained the number of new ICU beds, hospital beds and outpatients' clinics. Estimates of population by municipality in 2020 were obtained from IBGE and used to compute the rate of ICU beds, hospital beds and outpatients' clinics per 100,000 residents.

Three measures of primary care services from March 2020 to June 2021 were extracted from CNES: population coverage of the family health strategy, physician's coverage (%) and nurse's coverage (%).

The SVI was obtained from the Institute of Applied Economic Research (http://www.ipea.gov.br). This index estimates the degree of vulnerability and social exclusion of the population and is composed of 16 social indicators comprising domains of urban infrastructure, human capital, income, and work. The SVI score range from 0 to 1, and we classified the municipalities into very low (0-0.2), low (>0.2-0.3), moderate (>0.3-0.4), high (>0.4-0.5) and very high SVI (>0.5). [16,18]

3. Data analysis

3.1. Spatial analysis

We mapped the incidence and maternal mortality coefficients per 100,000 LB and the CFR for each Brazilian municipality. The spatial distribution maps were analysed in R (version 4.1.0), using the cartographic base of Brazil, divided by states and municipalities available on the IBGE website. [19] We applied the K-means clustering technique according to Hartigan-Wong algorithm to stratify municipalities into low or very high incidence, maternal mortality and CFR. [20]

The crude data rates were smoothed by the local empirical Bayesian estimator to minimize the instability caused by the random fluctuation. The rate was smoothed by applying weighted averages, resulting in a second adjusted rate. This method considers not only the value of the municipality, but weights it in the relationship of boundaries between municipalities through a spatial proximity matrix, considering the contiguity criterion in which the value of 1 is assigned to municipalities that border on and 0 to municipalities that do not share boundaries. [21]

The Global Moran statistic was used to identify spatial autocorrelations, and when these were identified, we used the Local Index of Spatial Association to quantify the degree of spatial association to which each location of the sample set is subjected to as a function of a neighbourhood model. This method allows to infer local patterns of spatial distribution of the variables analysed.

The local autocorrelation (local index of spatial association [LISA]) generated the Moran scatter diagram for the identification of critical or transition areas, in which the value of each municipality is compared with the values of neighbouring municipalities. The quadrants generated were interpreted as follows: Q1 - High/high (positive values and positive averages); Q2 - Low/low (negative values and negative averages); Q3 - high/low (positive values and negative averages); Q4 - low/high (negative values and positive averages). The LISA Map departs from the Local Moran Index for the identification of different patterns of statistical significance (non-significant, 5% significance, 1% significance and 0.1%

significance). The Moran Map only considers areas whose Moran indexes were significant (P-value < 0.05).

3.2. Regression modelling

After identifying the spatial clusters, we used demographic, socioeconomic and health indicators to explore their association with incidence rate per 100,000 LB, maternal mortality rate per 100,000 LB and CFR. The correlation structure between the variables was assessed using the Spearman correlation matrix (P < 0.05). To solve the multicollinearity problem observed in Spearman's correlation matrix, the multivariate technique of Principal Component Analysis (PCA) was used. [20] The aim of the PCA is to reduce the dimension of the independent variables by using the Varimax rotation method and Kaiser normalization. The dependent variables (incidence, maternal mortality and CFR) were modelled by Beta regression, assuming as independent variables the factors extracted from the PCA. [22,23] A total of 21 independent variables were transformed into orthogonal factors. Factors with value ≥ 1 were selected to compose the PCA. In this study, we observed that the 5th factor presented a value equal to 1.01 and an accumulated variance of 75.8%. The components were distributed as follows:

CPA-1: municipalities with lower percentage of people living with low income and lower percentage of unemployed people (lower than the average), lower SVI score, lower SVI human capital and SVI labour and income scores, lower percentage of illiteracy (lower than the average), higher municipality HDI (MHDI), higher MHDI longevity, MHDI education and MHDI income.

CPA-2: municipalities with lower pre-existing COVID-19 ICU bed rate and lower response COVID-19 bed rate (lower than the average).

CPA-3: lower rate of outpatient clinics per 100,000 population and lower percentage of family health strategy teams.

CPA-4: higher social inequality (higher Gini index), higher SVI Infrastructure score (i.e., greater social vulnerability), lower percentage of households with piped water and sewage collection and lower percentage of households with regular rubbish collection.

CPA-5: lower rate of hospital beds, lower percentage of physicians' and nurse' coverage.

3.3. Ethical consideration

Institutional review board approval and informed consent were not required because all data were obtained from public domain database and were deidentified.

Role of the funding source

There was no funding source for this study. The corresponding author had full access to all the data in the study and had final responsibility for the decision to submit for publication.

4. Results

A total of 13,858 cases and 1,396 deaths among pregnant and postpartum women were recorded in Brazil from March 2020 to 26 June 2021. Figure 1 describes the spatial distribution of the COVID-19 incidence per 100,000 LB. There was a variation in the number of cases per municipality, with 3,435 municipalities with rates below 211 cases per 100,000 LB; 105 municipalities with rates between 2,210 and 3,884 cases per 100.000 LB; and 45 municipalities with rates between 3,884 and 7,418 cases per 100.000 LB. A total of 1985 municipalities had no cases of COVID-19 among pregnant and/or postpartum women. There was spatial dependence on crude (I Moran 0.06; P <0.001) and smoothed indicators (I Moran

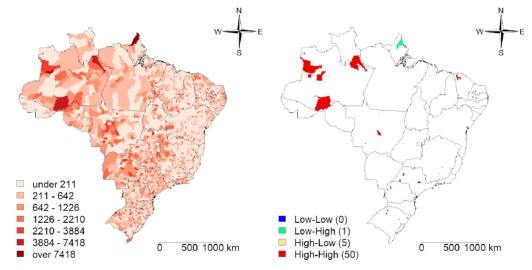


Figure 1. Spatial distribution of the COVID 19 incidence rate per 100.000 livre birth among pregnant and postpartum women in Brazil.

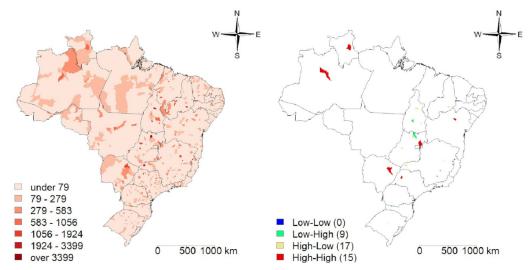


Figure 2. Spatial distribution of the COVID 19 maternal mortality per 100.000 live birth in Brazil.

0.13; P < 0.001). With the local Moran, there was an increase in the random fluctuation of COVID-19 incidence rates among pregnant and postpartum women after using the Bayesian model, with 164 significant municipalities with the crude rate and 56 with the Bayesian estimator. Fifty municipalities showed very high incidence rates of COVID-19 among pregnant and postpartum women and were considered at high risk of infection in this population (Q1 Moran Map). The municipalities with high incidence rates were in the states of Paraíba (n =13 municipalities), Ceará (n = 7), Amazonas (n = 7), São Paulo (n = 7), Rio Grande do Sul (n = 6), Minas Gerais (n = 4), Paraná (n = 3), Mato Grosso (n = 2) and Santa Catarina (n = 1).

There was also spatial dependence on smoothed maternal mortality rates by COVID-19 per 100,000 LB (I Moran 0.10; P=0.010). Stratum Q1 (high/high - municipalities with high maternal mortality rates and surrounded by municipalities with high maternal mortality by COVID-19) was composed of 15 municipalities and they were in the states of Minas Gerais (n=4), São Paulo (n=3), Goiás (n=2), Mato Grosso do Sul (n=1), Amazonas (n=1), Roraima (n=1), Pernambuco (n=1), Bahia (n=1) and Rio Grande do Sul (n=1) (Q1 Moran Map) (Figure 2).

Figure 3 shows the spatial distribution of crude maternal CFR due to COVID-19. High CFR (higher than the average) were found

throughout Brazil. There was spatial dependence on crude CFR (I Moran 0.05; P = 0.024) and a total of 72 municipalities were identified as having a high maternal lethality rate due to COVID-19, with 25 municipalities in the Southeast, 20 in the Northeast, 16 in the North, seven in the Central-West and four in the South region.

Correlation analysis showed an increase in incidence, maternal mortality rates and CFR with increasing social vulnerability index (global and in the domains of infrastructure, human capital and, work and income), increasing Gini index and increasing percentage of unemployed. There was a negative correlation between the incidence, maternal mortality and CFR rates and the increase in MHDI education and income, percentage of the population living in households with inadequate water supply, sewage or rubbish collection services and percentage of illiteracy people. There was an increase in the burden of COVID-19 with the increase in the proportion of hospital and ICU beds per 100,000 people and the increase in the coverage of physicians and nurses. However, the incidence, maternal mortality and lethality rates were inversely proportional to the coverage of family health teams and availability of outpatient clinics (Table 1).

Due to the high multicollinearity observed in the correlation matrix, we perform the Beta regression analysis using the multivariate technique of PCA (Table 2), Municipalities characterized

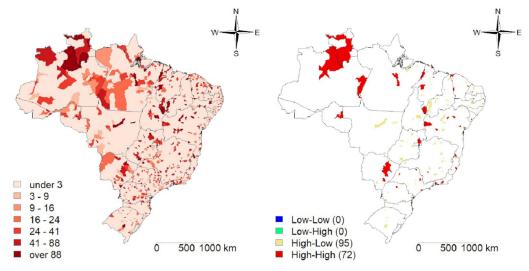


Figure 3. Spatial distribution of the COVID-19 case fatality rate in Brazil.

Table 1Correlation between socioeconomic and social vulnerability indicators and incidence of COVID-19 among pregnant and postpartum women, maternal mortality and case fatality rate in Brazil.

Variables	Incidence per 100,000 Live Birth	P-value	Maternal Mortality per 100,000 Live Birth	P-value	Case fatality rate	P-value
Gini index	0.07	< 0.001	0.10	< 0.001	0.11	< 0.001
Social Vulnerability Index (SVI)	0.17	< 0.001	0.14	< 0.001	0.14	< 0.001
SVI infrastructure	0.11	< 0.001	0.09	< 0.001	0.09	< 0.001
SVI human capital	0.17	< 0.001	0.15	< 0.001	0.15	< 0.001
SVI work and income	0.17	< 0.001	0.14	< 0.001	0.14	< 0.001
Municipal human development index (MHDI)	-0.08	< 0.001	-0.04	0.003	-0.04	0.004
MHDI longevity	0.03	0.016	0.07	< 0.001	0.07	< 0.001
MHDI education	-0.09	< 0.001	-0.07	< 0.001	-0.07	< 0.001
MDHI income	-0.16	< 0.001	-0.12	< 0.001	-0.12	< 0.001
Population living in households with inadequate water	0.03	0.011	0.01	0.271	0.01	0.316
supply and sewage services (%)						
Population living in households with inadequate rubbish	0.05	< 0.001	0.02	0.230	0.01	0.270
collection service (%)						
Illiteracy people (%)	-0.18	< 0.001	-0.16	< 0.001	-0.16	< 0.001
Percentage of people with low income (%)	-0.13	< 0.001	-0.08	< 0.001	-0.08	< 0.001
Unemployment (%)	0.09	< 0.001	0.14	< 0.001	0.14	< 0.001
Hospital beds per 100,000 people	0.18	< 0.001	0.15	< 0.001	0.15	< 0.001
ICU beds (pre-existing) per 100,000 people	0.27	< 0.001	0.35	< 0.001	0.36	< 0.001
Outpatient clinics per 100,000 people	-0.04	0.003	0.00	0.822	0.00	0.776
Family Health Strategy coverage (%)	-0.31	< 0.001	-0.26	< 0.001	-0.26	< 0.001
New ICU beds per 100,000 people	0.26	< 0.001	0.36	< 0.001	0.36	< 0.001
Physicians' coverage (%)	0.17	< 0.001	0.18	< 0.001	0.18	< 0.001
Nurses' coverage (%)	0.12	< 0.001	0.14	0.000	0.14	< 0.001

by PCA-1 (highest social and economic indicators), PCA-3 (lower outpatient clinics and family health team coverages) and PCA-4 (higher social inequality and lower urban infrastructure) presented the highest rates of incidence, maternal mortality and CFR (Table 3).

5. Discussion

Several studies have described the clinical characteristics related to deaths among pregnant and postpartum women due to COVID-19; [10,24–29] but few have explored how social, economic and demographic features are associated with the maternal mortality risk. [13] In this study, we describe the spatial distribution of COVID-19 cases and deaths in an obstetric population and their association with socioeconomic vulnerability. In Brazil, COVID-19 cases and deaths among pregnant and postpartum women had a heterogeneous geographical distribution, with well-defined spatial clusters mostly located in the countryside. Our findings also showed that the burden of COVID-19 in terms of incidence rates

and maternal mortality affected municipalities with the following characteristics: a) municipalities with better social and economic indicators; b) municipalities with low availability of outpatient clinics and low coverage of family health teams; and c) municipalities with precarious urban infrastructure and high social inequities.

Anticipating the advance of SARS-CoV-2 infection, most Brazilian municipalities increased the health services capacity in order to address the pandemic. [16] In 63.6% of the municipalities, temporary health units intended for the care of people with like-flu symptoms were implemented, expanding their capacity for testing of COVID-19 suspected cases. [15] New hospital and ICU beds were opened in 12.6% of the municipalities. These actions were added to the already existing health network, increasing the people's access to health services, particularly in localities with higher (than average) socio-economic indicators. The more health facilities providing care and testing for COVID-19 the greater the chance of detecting incident cases, which may account for the high incidence seen in high socio-economic areas in our analysis.

 Table 2

 Principal component matrix using varimax rotation method with Kaiser normalization.

Variables	CP1	CP2	CP3	CP4	CP5
Gini index				0.48	
Social Vulnerability Index (SVI)	-0.76				
SVI infrastructure				0.84	
SVI human capital	-0.85				
SVI work and income	-0.87				
Municipal human development index (MHDI)	0.92				
MHDI longevity	0.81				
MHDI education	0.85				
MDHI income	0.90				
Population living in households with inadequate water supply and sewage services (%)				-0.62	
Population living in households with inadequate rubbish collection service (%)				-0.75	
Illiteracy people (%)	-0.88				
Percentage of people with low income (%)	-0.89				
Unemployment (%)	-0.40				
Hospital beds per 100,000 people					-0.70
ICU beds (pre-existing) per 100,000 people		-0.96			
Outpatient clinics per 100,000 people			-0.80		
Family Health Strategy coverage (%)			-0.70		
New ICU beds per 100,000 people		-0.96			
Physicians' coverage (%)					-0.50
Nurses' coverage (%)					-0.71

Table 3Beta regression model for the incidence, mortality and lethality rates due to COVID 19 in pregnant and postpartum women in Brazil

Variables	Estimate	Std. Error	CI 95%	P-value	
Incidence rate (Pseudo-R ² = 0.15)					
Intercept	-5.60	0.03	-5.67 to -5.54	< 0.001	
PC1	0.15	0.01	0.13 to 0.18	< 0.001	
PC2	-0.15	0.01	-0.17 to -0.12	< 0.001	
PC3	0.22	0.01	0.20 to 0.25	< 0.001	
PC4	0.09	0.01	0.06 to 0.12	< 0.001	
PC5	-0.08	0.01	-0.10 to -0.05	< 0.001	
Maternal Mortality rate (Pseudo- $R^2 = 0.11$)					
Intercept	-7.76	0.05	-7.86 to -7.66	< 0.001	
PC1	0.05	0.01	0.02 to 0.08	< 0.001	
PC2	-0.07	0.01	-0.10 to -0.05	< 0.001	
PC3	0.06	0.01	0.04 to 0.09	< 0.001	
PC4	0.04	0.01	0.01 to 0.07	0.003	
PC5	-0.04	0.01	-0.07 to -0.02	0.001	
Case fatality rate (Pseudo- $R^2 = 0.07$)					
Intercept	-1.75	0.01	-1.77 to -1.72	< 0.001	
PC1	0.01	0.01	-0.01 to 0.03	0.235	
PC2	-0.06	0.01	-0.08 to -0.04	< 0.001	
PC3	0.06	0.01	0.04 to 0.09	< 0.001	
PC4	0.03	0.01	0.01 to 0.05	0.007	
PC5	-0.04	0.01	-0.06 to -0.02	0.001	

However, presenting above-average percentages of urban and capital infrastructure does not mean that the municipality has a well-established health network. Brazil has a hierarchical health system based on regionalization, where larger municipalities can offer health services in the three levels of complexity (primary health care, specialized health services and hospital services [including maternity hospitals]). In this study, 43 (86%) out of 50 municipalities with high rates of COVID-19 incidence and maternal mortality had a population of less than 50,000 inhabitants and they were classified as having low social vulnerability.

Inequalities in access to health services and diagnostic tests occur within the same municipality and this may partly explain why municipalities with a population ≥50,000 inhabitants and high socioeconomic indicators had a high burden of COVID-19 in the obstetric population.

The most vulnerable populations have been disproportionately impacted by COVID-19, where areas with the greatest inequities are those most affected. We found a relationship between the municipalities' socioeconomic inequality and the burden of COVID-19, with COVID-19 maternal deaths clusters being detected in munic-

ipalities with precarious urban infrastructure and high social inequities. In other words, the more heterogeneous the distribution of resources in a municipality, the higher the odds that the municipality would report COVID-19 maternal death as an important health problem.

Social and financial deprivation affects people's lives in complex ways. Areas with large income inequalities often have the worse living conditions, poor sanitation, inadequate housing, crowding and difficult access to health services. Additionally, the difficulty of maintaining social distancing in subnormal agglomerates contributes to SARS-CoV-2 spread and mortality in vulnerable populations. [30]

Disparities can also be observed in relation to access to prenatal and deliveries care services. Women living in areas of high social inequalities tend to have greater difficulties in accessing prenatal care. In Brazil, the proportion of women without prenatal consultations is higher in regions with poor socioeconomic indicators and living conditions. A Brazilian national survey in 266 maternity hospitals showed that about 60% of pregnant women living in the North region did not have any prenatal consultation during their

pregnancies. [31] In the Northeast, the proportion of women with no pre-natal visits was 32%, while for the Central-West, South and Southeast regions it was 31%, 26% and 23% respectively. [32] Furthermore, only 15% of the maternity hospitals have ICU beds, and their distribution is heterogeneous across regions, with a higher concentration in the Southeast and Southern regions. [33] Moreover, the allocation of resources directed to the control of the pandemic may have impacted the obstetric healthcare, as many antenatal care services have been disrupted, creating barriers to access to routine prenatal consultations and laboratory tests. [34]

In Brazil, a study conducted by IBGE's National Household Sample Survey (PNAD) showed that there were disparities in the population's access to COVID-19 diagnostic tests and health care. People living in areas of lower social vulnerability performed four-times more COVID-19 tests than those living in areas deprived of financial resources. [35]

Identifying the areas at highest risk of maternal mortality from COVID-19 would be beneficial for decision makers in allocating financial and material resources and promoting contingency measures to mitigate the spread of SARS-CoV-2. Furthermore, policymakers should include pregnant and postpartum women in the priority groups for vaccination against COVID-19, since this population is at high risk of infection and death. [11,12,36,37] Recent trial data has demonstrated the safety of mRNA based COVID-19 vaccines during pregnancy. [37]

This study assessed a large sample size of pregnant and postpartum women with laboratory-confirmed COVID-19 and how social determinants of health are associated with maternal mortality risk due to COVID-19 in a country with marked social inequalities. However, the data presented here need to be interpreted with consideration of the study limitations. The data were obtained from surveillance information systems and therefore only represent women who have accessed the health system, which may underrepresent women living in areas with a low SVI.

Furthermore, until August 2020 Brazil did not have a universal testing strategy for the obstetric population, and SARS-CoV-2 RT-PCR tests were offered only to women who presented symptoms suggestive of COVID-19 and had access to health services. Consequently, missing and undetected cases in poor communities could have influenced the detection rates, as higher underreporting is expected in areas with poor access to health services. Data on live births were for the year 2019, as official records are available for that year. Social, demographic and economic data were extracted from the 2010 National Census and are outdated, since the Brazilian federal government has cancelled the 2020 census. Secondary data in ecological studies are also unsuitable to establish disease causality, and therefore, the study only provides evidence of statistically significant associations between COVID-19 in the obstetric population, poverty and social inequalities.

The distribution of COVID-19 incident cases and maternal deaths occurred heterogeneously across Brazilian regions, with clusters being identified mainly in the countryside. This study also identified a relationship between social inequities and the burden of COVID-19 among pregnant and postpartum women. Identifying the geographical areas at highest risk of exposure to adverse maternal outcomes could be used to target interventions for mass testing, isolation of cases to mitigate the spread of the disease, as well as allocating the necessary health resources to prevent maternal deaths. Furthermore, our results support the recommendation to include all pregnant and postpartum women as a priority group for vaccination against COVID-19. The Brazilian Ministry of Health has issued a national guideline (Technical Note 02/2021) [38] to vaccinate all pregnant and postpartum women, and the rapid vaccination of this group would likely minimise future maternal deaths from COVID-19 in Brazil. Continued close monitoring of cases and deaths from COVID-19 in the obstetric population is necessary, even after the adoption of vaccination for this population

6. Contributors

TSS: conceptualisation, methodology, data collection, data analysis, and writing original draft. JRSS: data collection, formal data analysis, figures and interpretation. MRS, DL and RQG: literature search, data interpretation, and writing. VSS: conceptualisation, methodology, project administration, supervision, data curation and writing. All authors discussed the results and contributed to the final manuscript.

Declaration of competing interests

The authors declare that there is no conflict of interest.

Data sharing

SIVEP-Gripe dataset and all other databases used in this study are publicly available. Our analysis code is available upon request to the corresponding author.

Editor note

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Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.lana.2021.100076.

References

- Martins-Filho PR, Tavares CSS, Santos VS. Factors associated with mortality in patients with COVID-19. A quantitative evidence synthesis of clinical and laboratory data. Eur J Intern Med 2020 published online April. doi:10.1016/j.ejim. 2020.04.043.
- [2] Martins-Filho PR, de Souza Araújo AA, Quintans-Júnior LJ, Santos VS. COVID-19 fatality rates related to social inequality in Northeast Brazil: a neighborhood-level analysis. J Travel Med 2020:1–3.
- [3] Martins-Filho PR, Quintans-Júnior LJ, de Souza Araújo AA, et al. Socio-economic inequalities and COVID-19 incidence and mortality in Brazilian children: a nationwide register-based study. Public Health 2021;190:4–6.
- [4] Martins-Filho PR, Araújo BCL, Sposato KB, Araújo AA de S, Quintans-Júnior LJ, Santos VS. Racial disparities in covid-19-related deaths in brazil: Black lives matter? J Epidemiol 2021;31:239–40.
- [5] Santos VS, Souza Araújo AA, de Oliveira JR, Quintans-Júnior LJ, Martins-Filho PR. COVID-19 mortality among Indigenous people in Brazil: a nationwide register-based study. J Public Health 2020:1–2 Bangkok.
- [6] Baqui P, Bica I, Marra V, Ercole A, van der Schaar M. Ethnic and regional variations in hospital mortality from COVID-19 in Brazil: a cross-sectional observational study. Lancet Glob Heal 2020. doi:10.1016/S2214-109X(20)30285-0.
- [7] Zambrano LD, Ellington S, Strid P, et al. Update: Characteristics of Symptomatic Women of Reproductive Age with Laboratory-Confirmed SARS-CoV-2 Infection by Pregnancy Status - United States, January 22-October 3, 2020. MMWR Morb Mortal Wkly Rep 2020;69:1641–7.
- [8] Ko JY, DeSisto CL, Simeone RM, et al. Adverse Pregnancy Outcomes, Maternal Complications, and Severe Illness Among US Delivery Hospitalizations With and Without a Coronavirus Disease 2019 (COVID-19) Diagnosis. Clin Infect Dis 2021;73:S24–31.
- [9] Gurol-Urganci I, Jardine JE, Carroll F, et al. Maternal and perinatal outcomes of pregnant women with SARS-CoV-2 infection at the time of birth in England: national cohort study. Am J Obstet Gynecol 2021 published online May 20. doi:10.1016/j.ajog.2021.05.016.
- [10] Villar J, Ariff S, Gunier RB, et al. Maternal and Neonatal Morbidity and Mortality Among Pregnant Women With and Without COVID-19 Infection. JAMA Pediatr 2021 published online April 22. doi:10.1001/jamapediatrics.2021.1050.
- [11] Menezes MO, Takemoto MLS, Nakamura-Pereira M, Katz Leila, Melania MR, Amorim Heloisa O, Salgado Adriana Melo, Carmen SG, Diniz Liduina AR. Roxana Knobel CBA. Risk factors for adverse outcomes among pregnant and postpartum women with acute respiratory distress syndrome due to COVID-19 in Brazil. Int J Gynecol Obstet 2021;151:415–23.

- [12] de Souza Santos D, de Oliveira Menezes M, Andreucci CB, et al. Disproportionate Impact of Coronavirus Disease 2019 (COVID-19) Among Pregnant and Postpartum Black Women in Brazil Through Structural Racism Lens. Clin Infect Dis 2021:72:2068–9.
- [13] Prasannan L, Rochelson B, Shan W, et al. Social determinants of health and coronavirus disease 2019 in pregnancy. Am J Obstet Gynecol MFM 2021;3:100349.
- [14] da Silva BGC, Lima NP, da Silva SG, et al. Mortalidade materna no Brasil no período de 2001 a 2012: Tendência temporal e diferenças regionais. Rev Bras Epidemiol 2016;19:484–93.
- [15] Ranzani OT, Bastos LSL, Gelli JGM, et al. Characterisation of the first 250 000 hospital admissions for COVID-19 in Brazil: a retrospective analysis of nationwide data. Lancet Respir Med 2021;9:407–18.
- [16] Rocha R, Atun R, Massuda A, et al. Effect of socioeconomic inequalities and vulnerabilities on health-system preparedness and response to COVID-19 in Brazil: a comprehensive analysis. Lancet Glob Heal 2021;9:e782–92.
- [17] UNFPA, World Health Organization, UNICEF. World Bank Group the UNPD. Trends in Maternal Mortality: 2000 to 2017; 2019. p. 104.
- [18] de Souza CDF, Rocha VS, Santos NF, et al. Spatial clustering, social vulnerability and risk of leprosy in an endemic area in Northeast Brazil: an ecological study.

 J Eur Acad Dermatology Venereol 2019 jdv.15596.
- [19] Brazilian Institute of Geography and Statistics BIDS. Profile of Brazilian municipalities; 2017. 2017 [Internet]. Brazilian Institute of Geography Rio de laneiro p. 106.
- [20] Hair JF, Black WC, Babin BJ ARTR. Análise multivaridada de dados. Bookman; 2019. 6th.ed. Porto Alegre.
- [21] Chen Y. New Approaches for Calculating Moran's Index of Spatial Autocorrelation. PLoS One 2013;8. doi:10.1371/journal.pone.0068336.
- [22] Cordeiro G, Demétrio CGB. Modelos Lineares Generalizados e Extensões. Piracicaba. UFRPE /ESALQ 2010.
- [23] Madsen H, Thyregod P. Introduction to General and Generalized Linear Models. Chapman & Hall/CRCC; 2011.
- [24] Zaigham M, Andersson O. Maternal and perinatal outcomes with COVID-19: A systematic review of 108 pregnancies. Acta Obstet Gynecol Scand 2020:99:823-9.
- [25] Di Toro F, Gjoka M, Di Lorenzo G, et al. Impact of COVID-19 on maternal and neonatal outcomes: a systematic review and meta-analysis. Clin Microbiol Infect 2021;27:36–46.

- [26] Wei SQ, Bilodeau-Bertrand M, Liu S, Auger N. The impact of COVID-19 on pregnancy outcomes: A systematic review and meta-analysis. Cmaj 2021;193:E540-8.
- [27] Liu D, Li L, Wu X, et al. Pregnancy and Perinatal Outcomes of Women With Coronavirus Disease (COVID-19) Pneumonia: A Preliminary Analysis. AJR Am J Roentgenol 2020:1–6.
- [28] Adhikari EH, Moreno W, Zofkie AC, et al. Pregnancy Outcomes Among Women With and Without Severe Acute Respiratory Syndrome Coronavirus 2 Infection. JAMA Netw open 2020;3:e2029256.
- [29] Liu W, Wang Q, Zhang Q, et al. Coronavirus disease 2019 (COVID-19) during pregnancy: a case series. Preprints 2020:2020020373.
- [30] Cao Y, Hiyoshi A, Montgomery S. COVID-19 case-fatality rate and demographic and socioeconomic influencers: Worldwide spatial regression analysis based on country-level data. BMJ Open 2020;10:1–12.
- [31] C Leal M do, Esteves-Pereira AP, Viellas EF, Domingues RMSM, da Gama SGN. Assistência pré-natal na rede pública do Brasil. Rev Saude Publica 2020;54:1–12.
- [32] Tomasi E, Fernandes PAA, Fischer T, et al. Qualidade da atenção pré-natal na rede básica de saúde do Brasil: Indicadores e desigualdades sociais. Cad Saude Publica 2017:33:1–11.
- [33] Roberton T, Carter ED, Chou VB, et al. Early estimates of the indirect effects of the COVID-19 pandemic on maternal and child mortality in low-income and middle-income countries: a modelling study. Lancet Glob Heal 2020;8:e901–8.
- [34] Takemoto MLS, Menezes MO, Andreucci CB, et al. Maternal mortality and COVID-19. J Matern Neonatal Med 2020:1–7.
- [35] Brasil. Instituto Brasileiro de Geografia e Estatística (IBGE) Pesquisa Nacional por Amostra de Domicílios Contínua (PNAD) COVID-19; 2020. Rio de janeiro: IBGE
- [36] C Oliveira S de, da Silva TPR, Velásquez-Melendez G, et al. Social and obstetric inequalities and vaccination in pregnant women. Rev Bras Enferm 2020;73(4):e20190099.
- [37] Bardají A, Sevene E, Cutland C, et al. The need for a global COVID-19 maternal immunisation research plan. Lancet 2021;397:e17–18.
- [38] Brasil Secretaria Extraordinária de Enfrentamento à COVID-19. Nota Técnica No. 2/2021 - SECOVID/GAB/SECOVID/MS; 2021. Brasília, DF.