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EPIDEMIOLOGICAL ANALYSIS OF MATERNAL MORTALITY DUE TO COVID-19 AND ITS COMPLICATIONS BETWEEN APRIL 2020 AND JUNE 2021 IN BRAZIL

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Abstract: Introduction: The SARS-CoV-2 pandemic that started in December 2019 triggered significant consequences in the economic, psychosocial and health fields on a global scale. With the increasing number of cases, it was possible to identify groups more vulnerable to morbidity and mortality, with the maternal population being a prominent community due to relevant clinical outcomes. Thus, the study in question will provide a comprehensive understanding of maternal mortality, exploring qualitative and quantitative data from financial, social and ethnic perspectives, so far scarce in the literature. **Objective**: To carry out an epidemiological analysis of maternal mortality due to complications of COVID-19. **Materials and methods:** This is a descriptive, cross-sectional and retrospective population cohort, carried out on the platforms SIVEP Gripe and ``Observatório Obstetrico Brasileiro`` COVID-19 in order to look for cases of pregnant and puerperal women from the 14th epidemiological week of 2020 to the 26th of 2021. race, area of residence, age group, type of ventilatory support, level of education, Brazilian regions, gestational trimester and puerperium. **Results**: This study found that education is not associated with maternal mortality (p-value > 0.05). On the other hand, the less developed areas - North, Northeast (RR 1.30 [CI95% 1.09-1.40]) and rural areas (RR 1.26 [CI95% 1.19-1.70]), respectively - are significantly related to higher mortality, as well as the brown (RR 1.13 [95%CI 1.02-1.26]) and black (RR 1.41 [95%CI 1.17-1.71]) populations., women aged over 35 years (RR 2.30 [95%CI 1.77-3.00]), pregnant women in the 2nd trimester (RR 1.61 [95%CI 1.26-2.06]), puerperium (RR 1.99 [95%CI 1.80-2.20]) and/or who were exposed to invasive procedures (RR 26.63 [95%CI 21.87-32.43]). Conclusion: The morbidity and mortality resulting from COVID-19 during pregnancy and the puerperium is directly associated with the sociodemographic and socioeconomic profiles evaluated in the research, except for the level of education. That said, it will be possible to direct measures to reduce maternal deaths related to SARS-CoV-2.

Keywords: COVID-19; maternal mortality; risk factors.

INTRODUCTION

In December 2019, a new variant of the Coronavirus, SARS-CoV-2, emerged in the city of Wuhan, China, whose pathophysiology triggers an Acute Respiratory Syndrome (SARS) with notable pulmonary involvement and marked transmissibility (FURLAN et al., 2020). The COVID-19 pandemic is responsible for worldwide consequences, economic, social, ethical, moral and, above all, health crises. However, when it comes to health, death is undoubtedly the final and irreversible consequence for the affected individual (SOUZA and AMORIM, 2021). Therefore, in order to reduce the serious consequences of COVID-19, risk groups for complications and death were identified, which included pregnant women (SOUZA and AMORIM, 2021), even though it is still a controversial topic in pregnancy, childbirth and puerperium (ESTRELA, FERNANDA et al.). Initial studies in the obstetric population do not suggest a greater susceptibility of pregnant women to the complications of COVID-19, however, subsequent publications have reported cases of pregnant women with severe disease and maternal deaths resulting from the infection (NAKAMURA-PEREIRA and BARBOSA, 2020). Comparing pregnant women with and without COVID-19, those with the disease were shown to have a higher risk of death, admission to the intensive care unit and premature birth. (ALLOTEY et al., 2020; SANKARAN et al., 2021). In this sense, the risks shown can be justified by immunological

changes and physiological adaptations during pregnancy, such as elevation of the diaphragm, increased oxygen consumption and edema of the respiratory tract mucosa (FURLAN et al., 2020), which make them more susceptible to viral pneumonias (NAKAMURA-PEREIRA and BARBOSA, 2020). According to data from the Brazilian Obstetric Observatory COVID-19 (OOBr Covid-19), which uses data from the Influenza Epidemiological Surveillance System (Sivep-Flu), there are, from the start of the pandemic to April 2021, 9,985 confirmed cases of COVID-19. -19 among pregnant and puerperal women, with 815 deaths. This number of pregnant and postpartum deaths from COVID-19 more than doubled in 2021, with an average of 25.8 deaths per week, compared to the 2020 weekly average of 10.5 (an increase of 145%). It is possible that high birth rates and limited resources to provide health care, combined with social determinants, influence the increased risk of maternal death due to the illness caused by COVID-19, emphasizing the socioeconomic influence on the health of these women. (TAKEMOTO et al. 2020a; SOUZA and AMORIM, 2021). Thus, failures in prenatal care, precarious in-hospital care, discontinued care in the puerperium and social vulnerability can be cited as synergistic factors to the worsening situation. Taking them into account, especially the last one mentioned, researchers managed to show a discrepancy between ethnic groups, identifying that the risk of death was almost twice as high in black women when compared to white ones (KNIGHT et al., 2020; SOUZA and AMORIM, 2021). In this sense, this study will provide a comprehensive view of maternal mortality, since quantitative and qualitative data will be addressed from an economic, social and ethnic perspective, which will enable targeted and effective solutions by public administration bodies and, consequently, reduce maternal mortality rates in Brazil. Thus, the analysis seeks to deepen beyond technical issues associated with maternal mortality, explaining structural racism and the impacts of economic indices in each region of Brazil. It is evident, therefore, the relevance of this project both to the scientific and the administrative environment, since there are not enough studies in the literature that contemplate this approach. In addition, the present study systematized information that already existed and was registered in databases, respecting the ethical and legal aspects in force, without disclosing personal data of the analyzed population and without conflict of interests. Based on this information, it will be possible to increase the visibility of the theme, which will increase the number of actions in corrective measures, with the main objective of reducing the maternal mortality rates found, providing a contribution of great relevance to the scientific community and to the society.

MATERIALS AND METHODS

This is a descriptive, cross-sectional and retrospective population cohort, carried out on the SIVEP Gripe and Brazilian Obstetric Observatory COVID-19 (OOBr Covid-19) platforms in order to search for cases of pregnant and puerperal women from the 14th epidemiological week of 2020 to the 26th epidemiological week of 2021, that is, data obtained from 03/29/2020 to 07/03/2021. SARS cases diagnosed with COVID-19 by PCR, serology or antigen were included in the epidemiological data. Missing, unfinished cases and unknown gestational age belonged to the exclusion criteria. From this, the following items were listed: schooling, race, age group, area of residence, regions, gestational age by trimester and postpartum period, admission to the ICU, evolution from flu syndrome to acute respiratory syndrome, hospital-acquired

infection, need for ventilatory support and whether they had a cure or death outcome. This information was collected and organized in an Excel spreadsheet, which was submitted to statistical tests/calculations: Pearson's Chi-square test to determine the association between variables and clinical outcomes (cure and death), i.e., the probability of significance (p-value < 0.5). Absolute Risk and Relative Risk were also used to estimate the probability that a variable has to develop the death outcome, taking into consideration, a 95% confidence interval. Based on these results, tables were made, where a critical analysis of the data obtained was subsequently carried out, with the aim of confirming or refuting the information present in the literature.

RESULTS AND DISCUSSIONS

Based on the calculations, it was determined that only the level of education is not associated with maternal mortality in view of the probability of significance (p-value) above 0.5 (Table 8). It is worth noting that, although pregnant women without schooling have an absolute risk (AR) for mortality greater than women with higher education, from 20.51% to 12.76%, the relative risk (RR) was 1.61 (0.85 - 3.04), demonstrating the irrelevance of this variable (Table 1). Thus, regarding schooling, it is important to point out that the pandemic context of COVID-19 was not the norm in terms of health education, since there was a wide dissemination of information about the signs and symptoms of the disease, making the search to the health service occurred more appropriately, a fact that justifies the result found. Despite this, with regard to the Brazilian socioeconomic regions, those with the highest GINI coefficient (DATASUS, 2022) - North and Northeast - scored with a lower cure rate (Table 5), later ratified by the RR above 1 for mortality (Table 8). Likewise, residing in rural areas is significantly related to higher mortality compared to the urban region, regardless of the higher absolute risk in the peri-urban area, whose RR demonstrates similarity to that of the urban area (Table 4). Thus, it is possible to perceive that, in economic terms, although there is no clear association between schooling and mortality, there is a higher risk of maternal death in less developed areas.

Thus, the efficiency of the distribution system of health units in Brazil and the degree of access to them can be questioned, both in relation to socioeconomic territories and to countryside and metropolis areas. Furthermore, it is already known that private healthcare is delivered 32% to the urban sector and only 7% to the rural sector (SOUZA JÚNIOR et al., 2021). It is worth highlighting that the study by DE PINHO et al. (2021) points out the 1st and 3rd trimesters as the most relevant in terms of susceptibility to infectious diseases during the gestational period. Corroborating this idea, the studies by DASHRAATH et al. (2020) point out the 3rd trimester as the period in which the overwhelming majority of pregnant women acquire SARS-CoV-2 infection. However, regarding mortality, the 2nd trimester was the most relevant phase for maternal death during the gestational period, either due to the lower incidence of cure (Table 6) or due to the significant risk factor (Table 7). Furthermore, it was noticed that the puerperium phase was more relevant in the occurrence of the hard outcome, with an RR of 1.99 (1.80 - 2.20), a fact already evidenced by TAKEMOTO et al. (2020b). Evaluating the race, the brown and black population reveals both a significant AR and RR for death higher than those of the other races, highlighting the indigenous people with the lowest values, including with regard to the sample size (Tables 2 and 7). These data can be justified, either by the fact that the white population has the largest contribution

Degree of cure	TOTAL DEATH					
Education	Number					
Without schooling	31	79.49%	8	20.51%	39	100.00
Merged (1)	361	86.99%	54	13.01%	415	100.00
Fund2	892	86.35%	141	13.65%	1033	100.00
Average	2564	85.84%	423	14.16%	2987	100.00
Higher	930	87.24%	136	12.76%	1066	100.00
TOTAL	4778	86.25%	762	13.75%	5540	100.00

Table 1 - Distribution of the number and percentage of cure and death of pregnant women infected with SARS-CoV-2 according to the level of education from the 14th epidemiological week of 2020 to the 26th epidemiological week of 2021

Race	Cure		Death		TOTAL	
	Number	%		%		04
Yellow	80	87.91	11	12.09	91	100.00
White	4090	88.15	550	11.85	4640	100.00
Indigenous	75	89.29	9	10.71	84	100.00
Brown	4402	86.59	682	13.41	5084	100.00
Black	512	83.25	103	16.75	615	100.00
TOTAL	9159	87.11	1355	12.89	10514	100.00

Source: Adapted from Rodrigues et al. (2021)

Table 2 - Distribution of the number and percentage of cure and death of pregnant women infected with SARS-CoV-2 according to race from the 14th epidemiological week of 2020 to the 26th epidemiological week of 2021

Age range	Cure		Death		TOTAL	
Years	number	OK	number			%
<20	791	93.39%	56	6.61%	847	100.00
20-34	7058	88.47%	920	11.53%	7978	100.00
>=35	2949	84.77%	530	15.23%	3479	100.00
TOTAL	10798	87.76%	1506	12.24%	12304	100.00

Source: Adapted from Rodrigues et al. (2021)

Table 3 - Distribution of the number and percentage of cure and death of pregnant women infected with SARS-CoV-2 according to age group from the 14th epidemiological week of 2020 to the 26th epidemiological week of 2021

Zone of residence	Cure		Death		TOTAL	
			Number			
Periurban	37	82.22%	8	17.78%	45	100.00
Rural	525	83.07%	107	16.93%	632	100.00
Urban	9193	88.10%	1242	11.90%	10435	100.00
TOTAL	9755	87.79%	1357	12.21%	11112	100.00

Source: Adapted from Rodrigues et al. (2021)

Table 4 - Distribution of the number and percentage of cure and death of pregnant women infected with SARS-CoV-2 according to areas of residence from the 14th epidemiological week of 2020

Region	Cure		Death		TOTAL	
	number		number			
Midwest	1471	89.97%	164	10.03%	1635	100.00
North	1071	84.73%	193	15.27%	1264	100.00
Northeast	1978	85.52%	335	14.48%	2313	100.00
South	1718	89.25%	207	10.75%	1925	100.00
Southeast	4560	88.25%	607	11.75%	5167	100.00
TOTAL	10798	87.76%	1506	12.24%	12304	100.00

Source: Adapted from Rodrigues et al. (2021)

Table 5 - Distribution of the number and percentage of cure and death of pregnant women infected with SARS-CoV-2 according to regions of Brazil from the 14th epidemiological week of 2020 to the 26th epidemiological week of 2021

Age / Gestational	Cure		Death		TOTAL	
			number	%	No	%
1 tri[1]	809	92.25%	68	7.75%	877	100.00
2 tri [2]	2310	87.53%	329	12.47%	2639	100.00
3 tri [3]	5419	90.24%	586	9.76%	6005	100.00
Puerperium	1861	79.46%	481	20.54%	2342	100.00
TOTAL	10798	87.76%	1506	12.24%	12304	100.00

Source: Adapted from RODRIGUES et al. (2021)
Grades:[1] First quarter/ second quarter / third quarter

Table 6 - Distribution of the number and percentage of cure and death of pregnant women infected with SARS-CoV-2 according to gestational and postpartum age from the 14th epidemiological week of 2020 to the 26th epidemiological week of 2021.

Variable	p-value	Cohort of variables	RR (CI 95%)
degrees of Education	0.5556	no schooling	1.61 (0.85 - 3.04)
		Elementary 1	1.02 (0.76 -1.37)
		Elementary 2	1.07 (0.86 -1.33)
		High school	1.11 (0.93 - 1.33)
		University education	
Race	<0.01	White'	
		Yellow	1.02 (0.59 -1.79)
		brown	1.13 (1.02 -1.26)
		black	1.41 (1.17 -1.71)
		Indigenous	0.90 (0.49-1.69)
Residence zone	< 0.0005	<20'	
		Urban / Periurban / Rural	(0.80 - 2.81) (1.19 - 1.70)
		Southeast/midwest	0.85 (0.72- 1.01)
Region	<0.00001	South	0.92 (0.79- 1.06)
		North	1.30 (1.12- 1.51)
		North East	1.23 (1.09 - 1.40)
gestational age	< 0.0001	First quarter	
		2nd Quarter	1.61 (1.26- 2.06)
		3rd Quarter	1.26 (0.99- 1.60)
Pregnancy and Puerperium	<0.00001	Gestation*	
		Puerperium	1.99 (1.80 - 2.20)
Ventilatory Support	<0.00001	No SV*(1), With SVNi	4.00 (3.22 - 4.98)
		With SVI*(3)	26.63 (21.87- 32.43)

Table 7 - Relative risk and significance interval between education levels, races, age groups, areas of residence, regions, gestational ages and ventilatory supports, in relation to maternal mortality from the 14th epidemiological week of 2020 to the 26th epidemiological week of 2021.

to health insurance in the country (SOUZA JÚNIOR et al., 2021), or by the issue of black and brown women (SUS users) being more vulnerable to greater data for childbirth pilgrimage, absence of institutional bond, greater chances of post-term delivery, and lower number of prenatal consultations, contributing positively to complications and ICU admissions (THEOPHILO et al., 2018). In terms of age group, the younger the pregnant woman, the greater the probability of cure, approaching 94% of resolution of the infectious condition in women under 20 years of age (Table 3). On the other hand, being over 35 can double the risk of dying from SARS-CoV-2. These data corroborate the current literature, since KAYEM et al. (2020) and MARTINEZ-PORTILLA et al. (2020) point to a greater severity of the infectious condition caused by COVID-19 in older women. With regard to the use and type of ventilatory support, the non-invasive quadrupled the risk of mortality in pregnant women, while the invasive one can increase the risk by 27 times, whose death rate exceeds the cure rate (Table 7). It is known that pregnant women are predisposed to more severe and prolonged conditions of the disease due to their relative immunosuppression status, leading to a greater need for ventilatory support. Consequently, more invasive methods tend to cause a greater number of nosocomial infections, either due to direct injuries due to barotrauma or atelectasis (CRUZ et al., 2021; SANTOS NETO et al., 2021). In addition, it is worth noting that the relationship between increased ventilatory support and maternal death is greater in countries with less economic development, such as Brazil, when compared to countries such as Belgium and France (SOUZA and AMORIM, 2021). Therefore, it is worth pointing out that the complications associated with the use of ventilatory support in pregnant women are directly related to greater exposure to pathogens, however, the socioeconomic context of the country in which this pregnant woman is inserted becomes a bias that reinforces the aforementioned causality. This study had a large cohort acquired from an accessible and transparent platform about demographic and clinical data of the maternal population in the described period. Through this, it was possible to structure significant correlations through statistical calculations. However, it is important to consider that the use of these secondary data can lead to biased population estimates, since certain demographic data, such as race, can be either underestimated or overestimated. Furthermore, underreporting of infectious cases is a reality of the Brazilian health system due to lack of access and failure to diagnose the maternal population. It is also important to mention that the presence of minority groups, such as the indigenous population, may result in sampling bias, due to the questionable size of the population studied for statistical conclusion purposes. Fortunately, many studies have corroborated each other (including this one) regarding risk factors for mortality among pregnant and postpartum women infected with SARS-CoV-2. This provides a more targeted allocation of human, intellectual and financial resources to address these discussed vulnerabilities.

CONCLUSION

In view of the data obtained, it is clear that the morbidity and mortality resulting from COVID-19 during pregnancy and the puerperium is directly associated with specific sociodemographic and socioeconomic profiles in Brazil, highlighting race, area of residence, Brazilian region and age group. Regarding clinical data, both the type of ventilatory support and the maternal period are significantly associated with death rates.

Therefore, measures are needed to better target access to health care in order to reduce maternal deaths related to COVID-19 and the side effects of the pandemic. It is worth emphasizing the need for new studies with broad and primary data to resolve divergences that are still relevant about the impact of SARS-CoV-2 along with the clinical and demographic characteristics of the maternal population.

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