TRACKING EXCESS OF MATERNAL DEATHS DIRECTLY AND INDIRECTLY ASSOCIATED WITH COVID-19 IN BRAZIL: A NATIONWIDE DATABASE ANALYSIS

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Abstract

The COVID-19 pandemic brought a new challenge to maternal mortality in Brazil. Throughout 2020, Brazil registered 549 maternal deaths, mainly concentrated in second and third-trimester pregnant women. We estimate the excess of maternal mortality for Brazil in 2020. Assuming the average number of previous years as expected, or even correcting the expectation for excess female mortality due to COVID-19, we found that maternal mortality was more penalized. We also observed that the difference between the odds of occurrence of symptoms and comorbidities among COVID-19 maternal and female deaths was marginal. Differences between the two groups of deaths are significantly associated with social determination and (in)adequate obstetric care. 2021 has been more severe for maternal mortality. We need to increase immunization and monitoring among pregnant women immediately.

Main Text

Maternal mortality in Brazil ranged from 60 to 65 deaths per 100,000 live births between 2010 and 2017, with a considerable variation across the country[1]. As a result, Brazil did not accomplish the Millennium Development Goal (MDG) settled 35 deaths per 100,000 live births in 2015. In the Sustainable Development Goals (SDG) for 2030, a new compromise of 30 deaths per 100,000 live births was established. COVID-19 pandemic brought new challenges, with pregnant and postpartum women presenting a COVID-19 fatality rate of 7.2%, almost three times as much as the 2.6% in the general population in the country. The group had not been identified as particularly vulnerable before when COVID-19 was still majorly affecting developed countries.

Studies have addressed the impact of COVID-19 on pregnancy, childbirth, and the puerperium and whether the pregnancy-puerperal status changes the natural history of COVID-19[2,3]. COVID-19 infection in pregnant women has been associated with higher rates of cesarean section and mortality[4]. The effects on maternal outcomes have yet to be understood. However, we already know that the pregnant woman's risk includes relative immunodeficiency associated with maternal physiological adaptations, as well as an organic response to virus infections. Still, pregnant women can suffer from a multisystem disease, and comorbidities play a significant role in risk[5].

Maternal mortality is also certainly affected by healthcare quality, which involves access, availability of necessary resources, and acceptable practices for prenatal care, childbirth, and puerperium[6]. The impact of the pandemic on the provision of regular prenatal services and the aggravated lack of ICU beds for Obstetrics created additional difficulties in the clinical management of high-risk pregnancies, regardless of the COVID-19 infection condition[7]. Thus, we evaluated the excess of maternal deaths that occurred in 2020. After performed the decomposition of these deaths, we identified which ones were directly caused by COVID-19 and which ones could be attributed to the effects of the pandemic on healthcare services. Additionally, we verified differences between COVID-19 female and maternal deaths.

In 2020, 549 COVID-19 deaths in pregnant and postpartum women were reported in the country, with a weekly average of 12.1 deaths[8]. In addition to the significant increase in deaths, it was possible to identify that most of them occurred during pregnancy and not in the puerperium in all months of 2020 (μ=59.8%, SD=14.3%, range 50%-100%) with cases. Considering the first scenario for the excess maternal mortality estimation, we

found a statistically significant excess mortality from March to November 2020 (Figure 1a). In July, the peak of the first pandemic wave, there was a 79% excess of maternal deaths, compared to July in the previous five-year period. Considering the second scenario, which assumes an increase in maternal deaths due to the rise in female population mortality caused by the pandemic, we obtained a similar picture (Figure 1b). Excess maternal mortality was still estimated between April and November. This diagnosis reinforces the idea that even with an increase in general female mortality because of COVID-19, pregnant and postpartum women were additionally penalized, with an excess of maternal mortality higher than the excess of general female mortality.

Regarding the breakdown of excess maternal deaths, we found that in 2020 most of this excess was due to COVID-19 (μ=70.0%, SD=28.2%, range 6.1%-100%). However, an essential diagnosis was an excess of deaths that did not have to do with COVID-19 directly. Therefore, we assume that these deaths were related to barriers faced by women to timely adequate healthcare access and the worsening in the performance and quality of the care provided.

Table 1 shows the comparisons between maternal and female deaths due to COVID-19 by clinical, inpatient care and social variables using MOR (Table 1). Clinical variables suggest that the chances of occurrence of symptoms among maternal deaths were like those observed in the deaths of women of childbearing age, with no statistically significant difference. Regarding comorbidities recorded in the SIVEP-Influenza, the overall occurrence was lower among maternal deaths than among female deaths due to COVID-19 (MOR = 0.50; 95%CI 0.25-0.80). However, the reason for this difference was due to three groups: cardiovascular diseases (MOR = 0.36; 95% CI 0.09-0.66), diabetes (MOR = 0.32; 95% CI 0, 10-0.59) and obesity (MOR = 0.53; 95% CI 0.21-0.85). The weight of these comorbidities is high due to their prevalence. The chance of their occurrence among maternal deaths was lower than in the deaths of women of childbearing age.

The result suggests that clinical characteristics did not strongly impact the excess of maternal deaths. On the other hand, variables related to hospital care and social determinants of health seem to have an apparent effect.

The odds of being a black woman, living in a rural area and being hospitalized out of the residence municipality among maternal deaths were 44%, 61%, and 28% higher than those in the female deaths. These findings suggest that the COVID-19 pandemic has a synergistic effect with the inequalities already observed in maternal mortality regardless of the pandemic. Finally, inpatient care variables seem to differentiate more maternal from female deaths than the clinical variables. The odds of hospitalization, ICU admission, and invasive ventilatory support use among maternal deaths were, respectively, 4.37, 1.73, and 1.64 times as much as those among female deaths. This profile suggests that pregnant and postpartum women who died were managed as critical cases.

The findings indicate that Covid-19 deaths among pregnant and postpartum women, compared to childbearing age females, are not attributable to other clinical aspects such as comorbidities than the pregnancy itself. Therefore, once there is no stronger than marginal association to comorbidities, we can consider pregnancy an independent risk factor of dying from Covid-19. It requires attention to establish actions to reduce this risk. This situation gets worse when we consider all the problems due to access to health services from those women, which can explain why Brazil keeps the rates at this level.

Since mid-2020, publications on the deaths of pregnant and postpartum women due to Covid-19 in Brazil have alerted to the need to prepare and organize the complete healthcare services network. They focused on ensuring timely access and the adequacy of clinical practices because of the specificities of the disease in the pregnancy-puerperal cycle. Brazil has a maternal mortality ratio compared to countries with average sociodemographic development, according to a composed index of per capita income, average education, and fertility. Given that Brazilian fertility is at a lower level, the social and income inequalities are the elements that explain Brazil's position. High maternal mortality rates are mainly concentrated in countries with a peripheral economy and reveal a severe violation of the right to health. Maternal mortality is a preventable event in more than 90% of cases. It is a determining factor in the increase in poverty and starvation[9].

The more outstanding picture of social inequality plays the central role[10]. Differences among pregnant women's profiles in Brazil and other countries are not unlikely. There is a high occurrence of comorbidities in the country whose etiology involves inflammatory conditions, which are risk factors for complications from Covid-19, such as obesity, hypertension, diabetes and vasculopathies[11]. Social determinants of health strongly influence these chronic conditions. Racial, geographic, and socioeconomic disparities, therefore, require special attention. Social, economic and health policies would be benefitted from consideration of this contextual effect[12].

In developing, as opposed to developed countries, high birth rates and limited resources for healthcare delivery contribute to the increased risk of maternal death due to COVID-19[13]. Brazil, however, has had a declining birth rate since the 1970s, and poor quality prenatal and obstetrical care have a more powerful explanatory weight. Timely access to adequate obstetric services is essential for patient safety and quality of maternal care[14]. Delay in receiving it is associated with the severity of adverse maternal outcomes. Thadeus & Maine[15] developed a model called "Three Delays" to assess access to obstetric care, broken down into three components or phases: (1) delay in the decision to seek health care; (2) delay in identifying and reaching the appropriate health service; and (3) delay in receiving appropriate care at the right time. Even today, this model is used to explain most maternal deaths and some cases of severe maternal morbidity.

In Brazil, barriers to access obstetric services with specialized complex care, and inadequate monitoring of obstetric complications, persist[16]. It occurs despite the warning that the CDC has issued about COVID-19 increased risk for pregnant and postpartum women to develop into severe forms, requiring hospitalization, intensive care, use of mechanical ventilation, and even premature births[17]. In addition to the impressive number of 2020, over less than six months of 2021, maternal deaths had already surpassed the number reported in the previous year. There are 1156 deaths registered, more than twice of the previous year[18].

For all these reasons, the COVID-19 pandemic may represent a significant immediate obstacle to Brazils' achievement of SDG by 2030. The excess of maternal mortality and the significant increase in near-miss cases caused by COVID-19, directly or indirectly, put the country in a delicate situation.

Our analysis has limitations. Total mortality data represent data available at the time of research. We recognize that the data can change due to some updates over the next few months. However, even if there is a recovery of maternal death records for the database, maternal deaths pattern is already worrying in the current scenario. Another limitation concerns the low testing performed in Brazil. This limitation prevents us from

knowing precisely how many COVID-19 infected pregnant and postpartum women. However, this information does not compromise the estimate calculation we use. The Mortality Odds Ratio has the advantage that we can use it precisely in this type of circumstance, where the population base is unknown. We assume deaths in the general population (in our case, the childbearing age female population) to estimate the odds of factors we considered related to maternal mortality. We also know that there is some imbalance between the age group that concentrates most women who experience pregnancies (between 20 and 29 years old) and the group with the highest prevalence of comorbidities (40 to 49 years old). However, we performed the analyses disregarding pregnancies' order, and we believe this minimizes the potential selection bias.

The situation in Brazil demonstrates the importance of national leadership in confronting the pandemic. It is even more important to recognize the need for long-term global care to improve local public health[19]. High maternal mortality is an indicator of failure in the organization of health services. Moreover, the solution requires the involvement of the international community since it affects global development. This scenario does not repeat itself in other low- and middle-income countries, prolonging the pandemic's impact for all[20]. For this reason, the analysis of excess maternal mortality is a call of action at this point in the pandemic.

That said, we emphasize the need for adequate measures for adequate prenatal, delivery and postnatal care. It is fundamental to prepare the healthcare network so that pregnant and postpartum women do not remain unattended, further aggravating maternal mortality.

We assume that the vaccination performed on pregnant women in the first trimester is adequate to protect pregnant women during the second and third trimesters of pregnancy. Moreover, it is necessary to combine non-pharmacological measures and vaccination. We need to strengthen maternal health care, from access to prenatal care to the regulation of obstetric ICU beds. Prenatal consultations must be qualified, encouraging physical distance measures. We also need to screen pregnant women for respiratory symptoms, distribute good quality masks, adopt universal testing on admission to maternity hospitals with molecular tests (RT-PCR), and provide obstetric care in hospital units with access to ICU beds for moderate cases and ICU beds for severe cases.

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Table

Table 1: Maternal and female COVID-19 Mortality Odds Ratio (MOR) per social determinant proxy, clinical and inpatient care variables. Brazil, 2020.

Dimension of Risk Factors	MOR	CI 95%	P-value
Social Determinant Proxies			
Black vs Non-Black People	1.44	1.22 to 1.66	<0.01
Rural vs Urban/Periurban Place	1.61	1.24 to 1.98	<0.01
Out-of-City Hospitalization	1.28	1.09 to 1.48	<0.01
Symptoms			
Fever	0,91	0.69 to 1.14	0.48
Cough	1.15	0.90 to 1.40	0.29
Throat Pain	1.08	0.84 to 1.33	0.55
Dyspnea	0.75	0.48 to 1.03	0.19
Respiratory Distress	1.00	0.75 to 1.25	0.97
Oxygen saturation < 95%	0.82	0.82 to 1.06	0.13
Diarrhea	0.78	0.46 to 1.10	0.15
Vomit	0.68	0.32 to 1.04	0.09
Comorbidities			
Overall	0.50	0.25 to 0.80	<0.01
Cardiovascular Disease	0.36	0.09 to 0.66	<0.01
Hematological Diseases	0.88	0.15 to 1.60	0.85
Liver Diseases	1.33	0.68 to 1.99	0.49
Asthma	0.69	0.21 to 1.18	0.16
Diabetes	0.32	0.10 to 0.59	<0.01
Neuropathies	0.64	0.08 to 1.21	0.18
Lung diseases	1.02	0.51 to 1.55	0.97
Immunodepression conditions	0.64	0.25 to 1.04	0.08
Kidney Diseases	0.61	0.18 to 1.03	0.06
Obesity	0.53	0.21 to 0.85	<0.01
Hospital Care			
Hospital Admission	4.37	3.39 to 5.37	<0.01
ICU admission	1.73	1.50 to 1.98	<0.01
Invasive Respiratory Support (yes vs. no)	1.64	1.42 to 1.86	<0.01
Non-Invasive Respiratory Support (yes vs. no)	0.57	0.32 to 0.82	<0.01

Source: SIVEP-Gripe.

Figures

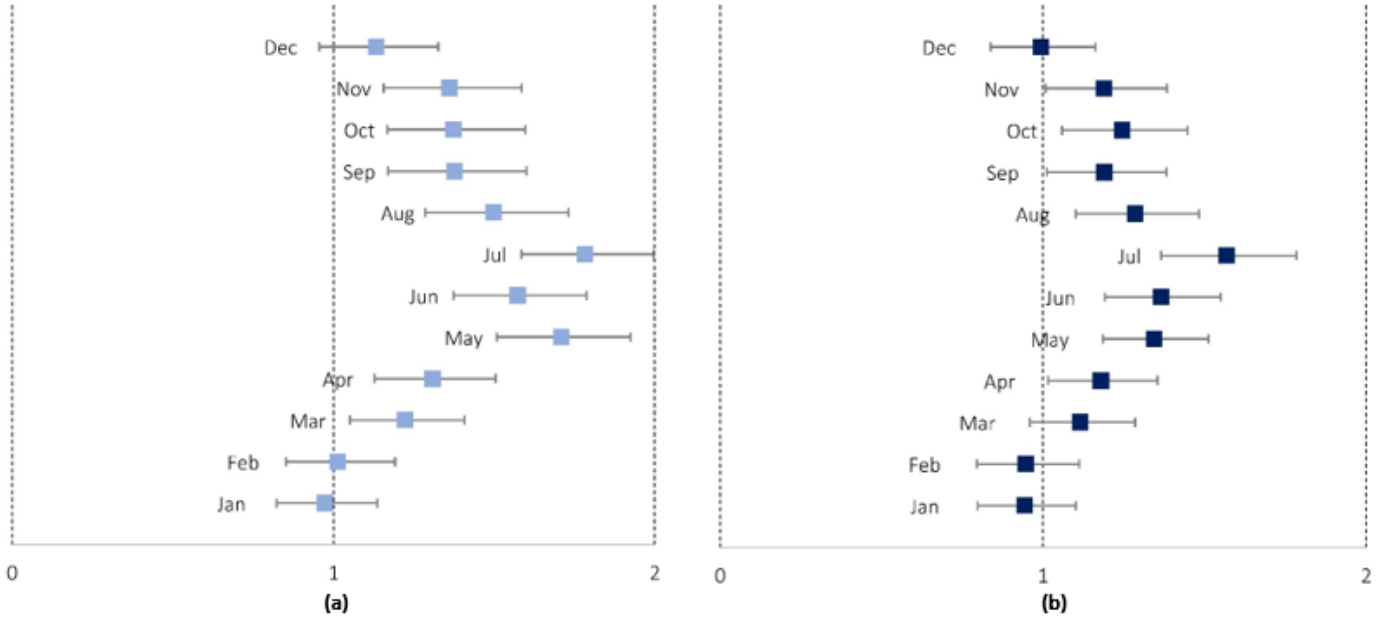

Figure 1

Excess maternal mortality per calendar month according to expected death scenarios. Brazil, 2020. Source: SIVEP-Gripe, 2021.

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