Preterm birth rates and caesarean delivery increased during the COVID-19 pandemic in Brazil: results from the national database.

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Summary (290 words)

Background: The SARS-CoV-2 (COVID-19) pandemic impacted the health systems between and within countries, and sexual and reproductive health (SRH) services were the most disrupted. Findings from high-income settings have reported significant changes in preterm birth (PTB) prevalence during the pandemic period. Our goal was to assess the PTB rates at the Brazilian national level during the COVID-19 pandemic year 2020 compared to three previous years.

Methods: We conducted a population-based cross-sectional study including data from January 2017 to December 2020. We extracted individual-level live birth data from the Brazilian Live Birth Information System (SINASC), which includes all live births from 22 weeks of pregnancy. The main outcome was the PTB rate. We estimated the odds ratio (OR) of PTB using propensity score weighting analysis. In addition to the analysis for the country, we performed a stratified analysis by region. Two-sided p-value of < 1% (0·01) was considered significant. All statistical analysis was conducted using statistical packages in python 3·9 languages.

Findings: The prevalence of preterm birth had a higher significant variation within Brazilian regions in 2020 compared to the pre-pandemic period (2017-2019). In Brazil, the OR of preterm births increased by 5·6% (OR: 1·052; 95% CI [1·044; 1·059]). Among the preterm births, the chance of childbirth by caesarean delivery also increased in the pairwise 2019-2020 (OR: 1·121; 95% CI [1·112 - 1·130]).

Interpretation: The OR of preterm birth increased during the first year of the COVID-19 pandemic in Brazil. Among the preterm births, the chance of childbirth by caesarean delivery was higher in 2020 than in previous years, suggesting a provider-initiated PTB.

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Keywords: Preterm birth, COVID-19, Brazil, Caesarean delivery, prevalence.

Research in context

Evidence before this study

We conducted a comprehensive search of PubMed, Scopus and Web of Science for research articles, from January 01st 2020, to May 20th 2022, with no language restriction, using the following search terms ((“Preterm Birth” OR “Birth, Premature”) OR (“Caesarean Section” OR “Caesarean delivery”)) AND (“coronavirus” OR “COVID-19” OR “SARS-CoV-2” OR “2019-nCoV” OR “COVID-19 Pandemic”). Preterm birth (PTB) is an important public health condition associated with a high prevalence of morbidity and death among children under five years old. However, most child death related to PTB is preventable. The COVID-19 pandemic provided a unique possibility to assess other not well established (public health and social measures at a large scale) preterm birth risk factors. Finding from observational studies (population-based) showed contradictory findings regarding the PTB rate in 2020 compared to the pre-pandemic periods. Data from health facility-based studies showed an increased caesarean delivery rate. Most of these findings are from high-income countries.

Added value of this study

Our population-based cross-sectional study assesses the prevalence of PTB and caesarean delivery during the first wave of the COVID-19 pandemic compared to the previous period. We set about 2.8 million annual live births records from 2017 to 2020, and our analysis was based on a quasi-experimental approach. Our findings suggest a significant variation within Brazilian regions in 2020 compared to the pre-pandemic period. Moreover, the overall caesarean delivery rate and the chance of childbirth by caesarean delivery among the preterm babies was significantly higher in 2020 compared to the pre-pandemic period.

Implications of all the available evidence

Brazil is one of the top countries with a higher burden of preterm birth and was most affected by the COVID-19 pandemic. Findings from individual studies have highlighted the association between the SARS-CoV-2 infection and adverse maternal outcomes, including preterm birth. The role of public health and social measure in curbing the effect of the COVID-19 pandemic on the onset of preterm birth are still unclear. Although these measures might have influenced the prevalence of preterm birth, our population-based study findings are not necessarily causal. The higher prevalence of preterm birth in the low resourced regions and regions with a lower Human Development Index may highlight the importance of addressing the social factors and equity in assessing adequate health care to prevent preterm birth.

Introduction (2953 words)

The SARS-CoV-2 (COVID-19) pandemic has reached Latin American countries later than other regions; nevertheless, we saw disrupting health systems, causing excess mortality and reducing life expectancy in middle and low-income areas.[1] Due to controversial health policies, conflicted message and long-time central government resistance to implement population mobility restrictions ,[2] Brazil was one of the main countries affected worldwide. Pregnant women were also a risk group, as the number of maternal mortality skyrocket during the pandemic.[3]

Maternal mortality is an important proxy for the quality of the maternal services countrywide. Another obstetric condition that is sensitive to suboptimal clinical care is preterm birth.[4] Studying preterm birth is important, because it is the primary cause of neonatal death, and its prevalence is rising in most low-income countries despite many efforts to revert it (9, 10). [5, 6] While several risk factors have been well-established, the key factor responsible for preterm deliveries is still unknown in half of the cases. [7] Since the onset of the pandemic, several studies identified an association between COVID-19 infection and adverse perinatal outcomes, such as stillbirths and preterm birth (PTB). [8-11] These findings are also contradictory, because while some analyses indicate that during the pandemic there were an increase preterm birth rates, other studies suggested a reduction.[10]

One of the most important underlying mechanisms for preterm birth is the inflammatory condition. The systemic inflammation may trigger cervical effacement and uterine contraction through increasing prostaglandins.[12] The SARS-CoV-2 infection is a systemic inflammatory disease, therefore, could lead to preterm birth. For example, among women with SARS-CoV-

2 pneumonia, there seems to be an increased preterm birth rate.[13] However, the infection itself may not represent the whole mechanism related to PTB.

We may also argue that individual behaviour changes associated with lockdown and other population restrictions, implemented to mitigate SARS-CoV-2 dissemination, may have influenced to some extent preterm birth rates. As an example, an Australian study showed a lower risk of preterm birth in pregnant women during lockdown in comparison to those born before the pandemic.[14] A populational-based study and metanalysis showed decreasing preterm birth rates,[15, 16] although the same empirical evidence was not corroborated in other study that fail to identify differences in the PTB rates. [(17)]

The COVID-19 pandemic period brought a challenge to health systems and, while many studies have been published since the breakdown of the pandemic, there is still scarce information about its real consequences on perinatal health, in different settings· In our study, we aim to assess the pattern of preterm births in a national dataset comparing the initial pandemic period to pre-pandemic periods in Brazil·

Methods

Study design and Data sources

This is a population-based cross-sectional study. We performed extensive use of the publicly available microdata of live birth, collected by the Brazilian Ministry of Health, and launched by the Brazilian Live Birth Information System (SINASC in Portuguese). [18] The SINASC is an e-birth registration system developed by the Department of Informatics of the National Unified Health System (DATASUS). This system was implemented in 1990 and the data are collected

routinely immediately after each birth through a standardized document (declaration of live births), which was updated in 2010 to ensure a better quality of the information recorded. [19] The updated version included many important variables for the study of PTB, such as sociodemographic and obstetric variables. This study was part of the REBRACO initiative, and the study protocol was approved by the Institutional Review Board (Letters of Approval numbers 4.047.168).[20]

Data acquisition and pre-processing routines·

Data were downloaded from http://svs·aids·gov·br/dantps/cgiae/sinasc/ on February 20th, 2022. All live births equal or superior to 22 weeks, from January 2017 to December 2020 were included. We extracted individual-level data regarding gestational age at birth, sex, maternal age, ethnicity, schooling, parity, gravidity, mode of delivery, region and federal state of residence, number of living children, number of antenatal care (ANC) visits, and newborn's weight. These variables are available in the SINASC for each birth and, according to the literature, they are highly associated with PTB. We did not exclude multiple pregnancies and neonates with congenital anomalies for the analysis. All categorical variables were converted to binary dummies by using the one hot encoding procedure. Less than 5% of the samples had some missing value, or unknown data, we excluded from the sample individual-level data with missing information for gestational age at birth.

To reduce the influence of a possible trend in PTB prevalence, we based our analysis on a pairwise comparison of years from 2017 to 2020. We did not include data before 2017 to avoid the influence of the Zika virus outbreak in 2015 in Live Births and Fertility. [21] We created three stacked datasets [2017-2018; 2018-2019; 2019-2020] and we added, for each dataset, two dichotomous control variables: one to indicate whether the birth was preterm (y=1) or term

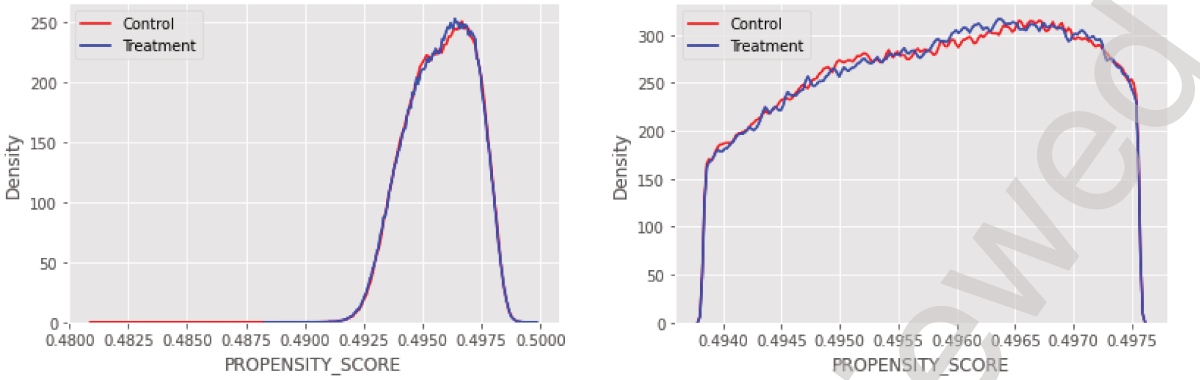
(y=0) and another to indicate whether the first year in the dataset (z=0) or the following (z=1)· The control variable (z) was useful to identify the control group (births in a previous year) and the treatment group (births in the following year)·

Statistical analysis

Our analysis was based on a quasi-experimental approach by means of the Propensity Score Weighting (PSW) method. [22, 23] PSW was designed to control for selection bias in non-experimental studies, for which it is desirable to assess the average effect of some variable that emulates a control/treatment process. Propensity scores are used to match untreated versus treated individuals, understanding that there is a probability of these last being exposed to certain stimulus or intervention. [24]

In a first step, a multiple logistic regression analysis was used to fit the binary control variable (z) as a function of mother's and obstetrics' characteristics: age, ethnicity/skin colour, schooling, parity, mode of delivery, number previous children, number of ANC visits and new-born weight. From this first regression we extracted a vector (e) that estimates the probability of treatment assignment conditional on baseline covariates (x), i·e· $e(x) = P(z = 1|\ x)$.

The vector (e) is called the *Propensity Scores* and it was used to control for selection bias and to derive the weights of a second regression model. The control was made by pruning samples corresponding to the tails of the Propensity Score vector, to keep only samples that can be considered comparable to each other. Figure 1 shows the kernel density estimate (KDE) plot for the Propensity Score referring to births in Brazil in the years 2019 and 2020, before (a) and after (b) a 10% pruning of each tail. In this example, 80% of the original dataset was selected for the final phase of the analysis·



(a) (b)

Figure 1: Kernel density estimate (KDE) plot for the Propensity Score referring to births in Brazil in the years 2019 and 2020, before (a) and after (b) a 10% pruning of each tail.

The set of weights was estimated as follows: for the individuals in the treatment group, $w = \frac{1}{e(x)}$, and for the individuals in the control group

$$w = \frac{1}{1 - e(x)}.$$

The final step in the PSW analysis was to run a new regression, fitting the outcome of interest (preterm birth) controlled by the covariates and using the propensity scores as weights. The coefficients of each variable from this regression can be converted to Odds-Ratio (OR) to help interpretation.

Role of the funding source

CMC is a PhD student, and RTS is a Postdoc fellow, supported by the SRH, part of the UNDP-UNFPA-UNICEF-WHO-World Bank Special Programme of Research, Development and Research Training in Human Reproduction (HRP), a cosponsored programme executed by the World Health Organisation (WHO). However, the study funders had no role in the study

design, data collection, analysis, interpretation, report writing, or decision to submit the manuscript· Therefore, this article represents the views of the named authors only and does not represent the views of the mentioned organization.

Results

About 2·8 million live births were recorded annually from 2017 to 2020. Table 1 presents the distribution of some clinical and epidemiological data comparing 2019 and 2020. Overall, for Brazil, the prevalence of preterm birth was 11·32% in the pandemic period 2020 compared to 11·09% in 2019.

In the multiple analysis using PSW, the OR for preterm birth for Brazil had a significant variation in 2020 compared to 2019 when controlled for clinical and demographical variables. The pairwise comparison of years from 2017 to 2019 did not show an increment in the OR for preterm birth, suggesting non increasing trend of PTB rates from 2017 to 2019 (figure 1 and table 2). However, the 2020-2019 comparison showed a significant 5·1% increase in the odds ratio for preterm birth (OR 1·051; 95% CI [1·044 - 1·059]).

Figure 1 also shows that this result was similar to the regional analysis for Northeast, South and Southeast, the most populated regions of Brazil. No significant effect was seen for the Midwest region. An opposite effect was observed in the North region, which significantly increased PTB in the 2018-2019 pairwise comparison and a reduction in the consecutive period analysis. Most clinical and demographic variables were significantly associated with PTB and showed consistency in this association in all pairwise comparisons. Caesarean delivery showed a higher increase in the OR for PTB in the pairwise 2019-2020 (table 2).

Caesarean delivery showed similarly OR for PTB in the 2017-2018 and 2018-2019 comparison (OR 1·076 and 1·081, respectively), and had a higher OR for PTB in the 2019-2020 comparison (1·121; 95% CI [1·112 - 1·130]). The analysis of caesarean delivery by gestational age groups showed a trend of increased caesarean delivery in all gestational age groups. The Odds-ratio for caesarean delivery among the preterm birth population is presented in Figure 3 and shows a more pronounced risk of being delivered by caesarean in the pairwise comparison 2019-2020 than in previous years. In the regional analysis, this pattern is also present in the South and Southeast.

Table 1 Descriptive statistics for Brazil live births 2019 and 2020·

	2019		*2020*	
	%	**Full Sample**	*%*	**Full Sample**
	100	**N=2,849,146**	***100***	**N=2,808,737**
Term	*88·88*	2,532,313	*87·13*	2,447,268
Preterm	*11·09*	315,831	*11·32*	318,052
Not stated/Unknown	*0·04*	1,002	*1·5*	43,417
Parity				
Primiparous	*37·54*	1,069,586	*37·05*	1,040,773
Multiparous	*62·46*	1,779,560	*62·95*	1,767,964
Mode of delivery				
Vaginal	*43·63*	*1,243,104*	*42·49*	*1,193,528*
Caesarean	*56·3*	*1,604,189*	*57·39*	*1,612,028*
Not stated/Unknown	*0·07*	*1,853*	*0·11*	*3,181*
Sex				
Male	*51·15*	1,457,226	*51·21*	1,438,304
Female	*48·84*	1,391,486	*48·78*	1,369,973
Not stated/Unknown	*0·02*	434	*0·02*	460
Race/colour				
White	*33·85*	964,557	*32·26*	905,98
Black	*6·19*	176,224	*6·34*	178,07
Asian	*0·45*	12,738	*0·44*	12,236
Brown	*55·96*	1,594,267	*57·06*	1,602,628
Indigenous	*0·93*	26,373	*0·91*	25,619
Not stated/Unknown	*2·63*	74,987	*3·00*	84,204
Mother's schooling				
0 to 7 years	*16·22*	*462,063*	*15·36*	*431,144*
8 to 11 years	*61·36*	1,748,186	*62·23*	1,747,742
12 and more	*21·27*	606,145	*21·12*	593,141
Not stated/Unknown	*1·15*	32,752	*1·31*	36,71
Type of pregnancy				
Single	*97·76*	2,785,200	*97·73*	2,745,068
Twin	*2·13*	60,61	*2·10*	58,996
Triplet and more	*0·05*	1,467	*0·05*	1,287
Not stated/Unknown	*0·07*	1,869	*0·12*	3,386
Number of ANC visits				
None	*1·52*	43,406	*1·77*	49,826
1 to 3	*5·35*	152,483	*5·96*	167,278
4 to 6	*20·26*	577,17	*20·64*	579,803
7 and more	*72·43*	2,063,669	*71·14*	1,998,224
Not stated/Unknown	*0·44*	12,418	*0·48*	13,606

Source: Brazilian Live Birth Information System (SINASC) (2022).

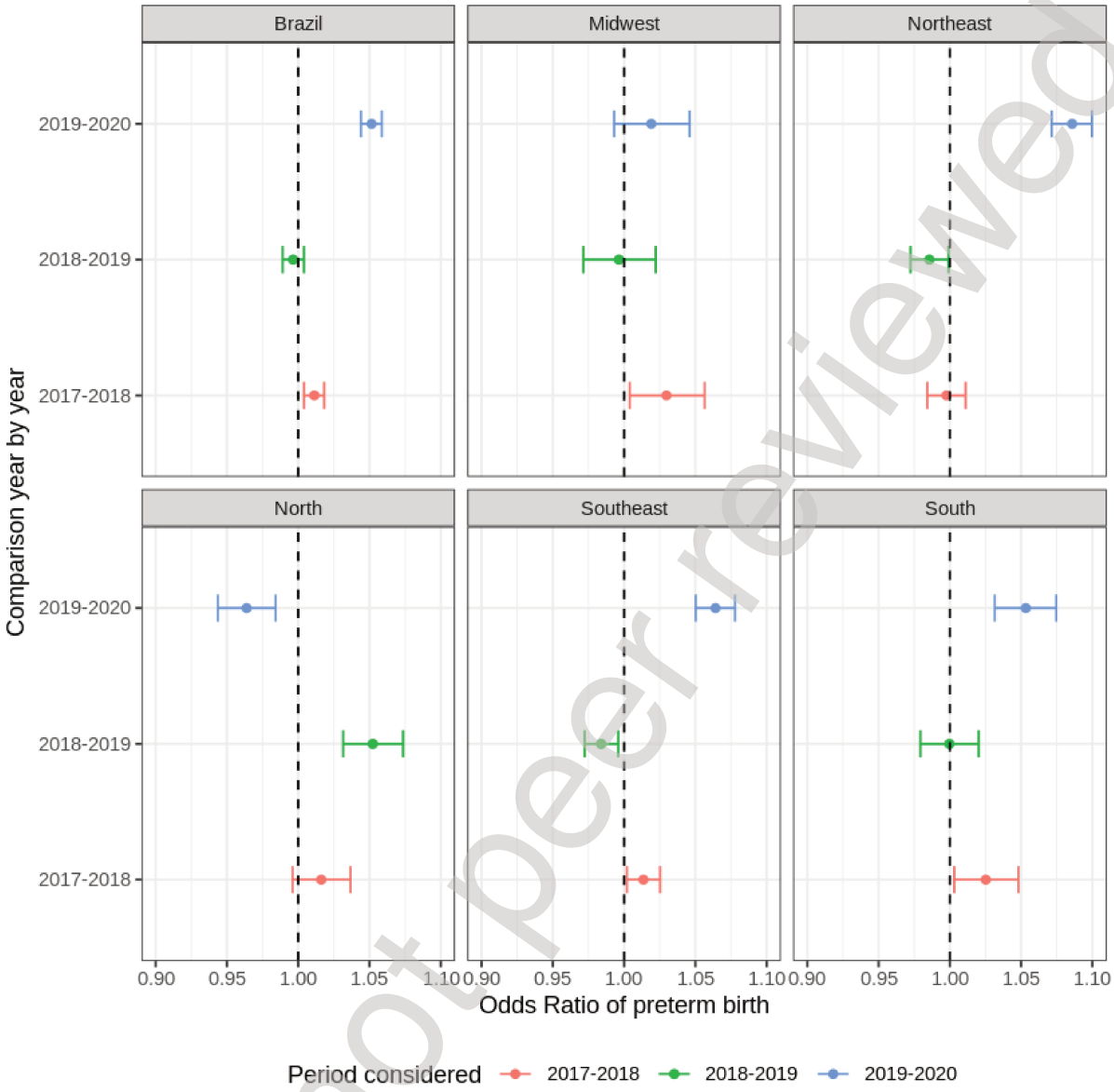


Figure 1 Comparison year by year of odds-ratio of preterm birth for Brazil and regions·

Table 2 - Multiple analysis using Propensity Score Weighting for preterm birth in Brazil.

Brazil	Odds Ratio (95% CI)		
	2017-2018	**2018-2019**	**2019-2020**
Intercept	116·956 (109·180 - 125·211)***	109·445 (104·899 -114·091)***	94·827 (91·012 – 98·790)***
Year	1·011 (1·004 - 1·018)**	0·996 (0·989 - 1·004)	1·052 (1·044 - 1·059)***
Weight	0·997 (0·997 - 0·997)***	0·998 (0·997 - 0·998)***	0·998 (0·998 - 0·998)***
Mother's age	1·011 (1·010 - 1·011)***	1·011 (1·010 - 1·012)***	1·016 (1·015 - 1·017)***
Multiparous	1·107 (1·097 - 1·116)***	1·108 (1·099 - 1·117)***	1·126 (1·116 -1·134)***
Caesarean delivery	1·076 (1·068 - 1·084)***	1·081 (1·073 - 1·090)***	1·121 (1·112 - 1·130)***
Sex			
Female	ref.	ref.	ref.
Unknown	1·884 (1·478 - 2·401)***	2·288 (1·761 - 2·974)***	1·950 (1·542 - 2·474)***
Male	1·381 (1·370 - 1·391)***	1·392 (1·381 - 1·402)***	1·400 (1·390 - 1·412)***
Race/colour			
White	ref.	ref.	ref.
Black	0·885 (0·871 - 0·899)***	0·894 (0·879 - 0·908)***	0·892 (0·877 - 0·905)***
Asian	0·904 (0·854 -0·958)**	0·936 (0·884 -0·991)*	0·962 (0·911 - 1·015)
Brown	0·972 (0·965 - 0·980)***	0·997 (0·988 - 1·005)	0·971 (0·963 - 0·979)***
Indigenous	1·054 (1·018 - 1·091)***	1·108 (1·071 - 1·145)***	1·076 (1·038 - 1·116)***
Mother's schooling			
0 to 7 years	1·119 (1·104-1·134)***	1·142 (1·127-1·158)***	1·028 (1·014 - 1·041)***
8 to 11 years	1·059 (1·048-1·071)***	1·074 (1·062-1·086)***	1·014 (1·004 - 1·024)***
12 and more	ref.	ref.	ref.
Type of pregnancy			
Single	ref.	ref.	ref.
Twin	2·838 (2·787 - 2·889)***	2·948 (2·889 - 3·004)***	3·061 (3·010 - 3·114)***
Triplet and more	6·639 (5·228 - 8·415)***	6·209 (4·613 - 8·356)***	8·488 (6,848 – 10,517)***
Nº of ANC visits			
None	ref.	ref.	ref.
1 to 3	1·553 (1·509 - 1·598)***	1·548 (1·496 - 1·592)***	1·42 (1·372 - 1·458)***
4 to 6	1·255 (1·221 - 1·289)***	1·288 (1·246- 1·320)***	1·248 (1·206 - 1·276)***
7 and more	0·637 (0·619 - 0·653)***	0·666 (0·638 - 0·676)***	0·648 (0·630 - 0·666)***
N	4,402,402	4,386,039	4,281,830

p <0·05*, p <0·01 and p <0·001*****

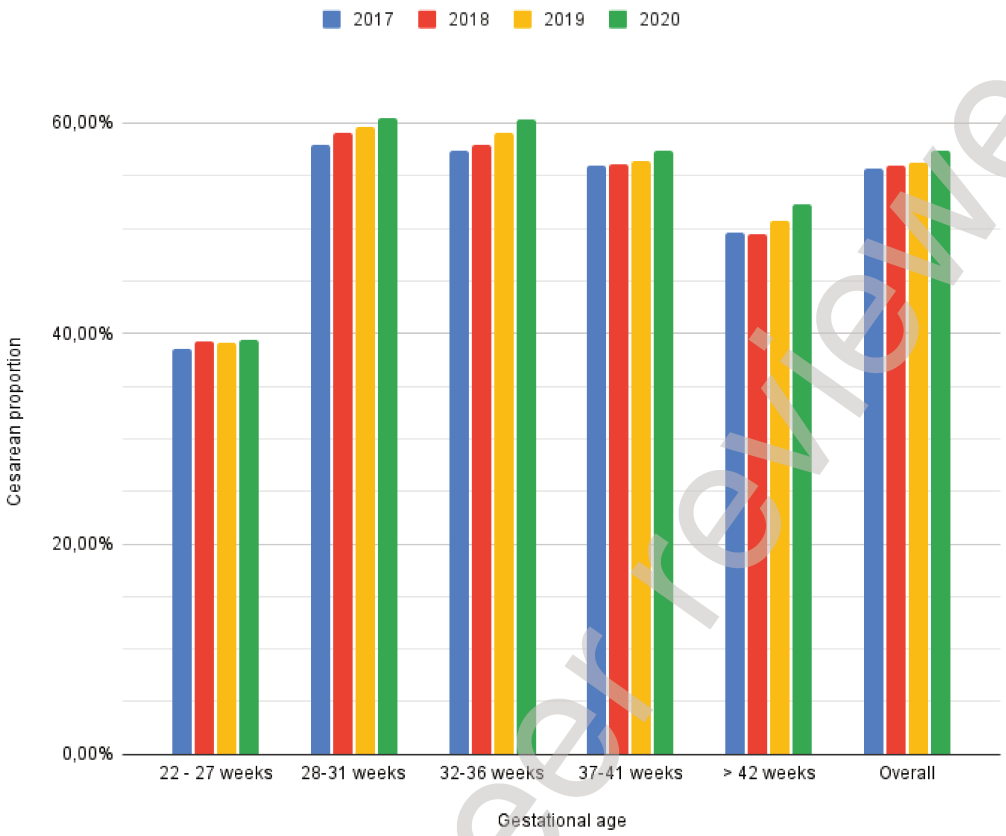


Figure 2: Caesarean delivery proportion for categorical gestational ages from 2017 to 2020.

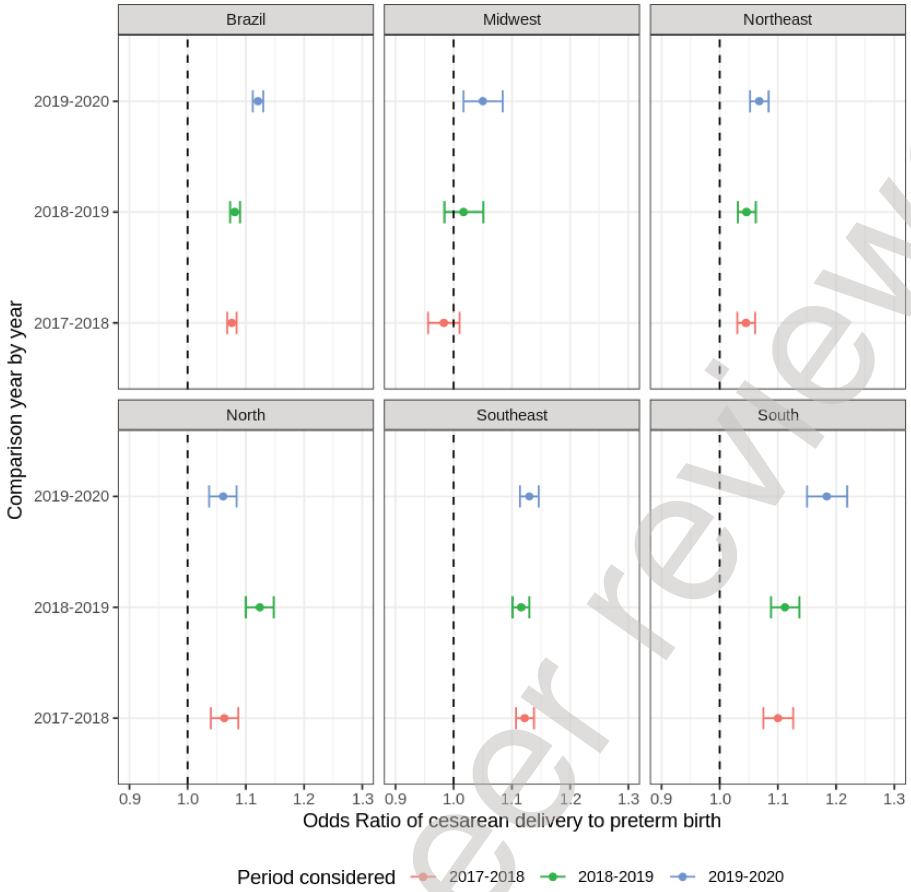


Figure 3: Odds-ratio of caesarean delivery to preterm birth for Brazil and regions.

Discussion

We evaluated the influence of the COVID-19 pandemic period on the PTB prevalence in Brazil using a populational database. We assessed the risk of PTB before and during the COVID-19 pandemic period with large and representative sample size, and we found an increased risk of PTB in the pandemic period compared to the three pre-pandemic years. Our finding suggested a small but significant variation in the prevalence of PTB in Brazil of about 5% after the onset of the COVID-19 pandemic (2020) compared to the pre-pandemic period (2017-2019).

Adult women, ethnicity (white and indigenous), 12 or more years of schooling, and multiparity were associated with an increased chance of PTB. These data are similar to the findings of other population-based studies. [25, 26]

The same pattern in the PTB rate was observed in the Northeast, Southeast, and South regions. The higher increased risk of PTB in the Northeast, a region with a lower Human Development Index, could be due to the difficulty accessing health services, [27, 28] and lack of strategy to mitigate the impact of the pandemic at different governmental levels.[2, 29] Moreover, a consequence of the greater economic inequality within Brazil. The COVID-19 pandemic brought an enormous burden to Brazil's North and Northeast regions 29) and revealed a sudden disruption of health care services. [30, 31]

Our findings are different from those observed in previous studies that indicated a reduced PTB chance during the COVID-19 pandemic.[8, 14, 32-36] This could be explained by the measures to face the pandemic implemented in an uncoordinated way in Brazil. [27] Also, due to inequality in health services access and the degree of responsiveness of the Brazilian National Health System to the pandemic. In addition, the previous studies were conducted in high-income countries with strict lockdown policies and with health services according to the needs posed

by the pandemic. On the other hand, our data may highlight PTB onset's multifactorial aetiology and mechanism. [37]

Another important finding is regarding the increased chance of caesarean delivery. Although there is a trend of increasing caesarean delivery rates, the risk of a PTB after caesarean delivery was increased in 2020 compared to previous periods. We may speculate that the increased chance of PTB in 2020 may be related to non-spontaneous (provider-initiated) preterm birth. Other maternal conditions might have influenced this PTB pattern with an increased chance of caesarean delivery as an inadequate ANC (leading to undiagnosed and untreated conditions such as diabetes, pre-eclampsia, and eclampsia, among others). [38, 39] Otherwise, it is probably an increment of caesarean delivery because, in 2020, it was uncertainly the effect of the SARS-CoV-2 infection on the mother and the baby and the possibility of vertical transmission.[40] Probably, many healthcare providers think that childbirth by caesarean delivery protects both the woman and the neonate. Moreover, caesarean delivery on maternal request and in some health facilities, there was a lack of structure for adequate labour induction procedures, increasing unnecessary caesarean deliveries.

Our study has some strengths and limitations. Our study has an adequate sample size and nearly 95% of the population of live births in Brazil, with data extracted at the individual level.[41] Moreover, the analysis of the different geographic regions allowed us to picture preterm birth among the different Brazilian contexts. Our results are robust in the additional analyses performed (simple and multiple regression analysis). The main limitation is related to the study design that does not allow causality association. We also did not assess the direct impact of COVID-19 on the occurrence of PTB, we considered the year of 2020 as a risk factor with all changes (social, economic, and epidemiological) brought from the pandemic onset.

Likewise, our regression model did not include variables associated with the PTB, such as maternal morbidities, including maternal COVID-19 infection. Due to the lack of this data, we did not assess the prevalence of foetal deaths and the abortion rate. These outcomes could have increased in situations of reduced access to adequate SRH services and impacted the birth rates in Brazil. Moreover, the data analyzed in 2020 included those referring to January and February when there were no recorded cases of COVID-19 in Brazil.

Conclusion

Our data suggest a high prevalence of PTB (11·32%) and Caesarean delivery rate (57·39%) during the first year of the COVID-19 pandemic in Brazil. Moreover, the odds ratio of PTB increased significantly in 2020 compared with three previous non-pandemic years. In addition, among the PTB population, the chance of childbirth by caesarean delivery was higher in 2020 than in previous years.

Contributors

RCP, CMC, LGB, JGC, CT and RTS conceived the study. CMC, AM, LAN, TA, and CFS extracted the data from the SINASC. RCP, CT, EECL, LAN, PR, and CFS conducted the statistical analysis, and collaborate in writing the manuscript first draft. RCP, LGB, MLC, CMC, and CFS collaborated to statistical analysis. RCP, CT, EECL, LAN, PR, EECL, and CMC wrote the first Draft. All authors critically reviewed the manuscript. All the authors read and approved the final version of the manuscript.

Declaration of interests

The authors declare that they have no conflict of interest.

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