

## CLINICAL ARTICLE

## Obstetrics

# Increased spontaneous preterm births during the second wave of the coronavirus disease 2019 pandemic in India

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**Abstract**

**Objective:** To compare spontaneous preterm birth (SPTB) and iatrogenic preterm birth (IPTB) rates during both waves of the coronavirus disease 2019 (COVID-19) pandemic.

**Methods:** Retrospective analysis of the PregCovid registry of pregnant women with COVID-19 was performed at a dedicated COVID-19 hospital in Mumbai, India. The data of 1630 women were analyzed for this study between April 4, 2020 and July 4, 2021. Prepandemic data were analyzed and compared with pandemic data. Main outcome measure was spontaneous preterm birth rate.

**Results:** Preterm deliveries were higher during the second wave (46/329; 14%) compared with the first wave (82/807; 10.2%) of the COVID-19 pandemic ( $P = 0.065$ ). Higher SPTBs were reported during the second wave than the first wave (12.5% versus 8.3%) ( $P = 0.03$ ) as well as the prepandemic period (12.5% versus 10.5%) ( $P = 0.286$ ). IPTBs were significantly lower in the pandemic period than in the prepandemic period (1.8 versus 3.3) ( $P = 0.012$ ).

**Conclusion:** In Mumbai, India, we found an unusual change in SPTBs during the 6 months of the second wave of COVID-19 compared with the previous 10 months of the first wave of pandemic and 1 year of prepandemic.

**KEYWORDS**

Coronavirus disease 2019, pregnancy, preterm birth, preterm labor, severe acute respiratory syndrome coronavirus 2 infection

## 1 | INTRODUCTION

Preterm birth (PTB) is a major cause of mortality and morbidity in the neonatal period, especially in developing countries.<sup>1</sup> The etiology of preterm birth is multifactorial. Higher preterm births were reported in women with coronavirus disease 2019 (COVID-19) (14%–25%)

mainly from high-income countries.<sup>2–6</sup> There is limited information on PTB rates in women with COVID-19 in low- and middle-income countries. A recent meta-analysis reported the disproportionate impact of COVID-19 on pregnant women residing in low- and middle-income countries.<sup>7</sup> Earlier, we reported higher rates of intensive care unit admission and maternal mortality among pregnant

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TABLE 1 Comparison of preterm birth rates of pregnancies with COVID-19 during two waves of COVID-19 pandemic and pre-pandemic period in India<sup>a</sup>

	Prepandemic period (October 1, 2019 to March 31, 2020)	COVID-19 pandemic period (April 1, 2020 to July 7, 2021)	First wave (April 1, 2020 to January 31, 2021)	Second wave (February 1, 2021 to July 7, 2021)	Pre-pandemic versus first wave P value <sup>b</sup>	Pre-pandemic versus second wave P value
Total number of pregnant and postpartum women managed at NH	3463	1630	1143	487	NA	NA
Symptomatic for COVID-19	NA	328 (20.1)	162 (14.2)	166 (34.1)	<0.001	NA
Number of deliveries	1879	1136 <sup>c</sup>	807 <sup>c</sup>	329 <sup>c</sup>	NA	NA
Total preterm deliveries	259 (13.8)	128 (11.3)	82 (10.2)	46 (14.0)	0.065	0.923
Iatrogenic preterm births	62 (3.3)	20 (1.8)	15 (1.9)	5 (1.5)	0.694	0.114
Spontaneous preterm births	197 (10.5)	108 (9.5)	67 (8.3)	41 (12.5)	0.030	0.286

Abbreviations: COVID-19, coronavirus disease 2019; NA, not applicable; NH, Nair Hospital.

<sup>a</sup>Data are presented as number (percentage).

<sup>b</sup>The  $\chi^2$  or Fisher exact test was applied at the significance level of  $P < 0.05$ .

<sup>c</sup>Included those patients who were admitted in the postpartum period, but delivered when they were suffering from COVID-19 and admitted at NH in the same episode of COVID-19.

women during the second wave of the COVID-19 pandemic in India.<sup>8</sup> Therefore, we aimed to analyze preterm deliveries and compare the rates of spontaneous preterm births (SPTBs) and iatrogenic preterm births (IPTBs) during the first and second waves of COVID-19. The SPTBs and IPTBs during the pandemic were compared with those in the pre-pandemic period.

## 2 | MATERIALS AND METHODS

We conducted a hospital-based, retrospective cohort study using data from the PregCovid registry database at BYL Nair Charitable Hospital (NH), Mumbai, India. The data of women with COVID-19 and PTB admitted to NH, Mumbai, India from April 4, 2020 to July 4, 2021.<sup>9</sup> Details of the PregCovid registry protocol and data collection methods are described elsewhere.<sup>10</sup> Data from 1630 pregnant and postpartum women with COVID-19 were analyzed for this study. PTB was defined as all births before 37 completed weeks of gestation.<sup>11</sup> PTBs were further classified as spontaneous (due to spontaneous preterm labor, or preterm prelabor rupture of membranes [PPROM]), or iatrogenic (due to provider-initiated cesarean, or labor induction, for a maternal, or fetal indication).<sup>12</sup> Gestational age was calculated based on last menstrual period and obstetric ultrasound. PTBs were sub-categorized based on gestational age: extremely preterm (less than 28 weeks); very preterm (28–32 weeks); and moderate to late preterm (32–37 weeks).

The COVID-19 pandemic period was divided into two waves: a first wave from April 1, 2020 to January 31, 2021 and the second wave from February 1, 2021 to July 4, 2021. Diagnosis of COVID-19 was made as per the existing National testing guidelines during both waves. All pregnant women with confirmed COVID-19 who were near-term or postpartum, those who needed obstetric interventions, with high-risk pregnancies, or with moderate or severe COVID-19 were admitted to NH.<sup>9</sup> The disease severity of COVID-19 was categorized as per the National Clinical Management Protocol for COVID-19.<sup>13</sup>

NH is a part of the PregCovid Registry network hospitals in India. Institutional Ethics Committee approval was obtained from the NH (ECARP/2020/63 dated May 27, 2020) and ICMR-NIRRH (D/ICEC/Sci-53/55/2020 dated June 4, 2020). The study is registered with the Clinical Trial Registry of India (CTRI/2020/05/025423). A waiver of consent was granted by the Institutional Ethics Committee because the data were collected from the medical case records of the pregnant women with COVID-19. The statistical analyses were performed using IBM SPSS Statistics Base version 26 (SPSS South Asia Pvt. Ltd., Bangalore, India). The data were presented as frequency (percentage) for categorical variables and mean (standard deviation) or median (interquartile range) for continuous variables. The Kolmogorov-Smirnov test was applied to evaluate the distribution of data. The  $\chi^2$  or Fisher Exact test were used to evaluate the differences in categorical outcomes and Student's *t* test or Mann-Whitney *U* test were used for continuous data accepting a *P* value less than 0.05 as significant.

TABLE 2 Characteristics of women with spontaneous preterm births with SARS-CoV-2 infection in India<sup>a</sup>

	Prepandemic period (October 1, 2019 to March 31, 2020) (n = 197)	COVID-19 Pandemic period (April 1, 2020 to July 7, 2021) (n = 108)	P value <sup>b</sup>	Pandemic		P value <sup>b</sup>
				First wave (April 1, 2020 to January 31, 2021) (n = 67)	Second wave (February 1 2021 to July 7, 2021) (n = 41)	
Age, years	25.0 (22.0–30.0)	29.0 (25.0–32.0)	<0.001	30.0 (25.5–32.0)	28.0 (24.0–30.0)	0.04
Sub-categorization of PTBs as per gestational age <sup>c</sup>						
<28 weeks	7 (3.6)	5 (4.6)	0.76	3 (4.5)	2 (4.9)	0.92
28–32 weeks	32 (16.2)	11 (10.2)	0.14	4 (6.0)	7 (17.1)	0.06
>32 weeks	158 (80.2)	92 (85.2)	0.27	60 (89.6)	32 (78.1)	0.10
Mode of delivery						
Vaginal birth	136 (69.0)	69 (63.9)	0.359	40 (59.7)	29 (70.7)	0.247
Cesarean section	61 (31.0)	39 (36.1)		27 (40.3)	12 (29.3)	
Clinical and pregnancy characteristics						
Primigravida	68 (34.5)	35 (32.4)	0.709	19 (28.4)	16 (39.0)	0.250
Multigravida	129 (65.5)	73 (67.6)		48 (71.6)	25 (61.0)	
Previous cesarean section	33 (16.8)	26 (24.1)	0.122	20 (29.9)	6 (14.6)	0.104
ART	NA	8 (7.4)	–	6 (9.0)	2 (4.9)	0.707
Previous stillbirth	NA	6 (5.6)	–	2 (3.0)	4 (9.8)	0.198
Previous abortion	41 (20.8)	34 (31.5)	0.039	25 (37.3)	9 (22.0)	0.135
PPROM	53 (26.9)	13 (12.0)	0.003	9 (13.4)	4 (9.8)	0.762
Multiple pregnancy	13 (6.6)	14 (13.0)	0.061	7 (10.4)	7 (17.1)	0.381
Blood transfusion	17 (8.6)	19 (17.6)	0.020	10 (14.9)	9 (22.0)	0.436
Pre-eclampsia	10 (5.1)	15 (13.9)	0.015	7 (10.4)	8 (19.5)	0.252
GDM	12 (6.1)	6 (5.6)	1.000	4 (6.0)	2 (4.9)	1.000
Comorbidities						
Anemia (haemoglobin <11 g%)	84 (42.6)	63 (58.3)	0.009	38 (56.7)	25 (61.0)	0.663
Chronic hypertension	2 (1.0)	3 (2.8)	0.350	2 (3.0)	1 (2.4)	1.000
Heart disease	5 (2.5)	4 (3.7)	0.725	3 (4.5)	1 (2.4)	1.000
Thrombocytopenia (<125K/ $\mu$ L)	4 (2.0)	7 (6.5)	0.057	3 (4.5)	4 (9.8)	0.423
Deranged liver enzymes	7 (3.6)	9 (8.3)	0.104	6 (9.0)	3 (7.3)	1.000
Maternal mortality	2 (1.0) <sup>d</sup>	3 (2.8)	0.350	1 (1.5) <sup>e</sup>	2 (4.9) <sup>f</sup>	0.556

Abbreviations: ARDS, acute respiratory distress syndrome; ART, assisted reproductive technologies; COVID-19, coronavirus disease 2019; GDM, gestational diabetes mellitus; NA, not available; PPRM, preterm prelabor rupture of membrane; PTB, preterm birth; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.

<sup>a</sup>Data are presented as median (interquartile range) or as number (percentage).

<sup>b</sup>The  $\chi^2$  or Fisher exact test was applied at the significance level of  $P < 0.05$ . The comparison of age between groups was performed using the Student's  $t$  test or Mann–Whitney  $U$  test at the significance level of  $P < 0.05$ .

<sup>c</sup>PTBs are sub-categorized based on gestational age: extremely preterm (less than 28 weeks); very preterm (28–32 weeks); moderate to late preterm (32–37 weeks).

<sup>d</sup>One mortality due to ARDS with acute renal failure and other mortality due to aspiration pneumonitis with subacute intestinal obstruction.

<sup>e</sup>Respiratory failure in severe ARDS.

<sup>f</sup>One patient died because of acute fulminant viral hepatitis with hepatic encephalopathy with coagulopathy with ARDS and other died because of lower respiratory tract infection with ARDS with septic encephalopathy with active pulmonary tuberculosis.

### 3 | RESULTS

A total of 1136 women with COVID-19 delivered during the first ( $n = 807$ ) and second ( $n = 329$ ) waves of the COVID-19 pandemic. Significantly more women with COVID-19 were symptomatic during the second wave (166/487; 34.1%) compared with the first wave (162/1143; 14.2%) ( $P < 0.001$ ). Out of 1136 deliveries, 128 (11.3%) were preterm. Preterm delivery rate was reported to be higher during the second wave (46/329; 14%) compared with the first wave (82/807; 10.2%) of the COVID-19 pandemic ( $P = 0.065$ ). Very preterm (28–32 weeks of gestation) SPTB rates were reported to be higher during the second wave (17.1% versus 6.0%,  $P = 0.06$ ). A higher rate of SPTBs was reported during the second wave than the first wave (12.5% versus 8.3%,  $P = 0.03$ ) as well as the prepandemic period (12.5% versus 10.5%,  $P = 0.286$ ). IPTBs were significantly lower in the pandemic period than in the prepandemic period (1.8% versus 3.3%,  $P = 0.012$ ). There was no significant difference in IPTB during the first and second waves of COVID-19 ( $P = 0.694$ ) (Table 1).

The median age of women with SPTB in the first wave was significantly higher than in the second wave (30 versus 28 years;  $P = 0.048$ ). Interestingly, the median age of women with SPTB during the COVID-19 pandemic period was significantly higher compared with the prepandemic period (29 versus 25 years;  $P < 0.001$ ). The majority of women with SPTB were multigravida during both the pandemic and pre-pandemic periods ( $P = 0.709$ ). The proportion of women with a previous history of abortion was significantly higher in the study cohort during the pandemic period compared with the pre-pandemic period (31.5% versus 20.8%;  $P = 0.039$ ). Women with anemia had a significantly higher SPTB rate in the pandemic period compared with the pre-pandemic period (58.3% versus 42.6%,  $P = 0.009$ ). PPROM rate was significantly lower during the pandemic compared with the pre-pandemic period (12% versus 26.9%;  $P = 0.003$ ). The proportion of women with pre-eclampsia was significantly higher among women with SPTB in the pandemic period compared with the pre-pandemic period (5.1% versus 13.9%;  $P = 0.015$ ). (Table 2).

COVID-19 symptoms were present in 23.1% (25/108) of women with SPTB, with no difference in the presentation of COVID-19 symptoms during both waves ( $P = 0.811$ ). Fever, dry cough, and dyspnea being the predominant symptoms, nine women (9/25, 36%) had moderate to severe disease and needed intensive care unit/high dependency unit admission, and six needed ventilator support. Out of the total three maternal deaths reported in the study cohort, one death was due to COVID-19 respiratory failure (see Table S1).

### 4 | DISCUSSION

The study demonstrates increased SPTB rates in the second wave compared with the first wave of the COVID-19 pandemic and the prepandemic period. In the present study, the SPTB rate during the first wave of the COVID-19 pandemic was 8.3%, higher than

the SPTB rate reported during the first wave in the UK (4.9%)<sup>2</sup> and Spain (6.1%).<sup>3</sup> The majority of the SPTBs in the present study were due to preterm labor, as PPROM was reportedly low (12%) during the COVID-19 pandemic period. The etiology of SPTB during the COVID-19 pandemic is largely unclear and possibly multifactorial, hampering effective prevention.<sup>12</sup>

The possible explanation for the increased SPTB rate during the second wave of COVID-19 could be the highly virulent  $\delta$  variant of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2; B.1.617.2) infection in pregnant women.<sup>14</sup> It is speculated that proinflammatory cytokines compromise the balance of cytokines at the maternal-fetal interface inducing PTBs in women with COVID-19.<sup>15</sup> Therefore, we can predict that SARS-CoV-2 delta (B.1.617.2) could be associated with more pronounced cytokine storm and inflammatory cascades,<sup>16</sup> which could have triggered preterm labor in our cases. Second wave of COVID-19 pandemic has witnessed significantly more maternal complications, such as maternal mortality in India.<sup>8</sup> However, the direct association of B.1.617.2 leading to SPTB can only be established with genome sequencing data.

In the present study, the SPTB rate during the first wave of the COVID-19 pandemic was 8.3%, higher than the SPTB rates reported during the first wave in the UK (4.9%)<sup>2</sup> and Spain (6.1%).<sup>3</sup> This could be because of the higher number of women who were anemic (58%) contributing to PTB in our cohort.

In contrast to other studies, from the UK<sup>2</sup> and Spain,<sup>3</sup> we did not find any increase in the occurrence of IPTB. Both studies reported a very high proportion of IPTB; 60% in the UK<sup>2</sup> and 32% in Spain<sup>3</sup> due to elective premature termination of pregnancy to improve the worsening maternal respiratory distress in severe COVID-19. The IPTB in our study cohort (1.8%) includes termination for obstetric and fetal indications only, and it is significantly less compared with studies from the UK (20.2%)<sup>2</sup> and Spain (7.7%).<sup>3</sup> The multidisciplinary team at our hospital decided on a case-to-case basis for emergency cesarean section or labor induction; either for facilitating maternal resuscitation or because of fetal health concerns.<sup>17,18</sup> Therefore the PTB rate remained low in the present study throughout the COVID-19 pandemic and consistent with the global prepandemic PTB rate of 11%.<sup>19</sup> A study from Kuwait also described management similar to that in the present study where all IPTB were as a result of termination for obstetric or fetal indication only.<sup>5</sup> We believe that labor induction or operative delivery in patients who are already medically unfit might increase the risk of maternal mortality and morbidity, as seen in other maternal infections. Premature termination increases cesarean section rates and neonatal morbidity and mortality, which was also observed globally during the pandemic. PTB also increases the financial burden on healthcare systems, especially in low- and middle-income countries. The increased rates of IPTB reported in other populations during the early phase of the COVID-19 pandemic could be a result of the lack of evidence on the impact of SARS-CoV-2 on pregnancy, resulting in the non-availability of evidence-based guidelines for obstetric management of COVID-19. As the pandemic advances, and with the availability of scientific evidence,

elective deliveries for the sole indication of maternal COVID-19 disease are now discouraged.<sup>17,18</sup> The universal screening that was implemented in the present study for detection of SARS CoV-2 infection in pregnant women, showed that 20% of the infected population was symptomatic. This is similar to a study from Spain (29%), which also incorporated universal testing<sup>3</sup> and much lower in comparison with a study from the UK (81%).<sup>2</sup>

We have observed a significant difference in age distribution of patients with SPTB in the pandemic period compared with the pre-pandemic period. Our results demonstrated that with advancing age, risk of SPTB increased among women with COVID-19. We speculate that older women are more susceptible for SPTB compared with younger women. The higher percentage of pre-eclampsia among the women with COVID-19 in the present study emphasizes the theory that the SARS-CoV-2 infection predisposes pregnant women to a greater risk of developing pre-eclampsia because of its pro-inflammatory state.<sup>20,21</sup> Anemia in pregnancy is an important risk factor for premature birth.<sup>22,23</sup> Our observations are consistent with this, showing higher incidence of anemia in the study cohort of SPTB during the pandemic period.

To the best of our knowledge, the present study is the first to describe the effects of both the first and second waves of the COVID-19 pandemic on SPTB and it generated contradictory evidence about the rates of IPTB among women with COVID-19. Limitations of the present study include that it is a single-center study, lacks testing for vaginal cytokines for detection of intra-amniotic inflammation, and lacks genome sequencing data on SARS-CoV-2 strains to definitively establish a direct relationship of SARS-CoV-2 infection with PTB.

Preterm birth not only causes an increased risk of long-term negative consequences such as adverse cognitive and motor development, behavioral and mental health problems, respiratory disorders, adding increased mortality and morbidity in early childhood but also leads to an increased financial burden on public health care.<sup>24</sup> Considering the increased burden of PTBs during the ongoing COVID-19 pandemic, appropriate healthcare policies are to be developed for achieving the Sustainable Development Goals.

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## CONFLICTS OF INTEREST

The authors have no conflicts of interest.

## AUTHOR CONTRIBUTIONS

NM, and RG had full access to all data, and take responsibility for data integrity, and the accuracy of the analysis. RG and NM were responsible for the study concept, and design. RP, CG, PM, MP, SK, and BJ acquired the data. All authors interpreted the data. NM performed the statistical analysis. NM, SM, and RG provided administrative, technical, and material support. RP, NM,

CG, and RG drafted the manuscript. NM, SM, and RG revised the manuscript.

## REFERENCES

- Muhe LM, McClure EM, Nigussie AK, et al. Major causes of death in preterm infants in selected hospitals in Ethiopia (SIP): a prospective, cross-sectional, observational study. *Lancet Glob Health*. 2019;7:e1130-e1138.
- Knight M, Bunch K, Vousden N, et al. Characteristics and outcomes of pregnant women admitted to hospital with confirmed SARS-CoV-2 infection in UK: national population based cohort study. *BMJ*. 2020;369:m2107.
- Martinez-Perez O, Prats Rodriguez P, Muner Hernandez M, et al. The association between SARS-CoV-2 infection and preterm delivery: a prospective study with a multivariable analysis. *BMC Pregnancy Childbirth*. 2021;21:273.
- Al-Matary A, Almatari F, Al-Matary M, et al. Clinical outcomes of maternal and neonate with COVID-19 infection – multicenter study in Saudi Arabia. *J Infect Public Health*. 2021;14:702-708.
- Ayed A, Embaireeg A, Benawadh A, et al. Maternal and perinatal characteristics and outcomes of pregnancies complicated with COVID-19 in Kuwait. *BMC Pregnancy Childbirth*. 2020;20:754. 10.1186/s12884-020-03461-2
- Figueiro-Filho EA, Yudin M, Farine D. COVID-19 during pregnancy: an overview of maternal characteristics, clinical symptoms, maternal and neonatal outcomes of 10,996 cases described in 15 countries. *J Perinat Med*. 2020;48:900-911.
- Gajbhiye RK, Sawant MS, Kuppasamy P, et al. Differential impact of COVID-19 in pregnant women from high-income countries and low-to middle-income countries: a systematic review and meta-analysis. *Int J Gynaecol Obstet*. 2021;155(1):48-56. 10.1002/ijgo.13793
- Mahajan NN, Pophalkar M, Patil S, et al. (COVID-19) in India. *Obstet Gynecol*. 2021;138(4):660-662. 10.1097/AOG.00000000000004529
- Mahajan NN, Pednekar R, Patil SR, et al. Preparedness, administrative challenges for establishing obstetric services, and experience of delivering over 400 women at a tertiary care COVID-19 hospital in India. *Int J Gynaecol Obstet*. 2020;151:188-196.
- Gajbhiye RK, Mahajan NN, Waghmare R, et al. Protocol for a prospective, hospital-based registry of pregnant women with SARS-CoV-2 infection in India: PregCovid Registry study. 10.1101/2021.07.21.21260823
- WHO: recommended definitions, terminology and format for statistical tables related to the perinatal period and use of a new certificate for cause of perinatal deaths. *Acta Obstet Gynecol Scand*. 1977;56:247-253.
- Goldenberg RL, Gravett MG, Iams J, et al. The preterm birth syndrome: issues to consider in creating a classification system. *Am J Obstet Gynecol*. 2012;206:113-118.
- MOHFW. Clinical Management Protocol for COVID-19 (in adults). <https://www.mohfw.gov.in/pdf/UpdatedDetailedClinicalManagementProtocolforCOVID19adultsdated24052021.pdf>. Assessed September 09, 2021.
- Cherian S, Potdar V, Jadhav S, et al. SARS-CoV-2 spike mutations, L452R, T478K, E484Q and P681R, in the second wave of COVID-19 in Maharashtra, India. *Microorganisms*. 2021;9:1542.
- Hanna N, Hanna M, Sharma S. Is pregnancy an immunological contributor to severe or controlled COVID-19 disease? *Am J Reprod Immunol*. 2020;84:e13317.
- Raman R, Patel KJ, Ranjan K. COVID-19: unmasking emerging SARS-CoV-2 variants, vaccines and therapeutic strategies. *Biomolecules*. 2021;11(7):993.
- Royal College of Obstetricians & Gynaecologists. Coronavirus (COVID-19) infection and pregnancy. <https://www.rcog.org.uk/en/>

- guidelines-research-services/guidelines/coronavirus-pregnancy/. Accessed September 09, 2021.
18. COVID-19 Clinical management: living guidance. <https://www.who.int/publications-detail-redirect/WHO-2019-nCoV-clinical-2021-1>. Accessed September 09, 2021.
  19. Walani SR. Global burden of preterm birth. *Int J Gynaecol Obstet*. 2020;150:31-33.
  20. Coronado-Arroyo JC, Concepción-Zavaleta MJ, Zavaleta-Gutiérrez FE, Concepción-Urteaga LA. Is COVID-19 a risk factor for severe preeclampsia? Hospital experience in a developing country. *Eur J Obstet Gynecol Reprod Biol*. 2021;256:502-503.
  21. Villar J, Ariff S, Gunier RB, et al. Maternal and neonatal morbidity and mortality among pregnant women with and without COVID-19 infection: the INTERCOVID multinational cohort study. *JAMA Pediatr*. 2021;175:817-826.
  22. Rahmati S, Azami M, Badfar G, Parizad N, Sayehmiri K. The relationship between maternal anemia during pregnancy with preterm birth: a systematic review and meta-analysis. *J Matern Fetal Neonatal Med*. 2020;33:2679-2689.
  23. Kempainen L, Mattila M, Ekholm E, et al. Gestational iron deficiency anemia is associated with preterm birth, fetal growth restriction, and postpartum infections. *J Perinat Med*. 2020;49:431-438.
  24. Been JV, Burgos Ochoa L, Bertens LCM, Schoenmakers S, Steegers EAP, Reiss IKM. Impact of COVID-19 mitigation measures on the incidence of preterm birth: a national quasi-experimental study. *Lancet Public Health*. 2020;5:e604-e611.

#### SUPPORTING INFORMATION

Additional supporting information may be found in the online version of the article at the publisher's website.

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