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Increased spontaneous abortions during the second wave of COVID-19 pandemic in India

Authors:

R. K. Gajbhiye[1]*, A. Tilve[2]*, S. Kesarwani[2], S. Srivastava[2], S. J. Kore[2], K. Patil[2], S. D. Mahale[1], N. N. Mahajan[2†]*

Affiliations:

[1]ICMR-National Institute for Research in Reproductive Health, Mumbai, India, 400012

[2]Department of Obstetrics and Gynecology, Topiwala National Medical College & BYL Nair Charitable Hospital, Mumbai, India, 400008.

*These authors contributed equally

† **Corresponding authors:**

Dr. N. N. Mahajan,

Associate Professor & Nodal Officer COVID-19 (Maternity)

Department of Obstetrics and Gynecology

B. Y. L. Nair Charitable Hospital and T. N. Medical College, Mumbai. 400008

Email: nirajdr@hotmail.com

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Lack of reliable data on the risk of spontaneous abortions (SABs) due to COVID-19 is leading to concern in patients, and obstetricians. Recent meta-analyses demonstrated the detrimental effect of COVID-19 in pregnant women in low-income and middle-income countries (LMICs) than high-income countries (HICs).[1] The second wave of the COVID-19 pandemic was reported to be more fatal than the first wave leading to increased severity and maternal mortality.[2] However, the impact of the second wave of COVID-19 on SABs is unknown. We present the analysis of a cohort of women with SAB and COVID-19 (n=1630) admitted at BYL Nair Charitable Hospital (NH), Mumbai, India from 1st April 2020 to 4th July 2021 during the first and second waves of COVID-19 pandemic (Figure 1).

SAB was defined as spontaneous pregnancy loss before 20 weeks of gestation or a fetus born weighing less than 500 g. Fetal demise was confirmed on ultrasound. The SAB rate (per 1,000 births) was significantly higher during the second wave as compared to the first wave of the COVID-19 pandemic (82.6 vs 26.7; p<0.001) as well as the prepandemic period (OR 1.7, 95%; CI 1.16-2.59; p=0.006). The incidence of SABs during the second wave of the COVID-19 pandemic was significantly higher than the first wave (p <0.004) as well as the prepandemic period (p=0.003) [Table 1]. The SAB rate was significantly higher during the February-July months of the prepandemic period (55.7 per 1000 births) compared to the April-January months of the prepandemic period (42.8 per 1000 births) [0.004]. However, there was a significant increase in the SAB rate during the second wave of COVID-19 pandemic (February-July 2021) compared to the same months in the prepandemic period in 2017 and 2018 at NH (p=0.044).

Fetal demise was reported significantly higher during the COVID-19 pandemic compared to the pre-pandemic period (p=0.006). The frequency of first and second-trimester fetal demise during the COVID-19 pandemic was more compared to the pre-pandemic period but did not reach statistical significance (p=0.09). The second-trimester SAB rate was significantly higher

in the COVID-19 pandemic as compared to the pre-pandemic period ($p<0.001$) [Table 1]. A higher number of COVID-19 symptomatic women with SABs were reported in the first wave (31.8%) as compared to the second wave (17.9 %) of the COVID-19 pandemic. The majority of women with SABs (96.4%) conceived spontaneously during the second wave of the COVID-19 pandemic ($p=0.07$).

Our study demonstrates three times increased risk of SAB during the second wave than the first wave of COVID-19 pandemic and two times higher risk than the prepandemic period. Although seasonal variation was observed for SABs during February-July months compared to April-January in the prepandemic period, we observed significantly higher proportions of SABs during the same months in the second wave of the COVID-19 pandemic. This is the first report on the increased SABs rate during the second wave of the COVID-19 pandemic. We observed an increased risk of SAB during the second wave of the COVID-19 pandemic which is similar to a study reported from Turkey[3] but in contrast to studies from USA[4] and Canada[5]. The findings of our study support the observations that COVID-19 could disproportionately affect pregnant women in LMICs[1] and women from an Asian background. The increased SAB rate during the second wave could be due to the highly infectious and virulent SARS-CoV-2 delta variant of concern (B.1.617.2) leading to more fetal deaths in both trimesters. The delta variant of SARS-CoV-2 was reported to be responsible for the second wave in India.[6]

The probable reasons for higher fetal deaths in our study could be explained by the fact that SARS-CoV-2 can infect the placenta and potentially affect fetal growth. Higher COVID-19 case rates, decrease in antenatal care visits, less access to nutritious food, travel restrictions during the second wave could have also led to increased SABs during the second wave of the COVID-19 pandemic. However, further studies are required to demonstrate the causal link

between fetal death and COVID-19. Limitations of this study include lack of SARS-CoV-2 testing of products of conception, and genome sequencing data on SARS-CoV-2 strains.

To conclude, our study provides evidence for counseling of the women who are desires of becoming pregnant during the ongoing COVID-19 pandemic and also for the women who got infected during their first trimester of pregnancy. COVID-19 appears to have an increased risk of SAB, especially during the second wave. Our findings are crucial for public health policy especially on prioritizing the vaccination of pregnant women in India and other LMICs in light of the predicted third wave of COVID-19 pandemic.

Disclosure of Interests: The authors report no conflict of interest.

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Contribution to Authorship:

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. AT, SK, SS, KP, and SJK acquired the data. All authors interpreted the data. NM and RG performed the statistical analysis. NM, SM, and RG provided administrative, technical, and material support. NM, AT, and RG drafted the manuscript. NM, SJK, SM, and RG revised the manuscript.

Ethics Approval:

The study was approved by the Ethics Committees of TNMC (No. ECARP/2020/63 dated 27.05.2020) and ICMR-NIRRH (IEC no. D/ICEC/Sci-53/55/2020 dated 04.06.2020). The study is registered with the Clinical Trial Registry of India (CTRI#2020-025423).

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Figure legend

Figure 1: Spontaneous abortions during first and second waves of COVID-19 pandemic in India**.**

Table 1. Comparison of spontaneous abortions during COVID-19 pandemic and pre-pandemic period at BYL Nair Hospital (NH), Mumbai, India

Parameter	**Pre-pandemic* period (October 1, 2016 - September 31, 2018)**	**COVID-19 Pandemic (April 1, 2020 – July 4, 2021)**	**Odds for COVID-19 Pandemic [95% CI]**	***P*-value**	**First-wave of COVID-19 (April 1, 2020 - January 31, 2021) (n=22)**	**Second-wave of COVID-19 (February 1 - July 7, 2021) (n=28)**	***P*- value**	***P*-value for Pre-pandemic *vs* First-wave**	***P*-value for Pre-pandemic *vs* Second-wave**
Total no. of pregnant and postpartum women with COVID-19 admitted at NH	11952	1630			1143	487			
Deliveries of women with COVID-19	7222	1136	-	-	807	329	-	-	-
Total births of mothers with COVID-19	7361	1161	-	-	822	339	-	-	-

Incidence of spontaneous abortion (%)	2.9	3.1	-	0.74	1.9	5.8	0.004	0.05	0.003
Spontaneous aabortions (per 1,000 births) #	349 (47.4)	50 (43.1)	0.91 [0.67-1.23]	0.53	22 (26.8)	28 (82.6)	<0.001	0.009	0.006
First trimester spontaneous abortion	281 (80.5)	30 (60.0)	0.36 [0.19-0.69]	0.001	13 (59.1)	17 (60.7)	>0.99	0.02	0.02
Second trimester spontaneous abortion	68 (19.5)	20 (40.0)	2.75 [1.48-5.14]		9 (40.9)	11 (39.3)			
Type of abortion									
Fetal demise	151 (43.3)	32 (64.0)	2.33 [1.26-4.31]	0.006	15 (68.2)	17 (60.7)	0.76	0.02	0.07
First trimester fetal demise	105 (30.1)	21 (42.0)	1.68 [0.92-3.09]	0.09	10[†] (45.5)	11 (39.3)	0.77	0.15	0.39
Second trimester fetal demise	46 (13.2)	11 (22.0)	1.86 [0.89-3.88]	0.09	5[‡] (22.7)	6 (21.4)	>0.99	0.20	0.25
Anembryonic pregnancy	73 (20.9)	6 (12.0)	0.52 [0.21-1.26]	0.18	3 (13.6)	3 (10.7)	>0.99	0.58	0.23

Second-trimester spontaneous abortion with live fetus	20 (5.7)	5 (10.0)	1.83 [0.65-5.11]	0.22	2 (9.1)	3[§] (10.7)	>0.99	0.38	0.23
Complete/incomplete abortion at admission	105 (30.1)	7 (14.0)	0.38 [0.16-0.87]	0.01	2 (9.1)	5 (17.9)	0.44	0.04	0.20

CI - confidence interval. The Chi-Square or Fisher exact test was applied at the significance level of P <0.05.

** Prepandemic period of two years (October 1, 2016, to September 30, 2018) was selected for comparison with COVID-19 pandemic period due to uninterrupted obstetrics and gynaecology services and data availability*

[†]First trimester fetal demise at 11 weeks had active tuberculosis; [‡] Second-trimester fetal demise at 24 weeks had Plasmodium vivax malaria; [§] Second-trimester abortion had Neurological complications of COVID-19 (Guillain-Barré syndrome) and autoimmune syndrome.

 # The denominator used for calculating the spontaneous abortion rate is all births of mothers who were infected with SARS-CoV-2.