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Correspondence

Increased stillbirth rate during the second wave of COVID-19 pandemic in India

Dear Editor,

The association of COVID-19 and stillbirths is still unclear due to conflicting evidence [1,2]. Moreover, there are challenges in low-income and middle-income countries (LMICs) as data for stillbirths are not well documented [3]. The highly virulent strain of SARS-CoV-2 is reported to be more lethal as higher intensive care unit/high dependency unit (ICU/HDU) admissions and increased maternal deaths were reported during the second wave of COVID-19 pandemic in India [4]. Herein, we present the comparison of stillbirth rates during the first and second waves of the COVID-19 pandemic in India.

A retrospective study of pregnant and postpartum women with COVID-19 (n = 1645) admitted at BYL Nair Charitable Hospital (NH), was conducted. The data was analysed for the first wave (1st April 2020 to 31st January 2021) and the second wave (1st February 2021 to 12th July 2021) of the COVID-19 pandemic. Stillbirths were defined as the death of a fetus that has reached a birth weight of 500 g, gestational age of more than 22 weeks [5]. For international comparisons and general statistics, stillbirths were further classified into late fetal deaths (greater than 1000 g or after 28 weeks) and early fetal deaths (500–1000 g or 22–28 weeks) [5]. Fetal death was confirmed on ultrasound.

Out of 1645 pregnant and postpartum women with COVID-19 which were managed at NH during the study period, 1142 women delivered. Out of 1645 pregnant and postpartum patients with COVID-19, 342 (20.8%) were symptomatic of the disease. The proportion of the symptomatic population is significantly higher in the second wave as compared to the first wave (35.9% vs 14.2%; $p < 0.001$). The stillbirth rate per 1000 births among pregnant women with COVID-19 was found to be significantly higher in the second wave than in the first wave (34.8 vs 14.6; $p = 0.027$) [Table 1].

Median gestational age was less during the second wave but the difference was not statistically significant (32 vs 36 weeks) ($p = 0.157$). Pregnant women with COVID-19 experienced more stillbirths at < 34 weeks gestational age during the second wave (7/12, 58.3%) compared to the first wave (3/12, 25%) ($p = 0.214$) but the difference was not statistically significant. The second wave witnessed twice the number of multigravida having stillbirths than the first wave (83.3% vs 41.7%) ($p = 0.089$).

A higher number of women with a history of previous abortion reported during the second wave as compared to the first wave (41.7% vs 16.7%) ($p = 0.371$). Anemia was more prevalent in women with stillbirths during the second wave compared to the first wave, (83.3% vs 66.7%) ($p = 0.640$); thus blood transfusions were higher during the second wave (50% vs 25%) ($p = 0.400$). Preeclampsia was reported higher in women with stillbirths during the second wave (25% vs 8.3%) ($p = 0.590$). 41.7% (10/24) of women with stillbirths were symptomatic for COVID-19. There was no difference in symptoms during both waves. Fever was the commonest symptom during both waves, whereas dyspnoea was only observed during the second wave. Moderate to severe COVID-19 disease was observed only during the second wave in 33.3% (4/12) and needed ICU/HDU admission, whereas all symptomatic women during the first wave had the mild disease (5/12, 41.7%). Three women had ARDS and needed ventilator support during the second wave. One maternal death was reported during the second wave but the cause was not directly related to COVID-19.

Our study demonstrates evidence of an increase in the stillbirth rate during the second wave of the COVID-19 pandemic in India compared with the first wave and pre-pandemic period. The stillbirth rate during the COVID-19 pandemic was higher (2.1%; 24/1142) in our study than other studies reported from UK (1.1%) [6], (0.8%) [7]; but lower than the USA (2.5%) [8]. One-fourth of the stillbirths (25%) in the second wave in our study could be directly attributed to COVID-19 disease as these patients had moderate to severe disease and had dyspnoea on admission and were admitted with intrauterine fetal death (IUFD). Additionally, during the second wave preeclampsia was reported higher, which could have contributed to higher stillbirths in the second wave. The higher percentage of preeclampsia in the study cohort indirectly supports the theory that the SARS-CoV-2 infection predisposes pregnant women to a greater risk of developing preeclampsia due to its pro-inflammatory state [9]. The highly virulent variant of concern B.1.617.2 (delta) is considered responsible for the second wave in Maharashtra, India [10]. Therefore, the increased stillbirth rate may be associated with the B.1.617.2 strain. However, in absence of genome sequencing data, it is difficult to prove this association.

Our study provides a strong basis to include stillbirths in all analyses on the global impact of COVID-19. The results of the study demonstrating the increased stillbirth rate during the second wave than the first wave are crucial to raising awareness and also for taking preventive measures. Limitations of our study are a single-center study, no comparison of stillbirths in pregnancies without COVID-19, lack of histopathological analysis or RT-PCR of placentas, and autopsies were not performed on fetuses, and lack of genome sequencing data on SARS-CoV-2 strains to definitively establish the direct relationship of SARS-CoV-2 infection with stillbirths.

Reducing preventable stillbirths during the COVID-19 pandemic should be a global priority. We suggest that the SARS-CoV-2 mitigation strategy needs to be integrated into a maternal, child, and new-born health care. The results of our study are useful for counselling pregnant women about the risks of SARS-CoV-2 infection during pregnancy.

Contribution to authorship

We declare that we participated in the study and have following contributions. NM, and RG had full access to all data, and take responsibility for data integrity, and the accuracy of the analysis.

Table 1
Comparison of stillbirth rates of pregnancies with COVID-19 in two waves of COVID-19 pandemic.

Parameters	First-wave (04.04.2020 to 31.01.2021)	Second-wave (01.02.2021 to 12.07.2021)	p value
Total number of pregnant and postpartum admissions at NH	1143	502	–
Number of deliveries	807	335	–
Total births	822	345	
Still birth rate per 1000 births	12 (14.6)	12 (34.8)	0.027
Still birth rate out of all deliveries (for international comparison)	12/807 (1.5)	12/335 (3.6)	0.025
Symptomatic for COVID-19	162 (14.2)	180 (35.9)	<0.001

Data are represented as n (%).
The Chi-square or Fisher-Exact test was performed at the significance level of $p < 0.05$.

RG, and NM were responsible for the study concept, and design. CG, RT, CS and RP acquired the data. All authors interpreted the data. NM performed the statistical analysis. NM, SM, and RG provided administrative, technical, and material support. NM, CG, RP and RG drafted the manuscript. NM, SM, and RG revised the manuscript.

We have seen and approved the final version and have the no conflicts of interest

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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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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