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ORIGINAL ARTICLE

Poorer Obstetrics Outcomes During the Second Wave of COVID-19 in India

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Abstract

Introduction Outcomes of pregnancy in COVID 19-infected mothers are worse than in the general population. Due to immunological changes, antenatal women are more vulnerable to severe complications. The India has experienced two waves of the disease. We analysed whether the second wave of the disease had affected pregnancy outcomes differently by comparing pregnancy outcomes with those of the first wave.

Materials and Method The study population included all the women delivered in the same tertiary centre during both the waves. Maternal outcome parameters include maternal oxygen requirement, maternal ICU admission and maternal death. Foetal outcome parameters include APGAR scores, preterm deliveries and NICU admissions, maternal and foetal outcome parameters between the first and the second waves were compared.

Results Demographic parameters were similar in both the waves of COVID 19. No significant differences were found in pre-pregnancy comorbidities, high-risk pregnancies and mode of deliveries between the two waves. Maternal oxygen requirement increased in the second wave [first wave 6(4.7%) vs second wave 25(40.3%) (p-value <0.001)]. There was also a significant increase in ICU admission [4(3.1%) vs 8(12.9%)], which was in positive correlation with maternal oxygen requirement during the second wave ($r=0.81$, $p<0.001$). However, there was no significant difference in maternal death [2(1.6%) vs 2(3.2%)]. No significant change noted in neonatal outcomes except for an increase in neonatal sepsis [0 vs 5(8.1%)].

Conclusion Mothers had more severe diseases during the second wave. But this did not translate into significant increase in maternal mortality and poor neonatal outcomes, possibly due to better preparedness.

Keywords COVID-19 · Pregnancy outcomes · Second wave

Introduction

The global COVID-19 pandemic has affected obstetrics practice as well as all other aspects of health infrastructure worldwide. Whereas in the first wave of the pandemic spread slowly in India, the second wave appeared to be more aggressive with many cases within a small period. India has been experiencing a massive surge of cases and deaths in the second wave starting from mid-February. As of mid-August, India is the second leading country in the number of cases worldwide [1]. Mutations in the virus have been reported during these waves. Out of all mutants, 'variants of concern' have generated attention because of their emergence in a particular area, global transmission as well as possible clinical implications [2]. The difference in infectivity, clinical presentation and severity between the first wave and second wave has been reported. This may be due to the variant of concern referred to above or due to change in public health policies. Some such policy changes were an increase in testing and tracing as well as a change in the threshold of admission and homecare [3]. We attempted to explore the differences in obstetrics outcomes between the first and second waves.

Pregnant women are also affected in this pandemic like the general population. During pregnancy, changes in the

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immune system make mothers more vulnerable to severe viral infections [4]. Some evidence suggests that the risk of critical illness may be greater in the later stage of pregnancy [5–8]. Data on pregnancy outcomes in the second wave and its comparison with the first wave are limited. It had been previously shown that the increased morbidities during the first wave could be attributed to a referral bias with COVID-19-positive cases having higher comorbid conditions or obstetric risks [9].

A report from the Royal Brompton Hospital in London mentions an increase in the number of pregnant women who required ECMO (extracorporeal membrane oxygenation) during the second wave [10]. However, this is circumstantial evidence only of worse outcomes of pregnancy as the pandemic progresses. It is very difficult to conduct population-based studies in the pandemic, because of the limitation of logistics. Thus, our centre data for the first and the second waves of COVID-19 were compared to test our hypothesis that outcomes were worse during the second wave.

Materials and Methods

Study Design and Setting

All pregnant women with a documented SARS-CoV-2 infection, who had delivered in a dedicated COVID-19 hospital (DCH) running in KIMS (Kalinga Institute of Medical Sciences) Bhubaneswar, India, were included. This centre was a dedicated COVID-19 tertiary care hospital as designated by the state government. For inclusion, the diagnosis of SARS-COV-2 infection had to be confirmed by real-time reverse transcription polymerase chain reaction (RT-PCR) using nasopharyngeal and oropharyngeal swabs.

Study Participants

The two waves of the pandemic in our state were defined as per ICMR (Indian Council of Medical Research) designation: all cases reporting between March and November 2020 were considered as representing the first wave while those delivered between April and June 2021 were taken as representing the second wave. Only COVID-19-positive pregnant women who delivered in the centre or expired were included. Anyone not delivering in the hospital or delivering after recovery from the infection were not included.

Outcome Variables

Primary maternal outcome parameters include oxygen requirement, ICU admission, post-partum complications like PPH, purpureal sepsis and maternal mortality. Foetal outcome parameters include a preterm or term foetus, foetal birth weight, APGAR score, neonatal sepsis, neonatal ICU admission, IUFD and neonatal death.

Statistical Analysis

Data are presented as mean ± SD for continuous data and number (and percentage) for categorical data. Statistical comparison of different variables like demographic characteristics, pregnancy risk factors, maternal and foetal outcomes between two waves of COVID-19 infections was made using χ^2/Fisher exact test (for categorical variables) or Student's *t* test (for continuous variables). Correlation has been done among maternal outcome parameters. A statistical software SPSS version 23.0 was used to analyse the data, and a p-value ≤ 0.05 was considered as statistically significant.

Results

A total of 189 patients were delivered in the COVID hospital running in KIMS. A comparison was made between 127 delivered during the first wave with 62 delivered during the second wave Fig. 1.

The geographical distribution of patients delivered at this centre in both waves has changed. At the beginning of the first wave, this centre was the only dedicated COVID hospital for maternity services in the state. But, the scenario changed during the second wave as more centres in various districts of the state (viz. Puri, Sundergarh, Jagatsinghpur, etc.) started providing maternity care [Fig. 2].

Table 1 shows that there was no statistically significant difference in age, gravida or parity of the pregnant women between the first and second waves (p-value > 0.05). No significant difference was found in pre-pregnancy comorbidities, pregnancy-associated comorbidities (i.e. hypertensive disease of pregnancy and gestational diabetes), high-risk pregnancies and mode of delivery (LSCS) between the two groups (p-value > 0.05). A significant difference was noted in the period of gestation at the time of delivery between the two waves (p-value < 0.028). Slight earlier delivery during the second wave may be due to an increase in the severity of disease and oxygen demand of antenatal women. We found a lower BMI status in the second wave as compared to the first wave, which can be explained by the earlier delivery during the second wave (p-value < 0.001) [Table 1].

Figure 3 shows the HRCT changes in randomly selected patients admitted to ICU during the first wave and the second wave. COVID-related abnormalities can be observed in both the HRCT images.

A significant difference has been noted in maternal outcome parameters between the two waves. There was a huge rise in oxygen requirement in the second wave (40.3%)

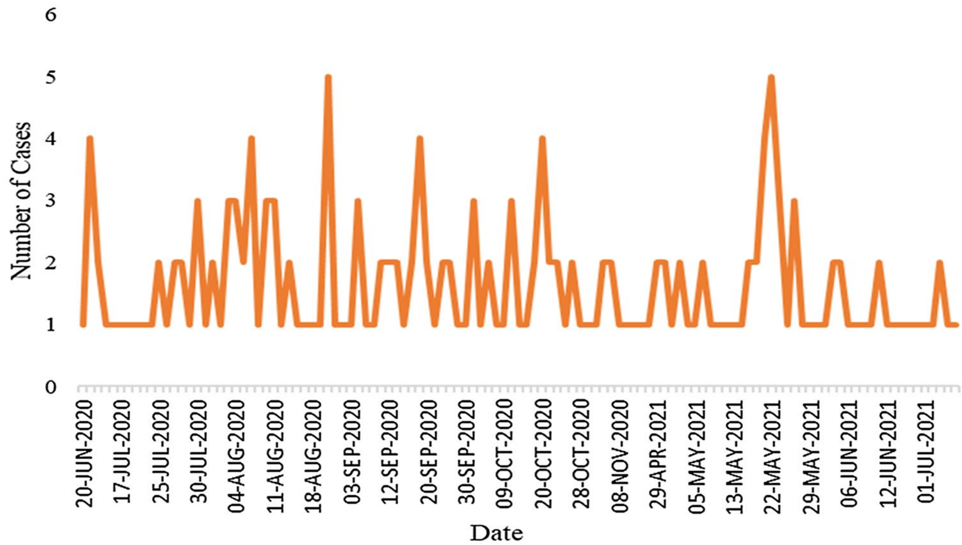

Fig. 1 Number of women with COVID-19 infection delivered per day over the entire study period

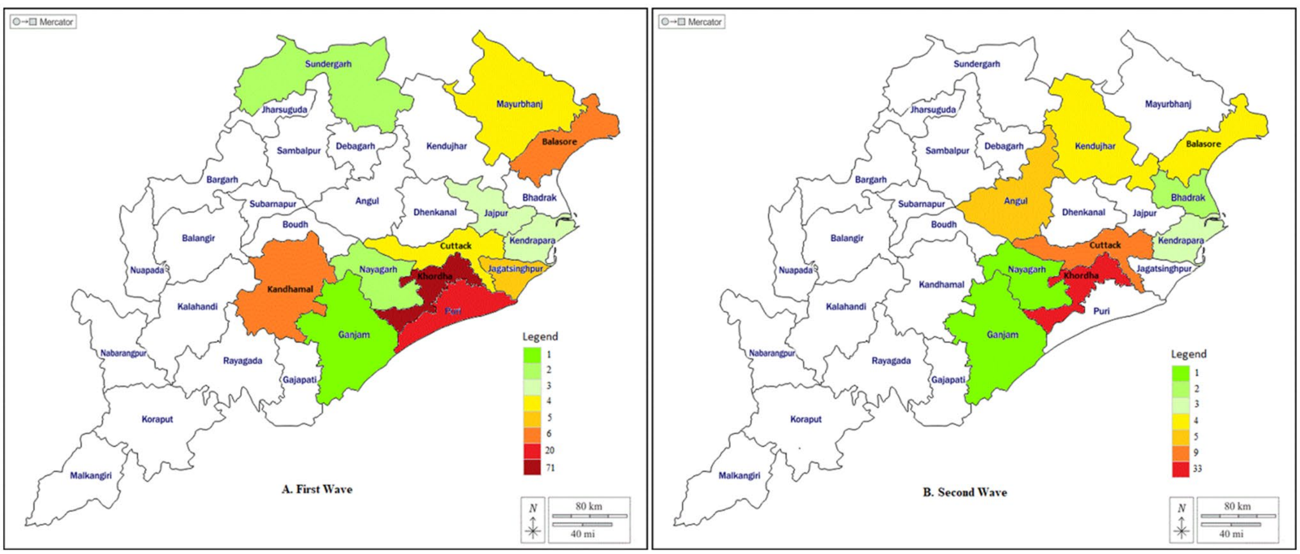

Fig. 2 Geographical distribution of the number of delivery of COVID-19-positive women

than in the first wave (4.7%). Though ICU requirement has increased in the second wave (p-value < 0.05), there was no significant rise in maternal mortality (p-value > 0.05) [Table 2].

Though there is a significantly positive correlation between ICU requirement and oxygen requirement in both the waves, the correlation coefficient was lower for the second wave ($r = 0.37$, $p < 0.05$) as compared to the first wave ($r = 0.81$, $p < 0.001$). A similar result was observed between ICU requirement and maternal mortality (the first wave $r = 0.70$, $p < 0.001$ versus the second wave: $r = 0.47$, $p < 0.001$). Also, oxygen requirement and maternal mortality had a significant correlation in the first wave ($r = 0.57$, $p < 0.001$). However, in the second wave, there was no correlation between maternal oxygen requirement and maternal mortality ($r = 0.22$, $p > 0.05$) [Table 3].

No significant changes in mean baby weight have been noted between both the waves of COVID-19 infection (2.4 ± 0.6 vs 2.5 ± 0.7; p-value > 0.05). Foetal outcomes including APGAR scores at 1 min (7.2 ± 1.7 vs 6.9 ± 1.0) and at 5 min (8.3 ± 1.5 vs 8.6 ± 0.9), neonatal ICU requirement (22.8% vs 30.6%) and neonatal mortality (1.6% vs 6.5%) were similar in both the first wave and second wave respectively (p-value > 0.05). However, significant changes were noted in neonatal sepsis, i.e. no neonatal sepsis was found in the first wave but 8% in the second wave [Table 4].

Table 1 Maternal demographic characteristics and pregnancy-related risk factors with COVID-19 infection.

	Category	Overall ($N = 189$)	First wave ($n = 127$)	Second wave ($n = 62$)	p-value
Demographic characteristics					
Age		27.7 ± 4.2	27.5 ± 4.3	27.9 ± 3.9	0.565
Gravida		1.7 ± 1.0	1.7 ± 0.9	1.8 ± 1.1	0.308
Parity	0	106 (56.1)	73 (57.5)	33 (53.2)	0.211
	1	69 (36.5)	48 (37.8)	21 (33.9)	
	2	11 (5.8)	5 (3.9)	6 (9.7)	
	3	3 (1.6)	1 (0.8)	2 (3.2)	
Gestation age at delivery		37.1 ± 3.4	37.5 ± 2.8	36.4 ± 4.3	**0.028***
Body mass index at delivery time		27.1 ± 2.1	28.1 ± 1.4	25.1 ± 1.9	**< 0.001****
Pregnancy risk factors					
Pre-pregnancy comorbidity		42 (22.2)	26 (20.5)	16 (25.8)	0.408
Hypertensive disease of pregnancy		18 (9.5)	11 (8.7)	7 (11.3)	0.563
Gestational diabetes		11 (5.8)	7 (5.5)	4 (6.5)	0.752
APH		3 (1.6)	1 (0.8)	2 (3.2)	0.251
PPROM or PROM		24 (12.7)	14 (11.0)	10 (16.1)	0.322
Mode of delivery					
LSCS		127 (67.2)	86 (67.7)	41 (66.1)	0.827

Bold indicates statistically significant results where $p < 0.05$

*Statistically significant at the 0.05 level (2-tailed)

**Statistically significant at the 0.01 level (2-tailed)

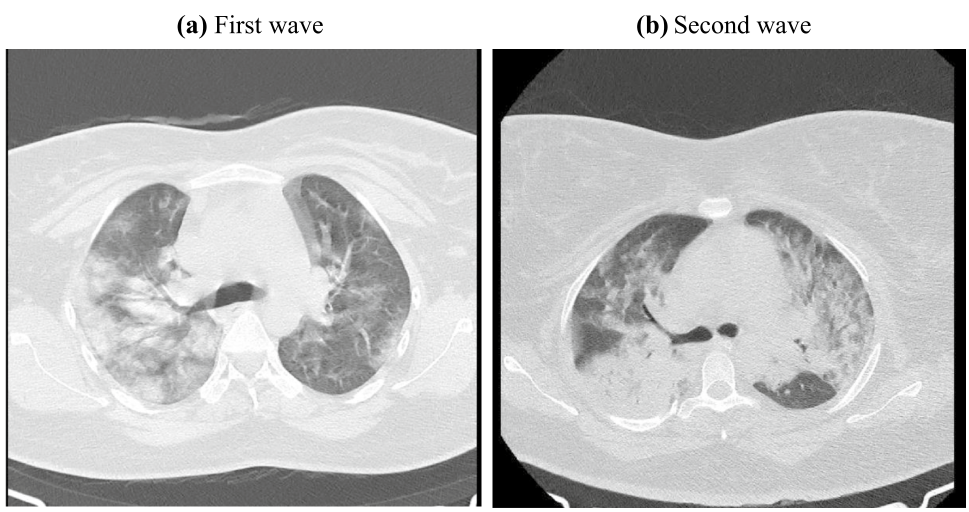

Fig. 3 HRCT of patients admitted in ICU during the first wave and second wave

Table 2 Comparison of Maternal outcomes between two waves of COVID-19.

Maternal outcome	Overall ($N = 189$)	First wave ($n = 127$)	Second wave ($n = 62$)	p-value
Oxygen requirement	31 (16.4)	6 (4.7)	25 (40.3)	**< 0.001****
Maternal ICU requirement	12 (6.3)	4 (3.1)	8 (12.9)	**0.021***
Maternal death	4 (2.1)	2 (1.6)	2 (3.2)	0.599

*Statistically significant at the 0.05 level (2-tailed)

**Statistically significant at the 0.01 level (2-tailed)

Table 3 Correlation among maternal outcomes in both waves of COVID-19

	First wave ($n=127$)		Second wave ($n=62$)	
	Correlation	p-value	Correlation	p-value
Maternal ICU requirement and oxygen Requirement	0.810**	< 0.001	0.370*	0.003
Maternal ICU requirement and maternal death	0.701**	< 0.001	0.474**	< 0.001
Oxygen requirement and maternal death	0.568**	< 0.001	0.222	0.083

*Correlation is significant at the 0.05 level (2-tailed)

**Correlation is significant at the 0.01 level (2-tailed)

Table 4 Comparison of foetal outcomes between two waves of COVID-19 infection

Foetal outcomes	Category	Overall ($N=189$)	First wave ($n=127$)	Second wave ($n=62$)	p-value
Baby weight (in kg)		2.4 ± 0.7	2.4 ± 0.6	2.5 ± 0.7	0.318
	0–1 Kgs	6 (4.7)	4 (6.5)	10 (5.3)	0.283
	1–2 Kgs	26 (20.5)	6 (9.7)	32 (16.9)	
	2–3 Kgs	76 (59.8)	41 (66.1)	117 (61.9)	
	3–4 Kgs	19 (15.0)	11 (17.7)	30 (15.9)	
APGAR score at 1 min		7.1 ± 1.5	7.2 ± 1.7	6.9 ± 1.0	0.244
APGAR score at 5 min		8.3 ± 1.5	8.3 ± 1.8	8.6 ± 0.9	0.206
Neonatal sepsis		5 (2.6)	0 (0)	5 (8.1)	
NICU needed		48 (25.4)	29 (22.8)	19 (30.6)	0.247
Neonatal death		6 (3.2)	2 (1.6)	4 (6.5)	0.092

Discussion

Analysis of 189 antenatal women with active COVID-19 infection delivered at the same health care facility during the first and second wave of COVID-19 showed significant differences in maternal and foetal outcomes.

Physiological changes during pregnancy make the response of COVID-19 in pregnant women different from other population. T2 shift during pregnancy over T1 makes humoral response dominant over cellular response. Hyper-response of T1 and T2 is supposed to the reason behind severe COVID-19 disease in pregnancy [11]. Progesterone is immunomodulatory and has role in repair of viral-infected lung tissue. High level of circulating progesterone potentially helps in recovery from viral lung disease [12]. Reduction in chest volume and increase in tidal volume by 30–40% during pregnancy increase susceptibility of pregnant women towards severe lung infections [13]. Pregnancy itself is a hypercoagulable state. Pathogenesis of SARS-CoV-2 is related to coagulation [14]. This synergetic effect makes pregnancy prone to thromboembolic phenomenon. Thus there are many factors that may potentiate the severity of COVID-19 during pregnancy. However, in our previous study during the first wave, we had shown that the increased risk of severe practically can be explained by presence of comorbidities or other pregnancy risk factors [9].

A change in the geographical distribution of admitted cases was seen during the second wave. It might have happened because in the first wave, this centre was one of the earliest dedicated centres for maternal care in the state. By the time of the second wave, more dedicated COVID-19 hospitals were available at peripheral districts and bed strength had been upgraded. This might account for lesser referrals from certain districts that had higher referrals during the first wave.

The second wave in India had spread much faster than the first wave [15]. Elsewhere the first wave had more severe disease as compared to the second wave, but they did not have universal RT-PCR testing and this might have led to a selection bias [16]. Europe fared better during the second wave possibly with the exception of Germany [17]. The serological survey from Odisha conducted in August 2020 suggests a higher number of asymptomatic infections in women [18]. Thus, during the second wave, some mothers might be having COVID-19 for a second time that may be more severe [19]. There is no significant statistical difference in maternal mortality between the two waves, but the absolute proportion had increased. Moreover, maternal oxygen demand, as well as ICU admissions, has increased significantly in the second wave, which is similar to the study coming from the UK [10]. Since ICU admission criteria in our institute have remained the same between the first and the second waves, it would remain comparable.

The average period of gestation at the time of delivery was less in the second wave than in the first wave. This may be due to the increased severity of COVID-19 (higher oxygen demand and critical care requirement) that may have led to the requirement for early delivery [20]. Material hypoxemia can lead to foetal distress and early delivery. Also, some studies have reported 'iatrogenic preterm deliveries' when the treating obstetrician might decide on early delivery before possible deterioration of the mother [21]. The BMI of the mothers was also lower in the second wave as compared to the first wave, which can be explained due to earlier delivery at an earlier gestational age [22].

The study was not designed to identify the cause behind the increase in severity, but one of the probable causes is the emergence of new variants of the SARS-CoV-2 virus [23]. Higher virulence of the COVID-19 variant B.1.617 has already been established, but whether this leads to an increase in disease severity is still unclear [18]. Usually severe COVID-19 occurs in women with concomitant comorbidities [24]. However, the proportion of women with comorbidities were similar in our first and second wave cohorts.

Correlation coefficients between oxygen demand, ICU admission and maternal death during the second wave were lesser than those in the first wave. In the second wave of COVID-19, there is a correlation between maternal ICU admission and death, but the correlation coefficient is not as strong as during the first wave. No correlation was established between maternal oxygen requirement and maternal death. This may be due to the strengthening of the healthcare system during the second wave such as resident doctors, paramedical staff and general practitioners being better experienced and trained since the beginning of the second wave. Although many healthcare facilities suffered a shortage of medical oxygen in different states of India, this was not so in the state of Odisha [25]. Oxygen support at tertiary care was enhanced during the second wave here, which was possibly a reason that helped reduce maternal mortality despite more severe disease.

Neonatal sepsis occurred during the second wave, whereas no cases had occurred during the first wave. A significant increase in neonatal sepsis can be explained by worse maternal disease, foetal hypoxia and thus increased susceptibility to other infections. Although NICU requirement and neonatal death were numerically more in the second wave, this was not statistically significant.

Though during the second wave, no vaccination was available for the antenatal population and less overall vaccinated population in our country, so the severity will be minimized with the current increase in vaccination.

Limitations

This study is a single-centre study and thus may have unique characteristics not generalizable to other centres.

Conclusion

Gestational age and BMI at delivery were significantly lower in the second wave. Mothers had more severe COVID-19 disease possibly due to novel mutants or variants. Oxygen requirement has significantly increased along with the ICU requirement in the second wave. Maternal mortality did not increase significantly despite more severe maternal disease possibly due to better knowledge, awareness and preparedness of the healthcare facility.

Declarations

Conflict of interest None of the author have any potential conflicts of interests.

Ethical considerations As per ICMR bioethics guidelines for research during COVID-19, since this was a non-interventional, retrospective study, a waiver of consent was granted. The study was approved by the institutional ethics committee of the Kalinga Institute of Medical Sciences, Bhubaneswar vide KIIT/KIMS/IEC/704/2021dated 27/07/2021.

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