

# Clinical Presentation, Maternal and Neonatal Outcomes in Pregnancies Affected by Coronavirus Disease 2019 and a Comparison between the Two Waves in Southern India

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## ABSTRACT

**Aim and primary objective:** To study the clinical presentations, maternal and neonatal outcomes in pregnant women with coronavirus disease 2019 (COVID-19) infection.

**Secondary objective:** To compare the clinical profile between the first and the second waves and to determine the risk factors associated with the maternal outcomes.

**Materials and methods:** This retrospective cohort study was carried out in pregnant women with confirmed COVID-19 infection who delivered from May 2020 to Dec 2021 in six hospitals in South India. Data on maternal demographics, severity of disease, and maternal and neonatal outcomes were collected from the medical records. Women who tested positive for COVID-19 infection were grouped into two cohorts, those who tested positive in the first wave between April and September 2020 and those who tested positive in the second wave between March and September 2021. A comparison was made between the two waves and risk factors for the outcomes were also analyzed.

**Results:** There were 471 COVID-positive pregnant women in the study, 252 in the first wave and 219 in the second. Demographic characteristics did not differ significantly between the two waves. The common symptoms of COVID-19 were cold/cough (50%) and fever (40%) and were similar in both the waves. Compared to the first wave, more women were symptomatic in the second wave (58.9% vs 24.21%) and needed hospitalization (55.71% vs 44.84%). Maternal morbidity/mortality (hospitalization for COVID treatment, oxygen administration, and maternal deaths) was significantly more in the second wave. Obstetric complications, cesarean section rates, preterm delivery, low birth weight babies, and neonatal intensive care unit admissions were not different between the two waves. There were six maternal deaths and three neonatal deaths in the second wave and none in the first. Symptomatic COVID was associated with increased maternal morbidity and mortality. Cesarean section rates were higher in those symptomatic after 34 weeks of gestation.

**Conclusion:** This study demonstrated that the severity of COVID and maternal and neonatal outcomes was significantly worse in the second wave. Symptomatic women were more affected though there were no identifiable risk factors.

**Clinical significance:** This study shows that different variants of the virus may cause different severity of presentation. The significant morbidity and mortality of the second wave reinforces the need for vaccination in reproductive age women.

**Keywords:** Comparison between the first and the second wave, COVID-19 in pregnancy, Maternal and neonatal outcomes, Risk factors for COVID outcomes.

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## INTRODUCTION

Coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has created a global health crisis. The first case of COVID in India was reported in South India on January 30, 2020, on the day that the World Health Organization (WHO) declared a public health emergency of international concern. The anatomical, physiological, and immunological changes of pregnancy make pregnant women more susceptible to viral infections<sup>1-3</sup> and the other corona infections in pregnancy (SARS, MERS) reported increased maternal morbidity and mortality.<sup>4</sup> While in the early phase of the present COVID-19 pandemic, some studies concluded that the disease does not run a more severe course in pregnant women,<sup>5</sup> more recent evidence shows worse outcomes in pregnant women.<sup>6,7</sup> India, like many other countries, witnessed high rates of infection in waves, the first one between April and September 2020. The second wave caused by a mutant strain saw exponential rise of cases within a short period and affected the young population and pregnant women much more severely.<sup>8</sup> In this study, we report the clinical presentation,

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severity, risk factors, and maternal and perinatal outcomes due to COVID and compare the first and the second waves.

**Table 1:** Demographic details

	All cases			Wave 1			Wave 2			p-value
	Mean	Median	SD	Mean	Median	SD	Mean	Median	SD	
Age	28.07	28	4.09	28.17	28	3.89	27.97	27	4.33	0.7
BMI	26.07	25	4.02	25.80	24.80	4.24	26.40	25.6	3.72	0.06

BMI, body mass index; SD, standard deviation; p-value <0.05 is significant

**Table 2:** Maternal characteristics

	All cases, number (%)	Wave 1, number (%)	Wave 2, number (%)	p-value
Primipara	258 (54.78)	140 (55.6)	118 (53.88)	0.8
Multipara	213 (45.22)	112 (44.44)	101 (46.12)	0.719
Obese (BMI >25)	208 (47.17)	106 (43.8)	102 (51.26)	0.053
Medical comorbidities	101 (21.82)	52 (20.72)	49 (23.67)	0.25

p-value <0.05 is significant

**Table 3:** Severity of COVID

COVID-19 severity	All cases, number (%)	Wave 1, number (%)	Wave 2, number (%)	p-value
Symptomatic	190 (40.33)	61 (24.21)	129 (58.9)	<0.0001
Hospitalization	235 (49.89)	113 (44.84)	122 (55.71)	<0.021
Oxygen requirement	65 (13.80)	6 (2.38)	59 (26.94)	<0.0001
HDU/ICU	7 (1.49)	1 (0.40)	6 (2.74)	<0.0001
Maternal death due to COVID	6 (1.27)	0	6 (2.74)	<0.0001
COVID-related maternal morbidity/mortality	78 (16.77)	7 (2.78)	71 (32.88)	<0.0001

p-value <0.05 is significant, <0.0001 is highly significant. HDU, high dependency unit

## MATERIALS AND METHODS

This was a retrospective study of pregnant women with confirmed COVID-19 infection who delivered from May 2020 to December 2021 in six hospitals in South India. The women were tested for COVID-19 infection according to the national guidance if they developed symptoms suggestive of COVID-19 or routinely at 38 weeks of gestation or when they were hospitalized for any reason.<sup>9</sup> Reverse transcription-polymerase chain reaction (RT-PCR) (SARS-CoV-2) test was done on nasopharyngeal samples according to the WHO guidance.<sup>10</sup>

The following data from medical records were entered into a structured questionnaire on Google forms from the different centers:

- Demographic data such as name, age, and hospital ID.
- Parity, BMI, medical comorbidities such as hypertension, pregestational diabetes, bronchial asthma, and immunosuppression.
- Gestational age at testing.
- Nature of symptoms.
- Severity of disease as assessed by hospitalization for oxygen therapy, steroids, Continuous positive airway pressure (CPAP), High dependency unit (HDU)/ICU admission, mechanical ventilation.
- Obstetric complications such as gestational diabetes, preeclampsia, PROM, sepsis, and fetal growth restriction.
- Mode of delivery and indications for cesarean sections.
- Preterm delivery (<37 weeks).
- Low birth weight babies (2500 gm), NICU admission for >12 hours, neonatal ventilation.
- Maternal deaths.
- Neonatal deaths.

The study population was grouped into two cohorts, those who tested positive in the first wave and the second wave. Those whose delivery details were not available were excluded from the study. A comparison was made between maternal factors (age, parity, BMI, and medical comorbidities), severity of COVID (symptomatic rate, hospitalization), maternal and neonatal outcomes as listed above.

## STATISTICAL ANALYSIS

Incidence of the maternal complications will be summarized as proportions. Relative risk for developing the outcome was calculated using a binary regression model and presented as crude and adjusted relative risk with its 95% CI. A p-value of less than 0.05 was considered significant. Data were analyzed using Epi-Info V7.

## RESULTS

A total of 471 pregnancies with COVID-19 infection were analyzed. Around 252 (54%) had tested positive in the first wave and 219 (46%) in the second wave. Demographic characteristics of these women in the two waves of the pandemic are presented in [Table 1](#) and maternal characteristics are shown in [Table 2](#). The mean age was 28 years (SD: 4.1) and mean BMI was 26 (SD: 4) with no difference between the first and the second wave ([Table 1](#)). More than half ( $n = 258$ , 55%) of the mothers were primi, and it is similar across both the waves. Overall, 47.17% ( $n = 208$ ) of the mothers are obese, with 43.8% ( $n = 106$ ) in the first wave and 51.26% ( $n = 102$ ) in the second wave ([Table 2](#)).

Severity of COVID manifestation is presented in [Table 3](#). Overall 40.34% of the positive mothers were symptomatic. There were significantly more symptomatic pregnant patients in the second wave (58.9% vs 24.21%). The common symptoms of COVID-19

**Table 4:** Obstetric outcomes

	All cases, number (%)	Wave 1, number (%)	Wave 2, number (%)	p-value
Maternal obstetric outcomes				
Obstetric complications (GDM, HDP, PROM, FGR)	86 (18.26)	40 (15.87)	46 (21)	0.1936
Cesarean delivery	331 (70.28)	177 (70.24)	154 (70.32%)	0.3222

FGR, fetal growth restriction, GDM, gestational diabetes mellitus; HDP, hypertensive disorders of pregnancy; PROM, premature rupture of membranes. *p*-value < 0.05 is significant

**Table 5:** Neonatal outcomes

Neonatal outcomes	All cases, number (%)	Wave 1, number (%)	Wave 2, number (%)	p-value
Live births	465 (98.73)	251 (99.6)	214 (98.17)	0.1285
Preterm delivery	49 (10.40)	25 (10.12)	24 (11.01)	0.7872
Birth weight <2500 gm	51 (10.83)	21 (8.33)	30 (13.70)	0.1615
NICU admission >12 hours	28 (6.29)	14 (5.76)	14 (6.93)	0.5352
Neonatal deaths	3 (0.64)	0	3	

*p*-value < 0.05 is significant

**Table 6:** Risk factors associated with maternal morbidity/mortality

	Risk ratio	95% CI
Age above 30 years	0.8	0.4–1.4
Multiparity	0.8	0.5–1.2
BMI >25	2.1	0.8–5.0
Medical comorbidities	1.5	0.9–2.3
Obstetric complications (preeclampsia, GDM)	0.8	0.4–1.2
Symptomatic COVID	2.7	1.7–4.2

were cold/cough (50%) and fever (40%). In total 49.89% of the COVID-positive pregnant mothers were hospitalized and more women needed hospitalization in the second wave (57.28% vs 44.84%). Coronavirus disease 2019-related maternal morbidity and mortality (represented as a composite of oxygen requirement, HDU/ICU care, mechanical ventilation, maternal deaths) was 32.88% in the second wave as compared to 2.78% in the first wave. There were six maternal deaths due to COVID pneumonia and related complications in the second wave compared to none in the first wave according to our study. The maternal mortality ratio in the second wave was 273 of 10,000 live births.

Obstetric outcomes are presented in Table 4. The cesarean section rate was 70.28% and was not statistically significantly different between the two waves. Around 9.43% of the sections were done exclusively because of COVID-positive status and an additional 9.05% were done on maternal request. Symptomatic COVID after 34 weeks was associated with a significantly higher risk of having a cesarean section delivery compared to developing symptoms earlier than 34 weeks (88.98% vs 49.15%, Relative risk (RR) 1.81, 95% CI, 1.39–2.37). Obstetric complications developed in 18.26% of cases and were not significantly different between the two waves.

Neonatal outcomes are presented in Table 5 and were similar across the two waves. Live birth rate during the study period among the COVID-positive pregnancies was 98.73%. The preterm delivery rate was 10.40%. Around 11.47% were low birth weight neonates weighing less than 2500 gm. Among the neonates, 5.95% were admitted to the NICU for more than 12 hours, 50% of the admissions owing to prematurity. There were three neonatal deaths in the second wave and none in the first wave.

In Table 6, potential risk factors for adverse maternal outcomes are listed. Of these, symptomatic COVID is associated with statistically significant increase in maternal morbidity/mortality.

## DISCUSSION

The COVID-19 pandemic exerted an enormous burden on the healthcare system across the world. Despite the efforts taken to control the devastation caused by the disease, after a prolonged first wave in India, the second wave due to the delta variant of the SARS CoV-19 virus affected the population in a much more intensive way. As the infectivity and virulence of the variant were very high, the spread of the infection was rapid causing devastating effects. This study compares the presentation and the differences in the outcomes in pregnancies during both the waves.

The demographic details of COVID-positive mothers did not differ significantly between the two waves. Though a significant 47.17% patients were obese with a BMI of >25, it was comparable to COVID-negative women during the same study period (46.4%) which was reported by one of the centers involved in the present study.

The symptomatic rate was significantly more in the second wave of the pandemic. During the first wave, most women were found to be positive on routine testing and were asymptomatic. They were hospitalized mostly for observation. However, during the second wave, those with symptoms needing COVID-related care were hospitalized. The higher symptomatic rate in the second wave is reflected in another study from India by Singh et al.<sup>11</sup>

The maternal morbidity comprising a composite of need for oxygen administration and HDU/ICU care was significantly more in the second wave than the first wave. There were six maternal deaths due to COVID pneumonia and complications in the second wave and none in the first wave. All the maternal deaths occurred in symptomatic patients. This high maternal morbidity and mortality figures are reported in other studies in India.<sup>11,12</sup> Living systematic review<sup>7</sup> has recognized increasing maternal age, high BMI and pre-existing medical comorbidities as risk factors for serious maternal morbidity and mortality. However, in this study, no risk factors achieved statistical significance, probably because of small numbers.

The cesarean section rates did not differ between the two groups. Overall the rate was 71.64%. This rate is higher than other

studies in India and inter-COVID study (38.35% in a study by Mahajan et al.,<sup>12</sup> 49% in another inter-COVID study).<sup>13</sup> This high rate was partly contributed by the fact that 18.48% of them were done for non-obstetric indications such as COVID positivity and maternal request (21.43% in the first wave and 15.53% in the second wave). During the early phase of the pandemic, the information about the risks to the pregnant mothers and the fetuses due to COVID was sparse and delivery was thought to be safer than continuing the pregnancy with the infection. Interestingly, this also resulted in 49.03% of the COVID-positive pregnancies being delivered at early term gestation between 37 and 39 gestation. Moreover, there might have been a low threshold for cesarean section in labor to avoid prolonged exposure to the staff. On further analyzing the data, there was significant difference in the cesarean section rates between those who tested positive before and after 34 weeks of gestation (49.15% vs 88.98%). This high cesarean rate was seen even in asymptomatic patients if tested positive after 34 weeks of gestation. It is possible that the risk was perceived to be higher if tested positive in advanced stages of pregnancy with a low threshold for cesarean delivery.<sup>14,15</sup> Further studies are required to understand the impact of disease in late pregnancy as compared to early gestation.

Living systematic review,<sup>6,7</sup> Pancovid registry (UK), and AAP-SONPM registry (USA)<sup>16</sup> reported higher preterm delivery rates in COVID-affected pregnancies compared to non-COVID-affected pregnancies. In our study, the preterm delivery rate in the entire study period was 10.54% and did not differ significantly between the two groups. Mahajan et al.<sup>12</sup> from India reported similar rates (9.32% in the first wave and 12.87% in the second wave), while Singh et al.<sup>11</sup> (India) reported higher rates (27.78% in the first wave and 24.71% in the second wave). To compare with non-COVID pregnancies, one of the centers that participated in our study reported an overall preterm delivery rate as 5.6% in non-COVID pregnancies during the same period. Interestingly, the spontaneous preterm delivery rate in LIVING study was 6% and was comparable to non-COVID pregnancies. Spontaneous preterm delivery rate in our study was low at 3.40%. As a significant number of preterm deliveries were iatrogenic for obstetric indications such as preeclampsia, gestational diabetes, and fetal growth restriction in our study as well as in other studies, the association of COVID and these conditions needs to be better understood.

The NICU admission rates were similar in both the groups, two third of them owing to preterm and late preterm neonates. There were no neonatal death in the first wave, and three neonatal deaths in the second wave. All the three neonatal deaths were in symptomatic COVID-positive mothers, one was extremely preterm (26 weeks), one was severe fetal growth restriction at 36 weeks, one was term due to severe respiratory distress.

The main limitation of this study is its retrospective nature. However, these data from six obstetric units in the private sector provide a good idea of the impact of the two waves on the pregnant population under their care. Though some risk factors for adverse outcomes were identified, due to the small sample size, statistical significance was not reached.

## CONCLUSION

The second wave of the pandemic resulted in worse maternal outcomes. This is in line with other studies comparing the two waves in India. There is more research needed comparing the outcomes in COVID-negative pregnancies during the same time to

determine the impact of the pandemic on pregnancy. To prevent complications and to improve outcomes, it is important to identify the risk factors for increased maternal/neonatal morbidity and mortality and this will need larger studies.

## Clinical Significance

This study adds to the existing recent evidence that pregnant women should be considered a high risk group and reiterates the impact of the COVID-19 on the vulnerable pregnant population. It has also demonstrated a more virulent impact from the mutated strain of coronavirus in the second wave in our country. As safety of COVID vaccination is well established now, vaccination in pre-pregnancy and pregnancy will play a major role in the prevention of adverse outcomes.

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