



# Second Wave of SARS-CoV-2: Impact on Pregnant Women and Newborns—A Tertiary Care Experience in North India

Sumitra Bachani<sup>1</sup> Jyotsna Suri<sup>1</sup> Anita Kumar<sup>1</sup> Suchandana Dasgupta<sup>1</sup>  Anjali Dabral<sup>1</sup>

<sup>1</sup>Department of Obstetrics & Gynecology, Vardhman Mahavir Medical College & Safdarjung Hospital, Delhi, India

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Address for correspondence Dr. Suchandana Dasgupta, MBBS, MS, Department of Obstetrics & Gynecology, Vardhman Mahavir Medical College & Safdarjung Hospital, Delhi 110029, India (e-mail: suchandana.dasgupta@gmail.com).

## Abstract

**Objectives** The aim of this study was to evaluate the clinical presentation, course of disease, and management of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in pregnant women. We also aimed to evaluate the fetomaternal outcomes in these women.

**Material and Methodology** This was a single-center, retrospective study performed in a tertiary care hospital for pregnant women with coronavirus disease 2019 (COVID-19) in India. The medical records of all antenatal or postnatal women who were admitted to COVID-19 facility from April 1 to June 30, 2021, were reviewed. The demographic characteristics, obstetric parameters, presence of comorbidities, disease severity, investigations, management, and fetal outcome were recorded.

**Statistical Analysis** The data were entered in MS Excel spreadsheet and analysis was done using Statistical Package for Social Sciences (SPSS) version 21.0.

**Result** A total of 94 women were admitted to the COVID-19 facility; 54 (57.45%) were antenatal and 40 (42.55%) were postnatal, 75.53% of them were between 20 and 30 years of age, and 62.96% were multigravida. In addition, 42.55% were asymptomatic and 32.98, 9.58, and 14.89% had mild, moderate, and severe disease, respectively. Also, 42.59% of women had cesarean delivery. Among these, 14 (14.89%) required intensive care unit (ICU) admission, and 24.46% needed oxygen therapy. Comorbidities were present in 48.94%, with hypertensive disorder being the most common (14.89%). Common residual complaints were malaise, body ache, and cough. Among women admitted in the ICU, eight (57%) had comorbidities such as preeclampsia, diabetes, heart disease, and anemia. All these women required oxygen therapy, antibiotics, and thromboprophylaxis. Six among them received steroid (methylprednisolone) and four received antiviral drug (remdesivir). Three women succumbed to death. The mortality rate was 3.19%. Among the neonates, six babies were affected with SARS-CoV-2 and all recovered. On follow-up after discharge, one woman with rheumatic heart disease expired after 2 days of discharge and one woman had a spontaneous abortion.

## Keywords

- ▶ COVID-19
- ▶ SARS-COV-2
- ▶ second wave of COVID-19
- ▶ pregnancy and COVID-19
- ▶ Delta variant
- ▶ oxygen therapy
- ▶ remdesivir

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**Conclusion** During the second wave, caused by the Delta variant, maximum requirement was for oxygen therapy, antiviral drugs, and steroids. We conclude that women with comorbidities and advanced period of gestation had a severe course and required critical care. The optimum care and counselling regarding possible outcome in such a vulnerable population is needed.

## Introduction

More than a year after its first appearance in Wuhan, China, the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) pandemic is raging in recurrent waves in countries around the world. The World Health Organization (WHO) had declared it a pandemic in March 2020.<sup>1</sup> Various countries adapted and applied many strategies to cut down the cases, imposing various restrictions and lockdowns. However, most of them experienced a second wave eventually and small but recurrent spurge of cases continues in clusters.

Delhi experienced a second wave with a surge of new cases since the first week of March 2021. A new variant was reported to be more contagious and virulent, and reached a peak daily active cases of more than 400,000 during the end of the first week of May 2021 and average daily deaths of 4,000 in India.<sup>2</sup>

During the first wave of SARS-CoV-2, the maternal mortality rate had been lower than the influenza (H1N1 virus) pandemic in 2009 and severe acute respiratory syndrome or Middle East respiratory syndrome in 2012. A recent study suggested that pregnant and peripartum women are experiencing more severe illness in the second wave of the coronavirus disease 2019 (COVID-19) pandemic than was observed during the first wave. However, the true cause of this change is currently unclear.<sup>3</sup>

Pregnant women are prone to infections as pregnancy is an immunocompromised state and risk of pneumonia is higher than in nonpregnant woman.<sup>4</sup> The possibility of vertical transmission is still a case of debate and research. Women with severe acute respiratory illness in pregnancy are more prone to develop complications such as high incidence of pneumonia, renal failure, thrombosis, and disseminated intravascular coagulation and need for intensive care. Fetal complications can be miscarriage, preterm delivery, growth restriction, and perinatal death.<sup>5</sup>

Few studies have been done during the second wave in India to evaluate the effect of the new variant (B.1.617.2). This has been labeled as Delta variant by WHO and was designated as variant of concern on May 11, 2021.<sup>6</sup> The differences in infectivity, clinical symptoms, and complications have not yet been established fully.

We aim to evaluate the fetomaternal outcomes in women who were admitted to the COVID-19 facility during the second wave. This will add to the evidence and research armamentarium on COVID-19.

## Methodology

### Study Design and Participants

This was a single-center, retrospective study performed in a tertiary care hospital of North India with 24,000 deliveries per year. The hospital has a separate COVID-19 facility for Obstetrics and Gynecology and a level II intensive care unit (ICU). A total of 98 women were admitted from April 1, 2021, to June 30, 2021, among whom 4 women were admitted with gynecological conditions and hence were excluded from the study. Finally, 94 antenatal and postnatal women comprised the study population.

The testing strategy was according to Indian Council of Medical Research (ICMR) guidelines. All women were tested with rapid antigen test (RAT) kit on admission. Antenatal women who tested negative with RAT underwent quantitative reverse transcriptase polymerase chain reaction (qRT-PCR). All RAT- and qRT-PCR-positive women were admitted to COVID-19 block unless they were fit for home isolation. The guidelines of Ministry of Health and Family Welfare (MoHFW), Government of India (GOI), were followed for classification and management of these women.<sup>7</sup> Women with mild and moderate symptoms were admitted to the isolation ward, whereas those with severe disease or those who deteriorated during hospital stay were transferred to the ICU. ICU care comprised oxygen therapy, antibiotics, antivirals, steroid, and thromboprophylaxis. In those women in whom chest imaging was indicated, chest X-ray (postero-anterior view) with abdominal shield for pregnant women was the modality of choice. Neither any pregnant female nor any postpartum female required computed tomography of chest. More of noninvasive oxygen therapy was used during ICU stay such as non-rebreathing mask and high-flow nasal cannula (which can deliver oxygen up to 60 L/min). In antenatal women with early gestation prone positioning was implemented and in advanced gestation lateral tilt was implemented. Antibiotics (oral antibiotics: azithromycin; parenteral antibiotics: penicillin [ampicillin, piperacillin/tazobactam], cephalosporin [ceftriaxone], clindamycin to prevent secondary bacterial infection) were administered according to hospital policy. Antivirals such as remdesivir were used in severe cases after appropriate counselling and written consent due to unproven teratogenicity. Methylprednisolone (40 mg 12 hourly) was used during the second wave instead of dexamethasone. Low-molecular-weight heparin, 0.4 mL/day by subcutaneous route in women with body weight < 60 kg and 0.6 mL/day subcutaneous route in women with body weight > 60 kg, was used for

thromboprophylaxis in all women. Women who were asymptomatic for 10 days after diagnosis, including 3 days after resolution of symptoms, were discharged. The test for SARS-CoV-2 was not repeated prior to discharge. All medical records regarding demographic characteristics, obstetric parameters, presence of comorbidities, disease severity, investigations, management, and fetal outcome were reviewed. The study was approved by the institutional ethics committee.

### Statistical Analysis

Categorical variables are presented in number and percentage (%) and continuous variables are presented as mean  $\pm$  standard deviation and median. The data were entered in MS Excel spreadsheet and analysis was done using Statistical Package for Social Sciences (SPSS) version 21.0.

## Result

### Study Population Characteristics

Among 94 women, 54 (57.45%) were antenatal and 40 (42.55%) were postnatal. A majority (75.53%) of them were between 20 and 30 years of age. Among 54 antenatal women, 34 (62.96%) were multigravida, 9 (20.37%) women were discharged undelivered and in subsequent follow-up 1 woman had miscarriage within 2 weeks of discharge, 5 continued their pregnancy without any adverse outcome, and the remaining 3 women delivered healthy baby at follow-up (1 had term and the other 2 had preterm deliveries).

### Severity of Infection and Comorbidity

A large number of women was asymptomatic (42.55%) during the second wave. Among the symptomatic population, most (32.98%) had mild symptoms such as fever, cough, loose stool, ageusia and anosmia, with fever being the most common symptom. Moderate disease was present in 9.58%, such as fever with either dyspnea (respiratory rate  $\geq$  24/min) or SpO<sub>2</sub>  $\leq$  93% on room air. Severe disease was present in 14.89% of women with breathlessness (respiratory rate  $>$  30/min) or SpO<sub>2</sub>  $<$  90% on room air; 14.89% required ICU admission and 24.46% needed oxygen therapy. Among the study population, 48.94% had some medical comorbidity, with hypertensive disorders being the most common (14.89%), followed by anemia (8.51%), diabetes, hypothyroidism, and intrahepatic cholestasis of pregnancy (6.38% each) (**►Table 1**). Three women succumbed to the disease: two became symptomatic in the postnatal period and were tested positive, and the third woman had severe COVID-19 disease at 34 weeks of gestation. One of them was overtly diabetic and another had rheumatic heart disease (**►Table 2**).

Women were discharged based on the government's (MoHFW) discharge policy. The average hospital stay was  $14 \pm 2$  days.

### Pregnancy Outcome

Among 43 antenatal women admitted to the facility, 20 (37%) had vaginal delivery and 23 (42.6%) underwent cesarean delivery while remaining 17 (20.4%) discharged undelivered. The

**Table 1** Demographic parameters of the study population

| Parameters                | Number (n = 94) | Percentage (%) |
|---------------------------|-----------------|----------------|
| Antenatal women           | 54              | 57.45          |
| Postnatal women           | 40              | 42.55          |
| Age (y)                   |                 |                |
| < 20                      | 2               | 2.13           |
| 20–30                     | 71              | 75.53          |
| > 30                      | 21              | 22.34          |
| Gravidity/parity (n = 54) |                 |                |
| Primigravida              | 20              | 37.04          |
| Multigravida              | 34              | 62.96          |
| Mode of delivery (n = 54) |                 |                |
| Vaginal delivery          | 20              | 37.04          |
| LSCS                      | 23              | 42.59          |
| Discharged undelivered    | 11              | 20.37          |
| RAT positive              | 48              | 51.06          |
| RTPCR positive            | 46              | 48.94          |
| Type of infection         |                 |                |
| Asymptomatic              | 40              | 42.55          |
| Mild                      | 31              | 32.98          |
| Moderate                  | 9               | 9.58           |
| Severe                    | 14              | 14.89          |
| Comorbidity               |                 |                |
| Diabetes                  | 6               | 6.38           |
| Hypertension              | 14              | 14.89          |
| Anemia                    | 8               | 8.51           |
| Heart disease             | 1               | 1.06           |
| Chronic kidney disease    | 0               | 0              |
| IHCP                      | 6               | 6.38           |
| Hypothyroidism            | 6               | 6.38           |
| Thrombocytopenia          | 2               | 2.12           |
| Bronchial asthma          | 1               | 1.06           |
| Others (seizure disorder) | 2               | 2.12           |
| ICU admission             | 14              | 14.89          |
| Oxygen requirement        | 23              | 24.46          |
| Mortality                 | 3               | 3.19           |

Abbreviations: ICU, intensive care unit; IHCP, intrahepatic cholestasis of pregnancy; LSCS, lower segment cesarean section; RAT, rapid antigen test; RTPCR, reverse transcriptase polymerase chain reaction.

indications for cesarean section in almost all cases were purely obstetric indications, with fetal distress with meconium-stained liquor being the most common indication. In one case, the mother presented with acute-onset desaturation and emergency cesarean section was performed to improve the outcome.

Among 20 women who delivered vaginally, 12 (60%) had term delivery and 8 (40%) women had preterm vaginal delivery. Among 23 cesarean deliveries, 16 (69.56%) were

**Table 2** Details of maternal mortality

| Parameters              | Case 1                                   | Case 2                      | Case 3                                     |
|-------------------------|--|-----------------------------|--|
| Presentation            | Postnatal                                | Postnatal                   | Antenatal                                  |
| Age (y)                 | 30                                       | 24                          | 30   |
| Parity                  | P2L2                                     | P2L1 (IUD)                  | G2A1                                       |
| Comorbid condition      | k/c/o RHD                                | Overt DM (on insulin)       | None                                       |
| Presenting symptom      | Fever                                    | Fever                       | Breathlessness with SpO <sub>2</sub> < 90% |
| Pregnancy complications | None                                     | None                        | IUD  |
| Mode of delivery        | Emergency LSCS                           | Vaginal delivery            | Emergency LSCS                             |
| Baby                    | Live, COVID-19 negative                  | Macerated still birth       | Twin, both fresh stillbirth                |
| Length of stay (d)      | 11                                       | 9                           | 14   |
| Place of death          | Home (2 d after discharge from hospital) | Hospital                    | Hospital                                   |
| Cause of death          | Not known                                | COVID pneumonia with sepsis | ARDS                                       |

Abbreviations: ARDS, acute respiratory distress syndrome; COVID-19, coronavirus disease 2019; DM, diabetes mellitus; IUD, intrauterine death; LSCS, lower segment cesarean section; RHD, rheumatic heart disease.

done for fetal distress and 7 (30.43%) had preterm emergency cesarean, with multiple pregnancy and antepartum hemorrhage being the common indications. Overall, the preterm delivery rate was 34.88%. Seven elective cesarean deliveries were done on maternal demand in term women with previous cesarean section as they did not give consent for trial of vaginal delivery after being explained regarding the risk of scar dehiscence or scar rupture. Health care workers are at additional risk and all appropriate COVID-19 protocols were followed.

## Maternal Mortality

### Neonatal Outcome

A total of 40 women were admitted postpartum and another 43 antenatal women delivered during their stay. Among 83 women, 1 woman was admitted with sepsis, 34.88% had preterm delivery and 13.95% (6 women) had intrauterine demise (IUD) and delivered a stillborn baby. Among the women who had IUD, two had severe COVID-19, resulting in hypoxia. Four of these had preterm vaginal delivery and two had diabetes, which may be the cause of intrauterine fetal demise. Two women with singleton pregnancy had an early neonatal death. One woman with twin pregnancy delivered by emergency preterm lower segment cesarean section at 32 weeks in view of both twin fetal growth restriction with one twin having reversed end diastolic flow but ultimately resulted in early neonatal death of both the twin babies. Two women with twin pregnancy had early neonatal death of one twin and another twin required nursery admission. Total neonatal deaths were 5 (11.62%). Among these, four had preterm vaginal delivery and three had twin pregnancy. Among 76 newborns, 6 (7.89%) babies had positive RTPCR report, but no mortality among them was observed. All babies were discharged in healthy state.

### Follow-up

All women were contacted telephonically after 2 weeks of discharge; eight were lost to follow-up as they could not be contacted. One woman with rheumatic heart disease expired after 2 days of discharge at home; the cause was not known. Among 11 women who were antenatal during discharge, 3 had vaginal delivery within the next 2 weeks, 1 had spontaneous abortion, 2 could not be contacted, and the rest were continuing their pregnancy well at the time of writing this paper. Common complaints after discharge were malaise, body ache, and cough. Few had complaints of persistent two or three spikes of fever. Another group complained of palpitation and breathlessness on exertion.

## Discussion

Pregnancy causes suppression of immune system and predisposes the woman to a higher risk of acquiring contagious diseases.<sup>8</sup> Reports from China and Europe corroborate that asymptomatic and mildly symptomatic infected pregnant women were more in number than women with severe symptoms. A report from New York City stated that 86% of COVID-19 pregnant patients presented with mild or no viral-associated symptoms.<sup>9</sup> In the current study, 42.55% of women were asymptomatic, 9.58% had moderate symptoms, and 14.89% had severe disease.

A meta-analysis of 11 studies in 2020, involving 9,032 pregnant women with COVID-19 and 338 infants, reported that the most prevalent symptoms was fatigue (54.5%), followed by cough (50.1%) and fever (27.6%). Other common symptoms such as dyspnea, myalgia, and sore throat were present in ~21, 16, and 11% of pregnant women with COVID-19, respectively. In less than 10%, atypical symptoms such as diarrhea were present.<sup>10</sup> In the current study, among the symptomatic population, most (32.98%) had mild symptoms

such as fever, cough, loose stool, ageusia, and anosmia. Fever was the commonest symptom. In the above-mentioned study, 30% of pregnant women with COVID-19 had preterm delivery, whereas premature rupture of membranes and fetal distress were observed in ~2% of women. Fetal death and neonatal death rate were reported to be 2 and 0.4%, respectively.<sup>10</sup> In the current study, 40% of women who delivered vaginally had a preterm delivery. Among cesarean deliveries, 69.56% were done for fetal distress and 30% had preterm emergency cesarean, with multiple pregnancy and antepartum hemorrhage being the common indications. Intrauterine death occurred in 13.95% of women, and in 11.62% of women, their babies had an early neonatal death. Preterm birth and stillbirth rate were higher than the contemporary non-COVID-19 population in the current study.

A systematic review and meta-analysis of 13 studies on pregnant women during the first wave of SAR-CoV-2 reported fever and cough as the most prevalent symptoms and clinical signs.<sup>11</sup> Pooled proportion of pregnant women having fever and cough was 76.0 and 38.0%, respectively. The most frequent complications during pregnancy, as reported in the study, were nonreassuring fetal heart (38.5%), premature rupture of membranes (38.5%), placenta previa (23.1%), preeclampsia (15.4%), gestational diabetes (15.4%), hypertension (7.7%), cholecystitis (7.7%), abnormal amniotic fluid (7.7%), umbilical cord abnormalities (7.7%), fetal asphyxia (7.7%), meconium staining (7.7%), and stillbirth (7.7%) from various published studies.<sup>4,12-20</sup> Although women were heterogeneously treated (antibiotics, antivirals, and corticosteroids, in different combinations), 45% of infected pooled proportion of women developed pregnancy-related complications. A relatively high number of pregnant women (13.0%) were admitted to the ICU, although there was no maternal mortality.<sup>4,12-22</sup> A low probability of vertical transmission was evident as the proportion of infected neonates was low (6%).<sup>10</sup> In the current study, maternal and fetal clinical profile was similar.

Mahajan et al in 2021 conducted a retrospective observational study in a dedicated COVID-19 hospital in Mumbai, and analyzed the data of 1,530 pregnant and postpartum women admitted during the first (1,143) and second waves (387) of the COVID-19 pandemic regarding the maternal and fetal outcomes. They reported that admission to the ICU or high-dependency unit, case fatality rate, and maternal mortality ratio were significantly higher during the second wave ( $p < 0.001$ ). The majority of maternal deaths (93%) were due to COVID-19 pneumonia and respiratory failure. They also reported the genome sequencing data to correlate the direct association of B.1.617 to adverse outcomes were not available, so definitive conclusions regarding the effect of the B.1.617 variant could not be made.<sup>23</sup> In the current study, the case fatality rate was 3.8% and both the maternal deaths were COVID-19 pneumonia and respiratory failure.

### Strength of the Study

It is a single-center study done in a tertiary referral hospital with COVID-19 facility and a fairly large cohort of women.

Guidelines of ICMR, WHO, and MoHFW, Government of India, were judiciously followed during admission, classification the disease severity, and management protocol and when deciding the discharge criteria.

### Limitation of the Study

A limitation of this study is the lack of long-term follow-up. No histopathological correlation could be done to determine possible vertical transmission.

### Conclusion

The course of this disease in pregnant and postpartum women can be rapid and aggressive, leading to death. During the second wave of SARS-CoV-2, women with comorbidities and advanced gestation were prone to severe disease and death, thus requiring more ICU admission, oxygen therapy, and antiviral therapy. There was a higher rate of preterm delivery and stillbirth. Operative deliveries were mostly done for fetal distress. It is thus recommended that all women planning a conception or currently pregnant must also complete the vaccination against COVID-19. This study will help in further evaluation regarding natural course of the disease and fetomaternal outcome of SARS-CoV-2 infection in pregnancy.

#### Funding

None.

#### Conflict of Interest

None declared.

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