Effects of COVID-19 during pregnancy on maternal and neonatal outcome: A retrospective observational study in tertiary teaching hospital, India

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ABSTRACT

Aim: This study aims to describe the clinical characteristics, maternal and neonatal outcome of pregnancies complicated with COVID-19 infection. Methods: This is a retrospective, single center, observational study conducted on all COVID-19 positive pregnant women who were admitted in our institution from 1st April 2020 to 30th November 2020. During the study period, a total of 201 pregnant and postpartum women with COVID-19 infection confirmed by RT-PCR test, regardless of their symptoms, were admitted and included in the study. Data were collected from hospital records about the demographic profile, clinical characteristics, maternal and neonatal outcomes. Results: The mean age was 26 years (SD = 5.21). Majority patients (71.6%) were asymptomatic and 22.3% had mild symptoms. Only 4 (1.99%) women had severe COVID pneumonia. Majority (75.62%) were admitted in 3rd trimester. Cesarean section rate in COVID-19 infected pregnant women was 53.8%, which was almost similar to 52.8% rate in COVID-19 negative pregnant population. Incidence of preterm birth was 11%. Most neonate were asymptomatic and only 2 of them tested positive on testing within 48 h of birth. Conclusion: There is no major effect of COVID-19 infection during pregnancy on maternal and neonatal outcome. The incidence of preterm birth and cesarean section is similar to COVID-19 negative pregnant population.

Keywords: COVID-19, maternal outcome, neonatal outcome, pregnancy, SARS-CoV-2

Introduction

Severe acute respiratory syndrome corona virus 2 (SARS-CoV-2) is a novel virus first reported to the World Health Organization (WHO) country office in China on 31st December, 2019. On 11th February 2020, WHO coined the new name for the disease as Corona Virus Disease 2019 (COVID-19). Due to its high transmissibility, it became a pandemic with 61.8 million reported cumulative cases and 1.4 million deaths globally on 1st December 2020 since the start of the pandemic. In India, the first case was confirmed on 30th January 2020. The incubation period of COVID-19 infection varies from 2 days to 2 weeks following exposure to the virus. The most common symptoms of COVID-19 are cold, cough, fever, anosmia, headache, myalgia, watering eyes. However, patients may also present with gradual worsening of respiratory discomfort, multi-organ failure, and severe pneumonia. Indian Council of Medical Research (ICMR) recommends the standard test for detection of the viral RNA by reverse transcriptase-polymerase chain reaction (RT-PCR) from the nasopharyngeal mucosa. The experiences from previous human coronavirus diseases - severe acute respiratory syndrome coronavirus (SARS-CoV) and Middle East respiratory syndrome coronavirus (MERS-CoV) suggests that disease is more likely to be severe in pregnant women and neonates are likely to have poor outcomes. Pregnancy is known to be a state of suppressed immune response and this make...
them susceptible to more adverse outcome in viral infections.[10] Immaturity of innate and adaptive immune systems of fetus and newborn make them highly vulnerable to infections.[11] Pregnant women and their newborn have been evaluated as being potential risk groups in the current pandemic. Some studies have shown that pregnant women are not more susceptible to COVID-19 infection than non-pregnant women.[12–14] Since SARS-CoV-2 is a respiratory virus, the chance of vertical transmission is likely to be low. But no clear evidence of vertical transmission from mother to fetus is reported in various studies.[15–17] Very few systemic reviews and meta-analysis are available till now and data are mainly taken from case report, case series, or observational studies. Further, the risk of postnatal transmissions and measures to prevent it has not yet been determined. Thus, there is need of more information and evidence on outcomes and clinical characteristics of COVID-19 infection in pregnancy to add to the continually evolving guidelines and management of such pregnancies and their neonates. Therefore, this study aims to describe the clinical characteristics, maternal and neonatal outcome of pregnancies complicated with COVID-19 infection.

Methods

Study design, Setting, Study Population

This is a retrospective, single center, observational (descriptive) study conducted on all COVID-19 positive pregnant women who were admitted in a tertiary care teaching institution, from 1st April 2020 to 30th November 2020. Our institution is a designated COVID care hospital of Eastern State in India. As a local policy, all pregnant women coming to the institution were screened for SARS-CoV-2 infection using travel, contact history and symptoms and were tested for SARS-CoV-2, RT-PCR test using nasopharyngeal and oropharyngeal swab. All pregnant women coming to labor room emergency were tested for SARS-CoV-2 by RT-PCR, irrespective of COVID-19 related symptoms or history. As a part of local policy, all RT-PCR confirmed COVID-19 positive pregnant women were admitted in COVID ward designated specially for obstetric patients, regardless of their symptoms or gestational age, till they became negative for SARS-CoV-2 infection on repeat RT-PCR done according to ICMR evolving guidelines. The management of symptoms related to COVID-19 infection categorized into mild, moderate, and severe cases was done as per hospital protocol following ICMR guidelines. The mode of delivery was decided according to obstetric indication.

The study was approved by the Institutional Ethics committee (IEC 130/29.11.2020)

Patient inclusion criteria

1. All pregnant women (irrespective of gestational age) who tested positive for COVID-19 infection by RT-PCR in our hospital or referred from other hospitals of our State.
2. Postpartum women who tested positive within one week of delivery in our institution or referred from outside.

Pregnant women with negative RT-PCR test were excluded from the study.

Neonatal assessment

All neonates born to COVID-positive pregnant women were tested on 1st day of life, if negative then, second test after 48 h and again after 7 days by nasopharyngeal swab for SARS-CoV-2, RT-PCR according to our institutional protocols. Babies who tested positive but had no symptoms were kept with the mother. Symptomatic neonates were admitted to designated NICU for COVID-positive new born. Routine separation of mother and baby was not done, unless either the mother or the baby was sick. Mothers were allowed to breastfeed their new born wearing mask and following hand hygiene. Babies who tested negative were allowed rooming-in according to the mother’s wish or were kept separately with healthy caregiver with provision of expressed breast milk. So, breastmilk was allowed regardless of COVID status.

Data collection

Hospital records, admission registers, investigation records, and patient case sheet and discharge registers were used to collect data using a standardized data collection sheet. For maternal characteristics, data recorded were demographic profile, period of gestation at time of admission, symptoms related to COVID infection, impact of COVID infection on course of antenatal period, other comorbidities (gestational diabetes, hypertension, pre-eclampsia, eclampsia, heart disease, anemia), mode of delivery and duration of hospital stay. Perinatal outcomes included were birth weight, preterm births, RT-PCR results of nasopharyngeal swabs, admission to NICU.

Statistical analysis

It was done using SPSS (Statistical package for Social sciences) Version 21.0 statistical analysis software. For continuous variable, we used mean and standard deviation (SD). Categorical variables are reported as number and percentage.

Results

During the study period of 8 months, a total of 201 cases with RT-PCR confirmed COVID-19 infection were identified in pregnant and puerperal women as per inclusion criteria and admitted in our institution. Total number of obstetric admission in non-COVID area of our institution during the study period was 2,724, thus giving incidence of COVID-19 during pregnancy as 6.87% of total obstetric admission. Maximum number of cases (90.5%) were admitted during the months of July to October 2020. First obstetric case admitted on 11th May 2020, then significant fall in COVID-19 positive cases in the month of November 2020 [Figure 1].

The demographic profile and other maternal characteristics of SARS-CoV-2 confirmed cases is depicted in Table 1. The maternal age ranged from 19 years to 42 years with a mean
age of 26.00 years (SD = 5.21). Nine (4.4%) women were diagnosed with COVID-19 infection during 1st trimester, out of which, 2 were ruptured ectopic pregnancy managed by salpingectomy, 4 cases had abortion (one case each of inevitable abortion and incomplete abortion, 2 missed abortion) managed by suction evacuation. All these 9 pregnant women in first trimester had mild symptoms for COVID-19 infection at the time of admission and were managed by giving symptomatic treatment only (no antiviral therapy) and discharged as per hospital protocol after testing negative. Maximum number of cases 152/201 (75.62%) were admitted in 3rd trimester.

Table 2 shows the obstetric outcomes of pregnant women with SARS-CoV-2 infection. 41 (20.3%) pregnant women were admitted remote from term and discharged undelivered without any major complications. The outcomes of these pregnancies are not known. 41.2% (83/201) delivered by cesarean section which were done for obstetric indications only. After excluding cases of abortion and antenatal cases who were discharged from hospital undelivered, the incidence of vaginal delivery was 71/154 (46.1%) and that of cesarean section was 83/154 (53.8%) among COVID-19 confirmed cases. Only 4 cesarean were elective done on maternal request, rest were emergency cesarean sections. Total number of delivery in non-COVID lab room during our study period were 1,978, out of which 52.88% were delivered by cesarean and rest 47.12% were vaginal delivery. Thus, the cesarean rate was almost similar in COVID and non-COVID area. The preterm birth rate in our study was 11% (17/154), out of which 7 were cesarean and 10 were vaginal deliveries.

The mean duration of hospital stay of COVID-positive antenatal patients who were discharged undelivered, those who delivered vaginally at term, preterm vaginal delivery and those delivered by cesarean was 9.65 (SD = 3.71), 8.35 (SD = 3.55), 7.42 (SD = 1.98), and 9.31 (SD = 3.08) days, respectively.

Table 3 depicts the associated risk factors and comorbidities. Majority 154/201 (76.6%) had no associated risk factors or comorbidities. The symptoms related to COVID-19 among SARS-CoV-2 confirmed cases is mentioned in Table 4. In our study, 4 (1.99%) women developed severe pneumonia requiring ICU admission with ventilatory support. Out of these, 2 were cases of antepartum eclampsia, one was severe preeclampsia, one was case of rheumatic heart disease with severe mitral stenosis. All delivered by cesarean except one case of eclampsia who came in active labor, delivered vaginally. Out of these, 2 women succumbed to death (case of rheumatic heart disease with severe mitral stenosis and pregnancy with antepartum eclampsia) in postpartum period. But 2 women recovered and got discharged from hospital after COVID-negative report. There were 2 maternal deaths among 201 cases giving case fatality

Table 1: Demographic profile of pregnant women with confirmed SARS-CoV-2 infection (n=201)

| Parameters                  | Number (%) |
|-----------------------------|------------|
| **Age**                     |            |
| ≤20 years                   | 31 (15.42%)|
| 21-35 year                  | 160 (79.60%)|
| ≥35                         | 10 (4.98%)  |
| **Place**                   |            |
| Rural                       | 49 (24.3%) |
| Urban                       | 152 (75.6%)|
| **Parity**                  |            |
| Nullipara                   | 84 (41.7%) |
| Multipara                   | 117 (58.3%)|
| **Gestation at time of diagnosis** |        |
| 1st trimester (≤13 weeks)   | 9 (4.4%)   |
| 2nd trimester (14-27 week)  | 12 (5.9%)  |
| 3rd trimester (≥28 week)    | 152 (75.62%)|
| Postpartum                  | 28 (13.9%) |

Table 2: Obstetric outcome of pregnant women with confirmed SARS-CoV-2 infection (n=201)

| Obstetric outcomes                  | Number (%) |
|-------------------------------------|------------|
| Discharged undelivered from hospital| 41 (20.3%) |
| Vaginal delivery                    | 71 (35.3%) |
| Cesarean section                    | 83 (41.29%)|
| Preterm Birth                       | 17 (8.45%) |
| Abortion                            | 04 (1.9%)  |
| Laparotomy for ectopic pregnancy    | 02 (0.99%) |

Table 3: Associated risk factors/comorbidities (n=201)

| Co-morbidities                  | Number (%) |
|---------------------------------|------------|
| Pre-eclampsia                   | 12 (5.9%)  |
| Antepartum eclampsia            | 08 (3.9%)  |
| Gestational diabetes mellitus   | 04 (1.99%) |
| Heart disease                   | 02 (0.9%)  |
| Obstetric cholestasis           | 02 (0.9%)  |
| Thyroid disorders               | 04 (1.99%) |
| Respiratory disorder (Bronchial Asthma, TB) | 04 (1.99%) |
| Severe anemia                   | 05 (2.48%) |
| Jaundice                        | 02 (0.9%)  |
| H/O malignancy                  | 02 (0.9%)  |
| Seropositive (HIV, HBsAg)       | 02 (0.9%)  |
| No risk factor                  | 154 (76.6%)|
rate of 0.99%. Total maternal death of our institute during the study period was 64. COVID-19 infection accounted for 3.12% of maternal deaths.

Neonatal outcomes are depicted in Table 5. Out of 154 COVID-19 confirmed deliveries, only 2 (1.2%) of the neonates were found COVID positive in the initial testing done on 1st day of birth. One was term baby delivered by cesarean for fetal distress, got admitted in NICU for sepsis and neonatal hyperbilirubinemia. Other baby was preterm vaginal delivery at 33 weeks, developed neonatal hyperbilirubinemia and got admitted in NICU. Both babies eventually got COVID negative on repeat test after 7 days of first test and were discharged from NICU. The incidence of intrauterine fetal death was 1 (0.65%) only. Twenty two babies required NICU admission- 14 babies for preterm birth, 5 babies for low Apgar score with meconium, 2 babies for sepsis, other 2 COVID positive babies for reasons explained above.

**Discussion**

This is a retrospective descriptive study describing the clinical characteristics, maternal and neonatal outcome of COVID-19 infection during pregnancy in a tertiary care teaching hospital of Eastern India. Studies have shown that pregnant women infected with SARS-CoV and MERS-CoV have more adverse outcomes in terms of spontaneous miscarriage, fetal growth restriction, preterm delivery, and maternal mortality rate of as high as 25% compared to 10% in normal population. Recent studies on COVID-19 have shown that compared to SARS-CoV, adverse mother and child outcomes are fewer in COVID-19 infection. Our retrospective study also seems to confirm to these. The incidence of COVID-19 infection during pregnancy was 6.87% of total obstetric admissions. Thus, pregnancy as such does not seem to increase the risk of getting the COVID-19 infection. In a prospective cohort population based study using United Kingdom Obstetric Surveillance System (UKOSS), estimated incidence of admission to hospital with confirmed SARS-CoV-2 infection in pregnancy was 4.9 (95% confidence interval 4.5–5.4) per 1,000 maternities, whereas Nayak et al. from India have reported incidence of 14.43%. Overall, 71.6% (144/201) of COVID-19 positive pregnant women in the present study were asymptomatic, 45 (22.38%) had only mild symptoms like sore throat, mild cough, loss of smell, and low grade fever. These observations are similar to a number of preliminary studies done on SARS-CoV-2 confirmed pregnant patients. A systematic review found low grade fever and cough to be the most dominant initial symptoms. PregCoV-19 Living Systematic Review reported that on universal screening in pregnancy, 74% (95% CI: 51–93) were asymptomatic and cough (41%) and fever (40%) were the most common symptoms. However, other studies have reported up to 88% and 67.4% as symptomatic at time of presentation.

Majority (75.62%) of COVID-19 positive pregnant women in our study presented in third trimester. This is similar to the finding of prospective cohort study using UKOSS where most women were admitted late 2nd or in 3rd trimester. Another study reported median age on diagnosis to be 29 weeks and half of them were in third trimester.

In our study, hypertensive disorders of pregnancy were found to be associated in 12% of COVID-positive pregnant patients. Other study has also reported increased risk of hypertensive disorder of pregnancy in pregnancy with SARS-CoV-2 infection. Evidence of association of gestational diabetes with pregnant women infected with COVID-19 is reported in some studies. But in our study only 1.99% of SARS-CoV-2 infected pregnant patients had gestational diabetes.

Our hospital being a tertiary care referral hospital, number of cesarean sections is relatively high. One of the key finding of our study was almost similar cesarean rate in COVID positive and COVID negative group, 53.8% and 52.88%, respectively. This finding is similar to cesarean rate of 50% in COVID-19 infected and 47% in COVID-negative group in study by Nayak et al. Another study suggested that majority of pregnant women had planned caesarean section to prevent neonatal transmission of the virus.

In our study, only 4 (1.9%) patients had developed severe COVID pneumonia requiring ICU admission with case fatality rate of 0.99%. Various preliminary studies done on COVID-positive pregnancies have also suggested low rate of ICU admission. UKOSS study suggested that rates of ICU admission and mortality in pregnant women admitted with COVID-19 were proportional to the rates among general population.

The neonatal outcome in our study were mostly reassuring in consistent with other studies. The incidence of preterm births in our study was 11% which is lower in comparison to 27% reported in UKOSS study. Out of 154 deliveries, only 2 neonate tested positive for SARS-CoV-2 by RT-PCR in their initial

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**Table 4: Symptoms of COVID-19 (n=201)**

| Symptoms       | Number (%) |
|----------------|------------|
| Asymptomatic   | 144 (71.6%)|
| Mild symptoms  | 45 (22.38%)|
| Moderate symptoms | 8 (3.98%) |
| Severe symptoms | 4 (1.99%)  |

**Table 5: Neonatal outcome (n=154)**

| Outcome                        | Number (%) |
|--------------------------------|------------|
| Intrauterine fetal death       | 01 (0.65%) |
| Birthweight <2.5 kg            | 30 (19.4%) |
| Preterm Birth                  | 17 (11.03%)|
| NICU admission                 | 22 (14.28%)|
| COVID 19 positive infants      | 02 (1.2%)  |
testing done, both babies were admitted in NICU. The mode of delivery does not seem to have a protective effect in neonatal transmission of virus in our study. Earlier studies have shown no risk of perinatal vertical transmission.\textsuperscript{[13,21]} Recent evidences show that vertical transmission is uncommon. Even if it occurs, it is not affected by mode of birth, delayed cord clamping, skin to skin contact, method of feeding and rooming in.\textsuperscript{[13-38]}

Major strength of this study is its large sample size while preliminary studies comprised of smaller sample size of 10–141 pregnancies. The findings of this study will help primary care physicians in better understanding of the clinical characteristics of COVID-19 in pregnant women and the maternal and neonatal outcomes. This will further aid in proper management, counselling, and timely referral of such patients. We acknowledge that being a retrospective study it has its limitation and we do not have the complete information of patients who were discharged from the hospital undelivered.

Conclusions

The key messages concluded from this study are that there is no major effect of COVID-19 infection in pregnancy on maternal and neonatal outcome. Majority of pregnant women with COVID-19 infection were asymptomatic or presented with mild symptoms and were discharged without complications. However, severe illness can occur when COVID-19 complicates hypertensive disorders of pregnancy. Cesarean section rates were similar to that in COVID-19 negative pregnant women. Our study is a preliminary study; Large multicentric studies are required to give a clear picture about vertical transmission and other maternal effects of COVID-19 infection. This study can provide the database and additional guidance to clinicians for counselling and policy making for pregnant women with COVID-19 infection.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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