

Foetomaternal Outcomes in COVID-19 Positive Obstetric Patients: An Observational Study

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ABSTRACT

Introduction: In Coronavirus Disease-2019 (COVID-19) pandemic, a serious concern has been raised regarding the health of the newborn and the pregnant mother. Limited data is available on the foetomaternal outcomes in this pandemic.

Aim: To assess the foetomaternal outcomes in COVID-19 positive pregnant patients.

Materials and Methods: A prospective cohort study was conducted from October 2020 to December 2020, at JSS Medical College, Mysuru, Karnataka, India, on 27 COVID-19 positive obstetric patients admitted to the ward who had confirmed COVID-19 on the basis of Reverse Transcriptase-Polymerase Chain Reaction (RT-PCR) or lung opacities. The study period belonged to first wave of COVID-19. The foetomaternal outcomes such as mode of delivery, abortions, foetal admission in Intensive Care Unit (ICU) and mortality among the mother and the baby were recorded. The data was collected and tabulated in Microsoft Excel sheet and frequency (n) and percentages (%) were calculated.

Results: Total of 27 COVID-19 positive obstetric patients (age 19-37 years; mean gestational age 34.84±7.75 weeks) formed the sample of the study. The mean age of the study

patients were 27.11±4.5 years. The primary symptoms included cough (18.52%) and breathlessness (11.11%). After diagnosis, seven cases (25.92%) continued pregnancy and were lost to follow-up while among those who delivered (n=20), the mode of delivery was Lower Segment Caesarean Section (LSCS) in 12 (44.44%), normal vaginal 6 (22.22%), emergency laparotomy in 1 (3.7%) and incomplete abortion in 1 (3.7%) women. Among the 20 who delivered, 1 was Intrauterine Death (IUD) and the rest of the 19 foetuses were negative for COVID-19. Of the total 20 foetuses delivered, 10 required Neonatal Intensive Care Unit (NICU) admission where one died. Repeat testing was done in 13 female subjects, all of them were negative, while rest of the seven patients did not turn in for repeat testing and were lost. Among the pregnant women, one patient died secondary to COVID-19 bronchopneumonia in the postpartum period.

Conclusion: If managed properly without any complications, the outcomes are good for the mother and the baby without a significant risk of transmission. However, the long-term follow-up is needed to assess the mortality of the patients.

Keywords: Coronavirus disease-2019, Newborn, Pandemic, Pregnancy

INTRODUCTION

The outbreak of Coronavirus Disease (COVID-19) was caused by Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2) in Wuhan, China and then it was declared as a public health emergency by the World Health Organisation (WHO) and an international concern was raised [1]. The high mortality rate necessitates recognition as well as protection of the susceptible individuals. The information acquired from outbreaks caused by human coronavirus such as SARS-CoV and the Middle East Respiratory Syndrome Coronavirus (MERS-CoV) indicates susceptibility of pregnant women to poor outcomes. Intensive care unit admission is common and 35% of case fatality rate is reported [2,3]. As pregnant women and newborns are at an increased risk of COVID-19, evaluation is required [4].

In spite of widespread studies related to the clinical manifestations and treatment of patients with COVID-19, there is scarcity of studies among pregnant women with COVID-19 in India [5-7]. The difference in the clinical characteristics of pregnant women with COVID-19 pneumonia from non pregnant women with COVID-19 is still not clear. Also, it is unclear whether COVID-19 pneumonia symptoms are aggravated by pregnancy and childbirth, and also if antiviral therapy is essential for pregnant women with COVID-19 [8]. Ongoing research has been vast which reports the data on foetomaternal outcomes. Since COVID-19 is a new disease, medical literature demands continuing research in this regard. Children have been spared from this disease but the newborn

susceptibility to COVID-19 in cases of infection to their mothers needs further research.

This study aimed at describing the clinical manifestations, treatment, and maternal and foetal outcomes in COVID-19 positive pregnant patients.

MATERIALS AND METHODS

This was a prospective cohort study conducted from October 2020 to December 2020 at JSS Medical College, Mysuru, Karnataka, India, where a total of 27 COVID-19 positive pregnant patients in third trimester were enrolled. Of the 27 cases, seven continued pregnancy and were lost to follow-up of whom the foetomaternal outcomes could not be determined. The study period belonged to first wave of COVID-19. Institutional Ethical Committee approval was obtained (JSSMC/IEC/310821/04NCT/2021-22).

Inclusion criteria: COVID-19 positive pregnant women, of age greater than 18 years, with confirmed RT-PCR or High Resolution Computed Tomography (HRCT) report (for COVID positivity) and in their third trimester were included in the study.

Exclusion criteria: Those pregnant women in their first and second trimester and those patients not willing to participate in the study were excluded from the study.

Sample size estimation: The study of Liu D et al., observed that 1 out of 15 patients got delivered vaginally [4]. Taking this value as reference, the minimum required sample size with 10% margin of error and 5% level of significance was 24 patients. To reduce margin of error, total sample size taken was 27.

Procedure

The diagnosis was made on the basis of RT-PCR or lung opacities on High Resolution CT scan (HRCT). HRCT was done in cases of clinical worsening. All women were tested for Complete Blood Count (CBC), liver profile, and D-dimer assays. The demography details (age, gestational age), treatment and foetomaternal outcomes such as mode of delivery, abortions, foetal admission in ICU and mortality among the mother and the baby were recorded.

Delivery protocols: The indications for caesarean section included eclampsia, imminent eclampsia, failed progression for more than 12 hours, failed induction, history of previous caesarean section and request by the mother. The indication for emergency laparotomy included ectopic pregnancy.

Treatment protocol: The patients were treated with antibiotics. Those who underwent normal delivery were given oral antibiotics (amoxiclav tablet 625 mg was given once daily for 5 days) and those who underwent caesarean were given injectables, that is, Augmentin 12 mg single daily dose for 3 days and Injection taxim 1 mg for five days or three consecutive doses. Multivitamin tablets (zinc and vitamin C) were given to all COVID-19 patients. For controlling fever, dolo 650 mg 4 times a day were given.

Indication of repeat RTPCR testing: The indications for repeat testing included the persistence of symptoms like fever, cough, cold and loose stools. The repeat samples were taken after two weeks of clinical improvement of the patient as per the discharge criteria. We followed this protocol only during the first wave of COVID-19. In the present study centre, as its a teaching institute, the authors followed the repeat testing protocol for psychological benefit for the pregnant women and lactating mother.

STATISTICAL ANALYSIS

The presentation of the categorical variables was done in the form of number (n) and percentage (%). On the other hand, the presentation of the continuous variables was done as mean±SD and median values. The data entry was done in the Microsoft Excel spreadsheet and the final analysis was done with the use of Statistical Package for Social Sciences (SPSS) software version 21.0.

RESULTS

The mean age of the study patients were 27.11±4.5 years with 13 primi and 14 multigravida. The gestational age of presentation was ≥37 weeks in majority of the women (59.26%) [Table/Fig-1]. Mean values of C-Reactive Protein (CRP), lymphocytes, neutrophils, Aspartate Aminotransferase (AST), Ferritin, and D-dimer were 70.24±64.21 mg/L, 17.6±6.41 µL, 77.43±7.92 µL,

Demographic characteristics	Frequency (n)	Percentage (%)
Age (years)		
Mean±SD	27.11±4.5	
Median (IQR)	27 (26-28.5)	
Range	19-37	
Gravida		
Primigravida	13	48.15%
Multigravida	14	51.85%
Co-morbidities		
Hypertension	5	18.52%
Hypothyroidism	2	7.41%
Gestational age (weeks)		
<37 weeks	11	40.74%
≥37 weeks	16	59.26%
Mean±SD	34.84±7.75	
Median (IQR)	37.29 (34.5-38.071)	
Range	8.86-41	

[Table/Fig-1]: Distribution of demographic characteristics of study subjects.

51.89±92.49 U/L, 61.04±45.89 ng/mL, and 1.61±1.27 mg FEU/µL, respectively [Table/Fig-2].

Blood investigation	Mean±SD	Median (IQR)	Range
CRP (mg/L)	70.24±64.21	53.4 (23.9-99.5)	0.17-239.4
Lymphocytes (µL)	17.6±6.41	17.4 (13.7-20.95)	2.5-29.7
Neutrophils (µL)	77.43±7.92	78.5 (72.8-81.35)	63.6-95.6
AST (U/L)	51.89±92.49	18 (14.5-29)	10-428
Ferritin (ng/mL)	61.04±45.89	42 (29-69)	13-175
D-dimer (mg /µL)	1.61±1.27	1.2 (0.7-2.1)	0.3-5

[Table/Fig-2]: Descriptive statistics of blood investigation of study subjects.

AST: Aspartate transaminase; CRP: C-Reactive protein; AST: Aspartate aminotransferase; IQR: Interquartile range

The signs and symptoms included cough in 5 (18.52%), breathlessness in 3 (11.11%), fever, loose stools, and pulmonary oedema in only 1 out of 27 patients each. In majority of patients, 18 (77.78%) showed no symptoms. All patients were positive for RT-PCR except one who showed ground glass opacities on HRCT.

After diagnosis, 7 (25.92%) women continued pregnancy and were lost to follow-up. Among 20 women who delivered, the mode of delivery was Lower Segment Caesarean Section (LSCS) in 12 (44.44%), normal vaginal 6 (22.22%), emergency laparotomy in 1 (3.7%) and incomplete abortion in 1 (3.7%) women [Table/Fig-3].

Mode of delivery	Frequency	Percentage
Continued pregnancy (Lost to follow-up)	7	25.92%
Emergency laparotomy	1	3.7%
Incomplete abortion	1	3.7%
LSCS	12	44.44%
Normal delivery	6	22.22%

[Table/Fig-3]: Distribution of mode of delivery.

LSCS: Lower segment caesarean section

Among the 20 who delivered, one was Intrauterine Death (IUD) and the rest of the 19 fetuses were negative for COVID-19. This case of IUD was born to a primigravida mother with 34 weeks of breech presentation who was diagnosed with preeclampsia and had symptoms of cough and cold. The reasons for IUD maybe lack of antenatal care probably due to the pandemic, preeclampsia and abruption because we found retroplacental clot in the postdelivery period. Though we did not find any patient in Disseminated Intravascular Coagulation (DIC), inflammatory markers such as CRP was increased in 10 cases, D-dimer in 8 cases with simultaneous lymphopenia in 3 cases.

Among 19 alive fetuses, 10 required NICU admission with ventilatory support where one died. The baby died due to prematurity and respiratory distress syndrome [Table/Fig-4]. Twelve fetuses were isolated from mother and none of them had vertical transmission from mother. Breast feeding was given in six fetuses (33.33%).

Augmentin, vitamin C, and zinc were given in 44.44% patients; amoxiclav, vitamin C, zinc in 40.74% patients; vitamin C, zinc in

Variables	Frequency (n)	Percentage (%)
Foetal outcome		
Died	1	5%
IUD	1	5%
Live	18	90%
NICU		
No	9	47.37%
Yes	10	52.63%
Positive/Negative of COVID-19		
Negative	19	100%

[Table/Fig-4]: Distribution of foetal outcome of study subjects.

IUD- intrauterine death; NICU: Neonatal intensive care unit; COVID-19: Coronavirus disease-2019

2 (7.41%) patients; amoxiclav, vitamin C, dolo in one patient; and antihypertensives, dolo, vitamin C, zinc in one patient [Table/Fig-5].

Treatment	Frequency	Percentage
Amoxiclav, vitamin C, zinc	11	40.74%
Amoxiclav, vitamin C, dolo	1	3.70%
Anti-HTN, dolo, vitamin C, zinc	1	3.70%
Augmentin, vitamin C, and zinc	12	44.44%
Vitamin C, zinc	2	7.41%
Total	27	100%

[Table/Fig-5]: Distribution of treatment of study subjects.
HTN: Hypertension

In present study, in 100% of patients, advice for home quarantine was given. Total of 51.85% patients underwent repeat testing in follow-up and report was negative. Among the pregnant women, one patient died secondary to COVID-19 bronchopneumonia. She presented to the hospital with oxygen desaturation of 59%, fever, cough, generalised weakness and loss of taste for six days. After admission to the COVID-19 ICU, the investigations showed imminent eclampsia with blood pressure 170 by 110 mm of Hg. She delivered a preterm male baby weighing 1.4 kg who was on ventilatory support after caesarean section. Serial arterial blood gas analysis was done and patient was maintained on non invasive ventilation. The condition of the patient deteriorated on day three where she had postpartum haemorrhage. She was managed medically with oxytocin and carboprost. She was also given antipyretics dolo 650 mg and injectable antibiotics. She had hypertension for which vasopressors were started. Despite efforts, the patient had cardiorespiratory arrest and she died. We suspect refractory hypoxia as an immediate cause of septic shock secondary to COVID-19 bronchopneumonia as a proceeding cause and pregnancy as the antecedent cause.

DISCUSSION

On December 2019, the first cases of COVID-19 pneumonia were reported from Wuhan, Hubei Province in China after which a rapid spread occurred worldwide [6]. Cases of COVID-19 in pregnancy were identified by Obstetricians. This study showed the findings from 27 pregnancies confirmed to have COVID-19 during the period of October to December 2020. Studies reported that COVID-19 during pregnancy may be associated with severe maternal morbidity and the possibility of maternal-foetal transmission could not be ruled out entirely [8-12]. The mean age of the patients in the present study was 27.11 ± 4.5 years. Higher mean age of the patients (32 ± 5 years) was reported in the study by Liu D et al., [4]. Mean age of the patients as reported in the studies by Zaigham M and Andersson O; Liu H et al., Chen H et al., and Zhang L et al., were 31, 30, 30, and 30 years, respectively [8,10,12,13].

In the present study, out of 27 patients, 13 were primigravida and 14 were multigravidas and most of the women presented at the gestational age of ≥ 37 weeks. Mean gestational age at the time of presentation in the studies by Liu D et al., Chen H et al., and Zhang L et al., were 224 ± 8 , 260 ± 14 , and 271 ± 10 , respectively [4,12,13]. The common symptoms were flu like such as fever, cough and breathlessness. Fever at the time of admission was the main symptom in pregnant women with COVID-19 in the study by Liu D et al., [4]. Other symptoms were cough, myalgia, fatigue, fever postpartum, sore throat, dyspnoea, and diarrhea [4]. Similarly, fever and coughing were present in most of the patients in previous studies conducted on pregnant women with COVID-19 [8,9,11].

As reported in the recent studies by Huang C et al., Chen H et al., and Li Q et al., pregnant women with COVID-19 pneumonia demonstrated a pattern of clinical characteristics that were comparable to that of non pregnant women with COVID-19 pneumonia [14,12,15]. With respect to the mode of delivery, many studies reported that most of the deliveries were done by caesarean section and foetal distress was the

main indication [10,12,13]. Similar was the case in the present study as the mode of delivery was LSCS in most of the women (44.44%).

Similar to present study, in study by Liu D et al., out of 15 patients, 10 were delivered by caesarean deliveries and one by vaginal delivery during the duration of the study period; four patients were pregnant: three were in the second trimester and one in the third trimester, at the end of the study period [4].

All the three patients in case report by Douedi S et al., delivered successfully by caesarean section. It was suggested that early caesarean section as well as mechanical ventilation for respiratory support to mention oxygen saturation was very beneficial for pregnant women with COVID-19 and their infants. All the three patients were extubated successfully [16]. Normal vaginal delivery in the present study and other studies indicate a potential role for natural delivery in pregnant women with mild COVID-19 pneumonia. In the study by Chen H et al., evidence of vertical transmission of SARS-CoV-2 infection in late pregnancy was not seen [12].

In the present study, all patients were positive for RT-PCR except one who had ground glass opacities on HRCT suggesting that there is a vital role of Chest CT in the diagnosis and treatment of COVID-19 pneumonia. Further, there is a significant role of CRP whose levels are increased beyond 20 ng/ml in COVID-19 patients, making it a potential marker of the disease especially in paediatric population. The frequent complications of COVID-19 include Disseminated Intravascular Coagulation (DIC) which necessitates the investigative role of D-Dimer as was done in the study.

In the study by Liu D et al., on chest CT, the most common early finding was Ground Glass Opacity (GGO), out of 15 patients, lymphopenia was seen in 12 patients and elevated C-reactive protein in 10 patients [4]. In another study by Liu H et al., elevated C-reactive protein was present in all 16 patients and lymphocytopenia was present in 9 patients. SARS-CoV-2 was confirmed in all patients [10]. In the study by Chen H et al., elevated C-reactive protein was present in all three patients and lymphocytopenia was present in one patient. SARS-CoV-2 was confirmed in all patients [12]. For management, author followed the standard protocol comprising of multivitamins, antipyretics, oral and injectable antibiotics as indicated. Liu D et al., reported that antibiotic therapy was given to all 15 patients, oxygen support (nasal cannula) in 14, and antipyretics in 11 patients [4]. A recent study on COVID-19 in pregnancy mentioned that management guidelines should be on the basis of data from the present epidemic instead of drawing on the experience from previous SARS-CoV-1 and Middle East respiratory syndrome- Coronavirus (MERS-CoV) outbreaks, because there may be difference in epidemiology, clinical manifestations and response to treatment [17]. In order to establish treatment algorithms for this patient group, multidisciplinary management of pregnant women with COVID-19 is of the paramount significance and the further larger studies are required [16].

After treatment, negative report was noted in patients who underwent repeat testing in the follow-up (51.85%). Home quarantine was advised to all patients however, one pregnant woman dies of bronchopneumonia in the ICU due to refractory hypoxia and pregnancy as the antecedent cause. Twenty foetuses delivered, 1 was IUD and 19 foetuses were negative for COVID-19. NICU admission was required in 10 foetuses, from which 1 died. In the study by Liu D et al., there were no cases of neonatal asphyxia, neonatal death, stillbirth, or abortion [4].

Breslin N et al., reported that there were two maternal ICU admissions of the mothers who had high Body Mass Index (BMI) ($>35 \text{ kg/m}^2$) as well as complicated medical history that resulted in question whether COVID-19 increases the risk of severe morbidity in high-risk pregnancies. There was one neonatal death and one intrauterine foetal death. Further studies should be conducted to address this issue [18].

Neonates delivered by caesarean section in the study by Douedi S et al., tested negative for COVID-19, which suggested no vertical transmission as was seen in the present study [16]. Further, infants were asymptomatic during hospitalisation which suggests that infants may acquire immunity from the mother. However, further research on this aspect is needed. The disease burden of COVID-19 is increasing and thus, the results will be helpful for understanding the nature of the disease and making informed decisions while treating pregnant women with COVID-19 infection.

Limitation(s)

Present study was limited by lack of age-matched non pregnant women as a control group.

CONCLUSION(S)

Cough, breathlessness, fever, loose stools and pulmonary oedema were the main symptoms in pregnant women presenting with COVID-19. Most of the pregnant patients delivered by caesarean section. All alive foetuses were negative for COVID-19 indicating that none of the foetus had vertical transmission from mother. All the women were COVID-19 negative after treatment however, one died due to bronchopneumonia. Though there was no vertical transmission of the infection to the neonate, careful monitoring and measures for the prevention of neonatal infection are warranted.

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