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Case Series

Clinical analysis of maternal and fetal outcomes in COVID-19 pregnant women undergoing cesarean section in a tertiary care center in Hyderabad, India

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ABSTRACT

The outbreak of coronavirus disease 2019(COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is spreading globally at an accelerated rate. A serious public health threat, it has caused a major impact on health care systems with a significantly high mortality and morbidity. Physiological changes and immuno-compromised state make pregnant women vulnerable during infectious disease outbreaks and hence need a more cautious approach. With this report we aim to share our experience regarding clinical characteristics, management and outcomes of 10 diagnosed COVID-19 pregnant women undergoing cesarean section at Medicover hospital, a tertiary-care center in Hyderabad, India between July to September 2020. All 10 pregnant women were referred in their third trimester with diagnosis of COVID-19. 2 out of 10 patients had severe COVID-19 and were managed in the ICU. All patients underwent emergency cesarean sections and none of the infants were infected with COVID-19. At discharge, all patients and the newborns were in a clinically stable condition. Effective management strategies incorporating integrated team approach, early cesarean section and low-threshold for mechanical ventilation has been shown to be associated with favorable outcomes for mothers diagnosed with COVID-19 and their infants. Also, the present data does not support any evidence of vertical transmission of SARS-CoV-2 virus in those manifesting during the third trimester of pregnancy.

Keywords: Cesarean section, COVID-19, Pregnancy, Vertical transmission

INTRODUCTION

First described in Wuhan, China, COVID-19 has been rapidly spreading globally, infecting millions of individuals with a significantly high mortality and morbidity rate. The International committee on taxonomy of viruses named the virus severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2).[1] SARS-CoV-2 is the newest pandemic, recognized as so by the world health organization (WHO) on the 11th March 2020.[2]

Most of the cases present with a mild seasonal flu-like illness, although some may have progressive respiratory failure and can even lead to death. With immuno-compromised status and physiological adaptive changes, pregnant women could be more susceptible to COVID-19 infection than the general population.[3] However limited data currently available indicate that pregnant women usually have mild disease and, according to most reports, there is no evidence of mother-to fetus transmission.[2]

This disease has compelled the clinicians to adapt to the ongoing pandemic with regards to the obstetric management. The recognition that the disease is highly contagious and the potential risk of vertical transmission has mandated planned intrapartum care for the patient, infant and the healthcare professionals. The paucity of reliable clinical guidelines, has necessitated ongoing

clinical trials to assess the effectiveness of drugs and their effect on fetus and to established standardized approach for treatment of pregnant women with COVID-19.

CASE SERIES

We present the clinical features and outcomes of 10 pregnant women with COVID-19, referred in their third trimester of pregnancy to Medicover hospital, a tertiary-care center in Hyderabad, India between July to October 2020. COVID-19 reverse transcriptase-polymerase chain reaction (RT-PCR) was positive for all patients.

All patients were quickly assessed by designated staff wearing appropriate personal protective equipment (PPE) in the isolation room, for the severity of COVID-19 and other comorbid conditions. Medical history, physical examination and fetal wellbeing were assessed and a multi-disciplinary team including obstetrics, anesthesia, critical care and infectious diseases team were involved. Basal electrocardiogram and laboratory workup were done including complete blood count, kidney function tests, liver profile and coagulation tests. Severity markers like lactate dehydrogenase (LDH), C-reactive protein (CRP), creatinine phosphokinase (CPK), ferritin, D-dimer and interleukin-6 (IL-6) were sent.

Patients were classified according to the severity of the respiratory infection into mild/moderate or severe cases. We used the CURB (confusion, urea, respiratory rate, blood pressure) adapted severity scale to assess the severity of the respiratory infection and the need for critical care was assessed by standardized criteria (adapted from the American thoracic society and infectious diseases society of America).[4] Abnormal radiological findings on HRCT chest were found in all cases with a CORADS score of 3 to 6. Lung involvement was <25% in mild cases, 25-50% in moderate cases and 50-75% in severe cases. Out of the 10 pregnant women, 6 had mild disease, 2 moderate and 2 exhibited severe disease which were managed in ICU. All 10 patients underwent cesarean sections under regional anesthesia. Necessary PPE was provided to staff attending to these women. Neonates from COVID-19-positive women were tested, isolated, and cared. All the infants were negative on throat swab RT-PCR.

The demography, clinical features and investigation profile of 10 patients are summarized in Table no 1 and 2. 3 cases with mild, moderate and severe COVID-19 infection are discussed here-

Case 1

Mrs. X, 25 year, primigravida came with 37+2 weeks pregnancy with altered doppler indices. She was asymptomatic for COVID but positive on RT-PCR. She had history of lung consolidation (RT-PCR negative) 2 months back for which she was hospitalized and was treated. Her HRCT chest showed fibrotic strands in medial area of right middle lobe with focal areas of air trapping with CT involvement score of <25% and CORADS score of 3 (Figure 1). Her inflammatory markers were WNL. She underwent LSCS in view of fetal distress and delivered an alive baby of birth weight 2.4 kg with APGAR 8/10. She had an uneventful intra-natal and post-natal period. Both mother and baby were discharged on 4th postoperative day (POD).

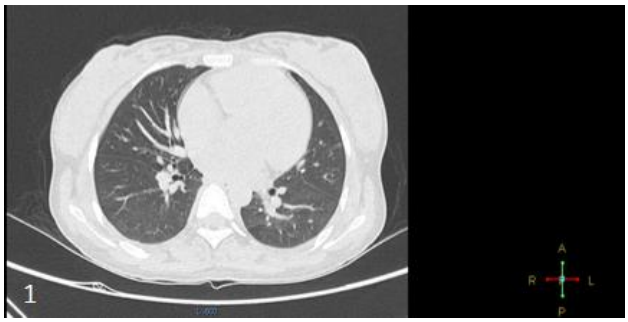

Figure 1: HRCT image of fibrosis of lungs (CT scoring <25%).

Case 2

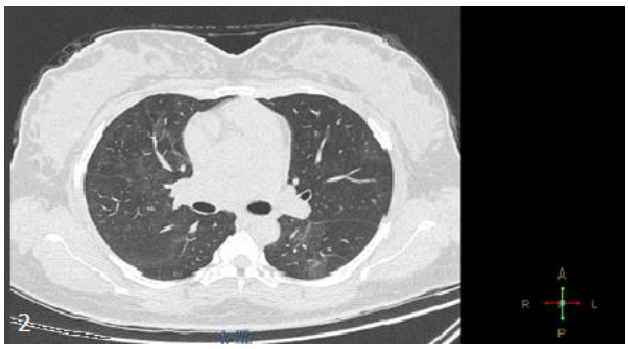

Figure 2: HRCT image of peripheral ground glass opacities (CT scoring 25-50%).

Mrs. Y, 31 year, G2P1L1 with 36+3 weeks pregnancy came with complaints of fever and dry cough for 5 days and SOB for 1 day. She had history of pregnancy induced hypertension (PIH) from 32 weeks of pregnancy managed with tab labetalol. On admission she was afebrile with PR 100/min, BP 136/100 mmHg, RR 14/min with SpO_2 of 93% on room air. Her HRCT chest showed CORADS score of 5 with CT involvement score of 25-50% (Figure 2) Her inflammatory markers were raised with proteinuria. Emergency LSCS was done in view of preeclampsia, oligohydramnios (AFI 6) and previous LSCS. Patient was managed postoperatively on remdesivir, IV antibiotics, anticoagulants, steroids and 4L O_2 support. She delivered an alive baby of weight 2.9 kg with minimal respiratory distress. Baby was discharged in stable condition on 2nd POD and mother on 6th POD.

Case 3

Mrs. Z, 26 years, G2P1L1 with 34 weeks pregnancy

came with complaints of fever for 15 days and shortness of breath (SOB) for 7 days. On admission she was afebrile with PR 98/min, BP 110/80 mmHg and RR of 30/min with SpO_2 of 98% on 15 L O_2. Her HRCT chest showed CORADS score of 6 with CT involvement score of 50-75% (Figure 3). Her inflammatory markers were raised with raised IL-6 (19.27). Emergency LSCS was done in view of fetal distress and meconium-stained liquor. Patient was managed postoperatively on remdesivir, IV antibiotics, anticoagulants, steroids and O2 support in ICU. She delivered an alive baby of birth weight 1.76 kg with respiratory distress needing CPAP. Baby had neonatal jaundice and sepsis which was managed conservatively and was discharged in stable condition after 9 days. Mother was discharged on 13th day from admission. Postoperative follow up was done at 1 and 6 weeks.

The median age of the women was 29.5 years. The median gestational age on admission was 37+1 with gestational age at birth ranging from 34 to 39+6 weeks. The most common symptoms were fever (5/10), shortness of breath (4/10), cough (3/10) with 4 patients being asymptomatic. One patient had features of preeclampsia and one presented with peripartum cardiomyopathy. Medical history of gestational diabetes and type 1 diabetes mellitus were present in 1 patient each. Lymphopenia was present in 4 out of 10 patients. Elevated levels of D-Dimers were seen in 7/10, LDH in 8/10, ferritin in 1/10 and CRP in 4/10. CPK was normal for all 10 patients. IL-6 was done for 2 ICU patients and it was raised.

The indications for LSCS were maternal reasons (2/10), fetal distress (3/10), preterm rupture of membranes (2/10) severe oligohydramnios (2/10) and previous LSCS (5/10). A total of 4 deliveries were preterm and betamethasone could be covered only for 2 patients. All patients received postpartum prophylactic low-molecular-weight heparin for thromboprophylaxis, azithromycin, ceftriaxone, vitamin C and supportive treatment. 2 ICU patients needed remdesivir, oxygen support and methylprednisolone. 4 neonates had respiratory distress and out of them 3 needed CPAP. 2 babies had sepsis and 2 had neonatal jaundice which was managed conservatively. Women used a dedicated breast pump to provide expressed breast milk for the neonate.

All the patients with their neonates were discharged in stable condition and were advised home isolation for a minimum of 14 days after resolution of clinical features. Telehealth follow-up was recommended to ensure maternal well-being.

Table 1: Demography and clinical features of 10 patients.

Age (year)	GA (weeks)	Symptoms	Comorbidities	Indication for LSCS
25	37+2	AS	-	FD
28	38+5	F/SOB	-	PCS
31	39+6	AS	-	PROM
29	34	F/C	GDM	PTL/FD
30	37	C	-	PROM
33	39	AS	-	PCS
32	38	AS	DM	PCS
26	34	F/SOB	-	FD/PCS
31	36+3	F/C/SOB	PE	PE/PCS/O
30	36+5	F/SOB	PPCM	O/twins

AS-asymptomatic, F-fever, SOB-shortness of breath, C-cough, GDM-gestational diabetes mellitus, DM-diabetes mellitus, PE-preeclampsia, PPCM-peripartum cardiomyopathy, FD-fetal distress, PCS-previous LSCS, PROM-premature rupture of membranes, PTL-preterm labour, O-oligohydramnios.

Table 2: Investigation profile of 10 patients.

CT-CORADS	CT- severity index	Lymphocytes	CRP	D-Dimer	LDH	CPK	Ferritin
3	M	11	1.81	284	201.2	13.7	17.16
4	M	27	1.84	1200	265.9	13.7	23.5
3	M	29	7.82	418	176.9	21	33.8
4	M	25	5.55	1499	224.8	19.9	19.6
4	MO	13	21.04	983	205.1	62	14.2
3	M	21	3.74	347	114.4	120	42.7
3	M	22	4.72	672	198.6	108	35.3
6	S	9	98.3	520	208.6	24.1	36.4
5	MO	22	13.6	1406	258	72	207
5	S	12	3.94	836.3	219.3	93.5	38.9

M-mild, MO-moderate, S-severe.

Figure 3: HRCT image of peripheral ground glass opacities (CT scoring 50-75%).

DISCUSSION

SARS-CoV-2 is a positive-sense, single-stranded RNA, group IV virus.[1] The disease caused by SARS-CoV-2, COVID-19 a respiratory illness varies from mild or no symptoms to severe respiratory failure that requires intensive care and can be fatal. Asymptomatic carriers of the virus have also been reported and pose a significant public health threat.[1] RT-PCR is the current gold standard for COVID-19 and shows a testing sensitivity of 95%.[1] CT Chest is essential to the management of COVID-19, and if indicated, should be promptly performed with an abdominal shield, avoiding delays due to fetal concerns.

In majority of the cases, the immuno-pathogenesis of COVID-19 infection involves disturbances of inflammatory mediators that do not cause the disease but helps in the progression of the disease.[5] Physiological and mechanical changes in the cardiovascular, respiratory, and coagulation systems increase susceptibility to infections and encourage rapid progression to respiratory failure in pregnancy.[6] An intense inflammatory response has been reported as one of the key features of severe COVID-19, and as there is relative immuno-suppression in pregnancy this may partly explain why many pregnant women do not develop severe respiratory symptoms.[7]

Presenting symptoms of COVID-19 in pregnancy are fever, cough, shortness of breath, nasal congestion, sputum production, headache, malaise, loss of appetite and diarrhea. In a systematic review including 790 pregnant subjects with COVID-19, the most prevalent symptoms were fever (58%), cough (52%), and shortness of breath (17%); 9 % of subjects were asymptomatic.[8] The main findings in laboratory tests during early stages of the disease include lymphocytopenia, transaminase elevation, proteinuria, as well as increased LDH and CRP levels.[4] Presence of co-morbidities like chronic hypertension, pregestational diabetes, cardiopulmonary diseases, chronic kidney disease stage III-IV, immuno-suppression or prolonged corticosteroid therapy may increase the risk of developing more severe clinical manifestations.[4] Complications include severe pneumonia with or without acute respiratory distress syndrome (ARDS), renal failure, multi-organ dysfunction, viral myocarditis and cardiomyopathy.[7] Serologic evidence of hepatic injury is common (15 to 50 percent of patients) and has been observed across the spectrum of the disease.[8] A New York study applying similar COVID-19 disease severity characteristics as described by Wu et al. observed that 86% of women possessed mild disease, 9.3% exhibited severe disease and 4.7% developed a critical disease with no maternal deaths.[7]

The usual protocols adopted for treating a severe COVID-19 infection like prone positioning, antiviral and supportive drugs specially thromboprophylaxis and steroids become an obvious and bothersome challenge for pregnant females. Other therapies such as methylprednisolone, tocilizumab, or remdesivir are being investigated in critically patients but there are safety concerns regarding their use during pregnancy.[4] International guidelines to date recommend thromboprophylaxis on an individualized basis, particularly women with mild symptoms who are self-isolating.[7] There is no evidence that giving steroids for fetal lung maturation causes harm in the context of COVID-19 infection.[7]

Preterm birth and cesarean delivery rates are increased. Fever and hypoxemia may increase the risks for preterm labor, pre-labor rupture of membranes, and abnormal fetal heart rate patterns.[8] While many of the preterm deliveries were iatrogenic and for maternal reasons due to concern for maternal respiratory function, there are reports of fetal distress as the indication in some cases.[7] With regard to the mode of delivery, cesarean section was performed in the majority of cases and several authors cited fetal distress as the reason behind the decision.[9] The cesarean section (CS) rate for women with confirmed COVID-19 infection has been reported as ranging from 42.9% to as high as 91-92% in other studies.[7] The systematic review by Di Mascio, with a CS rate greater than 90%, primarily included women who were hospitalized with COVID-19 pneumonia in over 90% of cases.[7] Further evidence is wanted to specify the timing and the preferred mode of delivery for pregnant women with COVID-19.

A systematic review of 33 studies described the outcomes of 385 pregnant women with COVID-19 with gestational age at birth ranging from 30 to 41 weeks' gestation and a preterm birth rate of 15.2%.[7] The largest cohort study would appear to be from the UK's obstetric surveillance system, which provides data on 427 COVID-19-confirmed pregnancies with a median gestation at symptom onset of 34 weeks. About one in 10 of those admitted required respiratory support, and 12% were delivered preterm solely because of maternal respiratory compromise. Of the 243 women who had given birth, 74% did so at term and 59% by cesarean section.[10]

Neither vaginal delivery nor cesarean section confers additional risks, and there is minimal risk of vertical transmission to the neonate from either mode of delivery.[11] A systematic review of 41 pregnancies in which the majority was delivered by CS, found no clinical signs of vertical transmission.[7] There is no evidence of vertical transmission of coronavirus 2 infection when the infection manifests during the third trimester of pregnancy.[12] Based on limited data, there is no evidence of the presence of the virus in genital fluids, urine, amniotic fluid, or breast milk.[4] The low maternal viremia found in this infection also suggests a negligible placental seeding.[4] In the study by Yu and colleagues,3 three neonates were tested for SARS-CoV-2, of whom two were negative. One neonate was positive, but the viral nucleic acid tests of the placenta and cord blood in this case were negative.[3] By a recently published study where three infants born by cesarean section tested positive for SARS-CoV-2, 2 days after birth. However, in their analysis of 38 infected pregnancies, Schwartz et al did not find any evidence for intrauterine transmission.[9] Neonatal complications have largely been related to preterm birth and to adverse uterine environments resulting from critical maternal disease.[8] The main risk for the infant is its exposure of airborne droplets from the feeding COVID-19 infected mother. The adherence to strict hand-hygiene measures and wearing of a facemask is imperative to limit such an exposure.

CONCLUSION

Until a definite cure and/or an effective vaccine is available, the current pandemic, will stay longer and thus will also determine the true maternal and fetal outcomes for those affected.

Given the uncertainties of the clinical course and its contagious nature, proper intrapartum planning would ensure safety of the mother and healthcare professionals.

The mode of delivery should, at present be determined individually keeping in mind the mother's well-being as a priority in severe COVID-19 patients.

Routinely isolating, testing, rooming-in and breast feeding should be initiated in neonates of COVID-19 patients while following contact prevention protocols.

The novelty of COVID-19 and its clinical uncertainties in pregnancy should prompt researchers and clinicians to conduct and report high-quality unbiased research thus laying the foundations for evidence-based protocols and better understanding of the disease as regards its severity, vertical transmission, perinatal and neonatal outcomes.

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