

# Pregnancy with COVID-19: Weal and Woe

Fahmida Rashid<sup>1</sup>, Shoyela Shahnaz<sup>2</sup>, Reshma Sharmin<sup>3</sup>, Mohammad Abdus Sattar<sup>4</sup>, Shahanara Chowdhury<sup>5</sup>

## ABSTRACT

**Background:** Coronavirus disease-2019 (COVID-19) has spread across the globe and has been declared pandemic by the World Health Organization (WHO). People of all age groups are at risk of getting the disease. Pregnant women are at an increased risk of acquiring the infection and developing moderate-to-severe pneumonia resulting in adverse outcome.

**Case Descriptions:** Published case series have shown that high-risk pregnancies have been associated with higher morbidity and mortality. Pregnancy-induced immune response might have an impact on maternal cardiovascular system and exaggerate the course of COVID-19 disease. Here, we report two cases of late pregnancy with COVID-19 one of which ended with complete recovery and another with adverse outcome.

**Conclusion:** These two case scenarios might add to the emerging evidence of pregnancy outcome in COVID-19.

**Keywords:** Comorbidity, COVID-19, Pneumonia.

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## BACKGROUND

In 2020, world experienced an awful pandemic due to Coronavirus disease-2019 (COVID-19) caused by noble corona virus (SARS-CoV-2), which originally started from Wuhan, China which engrossed almost all countries of the world. From fetus to elderly, all are at a risk of getting infected with this virus. The UN study found that during COVID-19 lockdown there had been over 7 million unintended pregnancies in the world. Pregnant women are at an increased risk of acquiring viral respiratory infection and developing severe pneumonia due to the physiological changes in their immune and cardiopulmonary systems.<sup>1,2</sup> As pregnant women are susceptible to severe acute respiratory syndrome (SARS)<sup>3</sup> that may result in increased risk of adverse pregnancy outcomes. In general, the clinical characteristics of pregnant women are similar to those of nonpregnant adults in terms of maternal and fetal outcome.<sup>4</sup> Majority of pregnancies with COVID-19 have good outcome and develop mild disease, while a few groups of pregnant women get adverse outcome following COVID-19. The most high risk among pregnant women are—those beyond 28 weeks of pregnancy, associated comorbidity, such as diabetes mellitus, hypertensive disease of pregnancy, asthma, heart disease, obesity, and maternal age >35 years. A systemic meta-analysis reported up to 3% pregnancy ended up with severe maternal morbidity.<sup>5</sup> Pregnant women with history of kidney transplantation, or on immunosuppressive agents have been defined as “extremely vulnerable” by Public Health England. As pregnancy is a prothrombotic state, 5–10% of women without risk factors and women of high-risk pregnancy have adverse outcome following COVID. These vulnerable groups should be hospitalized following COVID, as they are at increased risk of severe disease. They may require advanced oxygen therapy including intensive care unit (ICU) admission. With respect to maternal ICU admissions and mortality rates during COVID-19, the available data appear reassuring. In contrast, SARS and middle east respiratory syndrome (MERS), respectively, had 15–18% and 25–27% mortality rates; 30 and 60% ICU admission rates, and a requirement for mechanical ventilation in 35 and 41% of women.<sup>6,7</sup>

<sup>1-3,5</sup>Department of Obstetrics and Gynaecology, Chittagong Medical College Hospital, Chattogram, Bangladesh

<sup>4</sup>Department of Medicine, Chittagong Medical College Hospital, Chattogram, Bangladesh

**Corresponding Author:** Fahmida Rashid, Department of Obstetrics and Gynaecology, Chittagong Medical College Hospital, Chattogram, Bangladesh, Phone: +880 1711315190, e-mail: dr.fahmidaswati@gmail.com

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## CASE DESCRIPTIONS

### Case 1

A 28-year-old primi, physician by profession who was 35 weeks pregnant developed low-grade fever and mild cough during the first week of June 2020. She reported to her obstetrician after 5 days as she felt undue fatigue. She has been self-isolating for the last 3 months and went out only once for routine ultrasound scan as a part of routine antenatal checkup. Her husband who was a physician also developed similar symptoms. Following a telephone consultation with she underwent a reverse transcription polymerase chain reaction (RT-PCR) to rule out COVID-19. Her RT-PCR report came negative on day 5. But, COVID-19 suspect case she was advised to have home isolation and self-monitoring of oxygen saturation and monitoring of fetal heart rate by fetal Doppler and fetal movements. During this isolation period, her cough increased and also she developed respiratory distress and chest tightness. On seventh day of her symptom, her saturation fell to 93% and she was advised for hospitalization. But she refused hospitalization and instead decided to have oxygen at home @ 3 to 5 L/minute. During this time, she also had telephone consultation with an internal medicine specialist who advised some routine

investigations and to commence her on azithromycin, salbutamol inhaler, oxygen inhalation, and respiratory exercise. With these her saturation improved to 96%. Her routine blood test on day 7 revealed neutrophil-80%, lymphocyte-14%, white blood cell (WBC)-7,000/mm<sup>3</sup>, platelet-220,000/mm<sup>3</sup>, S. creatinine-0.8 mg/dL, C-reactive protein (CRP)-34.3 mg/L, D-dimer-1.52 µg/mL, S. ferritin-47.12 ng/mL, alanine aminotransferase (ALT)-128 U/L, chest x-ray (CXR)-with shield feature was normal. Although her RT-PCR was negative, her other parameters along with her symptoms were suggestive of COVID-19. And prophylactic low-molecular-weight heparin (LMWH) (clexane) 60 mg/day subcutaneously was started from the eighth day of symptom. Again she was advised to repeat RT-PCR in preparation for planning delivery as her estimated date of delivery (EDD) was 1 week later. On day 10th of her symptom, RT-PCR test was positive. From day 10th, her fever subsided but her respiratory symptoms persisted. One week after starting of LMWH on day 13th, all hematological investigation repeated that shows—N-68%, L-27%, WBC-10,100/mm<sup>3</sup>, platelet 250,000/mm<sup>3</sup>, D-dimer-1.98 µg/mL. After reviewing her report internal medicine specialist advised her to continue LMWH. From day 13th, her symptoms subsided. Apart from persistent cough, all her symptom subsided. On day 18th, a repeat RT-PCR was performed, which was negative. At her 39 weeks 1 day pregnancy at night, she started having labor pain and was admitted to the local tertiary hospital (Chittagong Medical College Hospital). Twelve hours after labor pain, she delivered vaginally a healthy male baby weighing 3.2 kg with normal appearance, pulse, grimace, activity, respiration (APGAR) score 5 minutes. The following day she was discharged home with LMWH for another 2 weeks. She was also advised to repeat prothrombin time (PT), activated partial thromboplastin time (aPTT), D-dimer, blood, and complete blood count (CBC).

### Outcome and Follow-up

She was followed up 2 weeks following the delivery when both the mother and the baby were doing well.

### Case 2

A 26-year-old physician (G2 P0 Ab1) was first diagnosed with glomerulonephritis at 12 weeks of pregnancy during routine antenatal checkup. She had a history of hypertension for 2 years. Following first antenatal checkup, she was prescribed antihypertensive (methyldopa, nifedipine) and methylprednisolone 40 mg daily for glomerulonephritis. As she was in high-risk pregnancy, additional aspirin 150 mg daily was prescribed. Also LMWH (clexane 40 mg) subcutaneously daily was added along with hematinic and calcium supplements. But she refused to continue LMWH. During her antenatal period, her blood pressure (BP) fluctuated between 170/110 and 150/100 mm Hg with antihypertensive and her renal function deteriorated further. She underwent cesarean section at 34 weeks of gestation due to superimposed preeclampsia, impaired renal function, and intrauterine growth restriction (IUGR). A female baby weighing 1.9 kg was born with APGAR score 8 at 5 minutes. Baby was sent to neonatal intensive care unit (NICU). Immediately after operation, mother was shifted to high dependency unit (HDU) for close monitoring. She was discharged on postpartum day 3 as both of their condition was stable with prophylactic antibiotic, antihypertensive (losartan potassium), and oral methylprednisolone. On postoperative day (POD) 7, she experienced low-grade fever and respiratory distress. She was monitoring her oxygen saturation at home and self-isolated her from other family members and newborn after consulting with her obstetrician over telephone.

At home when her saturation was fluctuating from 93 to 96%, she was advised to get admitted to the hospital by her obstetrician. But she remained at home and took oxygen at home @ 2 to 3 L/minute for the next 2 days. On POD 9, she was rushed to hospital emergency while her saturation became 85%. She was admitted to COVID ICU as a COVID suspect case. Initially, she was put on non-rebreather mask @ 15 L/minute. However, when her saturation deteriorates to 75% she was put on high-flow nasal cannula (HFNC) with FIO<sub>2</sub>-80%, O<sub>2</sub> flow @ 60 L/minute. With that her saturation was maintained 89 to 91%. Immediately after admission she was started—ceftriaxone, methylprednisolone drip, LMWH 40 mg 12 hourly, and antiviral oral favipiravir. As BP was high, previous antihypertensive was changed into combination of amlodipine and atenolol day after admission. Prone positioning was performed along with right and left lateral position for 3–4 hours interval, although postoperative wound pain made it difficult. Her baseline investigation day after admission Hb%-11.5 g/dL, N-94%, L-5%, platelet-21 × 10<sup>9</sup>/L, WBC 12.64 × 10<sup>9</sup>/L, S. creatinine-2.89 mg/dL, estimated glomerular filtration rate (e-GFR)-20 mL/minute/1.73 m<sup>2</sup>, D-dimer-2.90 µg/dL, CRP-265 mg/L, S. ferritin-321 ng/mL, S. urea-91 mg/dL, alkaline phosphatase-116 U/L, aspartate aminotransferase (AST)-44 U/L, urine R/E-plenty of red blood cell (RBC), troponin I-0.05 ng/mL, random blood sugar (RBS)-7.89 mmol/L, S. electrolyte-within normal limit. CXR showed bilateral consolidation. Her nasopharyngeal swab for COVID-19 came positive 2 days after admission on day 8 of symptom. On day 9 of the onset of symptom, donor plasma was transfused. But her condition was unchanged and saturation was maintaining 89%. Her investigation repeated on day 9, which reveals S. creatinine-3.08 mg/dL, e-GFR-19 mL/minute/1.73 m<sup>2</sup>, S. ferritin-252 ng/mL, lactate dehydrogenase (LDH) 889 U/L, D-dimer-1.187 µg/mL, S. procalcitonin-0.338 ng/mL, serum NT-proBNP 3,223 pg/mL, aPTT-patient-28 seconds, and control-29 seconds. During this time, she was diagnosed as a case of adult respiratory distress syndrome (ARDS). On day 20th, her oxygen saturation fell to 50–60%. And with FIO<sub>2</sub>-100% and oxygen rate @ 60 L/minute, her saturation was unchanged. Permission for ventilator was sought from patients' family, but it was refused. Despite close monitoring, after struggling for 11 days, she expired in COVID ICU at postpartum day 21 due to ARDS with multi-organ dysfunction.

### Outcome and Follow-up

After struggling for 11 days in COVID ICU, the patient died due to ARDS with multi-organ failure. Information of the neonate was taken from her husband over phone call after 2 weeks and the baby was doing well.

## DISCUSSION

Most of the pregnant women with COVID-19 infection usually have mild symptom. Pneumonia during pregnancy is associated with increased morbidity and mortality compared with the non-pregnant state.<sup>6–8</sup> A quarter of women diagnosed with pneumonia in pregnancy require hospitalization, often critical care, and many need ventilator support.<sup>9</sup> Review of 108 pregnant women with confirmed SARS-CoV-2 infection showed three cases of maternal intensive care admission (3%) and no confirmed fatalities.<sup>5</sup> A number of cases reported where mother needed ICU admission, where one case required invasive ventilation with extracorporeal membrane oxygenation.<sup>3</sup> The two maternal ICU admissions reported by Breslin et al.<sup>10</sup> involved mothers with high body mass

index (BMI) (>35) and complicated medical history, which leads one to question whether COVID-19 increases the risk of severe morbidity in high-risk pregnancies. It was observed that mother with comorbidity especially with prior chronic medical condition usually are usually at higher risk of poor outcome.<sup>11</sup>

In the first case, though she was in last trimester, did not have any comorbidity, BMI was normal, lungs were clear. She had moderate symptoms, only her D-dimer was a bit high which might be due to pregnancy itself. Prompt medical intervention and follow-up improved her condition. As delivery occurred while she was asymptomatic, it was assumed that her body physiology reverted back to normal by this time.

In the second case, patient had prior comorbidity—glomerulonephritis, hypertension, and she was on systemic glucocorticoid during whole pregnancy period. Also, during pregnancy, she was irregular on taking prescribed prophylactic LMWH from first trimester. All these risk factors made her vulnerable for acquiring COVID-19. Once infected during postpartum period, her condition worsen. Also, because of impaired renal function broad-spectrum antibiotic meropenem, antiviral remdesivir, and full therapeutic dose, LMWH could not be commenced which might have had adverse reactions. Despite all types of medical intervention, the best effort and critical care support she succumbed to ARDS after struggling for about 11 days in the ICU.

## CONCLUSION

COVID-19 in third trimester should be managed with utmost care especially if it is high-risk pregnancy and associated with comorbidity. They should be taken care of in a tertiary care center where ICU facilities prevail. Multidisciplinary approach toward management of pregnancy with COVID-19 and frequent and keen monitoring could save this high-risk group. However, despite the best effort, a small number of pregnant women who are particularly in the high-risk group may not survive.

## CLINICAL SIGNIFICANCE

COVID-19 in last trimester pregnancy is high-risk groups. Therefore, frequent follow-up, timely monitoring by necessary investigation,

and extended thromboprophylaxis and multidisciplinary care could save life of pregnant women who have COVID-19.

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