MEGA JOURNAL OF CASE REPORTS

Case Series

Published Date: September 07, 2022

Challenging Antenatal Cases in India during COVID 2.0

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Abstract

After a century, the world has come across a pandemic which has shown its dreadful effects. The second wave posed more danger to the antenatal patients. COVID 19 has complicated pregnancies with first and second trimester miscarriages, preterm labor, intrauterine death, fetal growth restriction. Here we discuss two interesting cases who were inflicted with mild to moderate COVID disease during second wave of pandemic and presented with abruption placentae and COVID induced coagulopathy. First case was a term uncomplicated pregnancy in labor with tense tender uterus and absent fetal heart, while second case was a 32 weeks' pregnancy with antepartum haemorrhage and intrauterine fetal demise. Both had markedly raised D dimer, hypofibrinogenemia 1with normal blood pressure, prothrombin time and low platelets. There arises a need for close monitoring of antenatal patients in post COVID period.

Keywords: Abruption placentae; COVID 2.0; Pregnancy; Second wave

Introduction

Pregnancy is a memorable experience in which each woman undergoes a wide range of physiological changes, mood changes, and minor ailments. It is a dream of each antenatal lady to undergo uncomplicated pregnancy. COVID 19 (Coronavirus), a newly discovered virus in 2019 with its origin in Wuhan, China was declared as a pandemic by the World Health Organization on March 11th, 2020. The etiologic agent of COVID-19 was isolated and identified as a novel coronavirus, initially designated as 2019-nCoV. The virus was named as severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) by the International Committee for Taxonomy of Viruses as it was genetically related to the SARS outbreak in 2003 **[1,2].** COVID 19 has complicated pregnancies with first and second trimester miscarriages, preterm labor, intrauterine death and fetal growth restriction. The majority of pregnant women diagnosed with COVID-19 disease have a mild course of illness

and will recover without needing to deliver, but the risks of critical illness and need for mechanical ventilation are increased compared to the general population. Various co-morbidities predispose to increased susceptibility of acquiring COVID infection like diabetes, elderly age group, hypertension, immunosupression, chronic kidney disease, persistent cardio respiratory disease and obesity. Vertical transmission of SARS-CoV-2 is possible but the studies are still inconclusive **[3].**

Case Series

Case 1

A 29 years' gravida 3, parity one, living one with one abortion with 9 months' pregnancy visited in emergency of our private hospital. She was a registered case and had only single antenatal visit at our clinic one week ago. She had history of fever, myalgia and sore throat 2 weeks back, when she was tested COVID 19 RT PCR positive. Subsequently, she was isolated and prescribed Tab Azithromycin, Vitamin C and paracetamol for the same. She became asymptomatic within a week, and also paid a visit at our clinic for regular antenatal checkup. On examination, she was 36 weeks, cephalic and fetal heart was 140/min regular. All her reports (liver and kidney function tests were reviewed and were within normal limits. The patient was advised daily fetal movement count, temperature and saturation monitoring every 4-6 hourly; and to continue her supplements. After one week, the patient landed in emergency with continuous pain abdomen. On examination, she had severe pallor and pedal edema. Her vitals were normal. Abdominal examination showed tense tender term size uterus, not relaxing in between the contractions. Fetal parts could not be palpated properly and on auscultation, fetal heart was not found. On vaginal examination, os was 1 cm dilated and Bishop's score was 4. Urgent ultrasonography revealed an intrauterine fetal demise. All blood investigations were sent and two units of Packed Red Blood Cells (PRBC), four units of Fresh Frozen Plasma (FFP) and four units of random donor platelet concentrate (RDPC) were arranged. Patient was taken up for emergency caesarean section in view of poor bishop score after having a negative COVID rapid antigen report, as RT PCR report takes long for reporting. Intraoperatively, the uterus was congested, bluish, couvelaire grossly **(Figure 1a).** Liquor was blood stained. It was a fresh intrauterine death with baby weighing 2.5 kg and no gross anomalies. Placenta was lying separated in the uterine cavity along with three large retroplacental clots measuring 1.5litres **(Figure 1b).** Postpartum Hemorrhage (PPH) was managed with medically. Generalised oozing was noted from multiple sites. Three units of PRBC and four FFP were transfused intraoperatively. Her postoperative hemoglobin -6.2g, TLC-20,600/mm3, C-reactive protein(CRP)-18mg/L; platelet count-1.01lac/mm3, PT-INR- 15.7/1.19; APTT-42 sec; D dimer->10,000 ng/ml; S fibrinogen level- 36ng/ml. Her liver and kidney function tests, sugar profile was normal and admission rapid antigen testing was negative. Postoperatively, patient was under strict monitoring. Intake output charting was done and higher antibiotics. Patient was allowed orally after 6 hours and ambulation; deep breathing exercises were encouraged after 12 hours. After 12 hours, the patient desaturated on room air, Spo2 was falling to 89%, and she was started on oxygen 5l /min. Urgent Chest X ray was done which showed subtle patchy areas in both the lung fields **(Figure 2).** By that time, her COVID RT PCR reported to be positive. She had a total of three more PRBC transfusions and injection low molecular weight heparin 40mg twice a day subcutaneously was begun and continued for one week. D-dimer levels after 72 hours were 6862 ng/ml and CRP was 9 mg/L. She was weaned off oxygen in next 13 hours after intensive monitoring. Her foley's catheter was removed after 48 hours and dressing was done on Day 3. Her repeat haemoglobin was 9.7g/dl. Patient was

discharged on LMWH injection which were continued till 16 days when her D dimer levels had fallen to 669 ng/ml. Suture removal was done on day 10, and was fine postoperatively. Patient was given oral Rivaroxaban 10mg once daily for 40 days for thromboprophyllaxis. Histopathological analysis of placenta showed placental injury in form of decidual necrosis adjacent to areas of haemorrhage **(Figure 1c)** and intervillous hemorrhage **(Figure 1d).** Autopsy of baby did not show any evidence of COVID infection.

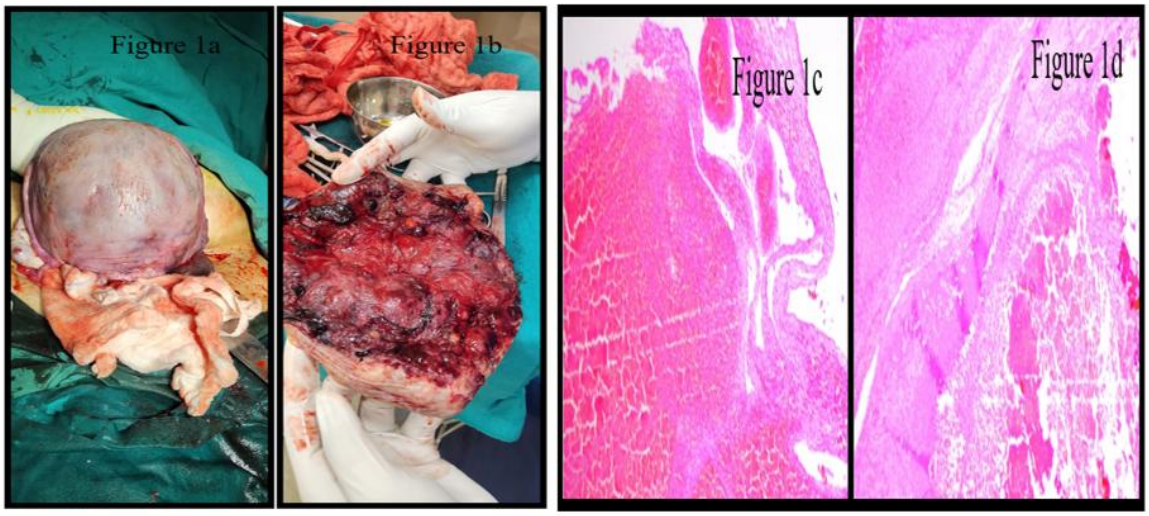

Figure 1: a) Couvelaire Uterus. b) Placenta lying separated in uterine cavity. C) Microscopic image of placenta showing decidual necrosis adjacent to areas of hemorrhage (100X). d) Microscopic image of placenta showing intervillous hemorrhage (100X).

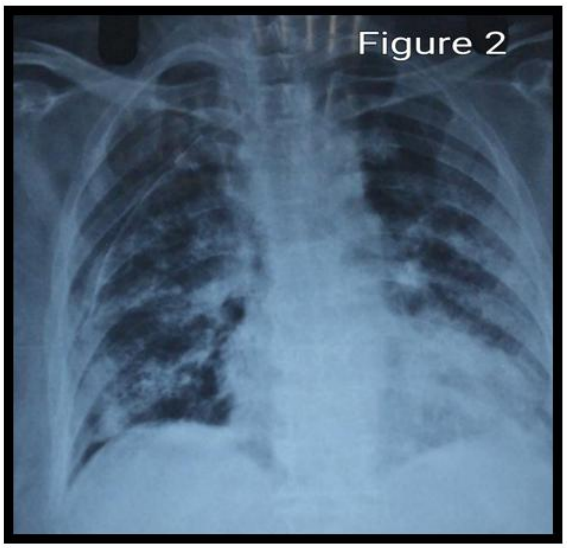

Figure 2: Chest X ray report of Case 1.

Case 2

33 years second gravida presented to emergency at 32weeks 6 days' pregnancy with sudden passage of clots from last 3hours. It was a well supervised pregnancy, with her last physical visit two weeks ago and a teleconsultation one day back for mild fever (99F) and running nose. She was prescribed on analgesics and antihistaminic for the same. She perceived fetal movements well before going to bed the previous night. She was pale looking, with no pedal edema, afebrile, normotensive with 98% Spo2. Abdominal examination showed

a 32weeks uterus in cephalic presentation, non-tender with absent fetal heart, and 2 moderate intensity contractions in 10 minutes lasting for 25-30 seconds, relaxing in-between the pains. Vaginal examination showed cervical os dilated by 4 cm, cervical length 2cm, with intact membranes and two clots measuring 100cc in the vaginal canal. Augmentation of labor was done by oxytocin infusion at 4mIU/min (30ml/hour) and escalated to 12mIU/min to establish good uterine contractions. COVID rapid antigen test was negative and RTPCR sample was taken. Her blood, urine samples were collected and two PRBCs were issued and started. Labor progressed well and she delivered a baby weighing 1.68kg after 4 hours. It was a fresh intrauterine death with no gross anomalies or skin changes. Liquor was blood stained and placenta was lying separated in the uterine cavity, expelled immediately after the delivery of baby. Two large retroplacental blood clots measuring 10x11 cm and 8x8 cm were passed **(Figure 3a).** Her hemoglobin was 6.5g, TLC -5050/mm3, neutrophil: lymphocyte ratio (NLR) = 5.2, platelet 1.01lac/mm3, PT-INR-12.1/0.90, APTT- 45sec; S.uric acid -9.2mg/dl, D dimer-14321 FEU/ml, S.Fibrinogen -236g /ml, CRP-16 mg/L. Her RTPCR report came out to be positive. Fetal autopsy did not reveal any COVID infection, while the placental histopathological examination showed blood accumulation beneath the decidua and short slender villi with increased syncytial knots **(Figure 3b and c).** Her D dimer, CRP levels were followed every 72 hours, and saturation and temperature were monitored every 6 hourly. She was started on LMWH 40mg twice a day and continued till 10 days when the D dimer levels fell to 936FEU/ml and CRP turned negative. Patient was discharged on day 3, and her haemoglobin prior to discharge was 8.2g/dl. She was started on oral Rivaroxaban 10mg once daily for 30 days for thromboprophyllaxis. Patient did well in the postpartum period and is still under follow up in post COVID clinic.

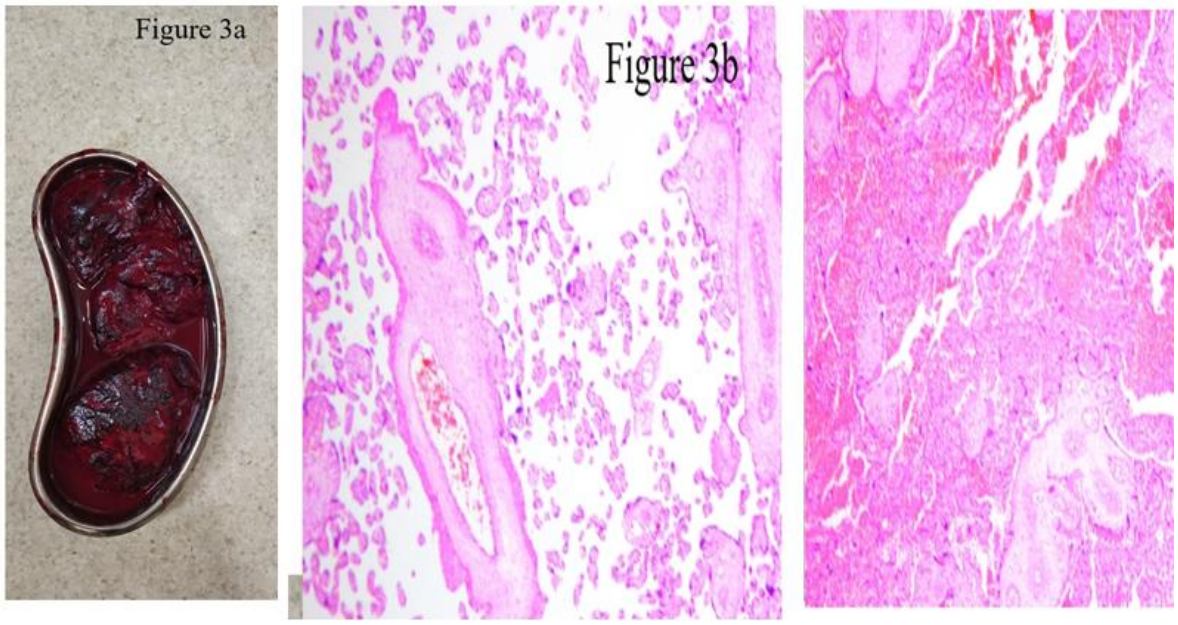

Figure 3: a) Large retroplacental clots. b) Microscopic section of placenta showing blood accumulation beneath and dissecting the decidua. (100X). c) Microscopic image of placenta showing short and slender villi with increased syncytial knots and intervillous space (100X).

Discussion

COVID 19 has emerged as an unsolved mystery for the scientists, physicians and gynaecologists. With each passing day, new aspects of this virus are coming up. As the COVID 19 began to decline in India, there came a

rapid upsurge of cases after Mid-March, 2021. Many studies had been done during the first phase of COVID 19. Many studies were done for evaluating the perinatal transmission of SARS-CoV-2 by testing the placenta, vaginal secretions, cord blood and amniotic fluid. Physiological changes in pregnancy have been reviewed and studied whether these changes increase the predisposition to COVID 19 infection. Shift of immune response from CD4+ Th1 to TH2 and decrease in Natural killer cells (NK) in pregnancy causes some altered infected cell clearance. Also, decrease in plasmacytoid dendritic cells which act as a precursor for type 1 interferon production against viruses seems to be one probable cause of increased susceptibility of pregnant patients to COVID 19 infliction. Anatomical changes in pregnancy like decrease in total lung capacity might cause difficulty in clearing the secretions thereby predisposing to severe respiratory infections **[4].** A study done by Kotlyar et al. **[5]** on 936 neonates from mothers with coronavirus disease 2019, showed 3.2% (27 neonates) being tested positive for severe acute respiratory syndrome coronavirus 2 viral RNA test using nasopharyngeal swab testing. Severe acute respiratory syndrome coronavirus 2 viral RNA testing in neonatal cord blood was positive in 2.9% of samples (1/34), 0% of urine samples (0/17), and 9.7% of fecal or rectal swabs (3/31).7.7% of placenta samples tested positive while none of the amniotic fluids samples detected the virus. Another study by Fenizia et al. **[6]** also reported the presence of the SARS-CoV-2 genome in vaginal swabs, placental tissue, cord plasma and confirmed congenital infection in a nasopharyngeal swab. Neonatal infection was suspected to be acquired in intrapartum period due to presence of specific antibodies in the umbilical cord plasma. Coagulopathy, non-reassuring fetal heart rate has been seen to develop in pregnancy even in the absence of severe clinical symptoms. Histopathologically, placenta showed increased perivillous fibrin deposition and intervillositis **[7].** Case series have been found in recent literature where intrauterine death was reported in the presence of mild/moderate and even asymptomatic COVID 19 infection between day1-day 22, marked by presence of acute chorioamnionitis on placental histopathology. SARS-Cov-2 was detected by RT-PCR in amniotic fluid in one case and in placental specimens in two cases **[8].** Another case reported a spontaneous miscarriage in a 19 weeks' pregnancy after having symptoms of COVID 19 like fever (102.5 °F [39.2 °C]), myalgia, fatigue, mild pain with swallowing, diarrohea, and dry cough for two days. Samples from vaginal mucosa, amniotic fluid, fetal blood, fetal urine, fetal mouth, fetal anus and other organs on autopsy did not show presence of virus on RT PCR testing, while placental submembrane and cotyledons were positive for the same **[9].** Pregnancy is a hypercoagulable state, and COVID 19 in pregnancy adds to the thrombotic complications especially in critically ill intensive Care Unit (ICU) patients. Cases have been seen with raised D dimer, low fibrinogen levels, mildly raised prothrombin time and thrombocytopenia in COVID 19 RT PCR infection. Although raised D dimer and hypofibrinogenemia have been poor predictors of mortality, but as per ISTH guidelines, raised D dimer above 3-4 fold the Upper Limit of Normal (ULN) must get admitted. Although these parameters are altered, but based on current literature, it is recommended to measure D-dimers, prothrombin time, and platelet count (in decreasing order of importance) in all patients who present with COVID-19 infection in order to stratify patients requiring admission/monitoring **[10].** Treatment includes the use of prophylactic dose Low Molecular Weight Heparin (LMWH) in all patients (including non-critically ill) who require hospital admission for COVID infection. Contraindications for its use include those with active bleeding and platelet count less than 25 $\times 10^9$/L. It can be given in patients with severe renal impairment with monitoring. Abnormal PT or Activated Partial Thromboplastin Time [APTT] is not a contraindication) for use of LMWH. In addition, LMWH has been shown to have anti-inflammatory properties which may be an added benefit in COVID

infection where pro-inflammatory cytokines are markedly raised **[11].** We encountered two cases at our hospital in which abruption occurred, concealed in case 1 and revealed in case 2, leading to intrauterine fetal demise in both the cases. Both the cases occurred after the patient was inflicted with COVID 19 mild to moderate disease. Both the patients required blood transfusions and had markedly raised D dimer, low fibrinogen levels, raised APTT and thrombocytopenia. However, the prothrombin time was normal, hence was a result of COVID 19 induced coagulopathy. It was seen that the hypercoagulation was seen in COVID 19 patients and hence increased thromboembolic events. But, the hemorrhagic manifestation of COVID in pregnancy is rare and not reported as yet. More studies need to be done to know the pathology behind abruption in COVID 19 in pregnancy.

Conclusion

We intend to convey a message that patients should be under strict monitoring in post COVID period, especially in this COVID 2.0 wave as we are coming across these cases due to COVID induced coagulopathy. Rising hemorrhagic manifestation in form of abruption has come up as a nightmare for the obstetricians and need more frequent monitoring in this dreadful second wave antenatal third trimester complication.

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Citation of this Article

Arunima S, Arti L, Vinod Kumar S, Daisy P, Vanita A and Ruchika C. Challenging Antenatal Cases in India during COVID 2.0. Mega J Case Rep. 2022; 1: 2001-2006.

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