Case Report

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# Outcome of pregnancy in sickle cell anemia patients with COVID-19 infection

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**Abstract:**

Sickle cell anemia (SCA) is a multisystem disease, associated with increased risk for infection and thromboembolic disease, and pregnancy is a stressor for patients with SCA. In general, coronavirus disease 2019 (COVID-19) infection in SCA is associated with a favorable outcome. Literature of pregnancy in SCA with COVID is scarce. We report a case series study of pregnant women with SCA, who are confirmed positive for COVID-19 from May 2020 to March 2021. These patients showed generally mild-to-moderate disease and presented predominantly with fever and painful crisis. They showed a significant drop in Hb from baseline, and they received low-molecular-weight heparin prophylaxis (LMWH) and blood transfusion. The outcome of pregnancy is satisfactory, although the mean birth weight was significantly lower than that reported from the same SCA population.

**Keywords:**

Coronavirus disease 2019, pregnancy, severe acute respiratory syndrome coronavirus 2, sickle cell anemia

## Introduction

Coronavirus disease 2019 (COVID-19) is caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2).[1] The clinical features of SARS-CoV-2 vary from mild in about 80%, severe in 15%, and critical in 5%, with more severe illness seen predominantly in the adults with advanced age, and those with underlying comorbidities.[2] Transmission occurs due to close contact and from contaminated surfaces. Vertical transmission from the mother to the fetus and baby is rare, and only a few cases are reported.[3] Pregnant women seem to contract the infection as likely as the general population, and course of COVID-19 in pregnant women resembles that of other populations.[4] Sickle cell anemia (SCA) patients are prone to pulmonary complications such as acute chest syndrome (ACS) and thromboembolic complications.[5] Furthermore, owing to the underlying immunocompromised state, SCA patients are at a higher risk of infection.[6] We have reported a large number of SCA with COVID, with favorable outcome.[7] Pregnancy in SCA has been associated with increased maternal and fetal complications including pulmonary complications.[8] Apart from the report by Justino *et al*., data on the outcome of pregnancy in SCA with COVID-19 are scarce.[9] Here, we report a case series of SCA patients with COVID, during pregnancy highlighting their outcome and placental histopathology, where available.

## Case Reports

Our case series included six pregnant women with SCA, who were confirmed to have COVID-19 confirmed by reverse transcription–polymerase chain

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reaction (PCR), using the GeneXpert machine (Cepheid, Sunnyvale, CA, USA). The course of the COVID-19 in these women, pregnancy complications, and delivery details were recorded. The placentas of two of them were sent for histology.

### Case 1

Mrs. A, a 30-year-old G3P1A1 (one previous cesarean section and one miscarriage), was admitted at 22-week gestation with fever, headache, cough, and chest pain. She had shortness of breath but maintained oxygen saturation throughout her stay without any supplemental support. In view of hemoglobin of 8 g% and severe vaso-occlusive crisis (VOC), exchange transfusion was performed, and she was discharged home after 7 days. She was readmitted in labor at 37 weeks and needed a cesarean section for cord prolapse. Placental histology showed focal infarction. The baby weighed 2130 g but did not need any special care in neonatal unit.

### Case 2

Mrs. B, G2P1, with a history of previous cesarean section was admitted with pain in the limbs at 31-week gestation. There was no history of fever. In view of history of contact with a positive patient, COVID-19 test was done and she was positive. She received a red cell exchange transfusion. She had a mild COVID illness, not needing any specific medications, and no oxygen supplement was given. She was delivered by elective cesarean section at 36 + 5 weeks as she had bilateral avascular necrosis of the femur. Her baby weighed 2500 g and did well. Examination of the placenta revealed increased perivillous fibrin deposition and scattered decidua calcifications. The mother and baby were discharged after 3 days of cesarean section.

### Case 3

Mrs. C, G2P1, previous cesarean section contracted COVID at 20+-week gestation with flu-like symptoms but no respiratory distress. She was managed as an outpatient as she did not have any respiratory symptoms. However, she was readmitted with VOC and needed an exchange transfusion in the third trimester. In view of her sickle cell disease and bilateral avascular necrosis of the femur, she had an elective cesarean section at 37 weeks and had a baby weighing 2.44 kg. The baby and mother were discharged home after 3 days of delivery.

### Case 4

Mrs. D, G2 P1, was admitted at 28 weeks with fever and back and limb pain. She reported contact with a COVID-positive patient, and hence, COVID test was done. She had a previous history of myocardial infarction, ACS, and avascular necrosis of the hip and shoulder. Furthermore, she had recurrent admissions for VOC in the recent past. She needed transfusion due to low hemoglobin and VOC, and received antibiotics and antiviral therapy as per protocol. She had a mild course. She had induction of labor at 37 + 2 weeks due to repeated admissions for sickle cell disease and delivered a baby weighing 2600 g. Both the mother and baby were discharged in good condition, and the placenta was not sent for histology.

### Case 5

Mrs. AH is a primigravida with moderate SCD, and had a complicated fat embolism syndrome and reflex nephropathy. She is on regular blood exchange, and was admitted with a painful episode at week 30 of gestation. She was confirmed to have COVID-positive PCR, and as she had contact with another family member, she received exchange transfusions and low-molecular-weight heparin prophylaxis (LMWH) prophylaxis. She was admitted for elective exchange and planned induction of labor at 37 + 1-week gestation. She had a vaginal vacuum-assisted delivery of a healthy baby boy of 2.73-kg weight.

### Case 6

Mrs. SA is a 43-year-old woman of S/C genotype and had a moderate sickle cell disease with recurrent ACS that needed intensive care unit admission, moderate asthma, and surgical splenectomy. She presented with cough and mild pain at week 8 of gestation, and she did not need hospital admission, however, she aborted at week 11, and histology showed a hydatidiform mole.

## Discussion

The PregCOV-19 Living Systematic Review has so far included over 54000 currently and recently pregnant women worldwide with suspected or confirmed COVID-19 (reported before November 29, 2020). Among the common, presenting features of COVID-19 in pregnancy include fever and cough, whereas dyspnea, loss of taste, and diarrhea were less common.[10] Furthermore, significant proportions may be asymptomatic according to the same study. An interim report from the UK Obstetric Surveillance System on pregnant women reported severe illness in the third trimester and <1% received extracorporeal membrane oxygenation. However, only symptomatic women were included in these data, limiting its applications to other categories.[11] Hence, overall pregnant women are at increased risk of severe disease with COVID-19.[11,12] If we consider SCA, there are a number of reports of COVID-19 in SCA, with variable outcome, however, the data on pregnant women with SCA and COVID-19 are scarce.[13] There is only one case report of a pregnant woman with SCA and ACS.[14] To the best of our knowledge, this is the largest series of

patients with SCA, COVID-19, and pregnancy. Our data suggest that patients with SCA and pregnancy handled COVID-19 the same as in general SCA population.[12] These patients presented predominantly with fever and painful episodes, and cough, not unusual from the general sickle cell patients, with mild to moderate in severity as per the WHO COVID-19 criteria.[7] Four patients needed admission (66.7%), with a mean hospital stay of 8.25 days, and two were treated at home. They had a significant drop in hemoglobin ($P < 0.001$), with a rise in WBC and lower platelets from baseline, but not statically significant [Table 1]. The management of these patients was predominated by attention to VOC and fever management during pregnancy, including antibiotics, low-molecular-heparin use and exchange, and blood transfusions (requiring on average 3–4 units of blood during the COVID episode). The outcome of pregnancy is satisfactory, although the mean birth weight was significantly lower than that reported from the same SCA population.[14] There were no confirmed cases of vertical transmission of the virus in a newborn in this case series.

In conclusion, this case series demonstrates that pregnant women with sickle cell disease and COVID-19, experienced a mild-to-moderate disease, with satisfactory outcome, provided they get the appropriate attention for VOC management during pregnancy, including LMWH prophylaxis and also simple and exchange transfusions. Our data indicated a significant drop in hemoglobin with low birth weight. None of the babies in our series showed evidence of vertical transmission.

## Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in

**Table 1: Clinical and laboratory features**

| Parameters | Cases | | | | | | Mean (±SD) |
|---|---|---|---|---|---|---|---|
| | Case 1 | Case 2 | Case 3 | Case 4 | Case 5 | Case 6 | |
| Age (years) | 30 | 26 | 28 | 35 | 25 | 42 | 28.8±3.54 |
| Genotype | S/S | S/B° | S/B° | S/S | S/S | S/C | |
| PMH | Splenectomy and cholecystectomy | ACS, bilateral AVN | ACS, AVN | Acute MI, ACS, AVN hips and shoulder, auto-splenectomy | Fat embolism syndrome, reflex nephropathy | Asthma, ACS, splenectomy, | |
| Presenting symptoms | fever, headache, cough, SOB, and chest pain | VOC, Mental Nerve syndrome | VOC, rhinorrhea | VOC, fever, tachycardia | VOC | Cough, mild pain | |
| Gestation at diagnosis | 22 | 31 | 20 | 28 | 30 | 8 | 26.2±4.4 |
| Gestation at delivery | 37 | 36+5 | 37 | 39 | 37+1 | Aborted at W11 | 37.4±0.8 |
| Birth weight (kg) | 2.13 | 2.50 | 2.44 | 2.66 | 2.73 | NA | 2.43 (0.2) |
| Length of stay | 7 | 12 | Home | 9 | 5 | home | 8.25 (2.5) |
| COVID severity | Moderate | Moderate | Mild | Moderate | Mild | Mild | |
| Therapy received | Ceftriaxone, azithromycin, oseltamivir, LMWH, exchange transfusions | Simple and exchange transfusions, LMWH | Oral pain medications | Tazocin, azithromycin, oseltamivir, LMWH, exchange transfusion | Exchange transfusions, LMWH | Cefuroxime and azithromycin | |
| Red cell units used during episode | 3 | 4 | 0 | 4 | 3 | | |
| Baseline Hb | 9.2 | 9.4 | 9 | 8.9 | 9.3 | 10.3 | 9.16±0.19 |
| Hb at presentation | 7.7 | 8.1 | 8.8 | 8.2 | 7.9 | NA | 8.14 (0.4) $P$<0.001 |
| Baseline WBC | 16.4 | 4.4 | 7.4 | 7.9 | 6.1 | 6.7 | 8.44±4.16 |
| WBC at presentation | 10.9 | 6.1 | 5.9 | 10.5 | 17.2 | NA | 10.12 (4.1) $P$=0.5 |
| Baseline platelets | 478 | 123 | 145 | 451 | 258 | 420 | 291±149.13 |
| Platelets ($10^9$) at presentation | 413 | 122 | 124 | 282 | 112 | NA | 210 (49) $P$=0.4 |
| LDH U/l | 1184 | 648 | NA | 243 | 597 | NA | 668 (36) |
| Serum ferritin µg/l | 7173 | 1161 | NA | 2286 | 7747 | NA | 4591 (290) |
| CRP µg/l | 48 | 74 | NA | 25 | 64 | NA | 52 (18) |
| D. Dimers mg/l | NA | 3.9 | NA | 3.2 | 3.86 | NA | 3.65 (0.3) |

VOC=Vaso-occlusive crisis, ACS=Acute chest syndrome, AVN=Avascular necrosis, PMH=Past medical history, NA=Not available, WBC=White blood cell, CRP=C-reactive protein, Hb=Hemoglobin, LMWH=Low-molecular-weight heparin, SD=Standard deviation, MI=Myocardial infarction, LDH=lactate dehydrogenase, SOB=shortness of breath

the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Nil.

## Conflicts of interest
There are no conflicts of interest.

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