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(CASE REPORT)

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Maternal and perinatal outcomes for women with Sickle Cell Disease (SCD) in resource-limited settings. A report of two cases at Iringa Regional Referral Hospital, Tanzania

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Abstract

Background: Sickle Cell Disease (SCD) in pregnancy poses challenges in management as the pregnancy period increases the chances of SCD complications such as vaso-occlusive crises, anaemia, acute chest syndrome (ACS) and foetal distress following placenta calcifications. The increased demands and physiological changes that occur during pregnancy contribute to the complications associated with managing SCD in pregnant women.

Case presentation: We report two cases of SCD in pregnancy for a 26-year-old primigravida and a 32-year-old multigravida G3P2L2 woman who were admitted to our hospital in the antenatal ward and the Intensive Care Unit (ICU) due to complications from SCD during their pregnancies. Our patients were managed and delivered preterm due to foetal distress and placenta calcification by caesarean section under regional anaesthesia. We managed to have successful maternal and perinatal outcomes.

Conclusion: Despite the challenges of antenatal care, patient monitoring, follow-up and management of complications among pregnant women with SCD in lower-resource setting health facilities, pregnant women with SCD can still be managed with vigilance, close follow-up and timely decisions when severe complications arise to achieve a favourable maternal and perinatal outcome.

Keywords: Sickle Cell Disease (SCD); Pregnancy; Vaso-occlusive Crisis; Anaemia; Acute Chest Syndrome (ACS); Blood Transfusion; Maternal Outcome; Perinatal Outcome

1. Introduction

Sickle cell disease (SCD) is a group of autosomal recessive haemoglobinopathies caused by mutations in the β-globin gene, resulting in the production of abnormal haemoglobin S [1, 2]. Worldwide, the population of people with SCD has been increasing profoundly, with an estimated increase of 41.4% between 2000 and 2021 [2]. It is the most common inherited haemoglobin disorder globally, the highest population prevalence being in sub-Saharan Africa, the Middle East/North Africa, India, Latin America, and Mediterranean countries [1]. However, despite its high prevalence in some areas, SCD is becoming more of a global condition due to the free movement of people as a result of migration and globalisation [1-3].

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People with SCD are characterised by frequent chronic haemolytic anaemia, intermittent vaso-occlusive crises (VOCs), and progressive end-organ damage as a result of recurrent ischaemia and inflammatory processes associated with the disease [1]. Due to advances in technology for newborn screening, prophylactic interventions, and disease-modifying therapies, the survival of people with SCD has improved, including women who are now reaching reproductive age in satisfactory health to achieve pregnancy [1, 4] and with a significant reduction in maternal and neonatal mortality rates among SCD women as well [4].

Pregnancy in women with SCD is associated with a profound maternal and foetal morbidity due to the effects of pregnancy-related physiological changes on their already compromised haematologic and vascular systems, which are further affected by recurrent inflammations [1-3]. Pregnant women with SCD are at increased risk of VOC, acute chest syndrome, osteonecrosis, hepatic necrosis, leg ulcers, and thromboembolic events. Additionally, vaso-occlusion within the placenta can lead to hypertensive disorders of pregnancy, foetal growth restriction, stillbirth, and other adverse maternal and perinatal outcomes [1, 2, 4, 5].

Management of women with SCD during pregnancy needs to consider placental status, as there is an increased risk of placental insufficiency and, therefore, a high potential need for induction of labour or caesarean section for the best maternal and perinatal outcomes [3]. The decisions about the timing of birth (whether to wait for spontaneous labour or opt for a planned birth) for women with SCD should be individualised, taking into account the woman's preferences while balancing the benefits of continuing the pregnancy for foetal maturation against the risks of maternal and neonatal morbidities associated with the continuation of the pregnancy [2].

We present two cases of SCD involving a primigravida and multigravida woman, both managed in low-resource settings with vigilance, close monitoring, and follow-up; the decision for preterm delivery by Caesarean section was made due to placental insufficiency leading to foetal distress, resulting in successful maternal and foetal outcomes. These cases highlight the diagnostic challenges and therapeutic considerations in a resource-limited setting.

2. Case Presentation

2.1. Case 1

A 26-year-old primigravida, a known patient with sickle cell disease and not on regular follow-up, presented to our hospital at 27 weeks' gestation with difficulty in breathing and joint pain lasting one week, indicative of a vaso-occlusive crisis. Initial analgesics and hydration did not alleviate the pain. Subsequently, she developed worsening difficulty in breathing, chest pain, and progressive respiratory distress. On examination, she appeared ill, was in severe pain, jaundiced, and dyspnoeic. Her blood pressure was recorded at 110/70 mmHg, her pulse rate was tachycardic at 130 beats per minute, and her respiratory rate was tachypneic at 30 cycles per minute. Despite receiving 10 litres of oxygen per minute via a non-rebreather mask, her oxygen saturation was only 84%. Additionally, she had a febrile temperature of 37.8 degrees Celsius. Respiratory examination revealed bilateral crepitations, while cardiovascular examination confirmed tachycardia. An abdominal examination showed a gravid uterus, a fundal height of 28 cm, and a foetal heart rate of 142 bpm. Other systemic examinations were essentially normal. On investigations, her Full Blood Count (FBC) revealed WBC: 37.7×10^9/L (leukocytosis); haemoglobin: 6.54 g/dL (severe anaemia); haematocrit: 20%; platelets: 444×10^9/L; and MRDT malaria test: non-reactive. Her lactate dehydrogenase (LDH) was high at 684.55 IU/L, with a positive sickling test; her urinalysis revealed blood and significant leukocytes. Her chest imaging findings revealed dilation of multiple heart chambers, along with right pleural effusion, pulmonary oedema, and infiltrates [Figure 1]. She was diagnosed with sickle cell disease, acute chest syndrome, severe community-acquired pneumonia, and severe anaemia. She was admitted to the Intensive Care Unit (ICU), where she received treatment that included oxygen therapy via a non-rebreather face mask, intravenous fluids, injectable analgesics (paracetamol and morphine), and a blood transfusion of two units. Additionally, she was administered antibiotics, bronchodilators and corticosteroids. Continuous monitoring of maternal vital signs, oxygen saturation, and foetal heart rate was conducted, along with weekly obstetric ultrasounds (biophysical profiles). She remained in the ICU for three weeks before being transferred to the antenatal ward for expectant management. The patient demonstrated gradual clinical improvement after eight weeks in the hospital, with stabilisation of oxygen saturation and a reduction in respiratory distress. Her follow-up haemoglobin level was 9.5 g/dL at 35 weeks' gestation, and she subsequently underwent a Caesarean section due to placental calcification, resulting in the delivery of a female baby, weighing 2.9 kg, with Apgar scores of 9 and 10 at 1 and 5 minutes, respectively. The gross examination of the placenta revealed placenta calcification [Figure 2]. Her postnatal progress was uneventful while on antibiotics and supportive care. She was discharged home two weeks postpartum with stable vital signs, and her postpartum follow-up period, which lasted up to 42 days, was also uneventful. Our patient was on low dose throughout pregnancy and puerperium period. She was discharged from the obstetrics clinic and referred to a medical clinic to continue her regular follow-up appointments for sickle cell disease (SCD).

2.2. Case 2

A 32-year-old gravida 3, para 2, living 2 at 6 weeks' gestation age with two previous caesarean sections and a known patient with sickle cell disease. She was on regular folic acid supplementation throughout the pregnancy. She presented to the emergency department with a two-day history of a progressively worsening headache. The headache was generalised throbbing in nature, gradual in onset, and associated with dizziness, awareness of heartbeat, generalised body malaise, and effortless fatigability. She also reported a three-day history of abdominal pain, which began gradually and progressively worsened, predominantly localised to the epigastric region. The pain was associated with heartburn, early satiety, and a sensation of abdominal fullness. There was no history of loss of consciousness, convulsions, abnormal vaginal bleeding, easy bruising, respiratory symptoms, fever, night sweats, vomiting, diarrhoea, or urinary complaints. On examination, the patient was alert but severely pale, with mild jaundice and no evidence of cyanosis, lower limb oedema or lymphadenopathy. Her vital signs revealed a blood pressure of 124/86 mmHg, tachycardia with a pulse rate of 112 beats per minute, a respiratory rate of 21 breaths per minute and an oxygen saturation of 94% on room air. Abdominal examination revealed epigastric tenderness on deep palpation, with no other remarkable findings. Other systemic examinations were unremarkable. Upon investigations, her haemoglobin was 8.71 g/dl, and FBP showed leukocytosis (WBC 17 $\times 10^3/\mu L$) and neutrophilia, suggestive of an underlying infectious process. The chest x-ray revealed pulmonary oedema [Figure 3]. The malaria rapid test (MRDT) was negative; urinalysis results were unremarkable. The HIV test was negative; the VDRL was negative. She was diagnosed with gastritis and anaemia and was managed with antacids and haematinics. She was scheduled for two weekly antenatal care follow-ups, which were uneventful up to 36 weeks' gestational age. At a gestation age of 36 weeks, she came with severe joint pain and difficulty in breathing. Her haemoglobin was 3.96 gl/dl, $Sapo_2$ was 87%, and an ultrasound revealed placenta calcification with foetal heart rates at 124/min. She was admitted to the ICU, where a blood transfusion of packed red blood cells (4 units) was given, showing improvement of haemoglobin to 9.67 g/dL, oxygen therapy and antibiotics were given. She was also on low dose aspirin throughout the pregnancy and puerperium. A Caesarean section was done at a gestational age of 36 weeks due to placenta calcification [Figure 4] and non-reassuring foetal heart rate tracing; she had a female baby weighing 1.3 kg with an Apgar score of 8-10. Her postnatal follow-up was uneventful with normal haemoglobin ranges, and she was discharged to medical clinics for follow-up 6 weeks postpartum.

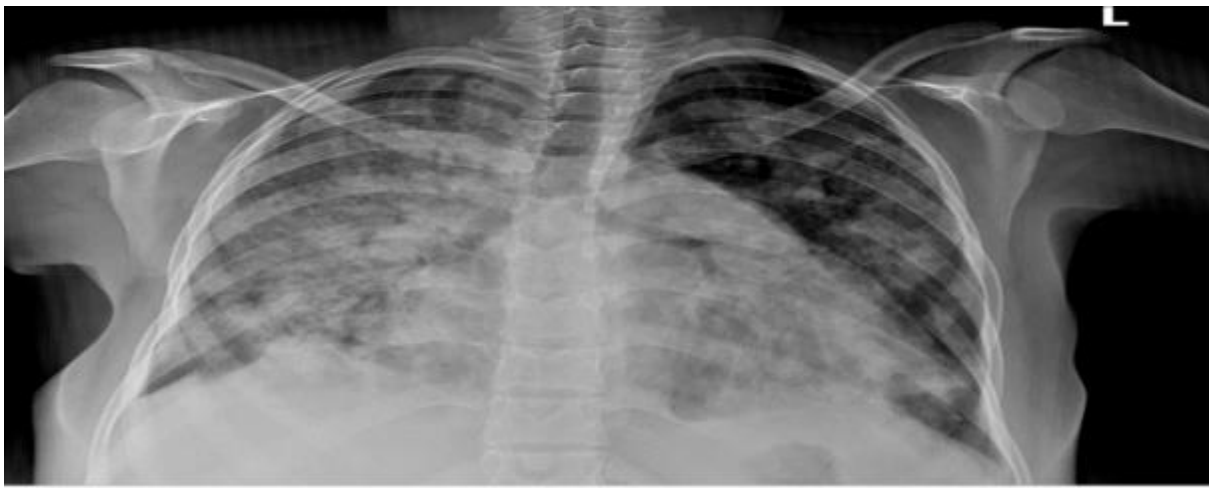

Figure 1 Chest x-ray showing bilateral fluffy opacities, more pronounced on the right side. The tenting of the bilateral hemidiaphragms suggests reduced lung volumes, accompanied by widening of the carina angle. The cardiac silhouette appears enlarged, and the right costophrenic angle is obscured. The imaging findings indicate dilation of multiple heart chambers, along with right pleural effusion, pulmonary oedema, and infiltrates

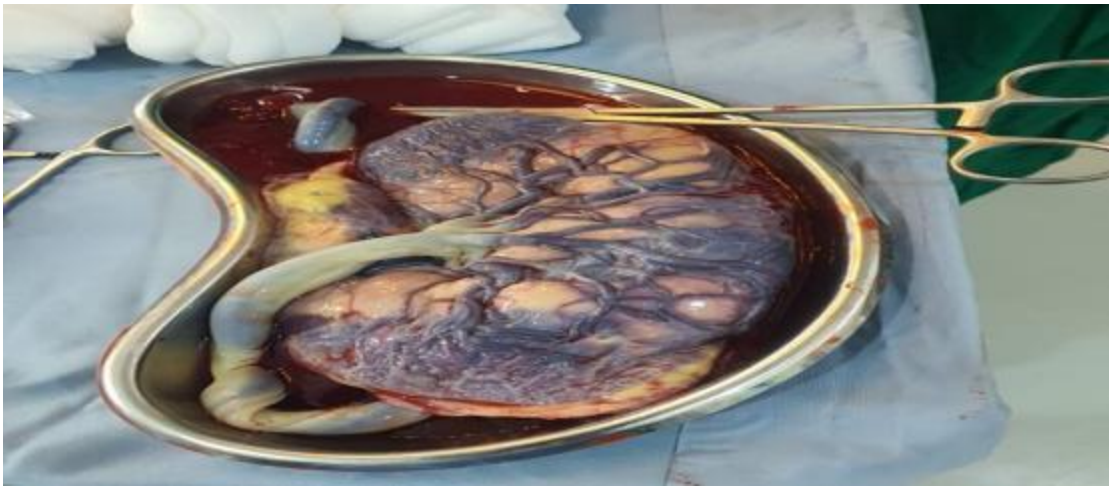

Figure 2 Post-delivery gross findings of severe placenta calcification

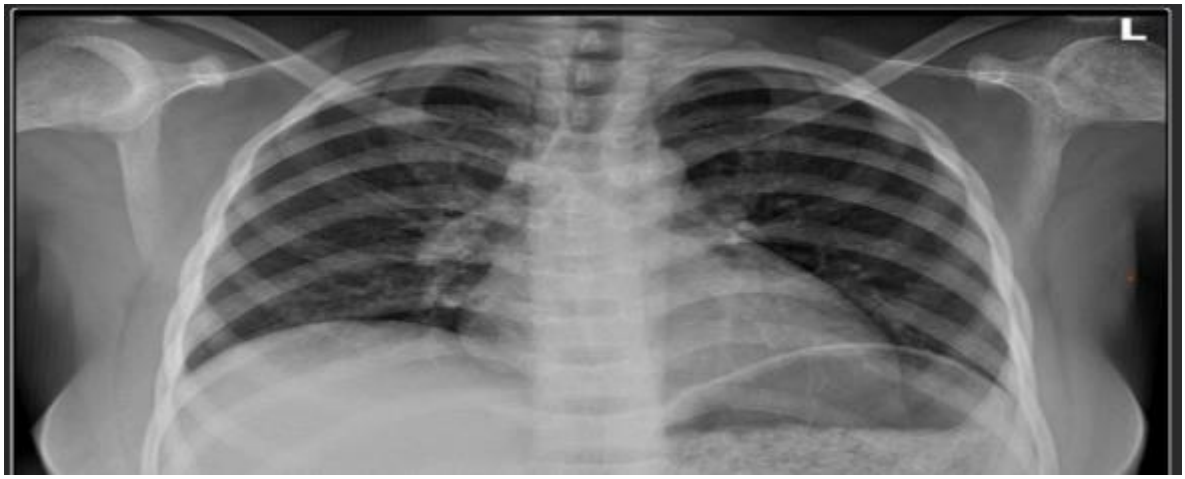

Figure 3 X-ray on admission suggestive of non-cardiogenic pulmonary oedema showing patchy infiltration in the right perihilar areas with normal other parts of pulmonary parenchyma, cardiac silhouette, bones and upper abdominal parts.

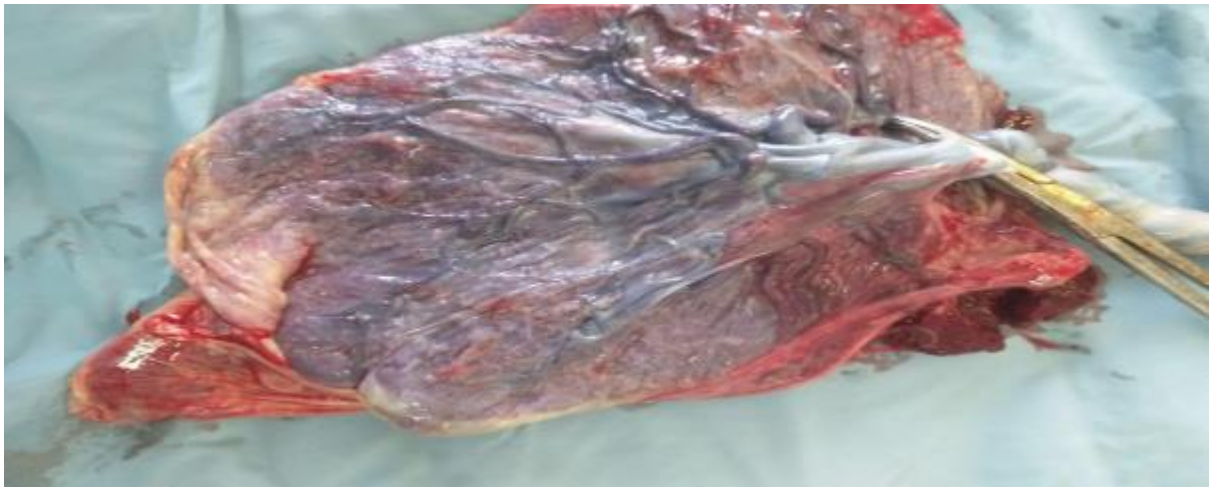

Figure 4 Gross appearance of a placenta calcification at delivery

3. Discussion

SCD is the most prevalent genetic disease in Africa, though it remains largely neglected, leading to multiple organ failure and premature death. For children under five years old, adolescents, and pregnant women, sickle cell disease imposes a financial burden on families, resulting in a frequent lack of adequate healthcare infrastructure, which includes access to specialised SCD clinics, diagnostic tools, and medications [6]. This situation was exemplified by our two presented cases, as neither patient had the opportunity to attend a specialised SCD clinic before pregnancy, and we lacked a haemoglobin electrophoresis machine to quantify the HBS percentage, which is essential for making informed decisions about the timing and mode of delivery. Therefore, the resource limitations in our countries pose a major obstacle and impact the management options for pregnant women with SCD [6].

Hydroxyurea and blood transfusions are documented as the main disease-modifying treatments for SCD [6]. In our cases, because specialised SCD clinics were unavailable, all patients were off hydroxyurea before pregnancy, even though hydroxyurea is not recommended during pregnancy. Effective and quality antenatal care management is recommended to minimise risks to the mother and foetus and for better outcomes, and studies have shown a high mortality rate in developing countries of 7-12% in Africa and 4-40% in India due to poor and insufficient antenatal care [7]. In both our cases the quality of antenatal care was questionable, as there was no early, timely referral of patients to a higher-level facility. Our cases were planned for normal routine antenatal contacts; like other low-risk clients, they sought higher-level facility services due to the onset of severe complications. Our cases did not receive preconception care despite being known for SCD, and this is the same observation for the majority of women [8]. Pre-existing anaemia and malnutrition among pregnant women, which are highly prevalent in low-resource countries, as is the case for our two cases, are important factors that might have affected maternal and perinatal outcomes [4].

As is well documented in various studies, pregnant women with SCD are at a higher risk of maternal and foetal morbidity [1, 2, 4, 5]. The antenatal maternal and foetal morbidity determines the surveillance, monitoring and management of patients, timing and mode of delivery as well as the maternal and perinatal outcomes among SCD-pregnant women. Providing improved antenatal surveillance and management is crucial for enhancing outcomes [9]. Our reported cases had multiple admissions, including in the intensive care unit (ICU), due to recurrent complications of vaso-occlusive crises (VOCs), low haemoglobin (anaemia) and chest infections, as has been observed in other studies [10].

We managed vaso-occlusive crises in our patient with analgesics, intravenous fluids, and on-demand blood transfusion. Due to lack of infrastructure, we had no option for prophylactic exchange blood transfusion (PEBT), which has been observed in studies to reduce infections and reoccurrence of vaso-occlusive crises and impact on postnatal prognosis [11], though a recent clinical trial has shown that PEBT has no impact on maternal, infant and postnatal outcome [12]. On demand/prophylactic blood transfusion has been recommended in several studies and guidelines [2, 6, 13, 14]. The benefit of transfusion includes a decrease in the percentage of HbS, increased oxygen-carrying capacity, improved haemoglobin, suppression of sickle erythropoiesis and dilution of HbS, thus preventing the sickle cell crises [15]. However, careful monitoring due to the risks of alloimmunisation and iron overload needs to be strengthened [6]. The pain relief was offered timely to our cases by use of analgesics. Options for pain management include oral paracetamol, nonsteroidal anti-inflammatory drugs (NSAIDs), or opioids at the lowest effective dose for the shortest necessary duration, taking into account the stage of pregnancy, contraindications for specific medications, the woman's views and preferences, her previous experiences with the medication, the risk of dependence, and the availability of these options [2, 4, 6]. Intravenous fluid hydration was also implemented for pain management with vigilant monitoring for early detection of fluid overload and pulmonary oedema [2]. The anaemia was managed by on-demand blood transfusion and haematinics with continued folic acid and iron supplementation as recommended in most literature [2, 6, 13]. Our cases had frequent screening for infection as recommended by the WHO [2] and treatment with appropriate antibiotics, oxygen support, hydration, analgesics and, if required, blood transfusion, especially for acute chest syndrome (ACS), which was provided [4]. Our patients also received low-dose aspirin for thromboprophylaxis throughout the pregnancy as recommended in studies to reduce the risk of pre-eclampsia [6, 13].

The incidence of SCD delivery in Tanzania has been on the rise in the past few years; the disease is associated with excessive maternal deaths that are by far attributable to infections and lack of standard guidelines to improve care of SCD in pregnancy [16]. There has been no international consensus on the timing of delivery among pregnant women with SCD [2, 17], and therefore there is a need for an individualised birth plan [6, 13, 17]. In our two cases we managed to have no maternal deaths; however, maternal and perinatal outcomes of premature delivery/low birth weight babies and caesarean deliveries are the same as in other studies [6, 18, 19]. The higher rate of caesarean section in pregnant women with SCD has been attributed to complications such as pre-eclampsia, foetal growth restriction and foetal

distress [6], and regional anaesthesia, as for all our cases, is preferred to general anaesthesia [13], as it offers superior intraoperative and postoperative analgesia, better peripheral blood flow and avoidance of intubation [18].

The postpartum period is as challenging as the pregnancy period for women with sickle cell disease (SCD), as they are at heightened risk for complications. We provided immediate postpartum care for our cases, focusing on the prevention and management of the complications through careful monitoring and targeted interventions. Ensuring adequate hydration and oxygenation is essential to prevent complications, along with breastfeeding, postpartum pain management, infection screening, mental health support, provision of postpartum contraception, and long-term follow-up care as recommended [6] to monitor for chronic complications and maintain overall health. Our cases' postpartum period was uneventful, and were linked with the medical department for routine SCD clinic follow-up.

4. Conclusion

Pregnancy in SCD women requires preconception counselling, proper antenatal follow-up, close monitoring and prompt management of complications, aiming at early recognition of complications and multidisciplinary care for significantly improved maternal and foetal outcomes. Despite the challenges of managing sickle cell disease in low-resource settings, it is possible to achieve successful maternal and perinatal outcomes through vigilant follow-up, close monitoring, and timely delivery of care in areas with a high prevalence of SCD among pregnant women.

Compliance with ethical standards

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Disclosure of conflict of interest

Authors declare no conflict of interest

Statement of informed consent

Informed consent was obtained from all individual participants included in the study and patients understands that their names and initials will not be published, and their identity will be concealed.

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