Pregnancy in Sickle Cell Disease, with Human-Immunodeficiency Virus (HIV) and Obstructive Jaundice

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Summary

Sickle cell disease (SCD) is an autosomal recessively inherited hemoglobinopathy whose pathology involves tissue anoxia occasioned by abnormally shaped red cells. Although its burden is higher in Sub-Saharan Africa, an improvement in the quality and accessibility of healthcare has led to a prolonged lifespan for the affected. In effect, as more SCD patients conceive, the impact of the disorder on pregnancy continues to unravel. Its ramifications on conception and pregnancy include intrauterine growth restriction, fetal death, miscarriages, and subfertility. Also, sickling crisis in labour, postpartum haemorrhage, pre-eclampsia, and the need for caesarian delivery, often ensue peripartum. Unpacking pregnancy in SCD from the antenatal care perspective, intrapartum considerations, and continuity of care in the postnatal period is thus an essential concept for all practitioners to improve care provision for these mothers. Through the lenses of a case of pregnancy in SCD, HIV infection, and obstructive jaundice, our review journeys the complex course of care for a patient for 7weeks in our facility. We outline concepts of comprehensive patient care for pregnancy in SCD based on currently available evidence, and how they were applied to ensure optimal outcomes for the fetus and mother, whose case posed a unique challenge to the obstetric team.

Keywords: *Sickle Cell Disease, Obstructive Jaundice, HIV, Cor-morbidities*

[*Afr. J.* *Health Sci*. 2022 35(3): 263 - 268]

Introduction

Sickle cell disease (SCD) is an autosomal recessively inherited hemoglobinopathy whose pathology involves tissue anoxia occasioned by abnormally shaped red cells. Its burden is greatest in Sub-Saharan Africa, and in Western Kenya, it stands at 0.2%.[1] SCD mortality estimates are at 4.5%, pointing to a particular menace for children and women in their reproductive years.[2] Whilst caregivers discouraged pregnancy in SCD women before, the improvement in healthcare services to SCD has occasioned a turnaround. Nevertheless, although patients now live longer and better, pregnancies in SCD remain high-risk and necessitate vigilance.

Studies on pregnancy in SCD in Kenya are scarce. However, in Ghana, researchers have demonstrated a higher incidence of maternal complications in SCD.[3] The complications included postpartum haemorrhage, pre-eclampsia, and the need for caesarian delivery. Closer on in Tanzania, Muganyizi et al. also assessed and revealed a higher risk of delivering low birth weight babies with poor APGAR scores and a higher risk of maternal mortality.[4] Consequently, understanding the interaction between pregnancy and SCD from an antenatal care perspective, intrapartum considerations, and continuity of care in the postnatal period is an

essential concept for all practitioners who encounter these mothers.

Our review unravels a more complicated case of pregnancy in SCD and HIV infection with suspected obstructive jaundice, and her complex course of care for 7weeks in our facility. We outline concepts of comprehensive patient care for pregnancy in SCD based on currently available evidence, and how they were applied to ensure optimal outcomes for the fetus and mother, whose case posed a unique challenge to the medical team.

Case Summary

This was a 37-year-old SCD and HIV+ African female, G7 P2+4 with 1 living child at 28 weeks GBD. She presented with dull, right upper quadrant (RUQ) pain for 7 months, preceded by scleral jaundice, and had associated fever, anorexia, dark stools, and weight loss. Reported no pruritus, nausea, vomiting, or fatty food intolerance, but also had easy fatigability, mild bilateral limb swelling, and mild exertional dyspnoea. Fetal movements were perceptible. She had lost 4 consecutive pregnancies at 4-5months, and currently, the ANC profile showed moderate anaemia, and underweight (42kg). She had multiple admissions and transfusions due to SCD complications, most recently in July 2020. No report of surgeries or allergies, or substance use.

Examination revealed a sick-looking, wasted, dehydrated, severely pale, and jaundiced patient. *Vital signs:* B/P 90/54, HR 89, SaO_2 87% on RA, T: 36.9^0C, RR 18BPM. Abdominal examination showed FH at 24/40 weeks with breech presentation, a tender epigastrium, and moderate non-tender hepatomegaly. Other systems were unremarkable. Therefore, an impression of severe anaemia/jaundice in pregnancy at 28weeks 1 day GBD in known SCD/HIV patient with BOH and possible IUGR was made on admission.

Tests done included: UECs- Normal sodium (133mEq/L), potassium (4.6mmol/L),, urea (5.7mM), creatinine (102micromoles), LFTs- elevated alkaline phosphatase and GGT, CBC/GXM- severe anaemia (Hb-4.2g/dl) with leucocytosis, HBsAg- negative, BS for MPS- negative. Abdominal ultrasound - hepatomegaly, and gall bladder calculus. Obstetric ultrasound- singleton pregnancy in breech at 28/40 gestation, with FHR of 141bpm, adequate liqua, and EFW of 1212g. She was started on dexamethasone IM 12mg OD 3/7 for lung maturity, IM diclofenac 75mg BD 3/7, transfusion with 1350mls of packed red cells, and physician/surgeon consult.

Repeat examination and labwork showed improving anaemia, and perceivable fetal kicks with FHR WNL. However, pancreatic enzymes were markedly elevated, and a coagulation profile showed increased PT and INR. She was therefore started on vitamin K 10mg OD 3/7, cefixime 400mg BD, omeprazole 40mg OD (for epigastric pain), continued on folate 5mg OD, HAART/CTX, and paludrine 500mg OD. An abdominal MRI was recommended, and delivery was aimed for 34/40.

Later, she developed grade 2 ascites, even higher pancreatic enzymes, and no change in baseline labwork. Active fetal monitoring continued through weekly biophysical profiles demonstrating a reassuring fetus. Ongoing treatment continued due to CT scan contraindication and MRI unaffordability to the patient. One week before delivery, LFTs/UECs normalized, and obstetric U/S was normal- FHR 133BPM and EFW 1995g. She was

eventually delivered via elective C/S owing to (1) breech presentation with possible IUGR and BOH, (2) relative contraindications to induction due to HIV+ status, grand multiparity, and the possibility of sickle cell crisis in labour, (3) epidural anaesthesia unavailability, and (4) improved CBC, UECs and LFTs. The outcome was LMI scoring 9/1, 10/5, 10/10 weighing 2.1kg.

The post-operative period was uneventful. Her medications were IM morphine 10mg BD for 2/7, PO diclofenac 75mg TDS for 7/7, PO paracetamol 1g TDS for 7/7, IV ceftriaxone 1g BD for 2/7, and Amoxicillin 1g TDS for 5/7. Vital signs were WNL. She continued HAART and sickle cell medication resumed 1-day post-op, and the newborn was admitted to NBU for feeding with no other complications noted. Both were discharged after 2 weeks with the baby at 2.8kg, with contraception and drug adherence education done and linkage to surgeons for follow-up on gallstones, and obstructive jaundice performed.

Discussion

The evolving demographics of SCD

SCD is the commonest hemoglobinopathy worldwide.[5] In Kenya, its prevalence is about 4.5%, predominantly in Western Kenya and Coastal regions.[5] SCD was associated with near-total mortality before adulthood before the 20th century. However, thanks to advanced care, 94% of SCD patients now transition into adulthood.[6] The improved care has also prolonged life expectancy, hence increasing the incidence of pregnancy in SCD in various obstetric centres in Western and Coastal Kenya.[7]

SCD, fertility, and pregnancy

SCD is associated with subfertility. Subfertility is attributed to a chronic inflammatory state, transfusion-related hemochromatosis with associated endocrine dysfunction, and ovarian sickling causing ischemic infarctions.[8] Poor nutrition also delays reproductive development. Consequently, most adult SCD female patients fail to conceive, and those who do undergo unique physiologic and psychologic upheavals.

Pregnancy in SCD increases the maternal and fetal risk for adverse outcomes. First, the increased metabolic demands and erythropoiesis predispose the mother to various vaso-occlusive crises and multiple end-organ dysfunctions.[9] Additionally, placental vaso-occlusion leads to hypoxia and adverse fetal outcomes such as IUFD, IUGR, stillbirths, and prematurity.[9] In this case, the mother had a bad obstetric history comprising four previous miscarriages and one perinatal death, possibly due to such complications. Also, effective management of SCD improves obstetric outcomes.[9, 10] Here, the mother was only initially managed on proguanil and folic acid, thus failure to initiate hydroxyurea in the patient care at diagnosis could have contributed to poor maternal health before conception hence increasing the risk of poor obstetric outcomes.[11]

Pregnancy exacerbates sickle cell crisis, hence hemolysis presents as jaundice and anaemia in pregnancy, both of which increase complication risk. [12] The IUGR was likely due to maternal anaemia, and cholelithiasis from the hemolysis. The latter likely led to obstructive jaundice, hence putting the fetus at risk of bilirubin-induced neurologic dysfunction (BIND).

Delivery and postpartum care in SCD

The recommended delivery route in SCD is vaginal delivery. However, hospitals should have emergency theatre provisions and proper obstetric analgesia. Employing epidural analgesia with continuous electric fetal monitoring optimizes outcomes, and NSAIDs are recommended in the puerperium.[13] Cesarean section is recommended in complicated cases, or other obstetric indications. Importantly, assessment and replacement of blood loss in the postpartum period are integral in mitigating sickling during puerperium.[13] Standard supportive care including hydration, oxygenation, warmth, and infection control remains the same as for other SCD patients.[14, 15] In the first seven days of vaginal delivery and 6 weeks of cesarean section, LMWH thromboprophylaxis is recommended instead of low-dose aspirin, and progesterone-only contraceptives are favoured. In Kenya, guidelines recommend the monitoring of SCD mothers for one week postpartum before discharge.

Role of multidisciplinary care

Management of SCD in pregnancy necessitates multidisciplinary action and effective caregiver collaboration. While obstetricians remained at the forefront, this case roped surgeons and physicians to review the optimal care for her jaundice. Also, care providers for HIV/AIDS along with physicians assessed the optimal strategies for compliance and minimizing vertical transmission. The nurses provided day-to-day care in the wards, anaesthesiologists were instrumental in the delivery process to prevent crises and the neonatologist managed the baby in the first days of his life. The nutritionist ensured optimal feeding regimen and laboratory technicians and radiologists kept results prompt and reliable. Effectively, most providers played a role in the successful delivery of the child, hence the undeniable importance of healthcare worker collaboration in such cases.

Patient education

Expectant women with SCD should be informed about the effects of pregnancy on SCD and various measures. The patient's follow-up including vaccinations, prophylactic antibiotics, and folic acid supplementation should continue into pregnancy. SCD mothers should only receive iron supplements after laboratory evidence of iron deficiency.[14] Those with transfusion siderosis and on chelation therapy should have it discontinued 3 months before conception,[9] similar to hydroxyurea since the latter is teratogenic.[11] This illustrates the importance of patient education and preconception optimization, which is often absent due to discontinuity in patient care. Prophylactic low dose aspirin (75 mg daily from 12 weeks) for preeclampsia and early transfusion in pregnancy improves obstetric outcomes. However, iron overload, alloimmunization, and transfusion reactions may impede this intervention.[12]

Conclusion

In sum, pregnancy in SCD constitutes a high-risk pregnancy. It, thus, requires close patient follow-up, multidisciplinary collaboration, and comprehensive patient education for optimal obstetric outcomes. Preconception counselling and patient optimization have an impact on the outcome of the pregnancy, further illustrating the importance of continuity of patient care.

Abbreviations

ANC	Antenatal Care
ARV/CTX	Antiretroviral Therapy/ Cotrimoxazole
BOH	Bad Obstetric History
BS for MPS	Blood Slide for Malaria parasite
CBC/GXM	Complete Blood Count/Grouping and Crossmatch
DMPA	Depot Medroxy-Progesterone Acetate
EFW	Effective Fetal Weight
FH	Fundal Height
FHR	Fetal Heart Rate
GBD	Gestation by Dates
HBsAg	Hepatitis B Surface Antigen
HIV	Human Immunodeficiency Virus
INR	International Normalized Ratio
IUGR	Intrauterine Growth Restriction
LFTs	Liver Function Tests
LMI	Live Male Infant
MRI	Magnetic Resonance Angiography
PT	Prothrombin Time
RA	Room Air
RUQ	Right Upper Quadrant
SCD	Sickle Cell Disease
UECs	Urea, Electrolytes and Creatinine
WNL	Within Normal Limits

Author contributions

Omoga D. O - Lead and corresponding author, compilation, and final review; Njonjo S W. - Approval seeking, manuscript writing, and review; Akong'o R - Manuscript writing and review.

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Source of funding

The research was self-funded by the authors.

Availability of data

The patient data used in advancing the case review can be requested from the authors.

Conflict of interest

The authors declare no conflict of interest.

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