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■ Original Article

Pregnancy Outcomes Among Patients with Sickle Cell Disease

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ABSTRACT

Background: Pregnancy is a serious problem to women with sickle cell disease. It is associated with increased risk of maternal and fetal morbidity and mortality. ***Objective:*** The objective of this study is to study and assess the pregnancy outcomes among women with sickle cell disease. **Materials and Methods:** This was a five-year retrospective study of the outcome of pregnancy in 56 women with sickle cell disease at the university of Abuja teaching hospital between January 1, 2014 and December 31, 2018. Pertinent information were obtained from labour, postnatal, and neonatal ward records as well as theatre records. The relevant demographic data such as age, gravidity/parity, concomitant medical/obstetric conditions, mode of delivery and maternal and neonatal outcomes were retrieved, documented and analyzed. The pregnancies were characterized by high maternal and fetal morbidity and mortality. Maternal complications noted were maternal mortality, hypertensive disorders of pregnancies, sickle cell crises and infections. Fetal complications included, intrauterine fetal deaths, still births, prematurity, low birth weights, fetal distress and asphyxia. The case notes of the patients were retrieved and analyzed using the statistical package for social science SPSS version 21 The results were presented and discussed using simple percentages and tables. **Results:** There were a total of 9, 682 deliveries during the study period, out of which 56 (0.6%) of those women were those with sickle cell disease. Fifty-two (92.1%) of the women had the genotype HbSS while 4(7.9%) were of the genotype HbSC. The age range was from 18 to 39 years with the mean age being 27.4 ± 4.7 years. Fifty-three (94.6%) of them were booked at our facility with the gestational age at booking ranging from 10 to 35 weeks gestation (Mean: 15.8 ± 1.3 weeks). The Antenatal complications included vaso-occlusive crises 24 (42.9%), Anaemia 22 (39.3%), Malaria 20 (35.7%), pregnancy induced hypertension 18 (32.1%), Pre-eclampsia and eclampsia 11 and 8 (11.7% and 8.9%), pyelonephritis 10 (17.9%). Majority of the women in this study (58.9%) had vaginal delivery while 41.1% had a caesarean section. About (17) 30.4% delivered before 37

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completed weeks of gestation. Birth weight below 2500g was noted to have occurred in (17) 30.4% of the neonates. Neonatal complications included prematurity 17 (30.4%), fetal distress 7 (12.5%) and birth asphyxia 5 (8.9%). Overall, there were four maternal deaths that occurred during this study (7.1%) while 9 (16.1%) of the babies suffered perinatal mortality. **Conclusion**: The study showed that sickle cell disease in pregnancy is quite common in the region and it is associated with adverse pregnancy outcomes for the sufferers of this medical condition. It does become pertinent that health workers should be knowledgeable and skilled in the management of these patients and that emphasis on effective antenatal care and skilled supervised deliveries, as well as female and health education to these women may be improved to further reduce the prevalence of the maternal and neonatal complications associated with pregnancy in sickle cell disease patients.

Keywords: sickle cell disease, pregnancy, complications, outcome.

Introduction

Sickle cell disease (SCD) refers to sickling disorders in which the sickling gene is present with another abnormal gene affecting the production (quantitative) or the structure (qualitative) of haemoglobin.[1] Sickle cell disease (SCD) is a preventable but irreversible non-communicable, genetically transmitted autosomal recessive blood disorder of significant public health concern.[2] It is the most common inherited disorder worldwide.[3] It is associated with varying clinical severity and potentially serious complications.[4]

The most common clinical phenotype is the homozygous, i.e. HbSS, also known as sickle cell anaemia.[5] Compound heterozygotes include HbSC, SD, SO-Arab and S-ß thalassemia, which are all collectively (in addition to SS) referred to as sickle cell disease.[6] Studies have shown there are more patients with sickle cell disease of the SS genotype compared with genotypes SC and S-beta thalassaemia.[5]

Sickle cell disease is prevalent in sub-Saharan Africa, South America, central America, Saudi Arabia, India and Mediterranean countries.[7] Sickle cell disease affects nearly 100 million people globally with over 300,000 children with sickle cell disease born annually with mortality rates of over 50%.[2] While sub Saharan Africa accommodates 75% of all SCD patients and 70% of all SCD births globally with majority dying before the age of 5 years, Nigeria is the most sickle cell endemic country in Africa with 2-3% of the total population affected, with an estimated 25% prevalence of sickle cell trait, 100,000 annual SCD births and 100,000 annual Sickle cell deaths.[2,5] Studies in Nigeria have given incidences and prevalences of Sickle cell disease in pregnancy to be 1.15%,[8] 0.2%,[9] and 0.3%[10] in Osogbo, port Harcourt and Jos respectively.

The primary pathophysiology of SCD is due to the polymerization of HbS in low oxygenated conditions with formation of long fibers within the red blood cells making them fragile and sickle shaped.[11] These cells are prone to increased breakdown, causing hemolytic anaemia, and vaso-occlusion in small vessels, resulting in most of the clinical features of this multi organ disease.[11] Red cell dehydration, abnormal adhesion of red blood cells to the vascular endothelium, inflammatory events, and activation of all the cells in the vessels and abnormalities of nitric oxide metabolism have been attributed to trigger a vaso-occlusive crises.[11]

Normal vascular, endothelial, and inflammatory adaptations in pregnancy may lead to exacerbation of these pathophysiologic change, with manifestation of resulting complications such as pre-eclampsia and fetal growth restriction.[11] Maternal problems can arise from chronic underlying organ dysfunction, such as renal disease or pulmonary hypertension, from acute

complications of SCD such as vaso-occlusive crises and acute chest syndrome, and from pregnancy related complications.[12]

The clinical presentation of Sickle cell disease is usually in the form of Crises.[1] Sickle cell crises is used to describe many of the acute events that occur in individuals with sickle cell disease.[13] The vaso-occlusive crises, which is most common during the latter half of pregnancy or puerperium and the haematologic crises are perhaps the most common in pregnancy.[7]

With advances in management, education, awareness and improved nutrition, men and women with sickle cell disease are enjoying an improved quality of life well into adulthood, when they may elect to plan a family, as a result, sickle cell disease is a common haemoglobinopathy encountered during pregnancy in Nigeria.[10]

Pregnancy in sickle cell women has numerous obstetrical, non-obstetrical and fetal complications.[7] It is associated with an increased maternal and fetal morbidity and mortality.[13] Maternal complications may include recurrent anaemia, bone pain crises, recurrent malaria infection, acute chest syndrome, spontaneous abortion, pseudo toxemia, hemolytic crises, pre-eclampsia, retained placenta and maternal mortality.[13] They are also at an increased risk of urinary tract infections, pneumonia and thrombo-embolic complications.[10,14]

Risks to the fetus include increased frequency of miscarriage, intra uterine growth restriction, preterm labour and preterm labour.[10] Fetal complications may include low birth weight (LBW), intrauterine fetal death, still birth and breech presentation.[13] Perinatal morbidity and mortality are higher than in the general population.[10] In HbSC, there are fewer reported adverse outcomes, but there is evidence of an increased incidence of painful crises during pregnancy, fetal growth restriction, antepartum hospital admission and postpartum infection.[15]

The management of Sickle cell disease in pregnancy requires a multi-disciplinary approach as this tends to be associated with better outcome for mother and baby.[1] The team should include a haematologist with special interest in sickle cell, an experienced midwife with experience in high risk pregnancies and led by an Obstetrician, a neonatologist and an Anaesthetist.[1]

Pregnancy in SCD patients should be considered a high-risk pregnancy because of the risk of frequent crises, background haemolytic anemia which may worsen and sometimes multiple end organ damage.[1]

Sickle cell disease in pregnancy is a high-risk pregnancy that requires a multidisciplinary approach in its management. The Care for such patients should start with preconception counselling. Adequate monitoring in the antepartum, intrapartum and postpartum period is important in other to reduce the associated perinatal and maternal morbidity and mortality that is found in these set of patients.

The objective of this study is to study and assess the pregnancy outcomes among women with sickle cell disease delivering at the university of Abuja teaching hospital.

Materials and Methods

This was a retrospective study of the pregnancy outcome of 56 women with sickle cell disease at the University of Abuja Teaching Hospital between January 1, 2014, and December 31, 2018. The University of Abuja Teaching Hospital is one of the tertiary hospitals in the Federal Capital Territory and serves the surrounding environs of Kogi, Nassarawa, Niger and Kaduna States. Attendance at the hospital is by self-referral, and referral from both public and private hospitals.

The relevant case file numbers of the patients were retrieved from the records in the antenatal, postnatal, labour, theatre, and neonatal wards. The case files were then traced to the medical records department of the hospital to identify these patients. Their case files (56) retrieved from the medical records department were then studied. The information obtained was coded and transferred onto a proforma designed for the study. The relevant data extracted from the patient case files included: Age, gravidity, parity, gestational age at booking, complications of the disease and

pregnancy during the antenatal period, labour and puerperium and information about mode of delivery and fetal outcomes.

The data was analysed using simple statistics. The results were presented and discussed using simple percentages and tables.

Results

During the study period there were a total of 9, 682 deliveries and 56 of those women had sickle cell disease in pregnancy constituting 0.6%. About 73.2% of them were within the age bracket of 25-34 years with a mean age of 27.4 ± 4.7 years. More than half (51.8%) of the patients were primigravidas and nulliparas while none of the women had parity greater than three. Moreover, 52 (92.1%) of the women had a genotype of HbSS while 4 (7.9%) had the genotype HbSC, out of which a larger percentage of them 43 (76.8%) had a stable packed cell volume that ranged between 21% and 25% with a mean value of 23.75%. Table 1.

It was noted that about 53 (94.6%) of the sickle cell disease women booked in our facility with the gestational age at booking ranging from 10 to 35 weeks gestation (Mean: 15.8 ± 1.3 weeks) and majority of them 33 (62.3%) booked during the second trimester. Only 17 (32.1%) booked or presented during the first trimester i.e. before 13 weeks of gestation. Three women who had their antenatal care elsewhere were referred during labour as a result of complications they developed while laboring at the respective referral centres as shown in Table 1.

In the same vein, about 35 (62.5%) of the patients required antenatal admission during the pregnancy due to one or more maternal or fetal complications, with majority of them having had more than one antenatal admission during the course of their pregnancy. Sickle cell crises, vaso-occlusive crises was the major antenatal complications noted in this study in 24 (42.9%) patients. This was by anaemia 22 (39.3%), malaria 20 (35.7%), pregnancy induced hypertension 18 (32.1%), pre-eclampsia 11 (19.7%), pyelonephritis (17.9%) and eclampsia 5 (8.9%), were other common antepartum maternal complications observed in order of frequency as shown in Table 2.

Of the 56 women reviewed, greater than 33 (58.9%) of the women in this study had vaginal delivery while 23 (41.1%) had caesarean section. Seventeen 17 (30.4%) delivered before 37 completed weeks of gestation. The instrumental delivery rate was 14.3%,[8] 5 women had vacuum while 3 women had forceps delivery. The most common complication observed during the intrapartum period in this study was anaemia 18 (32.1%), other complications noted were vaso occlusive crises, fetal distress and failure to progress in labour due to Cephalopelvic disproportion in decreasing order of frequency as shown in Table 3.

Intrauterine growth restriction was noted in 19 (33.9%) of the pregnancies while intrauterine fetal death occurred in 6 (10.7%) of the babies born to the sickle cell disease pregnant women. Most of the babies born 37(69.6%) had normal birth weights while birth weight below 2500g occurred in 17 (30.4%) of the neonates with the mean birth weight being 2.65kg. Neonatal complications in order of decreasing frequency included prematurity 17 (30.4%), fetal distress 7 (12.5%) and birth asphyxia 5 (8.9%). There were 9 perinatal deaths (16.1%). This was comprised of 6(10.7%) still births and 3(5.4%) early neonatal deaths as shown in Table 3.

In the postpartum period, the commonest puerperal complications wasanaemia (18, 32.1%). All of the women who had anaemia required blood transfusion with most requiring more than one unit of blood. Other puerperal complications were bone pain crises and post caesarean wound infection. One patient however developed puerperal psychosis which was managed adequately.

There were 4 maternal deaths during this study period giving the maternal mortality ratio of 41.2/100,000 live birth, (total live birth during study period 9,713). Two of the deaths occurred as a result of complications of Eclampsia while the other two maternal deaths had anaemia as a complication of their pregnancies with resultant anaemic heart failure as shown in Table 4.

Table 1: Maternal Characteristics of Pregnant Sickle Cell Disease Women

Genotype	Frequency	Percent
HbSS	52	92.9
HbSC	4	7.1
Age (years)		
18-24	13	23.2
25-34	41	73.2
=35	2	3.6
Parity		
Nullipara	29	51.8
Primipara	16	28.6
Multipara	11	19.6
Booking Status		
Booked	53	94.6
Elsewhere/Unbooked	3	5.4
Gestational Age at Booking		
= 13 weeks	17	32.1
14-28 weeks	33	62.3
29-36	3	5.6
Stable PCV (%)		
= 20	2	3.6
21-25	43	76.8
26-30	11	19.6

Table 2: Pregnancy Related Complications in Women with Sickle Cell Disease

Complication	Frequency	Percent
Sickle Cell Crises	24	42.9
Anaemia	22	39.3
Pregnancy Induced Hypertension	18	32.1
Malaria	20	35.7
Urinary tract infections	14	25.0
Pre-eclampsia	11	19.7
Pyelonephritis	10	17.9
Respiratory tract infections	8	14.3
Eclampsia	5	8.9
Abruptio placentae	5	8.9
PROM	6	10.7
Placenta Praevia	4	7.1
HIV	2	3.6

*Some patients had multiple complications

Table 2: Pregnancy Related Complications in Women with Sickle Cell Disease

Complication	Frequency	Percent
Live Births	50	89.3
Deaths	6	10.7
Gestational Age		
Full Term Birth	39	69.6
Preterm Birth	17	30.4
Birth Weight (Kg)		
>2.5	39	69.6
1.5-2.49	14	25.0
<1.5	3	5.4
Complications		
SCBU	22	39.3
IUGR	19	33.9
Fetal Distress	7	12.5
Asphyxia	5	8.9
Mode of Delivery		
Vaginal	33	58.9
Caesarean Section	23	41.1
Instrumental Vaginal Delivery	8	14.3

Table 4: Puerperal complications of patients with Sickle Cell Disease

Complication	Frequency	Percent
Anaemia	18	32.1
Vaso-Occlusive crises	8	14.3
Wound Infection (Post C/S)	6	10.7
Maternal death	4	5.4
Puerperal psychosis	1	1.2

*Some patients had multiple complications

Discussion

Pregnancy in women with Sickle cell disease is a high-risk condition fraught with higher rates of maternal and fetal complications, as well as sickle cell disease related complications.[20] A total of fifty-six pregnant women with sickle cell disease were seen and managed during the study period. The prevalence of sickle cell disease in pregnancy varies significantly in different parts of the world.[8] Olugbenga AO et al reported a prevalence of 1.15% in Osogbo, Ugboma HAA etal reported an prevalence of 0.2% in Port Harcourt, Kahansim et al reported a prevalence of 0.3% in Jos, Wilson et al reported a prevalence of 1.42% in Ghana and D'Couth et al reported an prevalence of 0.15% in India.[7,8-10,14] The prevalence of sickle cell disease in this study was 0.6%, this value is higher than prevalences in Port Harcourt (0.2%) and Jos

(0.3%)[9,10] but lower than the prevalence in Osogbo (1.15%). Pregnancy in sickle cell women is at a high risk for maternal and fetal complications than in the general population.[7] Similar to many studies, it was found that obstetric complications such as gestational hypertension and pre-eclampsia were high in women with sickle cell disease.[7-10] This study also showed a high prevalence of eclampsia consistent with earlier studies in Ghana and other states of Nigeria.[8-10,12,14]

As previously reported, this study showed over 40% prevalence of anaemia in the sickle cell disease pregnant women occurring both in the antenatal and puerperal period with all of them requiring transfusion. This was similar to studies conducted in Port Harcourt where about 50% of the women with sickle cell disease had anaemia and were transfused with blood.9 In the same vein, about 52.7% of the women with sickle cell disease in pregnancy required transfusion in a study conducted in India.[3] Anaemia results from chronic hemolysis from the sickle shaped cells as well as sequestration into the liver or spleen.[1] These patients usually have chronic compensated anaemia with their stable state haemoglobin ranging between 6.5 and 9.0g/dl.[1] In this study, majority of the sickle cell disease pregnant women had a stable packed cell volume ranging from 21 to 25%. This is similar to other studies conducted in other parts of Nigeria and India.[3,7-10]

In a meta-analysis study conducted by Baofor K et al, babies born to mothers with sickle cell disease compared with controls were at increased risk for intrauterine growth restriction and perinatal mortality.[16] The babies were found to be about three times more likely to be growth restricted compared to babies born to mothers without sickle cell disease (pooled OR 2.79, 95% CI 1.85-4.21, $p<0.001$).[16] Intrauterine growth restriction was seen in more than one third of the sickle cell disease women in this study, and such a high prevalence has also been reported in various literature.[7,9,14,16] Chronic maternal anaemia and hypertension in pregnancy resulting in reduced placenta perfusion is the most likely reason for intra uterine growth restriction.[7]

Pregnancy has been shown to exacerbate sickle cell crises.[14] Vaso-occlusive crisis, one of the acute complications of sickle cell disease has been shown to increase antepartum hospital admissions.[17] About 62.5% of the women in this study required antenatal admission on account of one or more antenatal complications of which sickle cell crises was inclusive. This could be due to the fact that majority of the women did not benefit from pre-conception counselling, were primigravidas and a high proportion of the women booked for antenatal care in the second trimester, showing that most of patients were poorly educated on the implications of pregnancy with their medical condition, as such they were not aware that their pregnancy was associated with a higher risk than their counter-parts with normal haemoglobin. These reasons could may have accounted for the high incidences of antenatal admissions in this study.

About 39.3% sickle cell crises were reported in this study. This value is comparable with the study done in Osogbo (40.43%). This is however much higher compared to studies done by D' Couth et al in India and Wilson et al in Ghana who reported incidences of 18.05% and 9.2% respectively.[14,18] More also, The prevalence is lower when compared to the studies done in Jos (51.4%) and Port Harcourt (50%).

Infective Complications observed in this study were mainly malaria, urinary tract infections, acute pyelonephritis and respiratory tract infections which were adequately managed without further sequalae. Infections was noted to be the cause of maternal mortality in 82% of sickle cell disease women in Tanzania.[19] Unlike many studies which showed a higher rate of malaria infections in pregnant women with sickle cell disease, some studies in India did not have a single patient with malaria.[7,20]

There was a high caesarean section and instrumental delivery rate of 41.1% and 14.3% respectively. Other studies also observed higher caesarean section rates and instrumental delivery in patients with sickle cell disease in pregnancy.[6-10,17,19,21] this could be due to the high prevalence of maternal and fetal complications often leading to

delivery by caesarean section. Moreover, the second stage of labour is preferably shortened in these patients to avoid excessive pushing that may precipitate crises.[1] This therefore explains the high instrumental delivery rate.

Women with sickle cell haemoglobinopathy have been found to have a higher prevalence of preterm delivery.[7-10,14] According to Desai G et al and Ugobama et al, the incidence of preterm birth was as high as 44-45%.[3,9] The prevalence in this study was 30.4% which was lower than that found in India and Port Harcourt and consistent with the 2-fold increased risk in sickle cell disease women.[12,16] Lower gestational age could be influenced by a high frequency of early surgical delivery or premature induction both of which are common interventions in the management of pregnancy among mothers with sickle cell disease, though this was not the case in this review.[10]

Sickle cell disease in pregnancy has also been associated with low birth weight (LBW) and was observed in about 50% of pregnancies by Ugobama et al.[9] and 44.4% by D'Couth et al.[7] Overall, the risk of LBW babies was twice that in mothers with SCD compared to women without sickle cell disease (pooled OR 2.00, 95% CI 1.42-2.83, p<0.001). 20 In another study, there was a nearly fourfold increased risk of infants being born small for gestational age (<10th centile) in women with sickle cell disease (RR, 3.72; 95% C I, 2.32-5.98) when compared with non-sickle cell disease women.[12] Factors responsible for this may be lower gestational age at delivery, maternal anaemia, preeclampsia and intrauterine growth restriction.[7] About 30.4% of babies weighed less than 2.5kg at birth, which was similar to reports obtained in Ghana, Jos and Osogbo.[8,10,14]

In view of prematurity, low birth weight and perinatal asphyxia due to intrauterine growth restriction, our neonatal intensive care admission was as high as 39.3%. This is comparable to the study done in India but however it is higher than the values found in other parts of Nigeria.[7-10]

The risk of neonatal death is shown to be significantly higher in women with sickle cell disease compared to women without sickle cell disease (pooled OR 2.71, 95% CI 1.41-5.22, p+0.003).20 The perinatal mortality (16.1%) was high in this study and this was primarily due to intrauterine growth restriction and asphyxia. This is comparable to the study in Osogbo.[10]

In Africa, a mortality rate of 7-12% persists as a result of sickle cell disease in pregnancy, reflecting limited services and inadequate antenatal care.[14] The mortality rate in this study was 7.1% The study in Ghana showed that there was still a significantly higher maternal mortality in women with sickle cell disease compared with women having no documented haemoglobinopathies suggesting that in sub-Saharan Africa, the health of women with sickle cell disease is severely compromised during pregnancy.[14] Acute chest syndrome, sepsis and multi organ failure have contributed to the higher incidence of maternal losses among sickle cell disease women.[9,12,17,21] However, in this study, two of the deaths occurred as a results of complications of eclampsia while the other two maternal deaths had anaemia as a complication of their pregnancies with resultant anaemic heart failure.

In Conclusion, the high rate of maternal and perinatal morbidity and mortality in pregnant women with sickle cell disease can be reduced significantly by improving the health care to women with sickle cell disease. This can be achieved by providing comprehensive health care comprising of proper education to promote awareness of sickle cell disease among affected women to present early for evaluation and management of symptoms to skilled and qualified health care providers who can provide continuity of care and prevention of high risk behaviors, provision and implementation of better and quality preconception care in our health care facilities, effective and adequate prenatal care, early identification, prompt management and treatment of pregnancy and sickle cell disease related complications in these women. This approach should ensure result in early identification and management of acute problems by the appropriate health caregivers at the appropriate place.

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