Pregnancy Outcomes in Women with Sickle Cell Disease (SCD) - A Tertiary Centre Retrospective Study in Nigeria. What has changed ?

ABSTRACT

Background

Sickle cell disease is the most common inherited condition. Due to recent advances in medical care for patients with sickle cell anaemia, more women with SCD are able to survive up to the reproductive age group. This has given rise to a higher number of pregnant women with SCD. It results in increased fetal and maternal risks due to the metabolic demands, hypercoagulable state and vascular stasis often associated with pregnancy. It has therefore become imperative to explore what progress has been made over the last decade as well as what can be done to achieve the best outcome in these women.

Method

This was a retrospective study of women with SCD who accessed antenatal care (ANC) at the Nnamdi Azikiwe University Teaching Hospital (NAUTH) Nnewi over a ten year period. Folder numbers were obtained from the obstetrics clinic and thereafter the folders were assessed and data retrieved using a checklist. Data analysis was done using SPSS 24.

Results

The prevalence of sickle cell disease among pregnant women in this centre was 0.03%. All the women had the HbSS variants. The mean age of the subjects was 28.3 ± 5.6years. Majority of the women were gainfully employed. The mean gestational age at booking was 26 9.5 weeks. Half of the neonates had fetal distress at birth. Commonest maternal complication was anemia (100%) followed by vaso-occlusive crisis(89%). Eighty nine percent of the women were delivered by emergency caesarean section prior to 37 weeks gestational age. Preterm birth and fetal distress were the commonest neonatal complications.

Conclusion

The study revealed that pregnancy associated with sickle cell disease still carries high maternal and fetal morbidity in this environment. Majority of the women with SCD in pregnancy did not receive preconception care and also did not commence their ANC early enough. There is need to educate women with SCD on the need for preconception care to ensure optimization of health prior to conception. They should also book early enough to facilitate close fetal monitoring throughout pregnancy.

Keywords: sickle cell disease, antenatal care, maternal outcome, neonatal outcome

INTRODUCTION

SCD is a group of hemoglobin disorders that result from the inheritance of the sickle cell β-globin gene. It can occur in the homozygous form as sickle cell anemia (SS) or in double heterozygous form with other types of abnormal Hb such as the Sc and Sβthal variants[1].It is a common disease of tropical origin affecting countries within the Mediterranean, Asia and Sub-Saharan Africa to which Nigeria belongs to[2]. The inheritance pattern is autosomal recessive and as such both parents must have the sickle cell gene. The mainstay of treatment has

often been prevention and appropriate management of any of the crises in individuals suffering from SCD with some advances in gene therapy. Nowadays, with recent advances and improved healthcare, the life expectancy of people with SCD has improved and many more women are reaching reproductive age. A pregnant woman with SCD is at risk of developing sickle cell crises.

During pregnancy, SCD can become more severe and pain episodes occur more frequently. This tends to pose a great challenge to their care because of the increased risk of pregnancy complications such as toxemia of pregnancy, postpartum haemorrhage, infections, prematurity, intrauterine growth, restriction (IUGR), low birth weight, abortions, stillbirth, urinary tract infections, stroke, thromboembolic episodes, heart failure, neonatal and maternal mortality[3]. Anaemia often occurs as a result of the deoxygenation of the sickle cells which become sickled and are then removed from the body by the reticuloendothelial system with a subsequent red blood cell life span reduction to 17 days and then a resultant chronic compensated anaemia.[4,5,6] There is also associated high perinatal mortality. Earlier studies on pregnancy outcomes in sickle cell patients revealed universal adverse outcome but with recent medical advances and care, the outcome seems to have greatly improved [4,7].

Maternal morbidity is increased in SCD due to infections (UTIs), cerebrovascular accident and sickle cell crisis. Maternal mortality is increased by as much as 25% due to pulmonary infarction, acute chest syndrome, congestive heart failure and embolism[3].The frequency of crises increases significantly especially in 3rd trimester as a result of increased oxygen consumption, blood viscosity & red cell mass. In addition, SCD constitutes a financial stress in view of the repeated hospital admissions, repeated transfusion and frequent pain medications given to these patients. While some studies have revealed improved outcomes for pregnant women with SCD as well as the majority of them being able to achieve a successful live birth, pregnancy with SCD is still associated with an increased incidence of morbidity and mortality[7].

In a study done in Enugu state, a state in the same geographical zone as the centre, the prevalence rate of SCD in pregnancy was 0.01% whereas that in Ebonyi state was 0.69%[8,9]. The study done in Port Harcourt (SS zone) had a prevalence rate of 0.14% in a ten-year study and 0.2% in a five-year study[10,11].

In West Africa, increasing rates of pregnant women with SCD are being seen. A study done in Ghana had a prevalence rate of 1.42% over a two year period[12]. Similar values were also seen in India where a 4 year study period revealed a prevalence of 1.2%[13].Considering the increasing prevalence in various parts of the world, it has become obvious that more pregnant women with SCD are being encountered now in medical practice. In the first half of 20th century, women with SCD barely survived to reproductive age. Early medical experience with SCD and pregnancy was a cause for concern. The first successful pregnancy was in 1931and with the major review that occurred a decade later, a 50% fetal loss was obtained.[11] Maternal mortality rates as high as 11.5% were reported from West Africa and from black American groups[11]. There has been a number of varying reports on maternal and fetal outcome in Nigeria as well as Africa.[8,9,10,11,12,14,15]

This study was undertaken to assess the current pregnancy outcomes among women with SCD in our centre as there has been no such previous study in this environment.

Objectives

The study sought to determine the maternal and fetal outcomes in pregnant women with SCD attending antenatal clinic at Nnamdi Azikiwe University Teaching Hospital, Nnewi , Anambra State of Nigeria

Materials and methods

Study Site: The study site was Nnamdi Azikiwe University Teaching Hospital (NAUTH) Nnewi, Anambra state Nigeria. NAUTH is the only federal government owned tertiary hospital in the state. It offers primary, secondary and tertiary services in the state. Nnewi is the second most populated town after Onitsha in Anambra state and is also located very close to Onitsha and Awka which are two densely populated areas in the State. The hospital in addition also serves as a referral centre for neighboring states.

Study Population: All pregnant women with SCD who had accessed care from NAUTH, Nnewi from January 1st 2011 to December 31st 2020.

Inclusion Criteria:
Pregnant women who had been previously diagnosed with SCD and accessed antenatal care (ANC) as well as had their deliveries at NAUTH from January 1st 2011 to December 31st 2020.

Exclusion Criteria:
Pregnant women who accessed ANC at the hospital but did not deliver in the hospital as well as those who had their delivery in the hospital but had accessed ANC care elsewhere

Sample size determination:
The sample size was determined using the Cochrane formula[16]
$N = Z^2pq/d^2$ with a p-value of 0.01 (proportion of SCD patients accessing antenatal care from a previous study)[8]

$$N = \frac{(2.96)^2 \times 0.01 \times 0.99}{(0.05)^2}$$
$$= 15$$

Sampling Technique: A non-random sampling technique was employed as all case folders that met the inclusion criteria within the study period were reviewed.

Data Collection
With permission from the records department, obstetrics records of women with sickle cell disease were identified, studied and required data retrieved with a checklist that had been designed to record patient's profile. This profile included age, highest educational qualification, occupation, marital status, parity, gestational age at booking, hemoglobin at booking,, transfusion history, obstetric and non-obstetric complications in all trimesters, mode and outcome of delivery, neonatal complications. The diagnosis of SCD was made using Hemoglobin electrophoresis machine.

Working Definition
Sickle Cell Disease (SCD) is the presence of homozygous HbSS on hemoglobin electrophoresis
Emergency LSCS is the surgical procedure performed via a horizontal incision on the lower part of the abdomen and usually done when there is immediate concern for the health of the mother and /or baby.
Anemia was defined as hemoglobin of less than 10g/dl
Vasoocclusive crisis was defined as a painful episode with subjective complaint of pain and exclusion of other causes of pain based on related symptoms.

Malaria was defined as presence of malaria parasites in thick or thin peripheral blood films in the laboratory. Tertiary Centre refers to a healthcare facility that offers specialized care to those referred from secondary or primary care centres which are unable to offer such specialized services.

Data Analysis:

All available data were analyzed using SPSS 25 with results presented in form of frequency tables. Descriptive statistics in the form of the frequency and percentages were calculated.

Ethical Considerations:

Approval for the study was obtained from the Nnamdi Azikiwe University Teaching Hospital Research and Ethics Committee.(date of approval 26th June 2021).

Results:

Out of 71, 737 women who accessed antenatal care during the period of study, 18 were diagnosed of SCD, giving a prevalence rate of 0.03%. The mean age of the respondents was 28.3 ±5.6years while the mean gestational age at booking was 26±9.5wks. Majority of them (77.8%) were married while 38.5% of them were nulliparous. More than half of them (55.6%) registered in their 3rd trimester. About 44% of the women had tertiary education. The booking haemoglobin was 6.5±3.5g/dl. All the women had the HbSS variant. The commonest complication was anemia (100%) with 72.2% of them being transfused. Majority of them (77.8%) had vaso-occlusive crisis while 88.9% of them delivered by caesarean section.

Half of the women (50%) had pre-term delivery while 50% of the newborn had fetal distress. The recorded neonatal death was 11% while stillbirth recorded was 5.6%. There were 33% newborns with low birth weight.

Tables:

Table 1: SOCIO DEMOGRAPHIC CHARACTERISTICS OF THE RESPONDENTS

VARIABLE	FREQUENCY	PERCENTAGE
AGE(years)		
21-25	7	38.9
26-30	6	33.3
31-35	2	11.1
36-40	3	16.7
TOTAL	18	100.0
MEAN	28.3±5.6 years	
HIGHEST LEVEL OF EDUCATION		
JSCE	2	11.1
SSCE	5	27.8
B.Ed	2	11.1
B.Sc	6	33.3
MISSING	3	16.7

TOTAL	18	100.0
OCCUPATION		
STUDENT	1	5.6
TEACHER	2	11.0
TRADER	7	38.9
CIVIL SERVANT	5	27.8
MISSING	3	16.7
TOTAL	18	100.0
MARITAL STATUS		
SINGLE	4	22.2
MARRIED	14	77.8
TOTAL	18	100.0
PARITY		
P_0	7	38.9
P_1	6	33.3
P_3	2	11.1
MISSING	3	16.7
TOTAL	18	100.0
GESTATIONAL AGE AT BOOKING		
(0 – 13WKS)	2	11.1
(14 – 26WKS)	6	33.3
(27 – 40wks)	10	55.6
TOTAL	18	100.0
MEAN	26 ± 9.5wks	
HAEMOGLOBIN AT BOOKING(g/dl)		
5.0	4	22.2
5.2	1	5.6
6.0	4	22.2
7.0	3	16.7
8.0	3	16.7
9.0	1	5.6
MISSING	2	11.1
TOTAL	16	88.9
MEAN HAEMOGLOBIN	6.5 ± 3.5g/dl	

TABLE 2: PREVALENCE OF SICKLE CELL DISEASE

VARIABLES	FREQUENCY	PERCENTAGE (%)
THOSE WITH SCD	18	0.03
THOSE WITHOUT SCD	71719	99.97
TOTAL	71737	
RECEIVED PRECONCEPTION CARE		
YES	0	0
NO	16	88.9
Missing	2	11.1
	18	100

TABLE 3: TABLE SHOWING THE VARIOUS TYPES OF SCD SEEN AMONG THE RESPONDENTS

VARIABLE	FREQUENCY	PERCENTAGE (%)
Hb SS VARIANT	18	100
Hb SC VARIANT	0	0
Hβ THAL VARIANT	0	0
TOTAL	18	

TABLE 4: COMPLICATIONS IN WOMEN WITH SICKLE CELL DISEASE ACCESSING ANC AT NAUTH WITHIN THE TEN (10) YEARS OF STUDY

VARIABLE	FREQUENCY	PERCENTAGE (%)
PRE ECLAMPSIA		
YES	3	16.7
NO	13	72.2
MISSING	2	11.1
	18	100
MALARIA		
YES	4	22.2
NO	14	77.8
	18	100
TRANSFUSION HISTORY		
YES	13	72.2

NO	3	16.7
MISSING	2	11.1
TOTAL	18	100
ANAEMIA		
YES	18	100.0
NO	-	0.0
TOTAL	18	100.0
VASO-OCCLUSIVE CRISIS		
YES	14	77.8
NO	2	11.1
MISSING	2	11.1
TOTAL	18	100
INTRAUTERINE FETAL DEATH		
YES	2	11.1
NO	14	77.8
MISSING	2	11.1
TOTAL	18	100
RESPIRATORY TRACT INFECTION		
YES	3	16.7
NO	12	66.7
MISSING	3	16.7
TOTAL	18	100
EMERGENCY CESAREAN SECTION		
YES	16	88.9
NO	2	11.1
TOTAL	18	100.0
WOUND INFECTION		
YES	2	11.1
NO	16	88.9
TOTAL	18	100.0
MATERNAL DEATH		
YES	1	5.6
NO	17	94.4
TOTAL	18	100.0

TABLE 5: NEONATAL OUTCOME AMONG THE RESPONDENTS WITH SICKLE CELL DISEASE ACCESSING ANC AT NAUTH WITHIN THE TEN (10) YEARS OF STUDY

VARIABLE	FREQUENCY	PERCENTAGE (%)
INTRA UTERINE GROWTH RESTRICTION		
YES	3	16.7
NO	13	72.2
MISSING	2	11.1
TOTALRESPONDENTS	16	88.9
PRE TERM DELIVERY		
YES	9	50.0
NO	7	38.9
MISSING	2	11.1
TOTALRESPONDENTS	18	100
FETAL DISTRESS		
YES	9	50.0
NO	7	38.9
MISSING	2	11.1
TOTALRESPONDENTS	16	88.9
CEPHALO PELVIC DISPROPORTION		
YES	1	5.6
NO	15	83.3
MISSING	2	11.1
TOTAL RESPONDENTS	18	100
NEONATAL DEATH		
YES	2	11.1
NO	15	83.3
MISSING	1	5.6
TOTAL RESPONDENTS	18	100
STILL BIRTH		
YES	1	5.6

NO	16	88.9
MISSING	1	5.6
TOTAL RESPONDENTS	18	100
BIRTH WEIGHT		
LBW(<2.5KG)	6	33.30
NBW (2.5KG AND ABOVE)	10	55.80
MISSING	2	11.10
TOTAL RESPONDENTS	18	100

Discussion

The prevalence of sickle cell disease in pregnancy in this study is 0.03%. This appears to be similar to the rate obtained at Enugu (0.01%) in Enugu state, a state in the same geographical zone as our centre. A higher value of 0.2% was obtained at Port Harcourt in South-South region of Nigeria[11]. Considering other West African countries, Ghana had a prevalence rate of 1.4% whereas 0.09% was obtained in Tanzania of East Africa.[12,17]

This lower value may have been as a result of the rule in this state where intending couples must present their genotype results before marriage institutions that end up discouraging those with the trait from getting married to each other. Studies done in other continents revealed relatively higher prevalence rates of 1.1% , 1.2% and 0.6% as seen in Saudi Arabia, India and USA respectively.[13,18,19.]

All the SCD cases seen in this study were of the HbSS variant. This is contrary to the findings in other centres where there were also other variants.[9,20,21]. This could be attributed to the fact that this centre uses hemoglobin electrophoresis machine for diagnosis instead of High Performance Liquid Chromatography.

Majority of the women (88.9%) in this study booked in their 2nd or 3rd trimester. Only 11% of the women booked in first trimester. The mean gestational age at booking was 26±9.5wks with only 2 women booking in 1st trimester. This is even later than the mean gestational age of booking recorded by Ugboma & George (16.6±3.3) in Port Harcourt and Kahansim ML et al (19.3±7.7) in Jos.[11,21] Booking early for antenatal care enables the health provider to monitor as well as identify risk factors related to poor maternal and fetal outcomes. Managing a pregnant woman with SCD requires close monitoring as anemia can worsen very quickly[6]. Initiating appropriate medical interventions will then decrease the risks for both maternal and fetal morbidity and mortality.[22,23] Other earlier studies in Africa had also recorded late booking in these women and majority of the women booking late in third trimester.[24,23,11] The commonest maternal complication in this study was anemia. Most of these women presenting late came in with severe anemia as shown by the mean booking Hb of 6.5±3.5g/dl. This is similar to the finding in other centers where anemia was present in many of the women. The value for anemia obtained in this study is higher than that obtained in Jos (62.9%) but similar to the study finding of 95.3% in Benin, Edo state.[21,25] . A study by Ogbonna et al in Rivers State recorded anemia of 94.2%.[26] Kahtani et al in Saudi Arabia found 86.2% of the women had anemia.[18]

Anaemia is one of the major complications of SCD and could be caused by hemolysis or red blood cell trapping in the spleen[4]. Anaemia in pregnancy has been found to be associated with increased risk of preterm premature rupture of membranes, spontaneous preterm labour, preterm delivery, intrauterine growth retardation as well as low birth weight babies.[4,5] The anaemia resulted in all the women in this study being transfused prior to delivery. This high rate of antenatal transfusion (72.2%) has serious implications in view of the risk of infection transmission and alloimmunization. Anemia was closely followed by vaso-occlusive crisis in form of bone pain with a frequency of 77.8%. This is much higher than that obtained in Port Hacourt (50%) and Jos (51.4%), Benin(23.8%) and Ibadan (7.3%) [11,21,25,27]Similar studies in Africa and outside Africa also recorded lower values than that discovered in our study centre – Benin Republic (19.5%), Cameroon (50%), USA (50%)[24,19.]and Baharain (65.3%).[28,24,19,29] .There was a low incidence of malaria in pregnancy

(22.2%) observed in this study. This is similar to the finding by Kahansim ML et al in Jos (25.7%) as well as that by Odum et al in Lagos (22.4%) but contrary to that by Ugboma in Port Harcourt (80%).[21,30,11] One would have expected a higher incidence of malaria in this study considering the fact that the study area is an area of high malaria transmission and SCD patients are more susceptible to malaria and other infections partly due to splenic dysfunction whereas the heterozygotes (Hb AS) are more protected against severe and complicated malaria.[31]

The incidence of pre-eclampsia in this study was 16.7%. This is quite lower than the 28.9% obtained in Jos.[21] While Ugboma in Port Harcourt recorded maternal deaths from pre-eclampsia, some other studies had no significant increase in pre-eclampsia amongst pregnant women with SCD.[11, 21, 29]. More studies may be needed in this area to know if pre-eclampsia has any relationship with SCD.

The incidence of intrauterine fetal death (IUFD) in this study was 11%. This is less than the 20% obtained in both North Central and South-South region of Nigeria but comparable to the 7.89% obtained in India.[21, 11, 32]. In this study, respiratory tract infection was found in 16.7% of the women and is similar to the 20% obtained in Jos.[21] Identification and treatment of underlying infections is key to reducing respiratory tract infections. Pneumococcal vaccines could be given where available. Wound Infection was the least maternal complication (11.1%) observed in this study.

The commonest mode of delivery was by caesarean section (88.9%) and all of them were emergency caesarean section(C/S). This centre had a higher CS rate than that obtained in Port Harcourt (60%) and Jos (26.3%).[11, 21] The caesarean section rates observed in Ghana (50%) and USA (42.4%) were far lower than that obtained in our centre.[12, 2, 19] Also, it was observed in similar studies outside Nigeria that the commonest mode of delivery was by vaginal delivery as recorded in Saudi Arabia (63.5%), Baharain (69.8%) and India (60.5%) respectively.[33, 32, 29] No record of instrumental delivery or epidural analgesia was performed among the women in this study. This is contrary to the study done in Benin by Omo-Aghoja and Okonofua where the CS rate was 20% whereas assisted vaginal delivery rate was 40%.[25] In view of economic cost of C/S with its morbidities and possible mortality, there is need for vaginal delivery especially assisted vaginal delivery with possible epidural analgesia to minimize pain. A similar study in South East Nigeria as well as India reported a lower caesarean section rate of 21.6% and 39.5% respectively.[9,33]

Fetal distress and pre-term delivery were the commonest fetal complications seen in this study with each having an incidence of 50%. This is much higher than the rate obtained in Jos where a 6.5% rate of fetal distress was recorded.[21] This brings to the fore the need for implementation of fetal surveillance in the third trimester. This study revealed 16.7% intrauterine growth restriction (IUGR) which is much lower than that recorded by Kahansim et al, in Jos(45.7%), Saudi Arabia(19.2%) and Rajauria et al in India(57.89).[21, 32, 33] More than half (55.8%) of the neonates in this study had normal birth weight of 2.5kg or more. This is similar to the finding in Port Harcourt where 50% of the neonates had normal birth weight.[11] However, while Olugbenga et al in Osun State and Nana et al in Ghana recorded higher normal birth weight babies of 87.8% and 88.9% respectively, Desai et al in India recorded 70.2% low-birth weight babies.[20, 12, 13] This highlights the need to monitor these women with serial sonograms for proper assessment of fetal growth. While the study recorded 2 neonatal deaths (11.1%) with one stillbirth (5.6%), a similar study in Abakiliki in the same South Eastern Zone recorded 20.4% stillbirth, higher than the figure obtained in the study centre[9]. Other similar studies in Port Harcourt and India recorded 20% and 7.9% stillbirth respectively.[11,33] The maternal death recorded in this study was 1 (5.6%) whereas Nwafor et al in their study at Abakiliki recorded no maternal death. Ugboma and George in South South Nigeria observed 20% maternal loss which is higher than the figure noted in this centre.

Conclusion

All the women did not receive preconception care and most did not commence antenatal care early. Women with SCD need to be educated on the need for preconception care to ensure optimization of health prior to conception. It is also important that pregnancy and conception discussions are held with women of child-bearing age with SCD during their periodic medical review/examinations.

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Conflicts of Interest
None

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