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PREGNANCY OUTCOME IN BOOKED NIGERIAN SICKLE CELL DISEASE PATIENTS

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SUMMARY

Background: As sickle cell disease patients now survive to reproductive age, their pregnancies and outcome remain a concern to obstetricians in view of the higher risk for complications.

Objective: To determine pregnancy outcome in sickle cell disease patients who had antenatal care and compare this with outcome in age and parity matched non sickle cell disease controls that had antenatal care.

Setting: The study was conducted at the Obstetrics and Gynaecology Department of the University of Ilorin Teaching Hospital [UITH], Ilorin, Kwara State, Nigeria.

Methodology: A five year retrospective case control study involving all sickle cell disease women who had antenatal care and subsequently delivered at the study site from 1st January 2007 to 31st December 2011 and age and parity matched non sickle cell pregnant women who also had antenatal care at the study site as controls. Data was collected from the individual patient case files and analyzed using SPSS version 18.

Results: The incidence of sickle cell disease [SCD] was 0.51% with mean age 28.2±2.41 years, mean parity 2.1±0.62, mean height 161±0.58cm and mean weight 58.2±3.12kg. Educational attainment was higher among SCD [subjects] compared to controls [P=0.044]. Subjects had higher percentages of all complications in pregnancy and delivery than controls; of these, maternal anemia, miscarriage and forceps delivery were

statistically significant while urinary tract infections, malaria in pregnancy, preterm delivery, caesarean delivery and postpartum haemorrhage were not significant. Neonatal outcomes were poorer among subjects but these were not statistically significant. The perinatal mortality rates were 178.6/1000 for subjects and 107.1/1000 among controls. Maternal mortality was 5.4% among subjects and none among controls.

Conclusion: Pregnancy outcome was poorer in sickle cell disease women compared to non sickle cell controls despite antenatal care; however, majority of these were not statistically significant. Maternal mortality remained relatively higher despite antenatal care in SCD women similar to other reports from low income countries.

Keywords: Sickle cell disease, Pregnancy, Outcome, Antenatal care.

INTRODUCTION

Sickle cell disease [SCD] is the commonest inherited disorder worldwide; it is most prevalent in individuals of African descent, Caribbean, Middle East, India and the Mediterranean¹. Pregnancy SCD women remains a concern to obstetricians especially as 25% of people of African stock carry the sickle cell gene and about 2-3% suffers from sickle cell anaemia². Variants of the disease include Hb SS, Hb SC, and Hb CC while the heterozygote form Hb AS is called sickle cell trait³.

There has been marked improvement in the management of women with sickle cell disease in the past decades, with more women reaching adulthood and reproductive age; fertility has been shown to be normal in SCD women⁴ but women with SCD who become pregnant are likely to suffer aggravated morbidity and mortality⁵. International evidence on pregnancy outcome in SCD has been inconsistent with low and medium countries reporting increased maternal and perinatal mortality^{6,7} while reports from high income countries showed more favourable foetal outcomes without appreciable risk for maternal mortality^{8,9}. Although there is scanty literature on SCD in pregnancy from Sub Saharan Africa, available ones suggest poor pregnancy outcome with maternal mortality ranging from 1.8-9.0%^{10,11}. Therefore, there is the need for more studies on pregnancy outcome in this category of women to increase the body of evidence. This study aimed at determination of the pregnancy outcome in sickle cell disease patients who had antenatal care and compare this with age and parity matched normal haemoglobin pregnant women who also had antenatal care.

MATERIALS AND METHODS

Study design: A retrospective case control study.

Study setting: The obstetrics and gynaecology department of the University of Ilorin Teaching Hospital, Ilorin, Nigeria.

Study population: Subjects were all 56 sickle cell disease patients who had antenatal care and delivered at the study site between 1st January 2007 and 31st December 2011 while controls were 112 [ratio 1:2 of subjects] age and parity matched non sickle cell disease patients who had antenatal care and delivered over the same period.

Inclusion criteria

Subjects were Sickle cell disease pregnant women who had modern antenatal care and had a record of pregnancy outcome at the study centre over the study period.

Controls were age and parity matched normal haemoglobin genotype [genotype AA] pregnant women who had modern antenatal

care and a record of pregnancy outcome at the study centre over the study period.

Exclusion criteria

Sickle cell disease women, who did not have antenatal care, had chronic medical conditions such as hypertension and diabetes mellitus or did not have a record of the pregnancy outcome were excluded from the study.

Sample size determination

The study was a total population study of all SCD patients managed over the study period. Controls were age and parity matched non SCD patients selected by random sampling.

Procedure/ Data collection

The case files of all Sickle cell disease patients managed during the study were retrieved and each evaluated to ascertain eligibility for the study. All relevant information for the study was retrieved from the case notes of these eligible cases. Thereafter, case files of non SCD controls were also retrieved and data extracted from them.

The sickle cell disease patients were managed in the same antenatal clinic as the rest of our pregnant patients, since there was no special obstetric clinic for such patients. They had routine antenatal investigations like Packed Cell Volume [PCV], Venereal Disease Research Laboratory Test [VDRL], Blood group and Rhesus typing and urinalysis done. At each antenatal clinic, a history of complaints were obtained, physical examination was performed followed by PCV estimation. Three doses of prophylactic antimalarial using Sulfadoxine/ Pyrimethamine was given after quickening at four weeks apart before 36 weeks. Folic acid 5mg daily was administered and blood transfusion with packed red blood cells was employed to correct anaemia as necessary. Serial ultrasonography every four weeks was used in assessing fetal growth; this was commenced at 24 weeks gestation to detect intrauterine growth restriction [IUGR] and assist in appropriate timing of delivery to reduce perinatal morbidity and mortality¹. Timing and mode of delivery were based on obstetric factors and other specific sickle cell crises were managed accordingly.

Labour was managed actively with the aid of partograph in all cases; in addition, subjects had measures to prevent intrapartum crisis including intravenous fluid to prevent dehydration, oxygen to prevent hypoxia, adequate analgesia with parenteral opioid, intravenous antibiotics and shortening of the second stage by instrumental vaginal delivery except when refused by the patient. The third stage of labour was managed actively with administration of 10IU of Oxytocin within one minute of the delivery of the baby followed by delivery of the placenta by controlled cord traction. Each parturient was observed at the delivery room for two hours before transfer out to the postnatal ward. Elective caesarean delivery was employed in patients with contraindication to vaginal delivery. Adequate monitoring and treatment of patients in labour was continued during the puerperium. Early ambulation to avoid embolic phenomena in the puerperium and close observation for infections were done postpartum. All parturient had counseling on contraception before discharge from the hospital.

Data analysis

Maternal and neonatal data were collected and analyzed using the SPSS version 18 statistical package. Results were expressed in tables; p-value and chi square were calculated as appropriate; statistical significance was set as p value <0.05.

Ethical issues/ Conflict of interest

Patient confidentiality was maintained during the study and it was conducted in accordance with institutional ethical standards. Personal identifying parameters like individual names of patients were not used; data collection sheets including electronic storage form were restricted only to researchers and kept away from where nonparticipants in the research can access them. There was no conflict of interest in the conduct of the study.

RESULTS

During the 5-year study period [1st January 2007-31st December, 2011], there were a total of

11,823 deliveries out of which 60 were SCD patients. Thus, the incidence of sickle cell disease in this centre was 0.51%. However, only 56 of the 60 SCD patients satisfied the inclusion criteria and were included in the study. From table 1, the age range of SCD patients was 19-38years [mean 28.2±2.41] while the parity ranged from 1-4 [mean 2.1±0.62]; this was the same for the controls by study design. The mean height for subjects was 161±0.58cm and 160.6±0.43cm for controls.

Of the sickle cell disease patients, 29[51.8%] were HbSS, 26[46.4%] were HbSC and 1[1.8%] was HbCC. A comparison of the educational status showed that subjects attained statistically higher education level than controls with χ^2 6.25 and p value 0.044 as shown in table 2.

Table 3 showed that subjects had higher occurrence of all complications during pregnancy and delivery. Of these, occurrence of severe anaemia [p=0.0042], mild to moderate anaemia [p=0.0000], miscarriages [p=0.0003] and forceps delivery [p=0.0042] were statistically significant. Others like malaria in pregnancy, urinary tract infections, preterm delivery, postpartum haemorrhage, vacuum delivery and puerperal sepsis were higher in SCD patients but were not statistically significant. The caesarean section rates were 14.3% among subjects and 12.5% among controls with p=0.7449. There were three maternal deaths among the 56 subjects giving a 5.4% maternal mortality; there were no maternal deaths among controls.

Table 4 showed that neonatal outcome was poorer among SCD patients with higher occurrences of low birth weight babies [p=0.5124], Apgar scores <7 [p=1.325], stillbirth [p=0.582], fewer cases of Apgar scores >7 [p=0.703] and fewer live babies at discharge [0.111]; however, these were not statistically significant. The perinatal mortalities were 178.6 per 1000 among SCD mothers and 107.1 per 1000 among controls.

Table 1: Maternal characteristics of sickle cell disease (SCD) patients and controls

	SCD		CONTROL	
	Mean	Range	Mean	Range
Age (yrs)	28.2±2.41	19 – 38	28.2±2.41	19 – 38
Height (cm)	161±0.58	151 – 176	160.6±0.43	146 – 172
Weight (kg)	58.2±3.12	43 – 76	63.5±4.18	42 – 79
Parity	2.1±0.62	1-4	2.1±0.62	1-4

Table 2: Educational status among sickle cell disease patients and control

	HbSS	HbSC	HbCC	SCD	Control
	n(%)	n(%)	n(%)	n(%)	n(%)
Educational Status					
Primary	6 (20.7)	2(7.7)	0	8(14.3)	24(21.4)
Secondary	4(13.8)	8(30.8)	0	12(21.4)	44(39.3)
Tertiary	19(65.5)	16(61.5)	1(100)	36(64.3)	44(39.3)

Chi square value (χ^2)= 6.25, df=2, p=0.044.

Table 3: Complications of pregnancy and delivery among subjects and controls.

Complication	HbSS	HbSC	HbCC	SCD	CONTROL	P value
	n(%)	n(%)	n(%)	n(%)	n(%)	
Severe Anaemia (PCV d 18%)	7(12.5)	-	-	7(12.5)	2(1.8)	0.0042
Mild - Moderate Anaemia 18% < PCV d 30%	21(37.5)	24(42.9)	1(1.8)	46(82.2)	30(26.8)	0.0000
Miscarriage	7(12.5)	4(7.1)	1(1.8)	12(21.4)	4(3.6)	0.0003
Malaria in Preg.	7(12.5)	4(7.1)	0	11(19.6)	12(10.7)	0.1153
UTI	3(5.3)	4(7.1)	1(1.8)	8(14.3)	6(5.4)	0.0512
Preterm Delivery	3(5.3)	1(1.8)	0	4(7.1)	5(4.5)	0.4818
Postpartum Hemorrhage	3(5.3)	2(3.6)	0	5(8.9)	5(4.5)	0.2580
Bone pain Crisis	9(16.1)	4(7.1)	0	13(23.2)	0	NA
Acute sequestration Crisis	2(3.6)	0	0	2(3.6)	0	NA
Pseudotoxaemia	0	1(1.8)	0	1(1.8)	0	NA
Puerperal Sepsis	1(1.8)	0	0	1(1.8)	2(1.8)	1.0000
Mode of delivery						
Spontaneous vaginal	10(17.9)	13(23.2)	0	23(41.1)	88(78.6)	0.0000
Forceps	3(5.4)	4(7.1)	0	7(12.5)	2(1.8)	0.0042
Vacuum	4(7.1)	2(3.6)	0	6(10.7)	4(3.6)	0.0688
Caesarean delivery	5(8.9)	3(5.4)	0	8(14.3)	14(12.5)	0.7449

There were three maternal deaths (5.3%) among SCD patients and none among the controls.

Table 4: Neonatal outcome among subjects and control

Neonatal outcome	Subjects n(%)	Control n(%)	P value
Birth weight (g)			
<2500	6(10.7)	7(6.2)	0.5124
2500-4000	49(87.5)	103(92.0)	0.593
Not recorded	1(1.8)	2(1.8)	1.000
Apgar Score			
< 7	6(10.7)	9(8.0)	1.325
≥7	28(50.0)	87(77.7)	0.703
Babies alive at discharge	46(82.1)	100(89.3)	0.111
Still Birth	10(17.9)	12(10.7)	0.582
Child take home rate per 1000 deliveries	821.4	892.9	
Perinatal mortality rate per 1000 deliveries	178.6	107.1	

DISCUSSION

From the study, the incidence of SCD in pregnancy was 0.51% and SCD did not deter the educational capability of the subjects as they were better educated than controls. However, SCD patients showed higher rates of all the complications in pregnancy, delivery and postpartum; of these, anaemia in pregnancy, miscarriage and forceps delivery were statistically significant while urinary tract and malaria infections in pregnancy, preterm delivery, caesarean delivery and postpartum haemorrhage were not. All parameters for neonatal outcome were poorer in babies of SCD women compared to controls in terms of low birth weight, low Apgar scores at birth and stillbirths. Maternal mortality was 5.4% among SCD compared to none among controls while perinatal mortality rates were 178.6 per 1000 among SCD babies and 107.1 per 1000 among controls.

These adverse outcomes were because in pregnancy there is an added strain on the already stressed physiological reserve of SCD women; the dilution anaemia may worsen their

anaemia, the reduced immunity increases their predisposition to malaria and other infections while the respiratory changes may result in hypoxaemia predisposing to vaso-occlusive crises. Thus, their pregnancies are associated with increased incidence of maternal and foetal morbidity and mortality mainly in late pregnancy, delivery and postpartum⁴. Reported common complications in them include anaemia, vaso-occlusive crises, urinary tract infections, miscarriage, intrauterine growth restriction, intrauterine foetal death and perinatal death from hypoxemia and placenta thrombosis; maternal death can also occur⁴.

A comparison of this study with descriptive studies from Nigeria showed its results were more favourable than those of these other studies. Ogedengbe *et al*¹³ in Lagos, Nigeria reported a maternal mortality rate of 129 per 1000 in Hb SS and 111 per 1000 in Hb SC pregnant women with a perinatal mortality of 233 per 1000 in HbSS patients; these were poorer than results from this study. In addition, Ocheni *et al*¹⁴ in Enugu, Nigeria reported higher maternal and perinatal mortalities while Odum

et al¹⁵ in Lagos reported a caesarean delivery rate of 43.2% compared to 14.3% in this study. The difference may be because of the lack of antenatal care in participants in these studies compared to subjects in this study who had modern antenatal care. These showed the positive improvement of antenatal care on pregnancy outcome in sickle cell disease patients.

Compared to comparative studies from other low resource countries, Addai et al¹⁶ in Ghana reported a statistical significance in the occurrence of low birth weight babies of haemoglobinopathy women compared to babies of normal haemoglobin mothers. Muganyizi et al⁵ in Tanzania from a cohort study reported a mean age at delivery of 24.0 ± 5.5 years at delivery among SCD patients which was comparable with the result in this study. However, they recorded lower fifth minute Apgar scores, higher stillbirths and an excessive risk for maternal mortality among SCD women compared to controls. These results were similar to the results from this study. They showed that antenatal care resulted in an improvement in the pregnancy outcome but the outcomes were poorer than those of normal haemoglobin genotype controls.

The beneficial effect of antenatal care among SCD women as demonstrated in this study was also documented by Rahimy et al¹⁰ in Cotonou, Republic of Benin who reported a maternal mortality of 1.8% which was lower than the result from this study. This further exemplifies the role of antenatal care in improving pregnancy outcome in SCD women.

Studies from developed countries showed higher caesarean delivery rates of 48% from France¹⁷ and 24% from United Kingdom [UK]¹⁸, lower maternal mortality of 1 in 68 participants in France¹⁷ but higher preterm delivery rates of 12.6%¹⁹ and 15.3%²⁰ from Saudi Arabia and 24%¹⁸ from UK coupled with lower perinatal mortality rates of 78.2 per 1000¹⁹ and 77.2 per 1000 deliveries²⁰ respectively. These has been partly attributed to the poor or nonexistent preconception care facilities in most countries in sub Saharan Africa²¹ unlike in

developed countries where well established preconception care and multidisciplinary specialist care in pregnancy are the rule. The participants in this study did not have the benefit of these services.

In conclusion, this study showed worse pregnancy outcomes in sickle cell disease patients compared to normal haemoglobin genotype women although majority of the parameters were not statistically significant.

We recommend that preconception care, collaborative multidisciplinary specialist care during pregnancy for sickle cell disease patients and improvement in support facilities for maternal and neonatal care in low income countries should be pursued.

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