Maternal–fetal prognosis of major sickle cell disease in pregnant women at a university hospital in a low–middle-income country

M B Dehi,[1,2] MD; **V A Angoi**,[1,2] MD; **C J Nsahlai**,[3,4] MD; **J Konan**,[1,2] MD; **K H Yeo**,[1,2] MD; **K Nguessan**,[1,2] MD; **S Boni**,[1,2] MD

[1]*Department of Gynecology and Obstetrics, Faculty of Medicine, University Hospital of Cocody and Université Félix Houphouët-Boigny, Abidjan, Côte d'Ivoire*
[2]*Department of Gynaecology and Obstetrics, Faculty of Medicine and Biomedical Sciences, University of Yaoundé I, Yaoundé, Cameroon*

Corresponding author: *M B Dehi (bostondehimian@gmail.com)*

Background. Sickle cell disease (SCD) is a common genetic disease in sub-Saharan Africa. The condition affects more than 7% of pregnant women worldwide, with complications including severe infections, vital organ damage, respiratory problems, bone marrow suppression and a high rate of maternal or fetal death.
Objective. To evaluate the prevalence, management and maternal–fetal prognosis of pregnancies in women with major SCD.
Methods. A prospective and descriptive study was conducted in the gynaecology and obstetrics department of the university hospital of Cocody, Abidjan, in Cote d'Ivoire over two years. Records of all pregnant women with homozygous SCD who had given birth or were followed up in the unit were reviewed. Women with an HbAA or HbAS genotype or any other normal electrophoretic profile or history of renal disease were excluded.
Results. Out of 14 819 delivery records, 118 (0.8%) women presented with an abnormal haemoglobin profile; 75 were classified as having major SCD (0.51%). The majority of women (82.7%) were younger than 35 and 68% worked in the informal sector. About a third (37.3%) had no formal education. Heterozygous HbSC profiles were the predominant (88%) presenting form; HbSS genotypes were found in 12% of cases. The occurrence of complications during pregnancy was significant (44%).
Conclusion. SCD in pregnancy is associated with an increased risk of maternal and fetal complications. Accurate and rigorous monitoring of these pregnancies by a multidisciplinary team, together with improved patient awareness and education, is required to reduce maternal and fetal health risks.
Keywords: Sickle cell disease, genotype, maternal and fetal prognosis, pregnancy, multidisciplinary management

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Haemoglobin (Hb) is responsible for oxygen transport in the blood and is composed of one haem molecule and four globin chains, with a genetically controlled chemical structure. The normal adult haemoglobin (HbA) molecule consists of one pair of α chains and one pair of β chains.[1] Globin, the protein fraction of haemoglobin, is affected by more than 1 500 mutations that modify its structure, function and expression.[1,2] Sickle cell disease (SCD), caused by a mutation in the gene that codes for β-globin, is the most common inherited genetic disease in sub-Saharan Africa, South and Central America, the Middle East, the Indian subcontinent and Mediterranean countries.[3,4] It results from a modification of the primary structure of globin. The predominant genotypes of SCD include HbSS, HbSC, HbSβ+-thalassemia and HbSβ0-thalassemia. Infrequent forms include HbSD and HbSE.[4] These structural variations affect the oxygen delivery functions of the molecule, its stability and resistance to oxidation.[4] Affecting approximately 5% of the world's population and more than 7% of pregnant women,[5,6] SCD is perceived as a global health threat by the World Health Organization. The main complications associated with this disease include severe infections, vital organ damage, stroke, kidney disease, respiratory problems, bone marrow suppression and a high rate of maternal and fetal deaths.[5-7] They occur mainly during pregnancy as many studies have shown that SCD is negatively associated with maternal health in pregnant women.[5-9] The fetal and maternal repercussions of SCD can be serious, with maternal complications such as anaemia, infection, painful vaso-occlusive crises, preeclampsia, premature labour and an increased risk of caesarean sections. Fetal problems can affect perinatal outcomes and include intrauterine growth retardation, premature birth, abnormal fetal heart rate and fetal death in utero. Furthermore, high rates of maternal and fetal mortality have been reported in pregnant women with SCD relative to rates in the general population.[8-10] Better management of women with SCD during pregnancy can improve the survival of both mother and child.[9]

However, without information about the disease and its different genotypes, appropriate pre- and postnatal care, including the development of guidelines for providing complete prenatal care can be challenging. In low- and middle-income countries (LMICs), women's limited access to education or prenatal care, a lack of medical coverage, and health facilities with limited technical resources are obstacles to efficient management of SCD in pregnant women. Implementing better management modalities for these patients should be handled by a multidisciplinary team composed of obstetricians, haematologists, paediatricians, anaesthesiologists and midwives. The objective of our work was to evaluate the hospital prevalence, management and maternal–fetal prognosis of pregnancies in women with major SCD in a reference health centre.

Methods

This was a prospective and descriptive study in the gynaecology and obstetrics department of the university hospital of Cocody in Abidjan, Côte d'Ivoire and ran over a two-year period (1 January 2015 to 31 December 2016). Our study included all pregnant women who had given birth in the department or had been followed up there. Patients with a homozygous SCD genotype (HbSS) and who have had single or multiple pregnancies with a gestational age greater than 6 months were eligible for inclusion. The genotype was confirmed by haemoglobin electrophoresis performed during prenatal care, or could have been known before the current pregnancy. Pregnant women were seen for prenatal visits every two weeks. Management was provided jointly with haematologists for major SCD. Women whose electrophoresis results showed genotype HbAA or HbAS, any other normal electrophoretic profile, or who had a history of renal disease or pre-existing diabetes, were excluded from the study. Data were collected from antenatal visit records, physical medical records, and death and delivery registers. Data were captured in a spreadsheet and analysed using EPI Info version 6.04 (CDC, Atlanta).

Ethical considerations

This study was conducted in accordance with the Helsinki Declaration and approved by the Ethics Committee of Felix Houphouet Boigny University (ref. no. N456588-CI/2024). All patients gave informed consent for participating in the study.

Results

Of the 14 819 deliveries recorded during the study period, 118 women (0.8%) had an abnormal haemoglobin profile. Major sickle cell disease was identified in 75 cases. Heterozygous HbSC genotypes accounted for 88% of these, and homozygous HbSS genotypes for 12%.

General patient data are summarised in Table 1. Patients were between 15 and 45 years old, with just over two-thirds (68%) being between 21 and 35. Patients under 20 made up 14.7% and those over 35 accounted for 17.3% of the sample.

About two-thirds (68%) of women worked in the informal sector. Roughly 37% had no formal education. Most patients (81.3%) lived with a partner. (Table 2).

The mean gestational age at delivery was 38 weeks (9 months), with a range of 28 - 40 weeks. Pregnant women who delivered at term accounted for 88% of cases. Caesarean sections accounted for 46.7% of the deliveries; the remaining were vaginal (53.3%). Other data on pregnancy and the immediate postpartum period are presented in Table 3.

Table 1. Sociodemographic characteristics of study sample (*N*=75)

Variables	*n* (%)
Age (years)	
≤20	11 (14.7)
21 - 35	51 (68.0)
≥36	13 (17.3)
Educational status	
No formal education	28 (37.3)
Primary school	14 (18.7)
Secondary school	13 (17.3)
Higher education	20 (26.7)
Occupation	
Informal sector	51 (68.0)
Student	5 (6.7)
School student	1 (1.3)
Housewife	18 (24.0)
Ethnic group	
Malinke	36 (48.0)
Akan	29 (38.7)
Krou	6 (8.0)
Foreign	4 (5.3)
Marital status	
Married	3 (4.0)
Single	11 (14.7)
Cohabiting	61 (81.3)

Table 2. Health profile of pregnant women presenting with SCD during the study period (N=75)

Variables	*n* (%)
Haemoglobin genotype	
HbSS	9 (12.0)
HbSC	66 (88.0)
Gravidity	
Primigravid	20 (26.7)
Paucigravid	19 (25.3)
Multigravida	36 (48.0)
Prior delivery history	
Nulliparous	39 (52.0)
Pauciparous	26 (34.7)
Multiparous	10 (13.3)
Prior obstetric history	
Induced abortion	4 (5.3)
Spontaneous miscarriage	23 (30.7)
In utero fetal death	15 (20.0)
Intrauterine growth restriction	6 (8.0)
Premature delivery	3 (4.0)
Neonatal death	4 (5.3)
None	20 (26.7)

Discussion

SCD, which is now known to be an autosomal recessive disease,[3] has been observed in Africa since the mid 17th century,[11] caused by a mutation in the β-globin gene. The predominant genotypes include HbSS, HbSC, HbSβ+-thalassemia and HbSβ0-thalassemia. Other rare forms include HbSD and HbSE.[12] The disease is characterised by the presence of elongated, sickle-shaped red blood cells, as described by James Herrick in 1910. The phenomenon of sickling, which occurs in deoxygenated blood, was first described *in vitro* by Victor Emmel in 1917.[13,14]

HbS results from a single mutation in the β-globin gene, with valine replacing glutamic acid at position 6 of the β chain. This modification makes HbS molecules more likely to polymerise under conditions such as hypoxia, dehydration and acidosis, forming the unique sickle shape of the red blood cells, and leads to anaemia, vaso-occlusion, adhesion and vasoconstriction.[7] Homozygous forms (HbSS) lead to SCD.[6,15] The heterozygous forms, known as sickle cell trait and in which HbS is seen in combination with other abnormal forms such as β-thalassemia, or haemoglobin C,[16] are usually asymptomatic and have little or no clinical consequences under normal physiological conditions.

The main consequences of SCD are painful seizures or organ damage in the form of cerebrovascular disease or retinopathy, acute chest syndrome, skin ulcers and avascular necrosis. Thus, management should aim to reduce the risk of SCD by suppressing HbS levels, treating complications and providing supportive care.

Haematopoietic stem cell transplantation may also be proposed.[7]

Our results showed a low frequency of major SCD in the study sample, as did other authors in sub-Saharan Africa.[17-19] Higher frequencies have been reported from Asia and North Africa.[3,7] The majority of pregnant women in our study were younger than 35, similar to findings from studies in other sub-Saharan African countries.[17-19]

Owing to cultural customs, many women in sub-Saharan Africa marry young and have early sexual activity. In many cases, the women have low levels of education, are unaware of family planning methods and live in precarious socioeconomic circumstances.[17-22] In our study we found 37.3% of the patients did not attain primary schooling and 68% worked in the informal sector.[17,18,20,22]

Most patients (88%) had a heterozygous HbSC genotype; HbSS genotypes were found in 12% of cases. This was similar to results from other studies.[3,5,7,8,10,16-21] As reported in other studies from LMICs,[3,5,7,8,10,16-21] our patients' earlier obstetric history showed high rates of spontaneous miscarriage (30.7%) and in utero fetal death (20%) in women with an HbSS genotype. Some studies have confirmed that the hypercoagulable state of pregnancy, coupled with mild gestational thrombocytopenia, may be indicative of the development of coagulation disorders. Therefore, multidisciplinary management, including coagulation monitoring during prenatal care, could greatly contribute to early diagnosis and interventions for pregnancy-associated coagulopathies in resource-limited settings.[21] In this study the occurrence of complications during pregnancy was significant (44%) and mainly included anaemia (54.5%) and painful vaso-occlusive crisis (36.4%).

The results of our study reported that most women delivered at term (88.0%), of which more than half (53.3%) were vaginal deliveries; caesarean section accounted for 46.7% of cases.

The proportion of caesarean deliveries was similar to what has been seen elsewhere;[10,17,18,21] caesarean delivery has been reported as the preferred route of delivery in developed countries.[12,16,22-24]

We noted a considerable number of delivery complications (21.3%), dominated by painful vaso-occlusive crisis (87.5%). Postpartum complications were mainly postpartum haemorrhage and anaemia. Similar findings have been described by other authors.[11,15,22-24] No maternal deaths were recorded in this study, in contrast to results from some studies in LMICs.[3,5,17-19,21] No neonatal deaths were recorded, although two fetal deaths (2.7%) were noted.

These numbers were lower than those described in developed countries.[11,15,22-24] Both maternal deaths were primarily related to chronic decompensated anaemia, commonly found in low-income patients.

The majority (82.7%) of newborns in our study sample had a normal birth weight and good Apgar scores (93.2%). Similar findings have been reported in studies from African[8,10,17,18,21] and Asian[3,5,12,20] countries. Early neonatal morbidity was dominated by prematurity (62.5%), intrauterine growth retardation (25%) and infection (12.5%) that required transfer to neonatology (15.1%). Similar reports were found in the literature, which recommended the implementation of common therapeutic measures during pre- and postnatal care.[6-8]

The results of our study are different from what was found in a meta-analysis by Oteng-Ntim *et al.*,[10] who reported that pregnancies in women with an HbSS genotype were associated with an increased relative risk (RR) of maternal mortality (RR=5.98), stillbirth (RR=3.94) and preterm labour (RR=2.21). Despite advances in protocols for SCD management in both obstetrics and neonatal medicine, there is still a strong association between the disease and pregnancy complications and comorbidities, including an increased risk of severe fetal and maternal outcomes,[10] and therapeutic interventions to improve pregnancy-related outcomes are not often implemented specifically in women with an HbSS genotype.[25] Interaction analysis showed that the HbSS genotype was associated with increased risk of premature birth, gestational hypertension, low birthweight and perinatal mortality.[10,22] Pregnancies in women with an HbSC genotype were associated with an increased risk of postpartum haemorrhage, caesarean delivery and low birthweight. In other studies, published before 2015, the HbSC genotype was associated with increased risk of eclampsia and in utero fetal death, whereas the HbSS genotype was significantly associated with the risk of fetal anoxia. Women with an HbSS genotype were sometimes noted to have an increased risk of urinary tract infections.

Finally, pregnancy complications were severe and more frequent in women with SCD, and more so in those with an HbSS genotype. Similar observations have been described in other studies.[10,25-27] Pregnancy outcomes in women with an HbSS genotype were worse compared with those who presented with an HbSC genotype, which often results in benign symptoms that may not be discovered until later in adulthood.[10,25-27] Results from a study in Brazil indicated that in women with SCD, the HbSS genotype was associated with a higher

Table 3. Data from current pregnancy or labour, and neonatal and birth characteristics

Variables	*n* (%)
Complications during pregnancy (N=75)	33 (44.0)
Anaemia	18 (54.5)
Vaso-occlusive crisis	12 (36.4)
Intrauterine growth retardation	2 (6.1)
Gravid hypertension	1 (3.0)
In utero death	2 (2.7)
Gestational age at delivery	
Preterm (<37 wk)	9 (12.0)
Full term (>37 wk)	66 (88.0)
Complications during delivery (N=75)	16 (21.3)
Vaso-occlusive crisis	14 (87.5)
Haemorrhage	2 (12.5)
Delivery modalities	
Vaginal delivery	40 (53.3)
Caesarean section	35 (46.7)
Maternal complications after delivery (N=75)	11 (14.7)
Anaemia	5 (45.4)
Vaso-occlusive crisis	3 (27.3)
Postpartum haemorrhage	2 (18.2)
Eclampsia	1 (9.1)
Birth weight (N=75)	
Small (<2500 g)	11 (17.3)
Normal (≥2500 g)	64 (82.7)
Apgar score at 5 min (N=73)	
≤6	5 (6.8)
≥7	68 (93.2)
Neonatal data (N=73)	
Prematurity	9 (12.3)
Neonatal infection	15 (20.5)
Hypotrophy	25 (34.2)
Transfer to neonatal unit	35 (47.9)

frequency of blood transfusion.[28] In the present study of women presenting with SCD (*N*=75), those with an HbSC genotype had better pregnancy outcomes although the incidence of SCD complications did not differ between those with an HbSS and HbSC genotype. However, Malinowski *et al*.[29] suggested that women with SCD who might be at high risk of adverse maternal–fetal outcomes could be identified early using routine clinical and laboratory data.

Study limitations

As this was a prospective study, patients presented at the unit just to give birth or were seen at the end of pregnancy, the course of antenatal care was unknown. However, prospective data collection could increase the quality and credibility of results. The small sample size may have influenced the outcome of the study, and undertaking a bigger multidisciplinary study could yield more representative results.

Conclusion

Our results showed SCD in pregnancy is associated with an increased risk of maternal and fetal complications such as anaemia, vaso-occlusive crisis, eclampsia, intrauterine fetal death and intrauterine growth restriction. Accurate and rigorous monitoring of pregnancies in women with SCD, by a multidisciplinary team that includes a haematologist, obstetrician and a paediatrician, is essential. Patient awareness and education through communication sessions and early screening for complications in women with SCD are essential to decrease associated risks.

Declaration. None.

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