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Pregnancy Outcome among Patients with Homozygous Sickle Cell Disease: Eight Years Retrospective Cohort in a tertiary Hospital in Sub-Saharan Africa

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ABSTRACT

Introduction: Sickle cell disease (SCD) is relatively prevalent in Sub-Saharan Africa and has been described to be associated with poor maternal and fetal outcomes in pregnancy. The objective of the study was to describe the trends, maternal and fetal outcomes of homozygous SCD in pregnancy in a cohort of patients hospitalized in Douala General Hospital (DGH) between March 2009 and February 2017.

Materials and methods: This was an eight year retrospective study of all registered maternal admissions seen at the obstetrics and gynecology unit of DGH over eight years period. Data was obtained using questionnaire and analyzed using SPSS version 20. The level of significance was set at a p value of 0.05.

Results: There were a total of 8804 maternal admissions in the service of obstetrics and gynecology unit of DGH over the 8 years period. Over this same period, 18 maternal admissions were admitted with homozygous sickle cell anemia in pregnancy. We had a prevalence of sickle cell anemia in pregnancy of 0.2% (2 cases per 1000 maternal admissions) with an annual admission rate of 2-3 cases per annum. The mean gestational age at booking and delivery were respectively 21 and 34 weeks. All our patients had anemia in pregnancy using WHO cut off point of hemoglobin <11 g/dl. A high prevalent rate of maternal, obstetric and neonatal complications was noted.

Conclusion: There is a high prevalence of sickle cell diseases among pregnant women in this region. Late antenatal booking and anemia are the predictive markers of poor pregnancy outcome in this population.

Keywords: Sickle cell diseases, Pregnancy, Outcome, Homozygous

INTRODUCTION

Sickle cell Disease (SCD) is the most common monogenetic disorder worldwide, affecting an estimated 30 million individuals and representing a major public health concern because of its associated significant morbidity and mortality [1]. It is one of the most severe monogenetic inherited conditions worldwide [2]. Sickle cell disease occurs in individuals homozygous for the β^S globin gene (SS) or heterozygous for the β^S allele and different abnormal β globin gene alleles, such as β^C (SC), $S\beta^0$ thalassemia or $S\beta^+$ thalassemia [3]. More than 75% of the global burden of SCD occurs in sub-Saharan Africa, where scarce health resources

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and inadequate awareness among health care providers and the general public contribute to shocking rates of early mortality [4,5]. Over the past 40 years numerous works have been done on SCD in the developed world, unfortunately, the status of SCD in Africa remains stagnant, with most affected persons lacking access to basic diagnostics and clinical care [5].

SCD can increase complication during pregnancy and in turn negatively influence the pregnancy outcomes [4,6]. Studies in Africa and United Kingdom (UK) have tried to estimate the negative influence of SCD on pregnancy outcomes [7]. SCD complicates about 1.42% of deliveries in Ghana [8]. Similar and very low incidence has been found in most sub-Saharan Africa countries [8]. Pregnant women with SCD are known to be at high risk of obstetrical complications and perinatal mortality as well as sickle-related complications [9]. The maternal and fetal complications include: vaso-occlusive crises (VOC), pulmonary complications, anemia, preeclampsia, eclampsia, premature delivery with associated risks, intrauterine growth restriction (IUGR), intrauterine foetal death (IUFD), increased caesarean section rate, low birth weight and all the acute and chronic complications of sickle cell [6,8,10].

There are not many studies in sub-Saharan Africa, which have explored the risk of negative pregnancy outcomes with SCD and to the best of our knowledge no study has been conducted in Cameroon on the subject despite the high incidence of SCD in Cameroon ranging between 20-30% [11]. This study reports the outcome of pregnancy in patients with homozygous sickle cell anemia in DGH over a period of eight years. The objective of the study was to describe the trends, maternal and fetal outcomes of homozygous SCD in pregnancy in a cohort of patients hospitalized in DGH between March 2009 and February 2017.

MATERIALS AND METHODS

Study design and setting

The study was a retrospective cohort study over a period of 8 years (March 2009-February 2017). The study was conducted in the obstetrics and gynecology unit of DGH. DGH is a 1st level reference hospital located in the economic capital of Cameroon, Douala. The hospital is well equipped with modern equipment and a bed capacity of 320beds. Amongst other units in the hospital is the obstetrics and gynecology unit which has a capacity of 30 beds and manages amongst other patients, patients with sickle cell in pregnancy. This is done in collaboration with the clinical hematology unit. The obstetrics and gynecology unit has 8 obstetricians and gynecologists, nurses and midwives. The unit also has modern bedside equipment for patient monitoring such as cardiotocograph. The unit is attached to a modern clinical laboratory and an imaging centre that functions 24/24. We included all patients with homozygous sickle cell anemia (HbSS) in pregnancy and excluded all other forms of SCD including Sickle cell trait and HbSS, patients with other hemoglobinopathies and incompletely filled files.

Data collection and analysis

We collected information from the medical records of the patients in the obstetrics and gynecology unit and the hematology unit. The following information was collected: socio-demographic data, obstetric history, medical history, current pregnancy including antenatal consultations, follow up during pregnancy, delivery and discharge from the hospital. Data was entered into epi-data version 3.1 and analyzed using SPSS version 20.0. We presented the data in the form of charts and tables. We determined the mean and standard deviation of continuous variables and the frequency and percentage of categorical variables. We compared categorical variables with chi square test and continuous variables with the student t-test setting the level of significance at a p value of 0.05.

Ethical consideration

Ethical clearance and administrative approval was obtained from the DGH ethics committee and administration respectively before starting data collection. Principles of ethics in research involving human participants were respected throughout.

RESULTS

There were a total of 8804 maternal admissions in the service of obstetrics and gynecology unit of DGH over the 8 years period out of which there were 8548 deliveries, 256 spontaneous abortions and 226 stillbirths. Over this same period, 18 maternal admissions were admitted with homozygous sickle cell anemia in pregnancy, out of which there were 2 spontaneous abortions and 2 still births (intrauterine fetal deaths). This gives a prevalence of sickle cell anemia in pregnancy of 0.2% (2 cases per 1000 maternal admissions) with an annual admission rate of 2-3 cases per annum. There were a total of 226 still births out of which 02 were from patients with sickle cell anemia. This gives a case fatality rate (CFR) of 0.9% (9 cases of stillbirths in SCD out of every 1,000 stillbirths) and a perinatal mortality rate or stillbirth rate of 12.5% in maternal admissions with sickle cell compared with 2.6% in maternal admissions without homozygous sickle cell. Similarly, there were a total of 256 spontaneous abortions out of which 2 occurred in patients homozygous for sickle cell anemia given an abortion rate of 11.1% in maternal admissions homozygous for SCD compared with 2.9% in maternal admissions without homozygous SCD.

From **Table 1** above showing baseline characteristics of maternal admissions with SCD in pregnancy. The mean age of patients homozygous for SCD was 29.7 ± 4.1 years, 66.7% of our patients were nulliparous at the start of follow-

Table 1. Baseline characteristics of maternal admissions with SCD in pregnancy.

Variable	Value
Age – Mean ± SD	**29.7 ± 4.1**
Marital Status – No (%)	
Single	12 (66.7%)
Married	5 (27.8%)
Divorced	1 (5.6%)
Level of education – No (%)	
Primary	2 (11.1%)
Secondary	9 (50.0%)
University	7 (38.9%)
Gravidity – No (%)	
Primigravida	8 (44.4%)
Multigravida	10 (55.6%)
Parity – No (%)	
Nulliparous	12 (66.7%)
Primiparous	4 (22.2%)
Multiparous	2 (11.1%)
Previous abortions	
One – No (%)	4 (22.2%)
Gestational age delivery – Mean ± SD	34 weeks, 6 days ± 5.4 weeks, 2 days
Antenatal Consultations – No (%)	
Average gestational age at booking – Mean ± SD	21.4 ± 2.2 weeks
1-3 ANCs	3 (16.7%)
4-8 ANCs	10 (55.5%)
≥ 9 ANCs	5 (27.8%)
Birth weight – Mean ± SD	**2256.7 ± 723.1 g**
Placenta weight – Mean ± SD	**508.9 ± 66.2 g**

up and 83.3% attended more at least four antenatal consultations (ANC).

The mean hemoglobin level during pregnancy was 7.5 g/dl. **Figure 1** shows the variation in the mean hemoglobin during pregnancy. In general hemoglobin level increases from 1st trimester to 3rd trimester. Compared to mean hemoglobin of 11 g/dl with 95 CI, the mean hemoglobin level was statistically significantly lower during all the trimester of pregnancy with a p-value set at 0.05 in univariate/multivariate analysis, none of the factors was significantly associated with anemia.

The dominant mode of delivery was caesarean section (CS) in 66.7% (12) of our patients. The indication included VOC, prolonged labor and premature rupture of membrane (PROM). Spinal anesthesia was used in all the patients who underwent CS. In 66.7% of the patients with vaginal delivery, epidural anesthesia was done. The most common

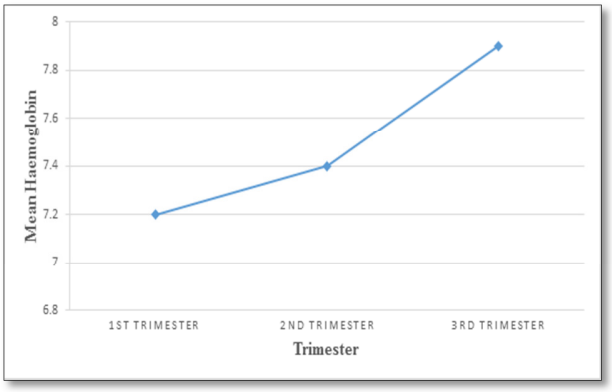

Figure 1. Variation of mean hemoglobin during pregnancy.

maternal medical complications in the peri-partum period were VOC in 44.4% (8) and hemolytic crisis in 33.3% while whereas obstetric complications were post-partum endometritis in 5.6% (1) and post-partum hemorrhage in 5.6% (1). VOCs and hemolytic crisis were significant different between patients homozygous for sickle cell and other patients. Other medical complications were not different. These obstetric complications were not significantly different between maternal admissions homozygous for sickle cell and the general maternal admissions. Common neonatal complications included: low birth weight (50.0%), need for hospitalization in neonatal unit 27.8% (5), still birth in 11.1% (2) and neonatal asphyxia in 11.1% (2) (**Table 2**).

Table 2. Medical and obstetric complications in SCD in pregnancy.

Complication	Frequency (n=18)	Percent (%)
Malaria in pregnancy	11	61.1
Vaso-occlusive crisis	9	50.0
Hemolytic crisis	8	44.4
Acute chest syndrome	6	33.3
Necrosis of the femoral neck	3	16.7
pulmonary embolism	1	5.6
Pre-eclampsia	1	5.6
Gestational diabetes	1	5.6
Urinary tract infection (UTI)	2	11.1
Abortion	2	11.1
Intrauterine fetal death	2	11.1
Intrauterine growth restriction	5	27.8
preterm labor	4	22.2
premature rupture of membranes (PROM)	2	11.1

The most frequent medical complications during pregnancy were: malaria in pregnancy 61.1% (11), VOC 50% (9) whereas the most frequent obstetric complications noted in our patients were intrauterine growth restriction 27.8% (5) and preterm labor 22.2% (4).

The dominant mode of delivery was caesarean section (CS) in 66.7% (12) of our patients. The indication included VOC, prolonged labor and premature rupture of membrane (PROM). Spinal anesthesia was used in all the patients who underwent CS. In 66.7% of the patients with vaginal delivery, epidural anesthesia was done. The most common maternal medical complications in the peri-partum period were VOC in 44.4% (8) and hemolytic crisis in 33.3% whereas obstetric complications were post-partum endometritis in 5.6% (1) and post-partum hemorrhage in 5.6% (1). VOCs and hemolytic crisis were significant different between patients homozygous for sickle cell and other patients. Other medical complications were not different. These obstetric complications were not significantly different between maternal admissions homozygous for sickle cell and the general maternal admissions. Common neonatal complications included: low birth weight (50.0%), need for hospitalization in neonatal unit 27.8% (5), still birth in 11.1% (2) and neonatal asphyxia in 11.1% (2) (**Table 3**).

Table 3. Mode of delivery and peri-partum maternofetal outcome.

Variable	Frequency	Percent (%)
Mode of delivery		
Caesarean Section	12	66.7
Vaginal	5	27.8
Instrumental delivery	1	5.6
Maternal Outcome		
Vaso-occlusive crisis (VOC)	8	44.4
Hemolytic crisis	6	33.3
Post-partum endometritis	4	22.2
Post-partum hemorrhage	1	5.6
Post-spinal headache	6	33.3
Neonatal outcome		
Neonatal asphyxia	2	11.1
Need for hospitalization in neonatal unit	5	27.8
Still birth	2	11.1
Low birth weight (<2500)	9	50.0

DISCUSSION

Our prevalence rate of SCD was 0.2% and the admission rate was 2-3 cases per annum. It is therefore estimated that one out of every 500 women seen in our antenatal consultations are homozygous for SCD (hemoglobin SS) and that yearly we receive in our antenatal consultations 2-3 patients with hemoglobin SS out of about 1073 maternal admissions per year. Our prevalence of 0.2% was similar to 0.2% and 0.14% obtained earlier in 2015 and 2016, respectively in Nigeria by Ubogma and George [12] and Nwabuko et al. [13]. The average gestational age of 21.4 weeks at booking ANC visit in this study indicate a late booking. This means that majority of the women registered at the second trimester. This was relatively similar to the gestational age of 22.1 weeks documented at a booking in South-South Nigeria by Nwabuko et al. [13], earlier in 2016. This may not be in the interest of the maternal and fetal well-beings. Antenatal care is one of the pillars of the Safe motherhood initiative aimed at preventing adverse pregnancy outcome. Early antenatal booking is recommended for this benefit. When a woman books late in the antenatal clinic, the benefit of safe motherhood is defeated. The advocacy has always been early booking as the panacea for a favorable outcome.

Pregnant women with SCD are classified as high risk. This is because SCD increases the risk of certain complications such as abortion, still births and anemia [13]. Anemia in pregnancy used in this study was based on the WHO definition as hemoglobin concentration <11 g/dl [14,15]. Based on this all our patients were anemic at booking and this persisted throughout pregnancy (**Figure 1**). This was similar to 94.6% obtained by Nwabuko et al. [13] in Nigeria in 2016. Anemia in pregnancy is very common in low- and middle-income countries [13]. Anemia, evidenced by low hemoglobin concentration, could be a predictive marker of women who may require blood transfusion during pregnancy or postpartum period: Other complications noted in our study included preterm labor, PROM, UTI, VOC, acute chest syndrome, low birth-weight, neonatal asphyxia, and need for hospitalization in the neonatal unit, etc.

CONCLUSION

There is a high prevalence of sickle cell diseases in pregnancy noted in our study. Late antenatal booking and severe anemia are predictive markers of poor pregnancy outcome. Obstetric complications in pregnancy noted were PROM, preterm labor, still births and abortions whereas medical complications included VOC, acute chest syndrome, hemolytic crisis and infections. Neonatal complications included low birth weight, neonatal asphyxia and the need for hospitalization in the neonatal unit after delivery.

DECLARATION

Ethics approval and consent to participate: Ethical approval was obtained from the ethical committee of Douala General

Hospital. A copy of is available for review by the Editor-in-Chief of this journal.

AVAILABILITY OF DATA AND MATERIALS

The datasets (details of all results) are available from the corresponding author on reasonable request.

COMPETING INTERESTS

The authors declare that they have no competing interests in this section.

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None.

AUTHOR CONTRIBUTIONS

PNT, TNN, EN, EK and CTN collected and analyzed the data; TNN and EK wrote the draft manuscript in French; PNT, JFN and CNN translated and wrote the draft manuscript in English language; TNN corrected the original manuscript; all authors corrected and approved the final manuscript.

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