



## **Prevalence of Sickle Cell Disease and Other Haemoglobin Variants in Calabar, Cross River State, Nigeria**

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### **Authors' contributions**

*This work was carried out in collaboration among all authors. Authors AK and O. Enang designed the study, performed the statistical analysis, wrote the protocol and wrote the first draft of the manuscript. Authors O. Essien and OC managed the analyses of the study. Author OO managed the literature searches. All authors read and approved the final manuscript.*

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### **ABSTRACT**

**Background:** Sickle cell disease (SCD) is the commonest genetic disorder worldwide with a global prevalence of 20-25 million. About 12-15 million affected persons are in Sub-Sahara Africa with Nigeria bearing the highest burden of people living with sickle cell disease. SCD is a disease characterized as an autosomal, recessive, heterogeneous, and a monogenetic disorder caused by an A-to-T point mutation in the  $\beta$ -globin gene responsible for the production of abnormal hemoglobin S (HbS), which polymerizes in the deoxygenated state and results in the sickling of erythrocytes. Haemoglobin variants are mutant forms of haemoglobin in a population usually occurring as a result

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of genetic changes in specific genes, or globins that causes change on alterations in the amino acid. They could affect the structure, behavior, the production rate and the stability of the specific gene. Well-known haemoglobin variants such as sick-cell anaemia are responsible for diseases and are considered haemoglobinopathies. Other variants cause no detectable pathology and are thus considered as non-pathological variants.

**Aim:** The study is aimed at evaluating the burden of sickle cell disease and other haemoglobin variants in Calabar, South-South Nigeria.

**Methods:** This is a retrospective study done at the haematology laboratory of University of Calabar Teaching Hospital, Calabar. Cellulose acetate electrophoresis at alkaline pH was used for the evaluation of haemoglobinopathies. The data were entered into Microsoft Excel 2016 spreadsheet and analysed with the IBM SPSS Version 22. Data were summarized into percentage of different phenotypes.

**Results:** Results of the total 3648 haemoglobin electrophoresis recorded, 1368 (37.50%) were male while the remaining 2280 (62.5%) females given a male to female ratio of 1:1.7. Five haemoglobin phenotypes were identified as HbAA, HbAS, HbAC, HbSC and HbSS. The overall average values of their prevalence were HbAA 64.78%, HbAS 32.62%, HbSS 2.14%, HbAC 0.33%, HbSC 0.14%. Thus, the prevalence of SCD (Prevalence of HbSS+HbSC) was 2.28%. The highest proportion of SCD was observed in 2011 with least in 2016 and 2017 respectively.

**Conclusion:** The prevalence of SCD and other haemoglobin variants in Calabar is similar to that of the national prevalence rate. There is need for continuous enlightenment and premarital counselling on the pattern of inheritance of SCD most especially with the increased burden of sickle traits in the environment has reported in this study.

*Keywords: Haemoglobin; phenotype; sickle cell disease; Calabar.*

## 1. INTRODUCTION

Haemoglobin (Hb) is a Greek word that is derived from two words: Haem and Globin which means blood and protein respectively. The globin comprises of a set of closely related protein formed by the symmetric pairing of dimer of polypeptide chains of  $\alpha$  and  $\beta$  globin into a tetramer with structural and functional unit in the red blood cell [1].

Haemoglobin is responsible for the transport of oxygen from the lung to the tissue and carry  $\text{CO}_2$  from the tissue to the lung for gaseous exchange. Also, haemoglobin serves as a buffer to maintain the pH of the physiology milieu of the body [2].

There are different types of Hb and their globin chain composition varies at different stages of life. During fetal life, Gower I, Portland, Gower II, and fetal Hb predominate in uterine life [2] there is a transition to adult Hb within 3-6 month of life [3].

Various genetic mutations affect the Hb. They could be quantitative or qualitative leading to various forms of haemoglobinopathies such as thalassaemias and HbS, HbC, HbE, and HbD among others [2]. These haemoglobinopathies arise from either homozygous, heterozygous or

compound heterozygous genetic mutations resulting in various clinical presentations. The inheritance of an S gene is termed sickle cell disorder. The HbS gene is due to point mutation at position 6 of the  $\beta$  globin chain with substitution of valine for glutamic acid while the C gene is due to substitution of lysine for glutamate at position 6 of the  $\beta$  chain [3].

Sickle Cell Disease (SCD) is a disease characterized as an autosomal, recessive, heterogeneous, and monogenetic disorder. The disease is caused by the inheritance of the sickle cell gene either the homozygous or heterozygous with another interacting gene [4]. The homozygous state is referred to as sickle cell anaemia and may be characterized by increased red cell destruction (haemolysis) amongst other clinical features. There is inconsistency and geographical variation in the available data on the Hb variants in our environment with paucity of study in our environment. The aim of this study is to evaluate the major Hb variants and the burden of sickle cell disease in Calabar.

## 2. MATERIALS AND METHODS

This is a retrospective study. Results of haemoglobin electrophoresis of patients done at the haematology laboratory of the University of Calabar Teaching Hospital (UCTH) Calabar from

Jan 2008 to September 2019 were analyzed. Cellulose acetate electrophoresis at alkaline pH was used for the evaluation of haemoglobinopathies. Various forms of haemoglobin phenotypes documented was used for the analysis. A total of three thousand six hundred and forty-eight haemoglobin phenotypes results were documented during the study period.

The data were computed into Microsoft Excel 2016 spreadsheet and analysed with the IBM SPSS Version 22. Data were summarized as percentage of different phenotypes including, normal HbAA and mutant allele(s) in the genotype; HbAS, HbAC, HbSS, and HbSC.

### 3. RESULTS

The eleven-year records of 3648 haemoglobin electrophoresis of patients showed that 1368 (37.50%) were male while the remaining 2280 (62.5%) females given a male to female ratio of 1:1.7 (Table 1). Five haemoglobin phenotypes were identified namely HbAA, HbAS, HbAC, HbAS, and HbSS. The overall prevalence was HbAA 64.78%, HbAS 32.62%, HbSS 2.14, HbAC 0.33%, HbSC 0.14%. Thus, the prevalence of SCD (Prevalence of HbSS+HbSC) was 2.28% (Table 2). The highest proportion of SCD was documented in 2011 and least seen in 2017 (Fig. 1). The mean age documented was 22.98 ± 2.84 (SD) years (Fig. 2).

### 4. DISCUSSION

SCD is the commonest genetic disorder worldwide with a global prevalence of 20-25

million. About 12-15 million affected persons are in Sub-Sahara Africa with Nigeria having the highest burden of people living with sickle cell disease [5]. SCD affects about 2-3% of the Nigerian population [6], in our study, a prevalence of 2.28% was reported.

This study found the prevalence of 64.78% for HbAA, 32.62% for AS, 2.14% for SS, 0.33% for AC, and 0.14% for SC with female preponderance. This is similar to the finding which showed HbAA at 55-75%, AS 20-30%, SS 1-3% [7] and a study by Olagunju et al. [8]. Nwogoh et al also reported similar findings [9], another study by Adu et al also reported similar findings in terms of SC and SS respectively [10]. Furthermore, a previous study conducted by Udomah et al. [11] on haemoglobin electrophoretic patterns, ABO and Rhesus D blood groups distribution among antenatal women in Sokoto, Nigeria reported a similar prevalence of SC (0.3%), AC 3.7%, AS 22.3% and AA 73.3%. Although, the findings are at variance with a similar study by Odunvbun et al which reported a higher prevalence of 75.3% for AA, 20.6% for AS, 1.1% for AC, 2.8% for SS and 0.2% for SC [12]. This difference can be attributed to the difference in study design and increase infant and under-five mortality.

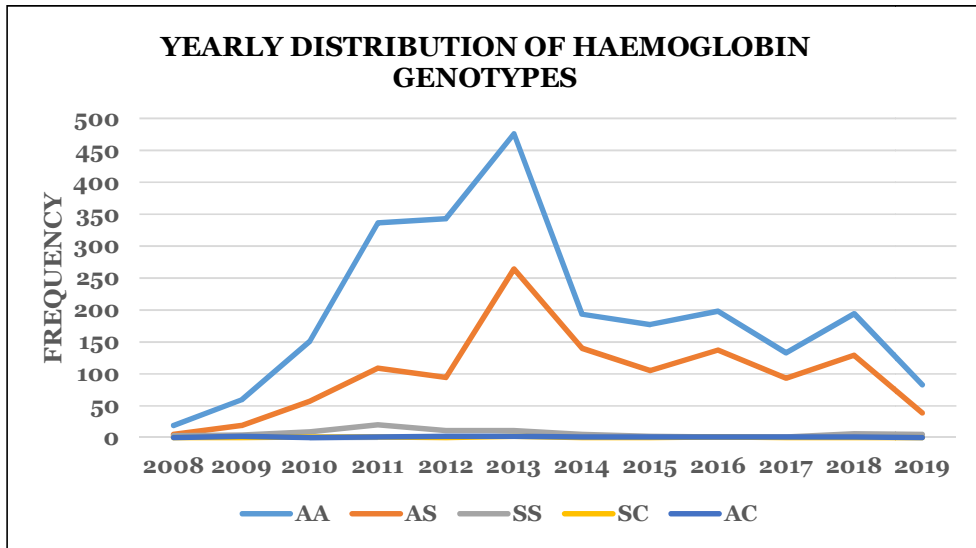
More so, a study conducted in Northern Nigeria by Baba Inusa et al. reported a higher prevalence of SCD when compared with our study. They reported a prevalence of 2.69% [13]. This also can be attributed to the difference in study design and consanguineous marriage encouraged by Islamic practice which may contribute to the high prevalence of HbSS in Northern Nigeria. Another study conducted

**Table 1. Gender distribution of haemoglobin variants**

Gender	Haemoglobin typing					Total
	AA	AS	SS	SC	AC	
Male	898	433	30	3	4	1368
Female	1464	758	48	2	8	2280
Total	2362	1191	78	5	12	3648

**Table 2. Prevalence of haemoglobin phenotype variants in Calabar**

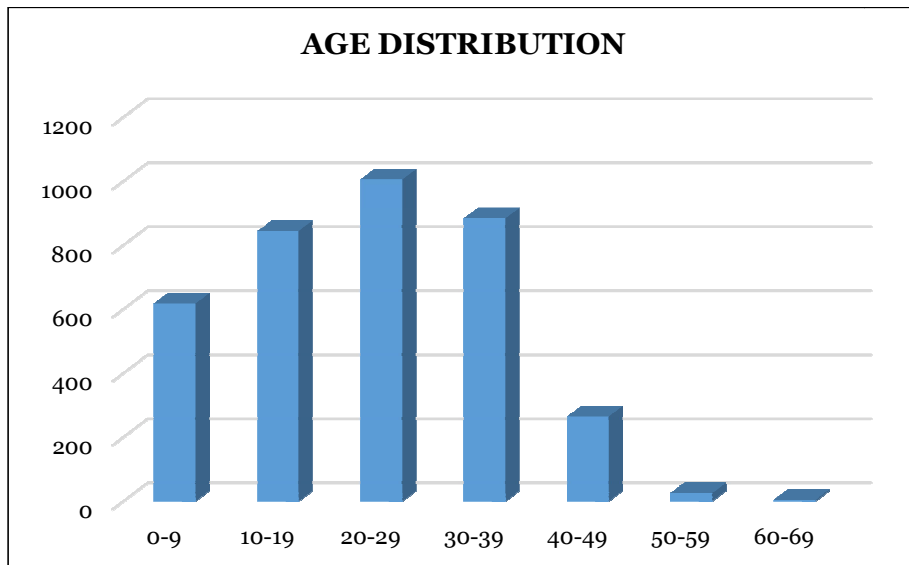
HB phenotypes	Frequency	Percentage
AA	2363	64.78
AS	1190	32.62
SS	78	2.14
AC	12	0.33
SC	5	0.14
SCD (SS+SC)	83	2.28



**Fig. 1. Yearly distribution of haemoglobin phenotype variants**

in Southwest Nigeria by Akhigbe et al. [14] reported a lower prevalence of AS (22.19%) and SS (0.56%). Similarly, Akinboro et al also reported a low prevalence of 10.23% for AS in a study conducted in Akure [15]. However, another study conducted by Bakare et al. [16] in Ogbomoso, south-west Nigeria, a higher prevalence of SS (3%) and SC (2%) was reported. The variation here could be attributed to the difference in literacy rate and increase in the number of specialist for easy detectability of the disease condition, and the high incidence of

HbC trait that is largely confined to the Yoruba people of southwestern Nigeria [17]. A similar study conducted by Nnaji in Southeast Nigeria [18] also reported a lower value for AS (26.4%) and SS (0.94%). Also, David Agatha Nikruka reported a lower prevalence of AS (18.8%) in the same region [19]. The difference observed in the Southeast region could be attributed to the increase in the availability of Specialists and even distribution of tertiary health facilities. These allows for early diagnosis and prevention of the disease condition.



**Fig. 2. Showing the age distributions**

In the index study, the peak incidence of SCD was in 2011 with least incidence in 2017. The high incidence could be attributed to high level of illiteracy, Spiritism, inadequate specialist (manpower), lack of infrastructure and difficulty in accessing health facility, inadequate enlightenment while the decline could be attributed to increasing manpower, education and establishment of advocacy groups.

## 5. CONCLUSION

The percentage of HbAA is maintained and the prevalence of haemoglobinopathies in the studied group is within the national prevalence. The study showed that the disease condition is not in the Hardy-Weinberg equilibrium (Hardy-Weinberg equilibrium is a principle stating that the genetic variation in a population will remain constant from one generation to the next in the absence of disturbing factors), indicating that with continuous enlightenment, pre-marital, genetic counselling and adequate political will, the disease can be curbed or ultimately eradicated.

## 6. LIMITATION OF THE STUDY

This study has some limitation, one of which is the bias for the methodology because some abnormal haemoglobin with similar electrophoretic mobilities must be detected using other techniques.

## 7. IMPLICATION OF THE STUDY

The implication of our finding is that the reducing trend of SCD in our environment is still characterized with the challenge of increased burden of sickle cell trait (AS) which allude to an upsurge of this disease condition if adequate enlightenment, premarital counselling and education on the pattern of inheritance of this disease condition is not done to mitigate this menace by all stakeholders involved in the management of sickle cell disease. Therefore, it is pertinent that a pre-marital counselling clinic should be established and strong legislation should be enacted to encourage genetic counselling and testing before marriage.

## COMPETING INTERESTS

Authors have declared that no competing interests exist.

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