Original Article

Prevalence of Chronic Complications in Adult Sickle Cell Anemia Patients in a Tertiary Hospital in South-South Nigeria

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Abstract

Background: Nigeria has the largest cohort of sickle cell anemia (SCA) worldwide; the chronic complication in adult sickle cell anemia patients is associated with increased morbidity and mortality. However, there is a paucity of studies describing the prevalence of the spectrum of chronic complications encountered by adult SCA patients. This study is aimed at increasing the awareness of chronic complications among adult SCA patients. **Methodology:** This was a cross-sectional hospital-based study involving 60 SCA patients visiting the University of Calabar Teaching Hospital, which was carried out from July 2017 to June 2018. The study involved 23 males and 37 females with ages ranging from 16 to 42 years. Information about the social demographic characteristics and any form of chronic complication of the participants were obtained using a questionnaire. A multisystemic examination was also done to ascertain their claims, and other information regarding chronic complications were obtained from their records at the Adult Haematology Clinic, Department of Haematology, UCTH. **Results:** The median age of the participants was 23 years. The participants consisted of 23 (38.30%) males and 37 (61.70%) females. The majority (86.70%) were single, whereas the remaining 13.30% were married. Most of the participants had tertiary education (73.30%), whereas the rest (26.60) had only secondary education. The most prevalent complication was avascular necrosis (AVN) with a prevalence of 8.33%, followed by retinopathy (6.67%), pulmonary hypertension, and leg ulcer had a prevalence of 5%, respectively. The least common complications were nephropathy, stroke, and hepatopathy, with a prevalence of 3.33%, respectively. **Conclusion:** The index study has exposed that adult SCA patients are associated with the spectrum of chronic complications ranging from AVN, retinopathy, pulmonary hypertension, leg ulcer, stroke, nephropathy, and hepatobiliary complication. The prompt intervention will help to improve their quality of life.

Keywords: Adult, chronic, complication, sickle cell anemia

Introduction

Sickle cell disease (SCD) is a heterogeneous group of autosomal recessive structural hemoglobin disorder with a highly variable clinical spectrum. The most prevalent form is sickle cell anemia (HbSS), which is due to the inheritance of the sickle gene in a homozygous state.[1] Other forms of SCD include the compound heterozygous forms, in which the sickle beta-globin gene is co-inherited with another abnormal hemoglobin gene such as HbC, β-thalassemia, and HbD among others.[2]

SCD is the most common genetic disorder worldwide. The global prevalence of SCD is 20–25 million, and about 12–15 million affected persons are in Sub-Sahara Africa.[3] The WHO estimated that 300,000 children are born annually with SCD, 75% of whom are in Sub-Saharan Africa. In Nigeria, >150,000 children are born with this disease annually. The overall prevalence of SCD in Nigeria is estimated to be between 2% and 3%; with slight variations from one region to another. Akaba *et al*. reported a prevalence of 2.28% in South-South Nigeria. Similarly, a prevalence of 2.4% SCD was reported in South-west Nigeria.[4]

SCD is characterized by numerous complications which affect every organ and or tissues in the body, often chronic

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in the long term. Chronic complications range from chronic pain, cerebro-vascular disease/stroke, pulmonary hypertension, leg ulcers, avascular necrosis (AVN), retinopathy, renal failure, and hepatopathy. Chronic complications can be attributed to the vicious cycle of sickling, which causes endothelial injury, inflammation, oxidative stress, and hypercoagulability, leading to a vasculopathy.[5] The aim of this study is to bring a paradigm shift from routine treatment of acute events in SCD to the more devastating chronic complications associated with morbidity and mortality, through the determination of the prevalence of chronic complications encountered by sickle cell anemia (SCA) patients at the UCTH, Calabar.

Methodology

Study design

This was a cross-sectional hospital-based study involving sickle cell anemia patients, carried out between July 2017 and June 2018.

Study area

This study was carried out at the adult hematology clinic of the Department of Haematology and Blood Transfusion, of the University of Calabar Teaching Hospital, government-owned tertiary institution situated in Calabar. The hematology unit is manned by Consultants, supported by; Resident Doctors, Trained Nurses, Medical Laboratory Scientists and Allied Staff, the unit also has a comprehensive medical records.

Subject

The study population comprises adults with SCA.

Sample size

A total of 60 SCA patients participated in the study.

Selection criteria

- Inclusion– All adults subjects who carry the SS gene attending the adult SCA clinic of the hospital
- Exclusion– All other hemoglobin genes
- Those with deformity following trauma or other condition not due to the sickle cell.

Methods

All patients who presented at the SCD clinic during the period of the study were given a questionnaire that captures their biodata and clinical information, which included any forms of chronic complication. All eligible participants underwent a comprehensive multisystemic examination to ascertain their complications. Other information regarding chronic complications was obtained from their records at the Adult Haematology Clinic, Department of Haematology, UCTH. A blood sample was collected into an ethylenediaminetetraacetic acid bottle for hemoglobin electrophoresis were those with the homozygous SS gene were reconfirmed after informed consent to participate in the study was administered.

Results

The median age of the participants was 23 ± 13.6 years. The participants consisted of 23 (38.30%) males and 37 (61.70%) females. Majority (86.70%) were single, while the remaining 13.30% were married. Most of the participants had tertiary education (73.30%), whereas the rest (26.60) had only secondary education [the demographic characteristics of the participants are shown in Table 1]. The most prevalent complication was AVN with a prevalence of 8.33%, followed by retinopathy (6.67%), while pulmonary hypertension and leg ulcers had a prevalence of 5%, respectively [Figure 1]. The least frequent complications were nephropathy, stroke, and hepatopathy, all with a prevalence of 3.33%. There was no observable significant statistical difference in the association between gender and chronic complications among adult SCA patients.

Discussion

The rising trend of chronic complications among adult SCA patients with the attendant increased morbidity and mortality poses a great challenge to both patients and caregivers. This study shows the profile and spectrum of chronic complications seen in adult patients with SCA attending a tertiary hospital in the South-South region of Nigeria. This study seems to be the first of its kind to describe the prevalence of chronic complications encountered by adult SCA patients in the South-South region of Nigeria. This rising trend of chronic complications among adult SCA patients in our study could be attributed to vasculopathy, which might have resulted from the vicious cycle of repeated inflammation, endothelial injury, oxidative stress, and hypercoagulability observed by earlier workers.[6]

Our study shows female preponderance with an M: F ratio of 1:1.6; this could be attributed to the good health-seeking behavior of females [Table 2]. Majority of the females in this study being single may be due to the social stigmatization of the SS gene individuals. Most of the SCA have attained tertiary education; this can also be attributed to the proximity of the hospital to a tertiary institution.

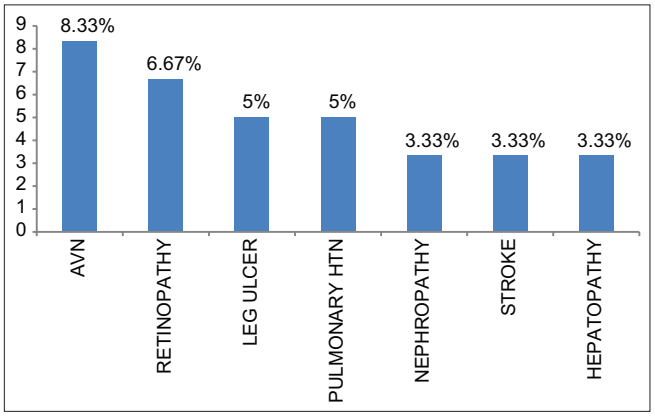

Figure 1: The distribution of chronic complications among adult sickle cell anemia patients

Table 1: The sociodemographic characteristics of the participants

Demographic data	Frequency (n=60), n (%)
Age group (years)	
<20	10 (16.70)
21-25	23 (38.30)
26-30	14 (23.30)
31-35	8 (13.30)
36-40	4 (6.70)
>40	1 (1.70)
Sex	
Male	23 (38.30)
Female	37 (61.70)
Marital status	
Single	52 (86.70)
Married	8 (13.30)
Educational level	
Secondary	16 (26.70)
Tertiary	44 (73.30)

Table 2: Gender distribution and chronic complications among adult sickle cell anemia patients

Complication	Male	Female	Total (%)	Statistics
Retinopathy	2	2	4 (6.67)	χ^2=4.531, P=0.424
Nephropathy	0	2	2 (3.33)	
AVN	3	2	5 (8.33)	
Leg ulcer	2	1	3 (5.00)	
Pulmonary HTN	1	2	3 (5.00)	
Stroke	0	2	2 (3.33)	
Hepatopathy	1	1	2 (3.33)	
None	14	25	39 (65.00)	
Total	23	37	60	

No statistical difference was observed in the association between chronic complications in sickle cell disease and gender χ^2 (6)=4.531, P=0.424.
AVN: Avascular necrosis, HTN: Hypertension

Most of our SCA patients were <40-years and the median age of the study population was 23 years. This may be due to the reduced life expectancy in patients with SCA in Sub-Sahara Africa[7] compared to the life expectancy of SCA in developed countries, which is >40 years.[8] The reduced life expectancy may be due to poverty, malaria, increase in the prevalence of communicable disease, illiteracy, lack of policy on routine newborn screening, limited access to healthcare, and disease-modifying drugs.[9]

AVN was the leading chronic complication encountered in our study, with a prevalent rate of 8.83%, and male preponderance with an M: F of 1.5:1. AVN is the leading cause of disability in SCA patients and invariably affects their quality of life.[10] In sharp contrast, Ladu *et al*., in a related study, reported a higher prevalence of 16.1%.[11] Similarly, other studies also reported a prevalence of 42%–48%.[12,13] In like manner, Balogun *et al*. reported a prevalence of 31.4% in South-West Nigeria.[14] The observed difference in the prevalence of AVN from the different regions could be attributed to the difference in study design and sample size. AVN is said to develop with age and common in the male gender.[14] AVN is also associated with hematocrit and high steady-state platelet count[15] because this leads to hyperviscosity within the sinusoids, which promote the sickling of the red cells, resulting in ischemia and subsequent infarction.

Retinopathy was the next most common chronic complication encountered in our study population, with a prevalence of 6.67%, with an M: F of 1:1. Retinopathy is reported more commonly in HbSc and HbS + thalassemia than HbSS due to the higher degree of fluid viscosity in the former.[16,17] In contrast to our study, Andong *et al*. reported a much higher prevalence of 26.9%,[18] while another study conducted in Accra, Ghana reported a prevalence of 3.5%.[19] Furthermore, a study conducted in Port-Harcourt, in South-South Nigeria, reported a prevalence of 34.0%. These large differences can be attributed to the study design and sample size.[20]

Pulmonary hypertension was also observed in 5.0% of our study population, with a female preponderance, M: F of 1:0.5, by the elevated Tricuspid Regurgitation Velocity. This is similar to the national prevalence rate of 3%–25% pulmonary hypertension in adult SCA in Nigeria.[21,22] Thus, the gold standard for determining pulmonary hypertension is the use of right heart catheterization, not readily available in our environment.

Leg ulcers in our index study reported a prevalence of 5%, with a male preponderance at a ratio of 1:0.5. This concurred with the findings of several studies conducted in Nigeria, in which leg ulcers range from 3% to 16%.[10,23-26] In variance to this study, a lower rate of 2.5% was reported in the United States,[27] while a significantly higher rate of 40% was reported among adult SCA patients in Jamaica. This variation may be attributed to the study population, sample size hemoglobin genotype, haplotype, and geographical location. There are several factors associated with the development of chronic leg ulcers; these include trauma, age (>20 years), sex (male), low hematocrit, and fetal hemoglobin level. The presence of chronic leg ulcers is also a known determinant of the severity of SC disease.[28] This complication requires a multidisciplinary management approach and safe blood transfusion.[29]

Nephropathy is also a form of chronic complication in SCA patients encountered in our study population, with a prevalence of 3.33% and female preponderance. This was lower than the reported prevalence of (20%–50%) from several studies in Nigeria.[30-32] This difference can be attributed to the study design. Renal involvement is a well-known documented complication of SCA.[33,34] The hypoxic, acidotic, and hypertonic state of the renal medulla favors vaso-occlusion, thereby affecting the medullary vasa recta. Early in life, SCD infants may develop hypothermia which might manifest as nocturia enuresis.[24] Studies have shown that the prevalence of enuresis is higher in SCA. Some studies have shown that increasing age, high hematocrit, high blood pressure, and

history of blood transfusion are associated with the risk of developing sickle cell kidney disease.[31,34]

Stroke, a fatal complication of SCA, was among the least encountered complications in this study, with a prevalence of 3.33%, with an overall female preponderance. Stroke is associated with significant morbidity and mortality in SCA.[35] SCA patients with stroke suffer a sudden onset of focal or global neurologic deficit of vascular origin lasting >24 h. A higher prevalence of 4.3% and 5.2% were reported in Port-Harcourt and Abuja, respectively.[36,37] This variation could be attributed to the difference in the study designs. The risk of stroke is said to be higher in those with low baseline hemoglobin, low fetal hemoglobin high white cell count, and high systolic blood pressure, higher in HbSS compared to the heterozygous forms and compound heterozygous forms. This complication requires a multidisciplinary management approach, exchange blood transfusion being pivotal.[29]

Hepatobiliary system involvement was among the least chronic complications of SCD among adult patients in this study, with an M: F ratio of 1:1. This complication in SCD is caused by transfusion transmissible infection, transfusion siderosis, intrahepatic trapping of sickled cells. In the current study, a prevalence of 3.33% was reported, which was similar to the studies reported by Solomon[38] and Fashola *et al*.[39] Risk factors that can influence hepatobiliary complications, especially cholelithiasis are local diet, genetic factors, crystallization of gallstone by ceftriaxone.[40]

Conclusion

The authors have concluded that adult SCA patients develop chronic complications ranging from a more frequent AVN to the least common hepatobiliary affectation. Prompt multidisciplinary interventions in the management of adults with SCA improve quality of life

Limitation

Financial constraints and inadequate available diagnostic equipment prevented further molecular evaluation of SCD patients with chronic complications

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Conflicts of interest

There are no conflicts of interest.

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