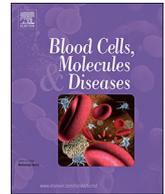




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journal homepage: www.elsevier.com/locate/bcmdSickle cell disease clinical phenotypes in Nigeria: A preliminary analysis of the Sickle Pan Africa Research Consortium Nigeria database[☆]

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ABSTRACT

Background/objective: Sickle cell disease (SCD) is a monogenic disease with multiple phenotypic expressions. Previous studies describing SCD clinical phenotypes in Nigeria were localized, with limited data, hence the need to understand how SCD varies across Nigeria.

Method: The Sickle Pan African Research Consortium (SPARCO) with a hub in Tanzania and collaborative sites in Tanzania, Ghana and Nigeria, is establishing a single patient-consented electronic database with a target of 13,000 SCD patients. In collaboration with the Sickle Cell Support Society of Nigeria, 20 hospitals, with paediatric and adult SCD clinics, are participating in patient recruitment. Demographic and clinical information, collected with uniform case report forms, were entered into Excel spreadsheets and uploaded into Research Electronic Data Capture software by trained data clerks and frequency tables generated.

Result: Data were available on 3622 patients enrolled in the database, comprising 1889 (52.9%) females and

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1434 (39.6%) children ≤ 15 years. The frequencies of Hb SS, Hb SC and Hb S β thalassemia in this data set were 97.5%, 2.5% and 0% respectively. Sixty percent, 23.8%, 5.9%, 4.8% and 2.5% have had bone pain crisis, dactylitis, acute chest syndrome, priapism and stroke respectively. The most frequent chronic complications were: leg ulcers (6.5%), avascular necrosis of bone (6.0%), renal (6.3%) and pulmonary hypertension (1.1%). Only 13.2% had been hospitalized while 67.5% had received blood transfusion.

Conclusion: These data on the spectrum of clinical phenotypes of SCD are useful for planning, improving the management of SCD across Nigeria and provide a foundation for genomic research on SCD.

1. Introduction

Sickle cell disease (SCD) is a genetic haemoglobin disorder arising from a single point mutation in the β -globin gene. It is the most common genetic disorder worldwide with the prevalence of the sickle cell trait reaching as high as 40% in some sub-Saharan African countries, Eastern Saudi Arabia and Central India [1]. The prevalence rates of sickle cell trait and the homozygous state in Nigeria, a country with the highest burden, are 25% and up to 2% respectively [2]. It is associated with acute and chronic complications of varying severity and high mortality [1,3]. The clinical manifestations arise from the tendency of the haemoglobin molecule to polymerize and deform red cells into the characteristic rigid sickle shapes which adhere to the microvasculature within tissues and organs, triggering a myriad of cellular events culminating in vaso-occlusion, ischaemia and infarction of tissues and organs. Repeated vaso-occlusions underly the chronic complications seen in SCD [4–6].

Nigeria is in West Africa with an estimated population of 202,041,733, and median age of 17.9 years [7]. The country is divided into six geo-political zones (Fig. 1b) with distinct ethnic and social backgrounds, indigenous languages, as well as unique cultural practices, which may impact their health. These include consanguineous marriages, nutrition and predominant occupation [7].

Also, the country has three major vegetation patterns, varying from the desert and savannah in the North to rainforest and mangrove in the Southern part of the country. The climate is tropical monsoon with a narrow temperature range maximum of 28 °C (82.4 °F) in the hottest month to 26 °C (78.8 °F). There are two main seasons, the hot dry season from October to April and the rainy season from May to September. A third season, the harmattan, is associated with low atmospheric humidity, increased wind speeds and dusty haze, which partially blocks the sun rays over northern Nigeria with a resultant fall in average temperatures to as low as 13 °C and even lower, especially in the evening and night times [8].

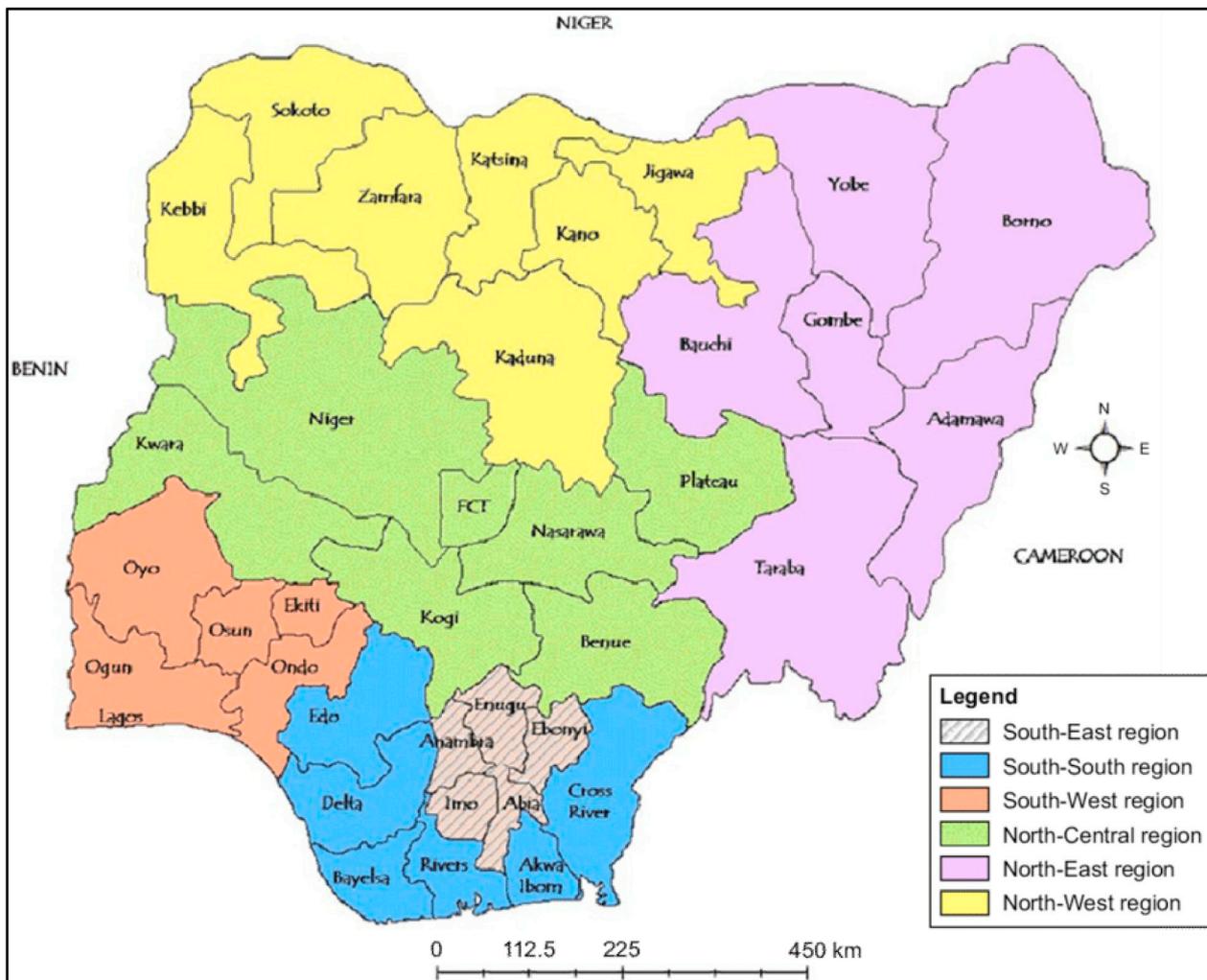


Fig. 1. Map of Nigeria showing the 6 geo-political zones in the country and their constituent states.

Several biological and environmental factors modify SCD phenotypic expression and account for unpredictable and variable clinical manifestations between patients and even within the same individuals with the disease [3,9,10]. Previous studies describing SCD clinical phenotypes in Nigeria were from single sites, limited to the regions where they were located [11–14] thereby failing to capture the spectrum of social, economic and tribally-diverse populations in both disease prevalence and complications noted in previous single-center studies. The roles of the varying prevalence of alpha thalassemia trait and malaria endemicity among the different ethnic groups have also not been taken into consideration. In this preliminary analysis of registry data, we describe the clinical phenotypes of SCD and how they vary across the geopolitical zones in Nigeria and between the various age groups.

2. Methods

The Sickle Pan African Research Consortium (SPARCO), with a hub in Tanzania and collaborative sites in Ghana and Nigeria, is establishing a single patient-consented electronic database with a target of 13,000 SCD patients in the three countries, as one of its objectives [15]. In collaboration with the Sickle Cell Support Society of Nigeria (SCSSN, <http://scsn.com.ng/>), 20 hospitals with paediatric and/or adult SCD clinics across the country, are participating in patient recruitment, using uniform case report forms (CRF) which is ongoing toward a target of 6000 patients for Nigeria. A typical SCD clinic in each institution runs once or twice a week and provides care including genetic counseling, the use of folic acid, antimalaria prophylaxis, with or without hydroxyurea and penicillin [16].

2.1. Methods of sampling

All patients previously confirmed to have SCD by alkaline cellulose acetate electrophoresis, and/or high-performance liquid chromatography (HPLC), who consented to be enrolled into the registry were recruited into the study at each collaborating site, using a uniform CRF. Both newly-diagnosed and known patients were included. The CRF contains the following information: data on sociodemographic characteristics such as age, sex, highest level of formal education, occupation, ethnicity, religion, state and local government of origin. Other data elements include age at diagnosis, methods of SCD diagnosis, episodes of blood transfusion, pain episodes and hospitalizations ever and in the 12 months preceding recruitment, presence or otherwise of acute complication(s) such as acute chest syndrome (ACS), priapism, severe haemolysis/anaemia; chronic complications such as stroke, leg ulcer; drug history and immunization. Only clinical non-laboratory data were analyzed. All acute and chronic complications of SCD were as previously defined [17,18].

- i. Hepatic complications in this study refer to any sickle cell-related liver disorder such as hepatic sequestration, hepato-biliary stone and liver abscess.
- ii. Renal complications refer to pyelonephritis, chronic kidney disease or nephrotic syndrome.
- iii. Stroke refers to acute neurologic events secondary to occlusion of and or haemorrhage from cerebral vessels confirmed on computerized tomography (CT) scan or magnetic resonance imaging (MRI)
- iv. Acute chest syndrome (ACS) - An acute illness characterized by fever and respiratory symptoms (dyspnea, chest pain) accompanied by new pulmonary infiltrates on chest radiograph
- v. Avascular necrosis (AVN): This is osteonecrosis of the head of femur or humerus, which is confirmed by radiography as irregularity of the articular surfaces of the head of femur or humerus
- vi. Priapism - Sustained, unwanted, and painful penile erection.
- vii. Leg ulcer - Ulceration of the skin and underlying tissues of the

lower extremities, especially on the medial or lateral surface of the ankle

2.2. Methods of data collection

Site leads as well as data collating personnel were trained centrally prior to commencement of data collection using uniform CRF and repeated a year later. A uniform set of data elements were determined by the consortium collectively to ensure harmonized data collection. Data was collected by both direct questioning of patients or parents/intermediate caregivers for paediatric patients, as well as checking of existing medical charts. As much as possible, all relevant information was obtained for each study participant. Data was collected and managed using Research Electronic Capture (REDCap) (Paul Harris, REDCap, Vanderbilt University Medical Center, 1211 Medical Center Drive, Nashville, TN 37232) software by trained data clerks. REDCap an electronic data capture tool, is a secure web-based application to support data capture for research studied. Data cleaning and quality checks from sites are carried out by the Data entry personnel at CESRTA before upload into REDCap. Data queries are referred to the sites for resolution before upload. The SPARCO Database Working Group hold monthly conference calls and data quality is assessed regularly by the Data Coordinator. Data inspection is carried out yearly by a team from the SPARCO Hub and Sickle Africa Data Coordinating Centre (SADaCC from the University of Cape Town (<https://www.sickleinafrica.org/data-management>)).

Ethical approval from the National Health Research and Ethics Committee (NHREC) Abuja was obtained. Some Centres in addition to the NHREC approval obtained ethics clearance from their Institutions' Health and Research Ethics Committee prior to patients' enrollment. Informed consent and assent were obtained from patients and or parent/caregiver as applicable.

2.3. Data analysis

SAS software (SAS Institute, Cary, North Carolina, USA) version 9.4 was used for database management and analyses. Graphical illustrations were done using SAS and Adobe illustrator. Subjects were assigned to each of the six (6) geopolitical zones of the country depending on the state where their clinics are located. Demographic and clinical information obtained were entered into Excel spreadsheet and sent to SPARCO Nigeria Site at the Centre of Excellence for Sickle Cell Disease Research & Training, University of Abuja (CESRTA) [15] for cleaning and entry into the Research Electronic Data Capture (REDCap) software by trained data clerks. Frequency tables were generated and descriptive statistics were subsequently applied. Categorical characteristics were expressed as proportions and percentages. Associations or differences between or among nominal characteristics were done using chi square while trend within ordinal characteristics were tested using Cochran-Armitage test. Statistical significance was set at 0.05 for all tests.

2.4. Attrition analysis

Analysis carried out on one or multiple variables were done independent of other variables. To that end, the total number of subjects analyzed for each variable tended to vary from variable to variable depending on the number of available observations for each variable.

3. Results

Three thousand, six hundred and twenty-two (3622) patients were enrolled as at the time of analysis from the 20 SPARCO collaborating centres with 25 SCD clinics comprising of 14 adult and 11 paediatric SCD clinics. Fig. 1 shows the states that make up the different geopolitical zones in the country, while Fig. 2 shows the collaborating centres of SPARCO Nigeria where patients are currently being enrolled into the

SPARCO registry. There were 1680 (47.1%) males and 1889 (52.9%) females. Fifty-three did not indicate gender. One thousand, four hundred and thirty-four (1434) (39.6%) were children up to the age of 15 years, remaining 2188 (60.4%) were older than 15 years.

Fig. 2
SPARCO Collaborating Centres.

S/NO	CENTRE	CLINIC
NORTH-CENTRAL		
1	University of Abuja Teaching Hospital (UATH)	Adult and Paediatrics
2	Zankli Medical Centre, Abuja	Paediatrics
3	Maitama District Hospital, Maitama	Paediatrics
4	General Hospital, Nyanya	Paediatrics
5	Federal Medical Centre, Keffi	Paediatrics
6	National Hospital Abuja	Adult and Paediatrics
NORTH-WEST		
7	Ahmadu Bello University Teaching Hospital, Zaria	Adult
8	Kaduna State University Teaching Hospital, Kaduna	Adult and Paediatrics
9	Aminu Kano University Teaching Hospital, Kano	Adult
10	Federal Medical Centre, Birnin Kebbi	Adult
NORTH -EAST		
11	University of Maiduguri Teaching Hospital	Adult
SOUTH-WEST		
12	Obafemi Awolowo University Teaching Hospital, Ile-Ife	Adult and Paediatrics
13	University College Hospital, Ibadan	Adult and Paediatrics
14	Lagos University Teaching Hospital, Lagos	Adult
15	Lagos State University Teaching Hospital, Lagos	Paediatrics
SOUTH-EAST		
16	University of Nigeria Teaching Hospital, Enugu	Adult
17	Nnamdi Azikiwe Teaching Hospital, Nnewi	Adult
18	Federal Teaching Hospital, Abakaliki	Adult
SOUTH-SOUTH		
19	Federal Medical Centre, Asaba, Delta state	Paediatrics
20	Irua Specialist Hospital, Delta State; Ambrose Ali University	Adult

3.1. Haemoglobin variants

Three thousand, five hundred and thirty-two (97.5%) of the patients had homozygous sickle cell anaemia (Hb SS) and 90 (2.5%) had compound heterozygous sickle cell disease (Hb SC). Table 1 shows the geographical distribution of SCD haemoglobin variants. A higher proportion of patients from the North, 68 (2.9%) of 2374 as against 22 (1.8%) of 1246 from the South had Hb SC.

3.2. Clinical phenotypes

3.2.1. Vasoocclusive crises

The available data on 2841 subjects were analyzed to ascertain the prevalence of bone pain crisis in the 12 months preceding recruitment into the study. Overall, bone pain crisis was reported in 1714 (60.3%) of the study population, significantly occurring more in females than males, 952 (62.7%) of 1518 females vs. 762 (57.6%) of 1323 males, $p = 0.0054$. Pain frequency also increased steadily from subjects aged ≤ 5 years to middle aged i.e. 46–50 years, 144 (40.1%) of 359 compared to 20 (83.3%) of 24 respectively, $p < 0.0001$.

3.2.2. Anaemia requiring transfusion

Data on blood transfusion across all the health centers were available in 3288 patients, of which 2219 (67.5%) had been transfused in the 12 months preceding recruitment. Frequency of blood transfusion increased steadily with age from 47.0% (209/445) among patients aged 5 years or less to 91.3% (21/23) of those aged 51–55 years, p for trend < 0.0001 . Table 2 shows variation in the transfusion rates across the six geopolitical zones of the country, ranging from 27.3% in the

North-West to 79.3% in the North-East.

3.3. Prevalence of SCD clinical phenotypes

3.3.1. Acute SCD phenotypes

As shown in Table 3a, 613 patients reported ever having dactylitis out of 2581 with available data in all the six zones, giving a prevalence of 23.8%. Similarly, of 2727 available data on ACS, 160 (5.9%) had experienced the complication.

3.3.2. Chronic SCD phenotypes

For stroke, 73 (2.5%) of 2876 who responded had history of stroke. One hundred and twenty-five (4.8%) had history of priapism of 2589 available data, while 27 (1.1%) of the 2504 who responded had echocardiogram-diagnosed pulmonary hypertension. For renal complications, of the 2639 who responded, 166 (6.3%) had the complications. Also, 379 (34.0%) of the 1116 who responded had hepatic complications, and for osteonecrosis, of the 2715 who responded, 163 (6.0%) had the complication.

The frequencies of dactylitis, liver and renal complications were significantly higher among patients from the Northern part of the country than those from the Southern part, $p < 0.001$, 0.007 and 0.002 respectively. On the other hand, ACS was significantly more common among patients from the South than from the North, $p = 0.017$. The frequencies of other complications were similar, $p > 0.05$ (Table 3b).

Tables 4a and 4b shows distribution of SCD phenotypes according to age group. For instance, 27.0% of infants and 41.7% of those aged 1–5 years reported dactylitis, as against only 15.3% of those older than 20 years. The frequencies of CLU, osteonecrosis and priapism however increased with age. While only 7.0% of children up to the age of 15 years had CLU, 19.1% of adults experienced the complication. This is similar to the distribution of osteonecrosis across age groups, 7.1% in children and 18.7% in adults.

4. Discussion

This is a preliminary analysis of the SPARCO Database in Nigeria which has as a target the enrollment of 6000 patients with SCD by 2021. The preliminary analysis of the data volume is necessary to appreciate the distribution of clinical phenotypes across the country in order to support the centres with skills development activities and in the use of the SPARCO standard of care guidelines for improved patient care which are components of the SPARCO network activities in the country [15]. The skewed age distribution of (39.6%) of children 15 years and below, compared to 2188 (60.4%) patients older than 15 years reflects the patient population in the clinics enrolled as there were more adult haematology SCD (14) versus 11 paediatric clinics.

Homozygous (Hb SS) variant was the most common, constituting 97.5% and the remaining were Hb SC. The North West had the highest frequency of Hb SC followed by the South-West. The relatively high percentage of Hb SC from the South-South may not reflect the true frequency because of the very small sample size from that region. The wide variation in Hb SC prevalence, (0.2–6.5%) may be explained by

Table 1
Geographic distribution of sickle cell disease haemoglobin phenotype.

Geopolitical zones	Number in the group	Hb SS (%)	Hb SC (%)
N/Central	1358 (37.5)	1343 (98.9)	15 (1.1)
N/East	200 (5.5)	199 (99.5)	1 (0.5)
N/West	816 (22.5)	764 (93.6)	52 (6.4)
S/East	532 (14.7)	531 (99.8)	1 (0.2)
S/South	14 (0.4)	12 (85.7)	2 (14.3)
S/West	702 (19.4)	683 (97.2)	19 (2.8)
Total	3622 (100.0)	3532 (97.5)	90 (2.5)

Table 2
Geographical distribution of blood transfusion.

Geopolitical zones	Number in group	Transfusion (%)	p value
N/Central	1146 (34.9)	697 (60.8)	< 0.0001
N/East	198 (8.70)	157 (79.3)	
N/West	752 (22.9)	605 (27.3)	
S/East	502 (15.3)	335 (66.7)	
S/South	14 (0.4)	10 (71.4)	
S/West	676 (20.6)	415 (61.4)	
Total^a	3288 (100.0)	2219 (67.5)	

^a Data for 3288 out of the 3622 were available on blood transfusion.

the genetic background of the various ethnic groups that make up the patient population. It may also indicate migratory and historic intermarital patterns across the groups. In this study, none of our patients was reported to have compound heterozygous Hb S β thalassemia, possibly because the β thalassemia allele is uncommon in Nigeria [19].

Dactylitis was reported more frequently in ages 0–5 years and thereafter the frequency decreases with age. This is similar to findings in Jamaica in which dactylitis occurred in 24% patients by 12 months and in 45% by 2 years [20]. Similarly, a study from South-West Nigeria recorded a frequency of 33% [11]. The frequency of dactylitis was highest in the North-West and North-Central zones and least in the South-East. The frequencies from the North-East and South-East were low probably because the data from these regions came from adult sickle cell clinics as dactylitis mostly occurs in infants and young children. Reporting dactylitis by adult respondents is a function of recall ability except in cases where these events were recorded in the patients' case notes; this may explain the lower prevalence in older patients. Another possible explanation is that this might be a feature of disease severity, leading to mortality in a subgroup of SCD patients who had these as children.

Our database showed that > 50% of patients have had bone pain crisis in all the age groups except in ages 1–5, making it the most common clinical phenotype in all age groups and across the geographical zones. Vaso-occlusive crisis has been shown in several studies to be the most common acute complication with bone pain being the most common clinical presentation and leading cause of hospital emergency visits [10,11,14,21]. Bone pain is the hallmark and end result of the basic pathogenetic concept in SCD and it is therefore, often the first and most consistent presentation of this condition.

The prevalence of acute chest syndrome (ACS) ranges from 2.9% to 7.1%, increasing with age and peaked at age group 11–15 years. Two studies in children from the South West and South-South reported frequencies of 11.3% and 3.5% respectively [11,22]. A prospective study in African Americans, the Cooperative Study of Sickle Cell Disease (CSSCD) recorded highest incidence in ages 2–4 with the incidence decreasing with age [23]. In the northern part of Nigeria, a study on seasonal variations in frequencies of acute vaso-occlusive morbidities among adult sickle cell anaemia patients in Maiduguri (North-East) and Kano (North-West) recorded frequencies of between 3.57% and 16.07%. The highest frequency was recorded in December, the peak of harmattan season (October to February) with a marked fall in ambient temperatures [24]. Acute chest syndrome prevalence ranges from 0% in South-South to 8.93% in the South-West.

The frequency of stroke increases with age and peaked at age group 11–15 years and thereafter begins to decrease. Geographically, the highest frequency was recorded in the North-West followed by the North-East zone while the Southern part of the country had lower frequencies. The frequency of stroke was generally low in this study ranging from 0 to 3.9% compared to some local studies which reported prevalence of between 2.9 and 8.9%, occurring mainly below the age of 10 years [11,24,25] as well as studies from some Sub-Saharan countries recording as high as 16.9% [26]. These studies were conducted in children below 17 years while our database has both paediatric and

adult patients, which may account for the difference.

The development of stroke is usually a clinically recognizable phenotype however, several other CNS manifestations such as loss of speech, vision and persistent headache and seizures are all indicative of CNS disease and may predate overt stroke. Therefore, the scope of CNS disease in each study needs to be evaluated and may explain the higher prevalence seen in some studies.

Previous comparative studies in the country demonstrated some regional differences. For instance, stroke prevalence among Nigerian patients with SCD ranged from 0 to 15% across the country in a multi-centre study [27]. Also, the Bini population in the South-south zone of the country was generally younger and had a slightly lower incidence of alpha thalassaemia, lower HbA2 and higher HbF and MCV values than the Yorubas from the South-western Nigeria. The Binis also had significantly less dactylitis but more episodes of acute chest syndrome [28].

There was a consistent increase in the frequency of priapism with age, from 0 in < 1 year to about 9% in > 20 years. This might be explained by the part played by male sex hormones, which increase with puberty, in the pathogenesis of this complication of SCD. The South-East recorded the highest prevalence, though the South-South recorded a frequency of 20%, but the sample size was very small (14) compared to the other regions and may not reflect the true prevalence. The incidence of priapism varies between 5 and 45% and up to 50% in Jamaican patients, depending on the study population as it is more common among adolescents and has been projected that up to 89% of males with SCD will experience priapism by the age of 20 [29,30]. A study from the South-West on the prevalence of priapism and its awareness among male homozygous sickle cell patients recorded a prevalence of 39.1%, which is significantly higher than the frequencies recorded in our database, probably because that study was conducted among teenagers and adults (age range 14–53 years) compared to 0.4% recorded among paediatric patients in the same region [11,31].

The prevalence of chronic leg ulcer (CLU) varied between 1.8 and 13.4% increasing with age and peaking among the young adults. Studies from the South-West and North-West reported 3.4% and 5.5% with mean and median ages of 28.3 and 17 years respectively [32,33]. The prevalence of CLU is generally low below the age of 10 and most frequent between 10 and 25 years of age. The CSSCD showed sharp increase in the incidence of CLU after the second decade of life ranging from 14.6 to 19.2% in SCA patients [34,35]. The causal associations and risk factors of CLU include Hb SS, low haemoglobin level, infection, poor nutrition and low socio-economic status [32,35,36]. Others are; inflammation, haemolysis, vasculopathy, thrombosis and neuropathy [37]. Genetic factors such as HLA-B35, as well as the presence of about 30 single nucleotide polymorphisms (SNPs) from Genome-wide association studies have been implicated in the pathogenesis of CLU [38–40]. This complication had been attributed to the heme-related endothelial activation, leading to increased nitric oxide scavenging [37]. Its occurrence has been found to correlate with the presence of other features of severe disease. The increase with age indicates either that there is a cumulative organ damage which becomes more clinically apparent with time or the increasing influence of environmental factors.

The frequency of osteonecrosis (based on clinical and radiographic findings) increased with advancing age, with distribution similar between the Northern and Southern parts of the country. A previous study from the South-East Nigeria documented prevalence of 13.1% and another from South-west Nigeria reported 15.9% [41,42]. Both studies were retrospective in nature and may explain the wide disparity from the overall prevalence of 6.0% in this study. In a comparative study to identify risk factors for avascular necrosis of the femoral head (AVNFH) among Nigerian patients with SCD, the group with AVNFH had significantly higher rate of painful crises and hospitalizations per year than the group without. The group with AVNFH also had a significantly higher euglobulin clot lysis time than the other group without [43].

Table 3a
Geographical distribution of sickle cell complications (six geo-political zones).

	North-Central		North-East		North-West		South-East		South-South		South-West	
	N		N		N		N		N		N	
Dactylitis	1024	305(29.8)	198	1(0.5)	480	147(30.6)	346	20(5.9)	14	0(0.0)	519	140(27.0)
Acute chest syndrome	1030	43(4.17)	198	2(1.0)	437	36(8.2)	515	46(8.9)	14	0(0.0)	533	33(6.2)
Stroke	1059	24(2.3)	198	6(3.0)	435	17(3.9)	514	12(2.3)	14	0(0.0)	656	14(2.1)
Priapism	1045	40(3.8)	143	7(4.9)	432	27(6.3)	442	40(9.1)	5	1(20.0)	522	10(1.9)
Pulmonary hypertension	986	1(0.1)	195	6(3.1)	378	5(1.3)	400	6(1.5)	14	0(0.0)	531	9(1.7)
Liver Complication	738	254(34.4)	96	7(7.3)	241	62(25.7)	173	33(19.1)	14	9(64.3)	71	14(19.7)
Renal complication	1029	20(1.9)	184	70(38.0)	434	32(7.4)	459	37(8.1)	14	0(0.0)	519	7(1.4)
Osteonecrosis	1026	29(2.8)	198	15(7.6)	444	61(13.7)	509	27(5.3)	14	4(28.6)	524	27(5.2)

N represent the number of patients with available data in each group.

Other risk factors include coexistent alpha-thalassemia trait, high haematocrit, leucocyte and platelet level [42,44].

5. Limitations

Data contributed to the database came mostly from the North with the North-Central zone contributing about 40% alone while the South-South zone contributed < 1%. There was a wide variation in the number of observations per variables thus the total number of subjects analyzed for each variable was based on the number of available observations for each variable. In addition to these, specific complications of the liver and the renal system were not captured as entities in the Case report form that was used in the collection of data. The prevalence of clinical phenotypes by age and region also did not take into consideration the expected high death rate in patients with SCD. As the registered patients are ‘survivors’, there is a possibility of bias toward less disease severity among study participants. However, with the planned commencement of newborn screening by the SPARCO network, enrolment and follow up of a cohort of newborn babies into the database will allow better observation of the clinical epidemiology of SCD in our environment.

6. Conclusion

This report of clinical phenotypes of 3622 persons with SCD enrolled in the SPARCO Nigeria Database shows variation across the six geo-political zones of the country. The age of the patient appeared to significantly influence the development of SCD complications. Bone pain crisis and blood transfusion suggestive of anaemia were frequent events across the country. Dactylitis and acute chest syndrome are also common. The most frequent chronic complications were leg ulcers, osteonecrosis, renal complications and pulmonary hypertension. Priapism and stroke are less commonly seen. This preliminary analysis of the database has helped to understand the distribution of clinical phenotype across the country to inform training of health care

Table 3b
Geographical distribution of sickle cell complications (northern and southern parts).

Phenotypes	North		South		Statistics	
	N	Frequency (%)	N	Frequency (%)	χ^2	P
Dactylitis	1702	453 (26.6)	879	160 (18.2)	22.656	< 0.001
Acute chest syndrome	1665	81 (4.9)	1062	79 (7.4)	5.665	0.017
Stroke	1692	47 (2.8)	1184	26 (2.2)	0.953	0.329
Priapism	1620	74 (4.6)	969	51 (5.3)	0.638	0.424
Pulmonary hypertension	1559	12 (0.8)	945	14 (1.5)	2.901	0.089
Liver complication	1075	323 (30.1)	258	56 (21.7)	7.218	0.007
Renal complication	1647	122 (7.4)	992	44 (4.4)	9.277	0.002
Osteonecrosis	1668	105 (6.3)	1047	58 (5.5)	0.650	0.420

N represent the number of patients with available data in each group.

Table 4a
Distribution of sickle cell complications according to age (< 1–10 years).

Complications	< 1 year		1–5 years		6–10 years	
	N		N		N	
Dactylitis	37	10(27.0)	417	174(41.7)	490	132(26.9)
Bone pain crisis	55	17(61.8)	386	170(44.0)	490	266(54.3)
Acute chest syndrome	35	1(2.9)	442	13(2.9)	502	25(4.9)
Stroke	36	0(0.0)	439	7(1.6)	502	12(2.4)
Priapism	37	0(0.0)	425	7(1.7)	494	9(1.8)
Chronic leg ulcer	35	0(0.0)	440	10(2.3)	499	9(1.8)
Pulmonary hypertension	27	0(0.0)	386	0(0.0)	470	1(0.2)
Liver complication	19	1(5.3)	237	52(21.9)	277	90(32.5)
Renal complication	37	0(0.0)	434	3(0.7)	493	5(1.0)
Osteonecrosis	37	0(0.0)	443	8(1.8)	499	14(2.8)

Table 4b
Distribution of sickle cell complications according to age (11– > 20 years).

Complications	11–15 years		16–20 years		> 20 years	
	N		N		N	
Dactylitis	382	83(21.7)	472	94(19.9)	783	120(15.3)
Bone pain crisis	387	346(70.0)	494	684(66.5)	1029	1714(60.3)
Acute chest syndrome	410	29(7.1)	469	32(6.8)	869	60(6.9)
Stroke	413	13(3.2)	496	15(3.0)	990	26(2.6)
Priapism	407	16(3.9)	439	23(5.2)	787	70(8.9)
Chronic leg ulcer	372	11(2.9)	389	22(5.7)	934	125(13.4)
Pulmonary hypertension	361	2(0.6)	432	3(0.7)	828	21(2.5)
Liver complication	212	62(29.3)	238	78(32.8)	350	96(27.4)
Renal complication	399	15(3.8)	454	27(5.9)	822	116(14.1)
Osteonecrosis	408	10(2.5)	469	35(7.5)	859	96(11.2)

providers to care for the patients using the standard of care guidelines which are the other components of SPARCO network activities within Nigeria.

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Declaration of competing interest

None.

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