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Sickle cell disease clinical phenotypes in children from South-Western, Nigeria

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Abstract

Background: The clinical phenotypes of children with sickle cell disease (SCD) are poorly described in many sub-Saharan countries including Nigeria.

Objectives: The objective was to highlight various clinical phenotypes of SCD in children and investigate the influence of sociodemographic indices on the development of SCD complications.

Methods: We carried out a cross-sectional study of 240 pediatric patients attending the sickle cell clinic and the emergency room in a teaching hospital in South-Western Nigeria over a 12-month period. The clinical phenotypes and severity of the disease were documented, and the influence of sociodemographic variables was investigated.

Results: The five leading clinical phenotypes in our patients were significant pain episodes, that is, vaso-occlusive crisis in 159 (66.3%); anemic crisis in 62 (25.8%); severe bacterial infections, 57 (23.8%); acute chest syndrome (ACS), 27 (11.3%) and stroke, 7 (2.9%). Forty-two (33.1%) had a previous history of dactylitis (hand-foot syndrome). Other clinical phenotypes such as avascular necrosis of the femur, 4 (1.7%); nephropathy, 2 (0.8%); priapism, gallstone and chronic leg ulcer, one (0.4%) each, were not commonly seen. More children with a history of asthma had ACS. Furthermore, high steady-state white blood cell count was associated with severe disease.

Conclusion: The clinical phenotypes of SCD in children from South-Western Nigeria are highly variable with the disease manifesting very early and about 10% having significant complications. Sociodemographic characteristics appear to have little influence on the development of SCD complications among our patients, but age and low-socioeconomic class are associated with anemic crisis.

Key words: Clinical phenotypes, Nigeria, sickle cell disease, sociodemographic variables

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Introduction

Sickle cell disease (SCD) is a monogenic disorder involving substitution of hydrophilic glutamic acid by hydrophobic valine at position 6 of β-globin chain. The disease exhibits phenotypic variability attributable to several environmental and multiple genetic modifiers linked and unlinked to the β-globin gene locus. Of particular importance, in this regard are the β-globin gene haplotype and Hb F levels.[1,2]

In Nigeria, the prevalence of SCD is 20-30/1000 live births annually.[3] The burden of the disease is, however, additive in that, apart from contributing 9-16% to under five mortality in many West African countries [4], about 10% of the survivors develop stroke by the second decade of life[5] and about 48% of adult patients frequently develop multiple organ failure by the fourth decade of life.[4,6]

The clinical phenotypes of children with SCD are poorly described in many sub-Saharan countries such as Nigeria. This has limited the understanding of the natural history

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of the disease in this part of the world and makes it difficult to design appropriate interventions. There is also a need to identify local relevant risk factors and the influence of socioeconomic class in predisposing to SCD complications and the prevailing co-morbidities that contribute to the overall clinical picture. In our previous study,[7] we evaluated the severity of SCD among our patients using a set of comprehensive clinico-laboratory parameters, including some SCD complications. In this report, we highlight various clinical phenotypes of SCD in children residing in a semi-urban town in South-Western Nigeria and investigate the influence of sociodemographic indices on the development of complications.

Methods

This was a cross-sectional study, including all children with SCD, who attended the Wesley Guild Hospital Ilesa Unit of Obafemi Awolowo University Teaching Hospital for routine follow-up care or emergency services over a 12-month period (January to December 2013). The hospital has a pediatric SCD clinic which runs weekly and attends to an average of 25 patients/week. A total of about 300 children with SCD is registered in the clinic. The clinic offers comprehensive care including the use of hydroxyurea when indicated. However, oral penicillin prophylaxis and pneumococcal vaccination are not currently routinely prescribed.

Written informed consents were obtained from the parents/caregivers before the commencement of the study. Furthermore, the study followed the ethical standards of the Helsinki declaration of the World Medical Association.

Data on the sociodemographics (age, sex, and socioeconomic class); medical history and physical findings were obtained from each patient through a pretested questionnaire and by review of relevant medical charts. Socioeconomic class was determined using the occupation of the father and the highest academic qualification of the mother according to Olusanya *et al*.[8] The father's occupation has scores ranging from 1 to 3, while the mother's educational qualification has scores from 0 to 2. The total score was then calculated for each patient with minimum and maximum possible scores of 1 and 5, respectively. The classification was such that the higher the total score, the lower the social class. For instance, those with a total score of 1 or 2 were in the upper social class (i.e. class 1); total score of 3 for middle social class (class 2) and score of 4 or 5 for lower social class (class 3). Other data included the age at diagnosis of SCD, age at first presentation in our facility and the presence of SCD complication(s) as defined by Ballas *et al*.[9,10]

- Acute significant painful episode was defined as a painful event requiring a hospital visit and the use of oral and or parenteral analgesics. Number of significant pain episodes in the 12 months preceding recruitment was documented
- Dactylitis/hand-foot syndrome: Painful nonpitting swelling of the hand/foot/digits
- Acute chest syndrome (ACS): An acute illness characterized by fever and respiratory symptoms (dyspnea, chest pain) accompanied by new pulmonary infiltrates on chest radiograph
- Avascular necrosis (AVN): This is osteonecrosis or aseptic necrosis of the head of femur or humerus confirmed by radiography as irregularity of the articular surfaces of the head of femur/humerus
- Stroke (cerebro-vascular disease): Acute neurologic symptoms/signs secondary to occlusion of and or hemorrhage from cerebral vessels confirmed on computerized tomography (CT) scan or magnetic resonance imaging (MRI)
- Hyper-hemolysis: Characterized by marked drop in hemoglobin concentration with evidence of increased red blood cell destruction such as worsening pallor and jaundice, passage of dark-brown urine, increase serum bilirubin, and reticulocytosis
- Splenic sequestration: Rapid enlargement of the spleen associated with anemia and hypovolemic shock
- Aplastic crisis: Transient aplastic situation characterized by clinical and laboratory evidences of severe anemia, reticulocytopenia, leucopenia and thrombocytopenia
- Severe bacterial infections: Pneumonia, sepsis, meningitis, osteomyelitis, septic arthritis confirmed by positive culture and or radiograph
- Chronic leg ulcer: Ulceration of the skin and underlying tissue of the lower extremities, especially on the medial or lateral surface of the ankle
- Cholelithiasis: Confirmed on abdominal radiograph in those with severe abdominal pain
- Priapism: Sustained, unwanted, and painful penile erection.

During the recruitment, a child was enrolled into the study only once. Splenic and hepatic enlargements by palpation, as well as laboratory tests (hematocrit and white blood cell counts), were done by standard methods during steady state. Massive splenomegaly was defined as steady state splenic size of at least 10 cm and persistent gross splenomegaly (PGS) as steady state splenic size of 10 cm or more in children with SCD aged ≥8 years.[11] Severity scoring of SCD was as previously reported, using some clinical and laboratory variables.[7] The parameters used in the severity scoring included frequency of significant painful episodes, blood transfusion, and SCD-related hospitalization in the previous 12 months; past or present histories of complications; the degree of splenic and hepatic enlargement; steady state levels of hematocrit and total white blood cell count. The parameters were scored 0-5 based on the frequency of occurrence and severity of the parameters, with a total score for each child ranging from 0 to 34. Patients with a total score of <8 were considered to have mild disease, score of 8-17 as moderate disease and score >17 as having severe disease.

Statistical analysis

We analyzed the clinical and hematologic profiles of the patients by proportions and percentages for categorical data and means ± standard deviation (SD), for continuous data. Categorical variables were compared with Chi-squared or Fisher's exact tests while metric data were compared with Independent's sample *t*-test, Mann–Whitney U-test, analysis of variance, or Kruskal–Wallis H-test as indicated. $P < 0.05$ were taken as statistical significance.

Results

Sociodemographic characteristics and age at diagnosis

A total of 240 children with SCD was recruited for the study. The male to female ratio was 1.7:1, 9 (3.8%) were infants and majority, 112 (46.7%) were from lower social class as shown in Table 1. They were diagnosed between the ages of 5 and 156 months; the mean age at diagnosis was 28.34 ± 9.11 months (median age was 28.0 months). Only 47 (19.6%) were diagnosed in infancy. The age at diagnosis was significantly ($P < 0.05$) lower in males than females (27.59 ± 3.77 months vs. 29.85 ± 9.70 months, respectively, and also in children from socioeconomic class 1 (27.11 ± 1.26 vs. 30.26 ± 5.12 vs. 29.84 ± 8.37 months). The mean age at first presentation with SCD-related symptoms in our hospital was, however, 31.31 ± 12.11 months (range: 5-154 months, median: 30.0 months).

Table 1: Sociodemographic characteristics, age at diagnosis, and age at first presentation of the children with SCD

Characteristics	Frequency (%)
Total number	240 (100)
HbSS/HbSC	217/23 (90.4/9.6)
Male/female	151/89 (62.9/37.1)
Mean age±SD/range (months)	70.83±44.35/6-180
Infants (<1 year)	9 (3.8)
Preschool age (1-5 years)	97 (40.4)
School age (>5-10 years)	102 (42.5)
Adolescents (>10 years)	32 (13.3)
Socioeconomic class 1	51 (21.3)
Socioeconomic class 2	77 (32.1)
Socioeconomic class 3	112 (46.7)
Mean age±SD at diagnosis/range (months)	28.34±9.11/5-156
Diagnosed during infancy	47 (19.6)
Diagnosed between 1 and 5 years	132 (55.0)
Diagnosed after 5 years	61 (25.4)
Mean age±SD at first presentation in WGH/range (months)	31.13±12.11/5-154

SD=Standard deviation; WGH=Wesley Guild Hospital; SCD=Sickle cell disease

Baseline clinical and laboratory profile

Thirteen (5.4%) of the children had asthma, and one (0.4%) had HIV infection as associated co-morbidities [Table 2]. About two-thirds, 159 (66.3%) of the children had at least one significant pain episode, 58 (24.2%) were transfused, and 127 (52.9%) had been hospitalized in the 12 months preceding recruitment for SCD-related complications. Thirty (12.5%) had massive splenomegaly and only 11 (4.6%) had PGS. The overall mean ± SD steady state hematocrit and total white blood cell counts were 18.65 ± 7.84% and 13,766 ± 11,227 cells/mm^3, respectively.

Table 2: Baseline clinical characteristics of the patients

Baseline characteristics	Number of children (%)
Number on hydroxyurea	13 (5.4)
Associated comorbidities	
G6PD deficiency	15 (6.3)
Asthma	13 (5.4)
Seizure disorder	3 (1.3)
Lymphoma	1 (0.4)
HIV infection	1 (0.4)
Congenital lymphangiectasia	1 (0.4)
Malaria infection*	68 (53.5)
Steady state hepatomegaly (frequency (%)/mean size/range in cm)	166 (69.2)/5.26±2.75/0-12
Steady state splenomegaly (frequency (%)/mean size/range in cm)	139 (57.9)/4.05±4.16/0-16
Massive splenomegaly	30 (12.5)
PGS	11 (4.6)

*Malaria parasitemia was demonstrated in 68 of the 127 children who were admitted during the study period. G6PD=Glucose 6 phosphate dehydrogenase; HIV=Human immunodeficiency virus; PGS=Persistent gross splenomegaly

Twenty-five (10.4%) were classified as having severe disease, 52.1% had moderate disease, and remaining 37.5% had mild disease using the SCD severity scoring system. The overall mean SCD severity score was 8.46 ± 4.65, with scores ranging from 1 to 21 [Table 3].

Sickle cell disease phenotypes

The five leading clinical phenotypes in our patients were significant pain episode, that is, vaso-occlusive crisis, 159 (66.3%); anemic crisis, 62 (25.8%); severe bacterial infections, 57 (23.8%); ACS, 27 (11.3%) and stroke, 7 (2.9%). Forty-two (33.1%) had a previous history of dactylitis/hand-foot syndrome. Other phenotypes such as AVN of the femur, 4 (1.7%); nephropathy, 2 (0.8%); priapism, gallstone and chronic leg ulcer, 1 (0.4%) each was not commonly seen.

Vaso-occlusive crisis

About two-thirds of the patients had at least one significant pain episode in the 12 months preceding the study. Forty (16.7%) of the patients experienced significant pain episode once, 23 (9.6%) twice and 97 (40.4%) thrice or more. The frequency of the pain episodes ranged from 0 to 15 during the study period. Using Mann–Whitney U-test and Kruskal–Wallis

H-test, the age, gender, and socioeconomic class did not significantly influence the frequency of pain episodes, $P = 0.123$, 0270 and 0.439, respectively. However, those with vaso-occlusive crisis (VOC) were older, 75.7 ± 45.9 versus 61.2 ± 39.9 months ($P = 0.016$).

The mean steady state hematocrit and the total white blood cell count of the 159 children with significant painful episodes were significantly higher than the 81 without pain episodes ($P = 0.001$ and 0.004, respectively) as shown in Table 4.

Table 3: Baseline laboratory characteristics and severity of the patients

Laboratory characteristics and disease severity	Number of children (%)
Hematocrit (mean/range in %)	18.65±7.84/18-31
Total white blood cell count (mean in cells/mm^3)	13,766±11,227
Pain episodes in the previous 12 months (mean/range)	2.48±2.85/0-15
Blood transfusion in the previous 12 months (mean/range)	0.78±1.08/0-5
Hospitalization in the previous 12 months (mean/range)	1.82±1.89/0-10
Mild disease (frequency (%)/mean SCDSS/range)	90 (37.5)/3.94±1.48/1-6
Moderate disease (frequency (%)/mean SCDSS/range)	125 (52.1)/9.76±1.74/8-14
Severe disease (frequency (%)/mean SCDSS/range)	25 (10.4)/18.54±1.05/18-21

SCDSS=Sickle cell disease severity score

Anemic crisis

Sixty-two (25.8%) had acute anemic crisis requiring blood transfusion during the study period, comprising 57 (23.8%) with hyperhemolysis, 4 (1.7%) with splenic sequestration, and 1 (0.4%) with transient aplastic crisis. As shown in Table 4, the 62 children who had anemic crisis were significantly ($P = 0.013$) younger than the 178 without anemic crisis (62.5 ± 43.1 months vs. 78.8 ± 44.4 months. Furthermore, a significantly ($\chi^2 = 4.363$, $P = 0.037$) higher proportion of children who experienced anemic crisis were from the lower social class, 36 (58.1%) of the 62 against 76 (42.7%) of the 178.

Severe bacterial infections

A total of 57 (23.8%) children had severe bacterial infections. Sepsis was the leading infection recorded (35 [14.6%]), followed by osteomyelitis (28 [11.7%]), pneumonia (19 [7.9%]), meningitis 4 (1.7%), septic arthritis and cerebral abscess (one case each).

Thirty-three (57.9%) of the 57 children with severe bacterial infections had positive cultures comprising 26 (45.6%); 7 (12.3%) and 4 (7.0%) with positive blood, bone/joint aspirate, and cerebrospinal fluid (CSF) cultures, respectively. The four with positive CSF culture also had positive blood cultures. The isolates in the blood included *Staphylococcus aureus* isolated in 13 (50.0%) children; *Klebsiella* spp in 9 (34.6%) children; *Haemophilus influenzae* and *Pseudomonas* species in 2 (7.7%) each, *Escherichia coli* and α-hemolytic streptococcus in one child each. Two children, however, had multiple growth of *S. aureus* and *Klebsiella*.

Table 4: Influence of sociodemographic characteristics and steady–state laboratory findings on the occurrence of vaso-occlusive and anemic crises

Characteristics	Vaso-occlusive crisis			Anaemic crisis		
	Present	Absent	*P*	Present	Absent	*P*
Number	159	81		62	178	
Mean age in month	75.7±45.9	61.2±39.9	0.016#	62.5±43.1	78.8±44.4	0.013#
Infancy, *n* (%)	4 (2.5)	5 (6.2)	0.120	7 (11.3)	2 (1.1)	0.001
Preschool age	61 (38.4)	36 (44.4)		29 (46.8)	68 (38.2)	
School age	68 (42.8)	34 (42.0)		23 (37.1)	79 (44.4)	
Adolescents	26 (16.4)	6 (7.4)		3 (4.8)	29 (16.3)	
Sex						
Male	106 (66.7)	45 (55.6)	0.092	42 (67.7)	109 (61.2)	0.361
Female	53 (33.3)	36 (44.4)		20 (32.3)	69 (38.8)	
SEC						
SEC 1	34 (21.4)	17 (21.0)	0.178	4 (6.5)	47 (26.4)	0.004
SEC 2	45 (28.3)	32 (39.5)		22 (35.5)	55 (30.9)	
SEC 3	80 (50.3)	32 (39.5)		36 (58.0)	76 (42.7)	
Hb type						
HbSS	144 (90.6)	73 (90.1)	0.912	59 (95.2)	158 (88.8)	0.141
HbSC	15 (9.4)	8 (9.9)		3 (4.8)	20 (11.2)	
Mean HCT (%)	21.8±7.7	18.0±8.1	0.001#	18.2±4.7	24.9±4.4	0.001#
Mean WBCC*	15.9±12.0	11.5±9.2	0.004#	15.4±13.0	14.2±9.0	0.425#

*WBCC and was expressed as $\times 10^3$/mm^3; #Done by Independent *t*-test, others by Chi-square test. SEC=Socioeconomic class; HCT=Hematocrits; WBCC=White blood cell count

Table 5: Influence of sociodemographic characteristics and some steady-state laboratory findings on the occurrence of severe infections and ACS

Characteristics	Severe infections			ACS		
	Present	Absent	*P* value	Present	Absent	*P* value
Number	57	183		27	213	
Mean age in months	82.4±52.4	64.1±37.6	0.004#	83.4±38.2	69.3±45.0	0.121#
Infancy *n* (%)	3 (5.3)	6 (3.3)	0.050	0 (0)	9 (4.2)	0.247
Preschool age	17 (29.8)	80 (43.7)		8 (29.6)	89 (41.8)	
School age	24 (42.1)	78 (42.6)		16 (59.3)	86 (40.4)	
Adolescents	13 (22.8)	19 (10.4)		3 (14.3)	29 (13.6)	
Sex						
Male	35 (61.4)	116 (63.4)	0.787	21 (77.8)	130 (61.0)	0.090
Female	22 (38.6)	67 (36.6)		6 (22.2)	83 (39.0)	
SEC						
SEC 1	15 (26.3)	36 (19.7)	0.314	13 (48.2)	38 (17.8)	0.001
SEC 2	14 (24.6)	63 (34.4)		2 (7.4)	75 (35.2)	
SEC 3	28 (49.1)	84 (45.9)		12 (44.4)	100 (47.0)	
Hb type						
HbSS	51 (89.5)	166 (90.7)	0.782	27 (100)	190 (89.2)	0.147
HbSC	6 (10.5)	17 (9.3)		0 (0)	23 (10.8)	
Mean HCT (%)	19.9±7.5	18.1±8.0	0.001#	20.4±8.4	18.4±7.8	0.215#
Mean WBCC*	17.7±12.7	11.4±9.6	0.004#	18.5±11.9	13.2±11.1	0.021#

*WBCC and was expressed as $\times 10^3/mm^3$; #Done by Independent *t*-test, others by Chi-square test. SEC=Socioeconomic class; ACS=Acute chest syndrome; HCT=Hematocrits; WBCC=White blood cell count

For the bone or joint aspirates, *S. aureus* was isolated in six children, *Klebsiella* in two and *Salmonella* spp. in one. There were multiple growths of *S. aureus* and *Klebsiella* in two children. The organisms isolated from the CSF were *H. influenzae* in two children, *Klebsiella* and α-hemolytic streptococcus in one child each.

Age was the only sociodemographic variable that significantly influenced the occurrence of severe bacterial infections [Table 5]. Those with severe bacterial infections were significantly older, 82.4 ± 52.4 months versus 64.1 ± 37.6 months, ($P = 0.004$).

Acute chest syndrome

Twenty-seven (11.3%) patients had confirmed ACS during the study period. These included 25 with one episode and two patients with two episodes. Significantly, more children with a history of asthma had ACS, that is, 6 (46.2%) of the 13 with a history of asthma as against 21 (9.3%) of the 227 without a history of asthma had ACS, $\chi^2 = 16.701$, $P = 0.001$. ACS also occurred more commonly among children from upper social class. Fourteen (51.9%) of the 27 children with ACS as against 38 (17.8%) of the 213 children without ACS were from upper social class, $\chi^2 = 7.764$, $P = 0.001$. However, age and gender did not significantly influence the occurrence of ACS [Table 5].

Stroke

Seven patients (2.9%) had overt stroke, in three of whom it occurred more than a year before the study period. The four with acute stroke were shown on CT/MRI to be infarctive. The age range of the seven patients was 26-97 months with a mean of 63.3 ± 26.3 months, which was not statistically different from that (71.1 ± 44.9 months) of the 233 children without stroke ($t = 0.46$, $P = 0.648$). Gender and socioeconomic class did not differ between the two groups.

Other phenotypes

Four patients (1.7%) had radiologically proven AVN. All of them were adolescents. Two males had nephropathy (nephrotic syndrome/chronic kidney disease), one child each had priapism, chronic leg ulcer, and gallstone.

Discussion

This study outlines various clinical phenotypes of SCD in children from South-Western Nigeria where the Benin haplotype (haplotype 19) which is associated with severe disease and Cameroun haplotype (haplotype 17) that is associated with variable severity are common.[12] Phenotypic variability has been reported even among patients in the Arabian Peninsula where the Arab/India haplotype which is associated with high Hb F and milder phenotypes, is prevalent.[13,14]

Sociodemographic characteristics, with the exception of age, appear to have little influence on the development of SCD complications, e.g. AVN and ACS among our patients. Earlier findings by Okany and Akinyanju in Lagos, Nigeria among 122 adults with homozygous SCD suggested that socioeconomic status has a modifying influence on the severity of SCD.[15] While socioeconomic

class may influence the quality of healthcare obtained, it could be that the patients in this study had similar access to healthcare facilities especially since they all attend the sickle cell clinic in our hospital. Moreover, socioeconomic class is less likely to influence the development of AVN or ACS, unlike severe acute anemia, which was seen in about one-quarter of the patients in this study with the majority resulting from hyper-hemolysis. Transient aplastic crisis was reported in only one child. These children with anemic crises were younger and from lower socioeconomic class, which is the group of children who are more likely to have recurrent malaria infection, nutritional anemia, and hookworm infestation.[16]

Although, we did not check for malaria parasites in all the 240 children recruited for this study, about half of those admitted (that is, 68 of the 127) had confirmed malaria parasitemia. Makani *et al*.[16] in their 5 years prospective surveillance study for malaria parasitemia among Tanzania patients with sickle cell anemia, observed that, though malaria infection was not common among outpatients with SCD, its presence during hospitalization was associated with a higher likelihood of death. Hence, current efforts at reducing malaria infection such as chemoprophylaxis and environmental manipulation must be intensified. In addition, prompt and effective treatment during severe illness is required.

Vaso-occlusive crisis was the leading clinical phenotype among our patients. These acute pain episodes occurred 1-15 times with about two-fifth of the patients having pain at least 3 times in a year. The most distressing aspect of pain crises was that the episodes were generally unpredictable. The approach to pain control, therefore, should include aggressive management of acute pain crises; prevention of future episodes and management of long-term sequelae of chronic pain such as osteonecrosis and osteomyelitis. Sadly, in our center, pain crises are often poorly evaluated and undertreated due to absence of specific physical findings and the fear of narcotic addiction and tolerance. As shown in Table 2, about 5% of our patients are currently using hydroxyurea. This, we hope, will significantly reduce the frequency of pain episodes among this group. However, its continuous use is threatened by its high cost and relative unavailability.

Bacterial infections contributed significantly to the clinical phenotypes of our patients with SCD. About a quarter had severe bacterial infections. SCD increases susceptibility to infections, which in turn, provoke a cascade of pathophysiological changes.[17] SCD impairs splenic function, causes defects in complement activation and deficiency in immune-boosting micronutrients like zinc.[18] Although many previous studies had reported low prevalence of invasive bacterial infections among children with SCD in Nigeria, it is still important that penicillin prophylaxis and hemophillus influenzae type b and pneumococcal conjugate vaccines be prescribed for these children who are at increased risk.[19,20] As reported by Obaro,[21] absence of evidence of pneumococcal infections in SCD patients might not necessarily imply evidence of their absence. The lack of evidence might result from prior use of nonprescription antibiotics, suboptimal laboratory isolation techniques, or death of those with the overwhelming infection before reaching the hospital.

In this study, the presence of complications such as VOC, anemic crisis, ACS, and stroke were associated with increased leucocyte count. Though SCD is a disorder of red blood cells, its severity increases with high leukocyte count.[22] The adherence of white blood cells to the vascular endothelium which is mediated by several adhesion molecules is thought to also facilitate vaso-occlusion. We also observed that SCD children with VOC had a higher mean steady-state hematocrit. High hematocrit is associated with increase blood viscosity; especially in patients with SCA whose stable hematocrit is usually low. This increased blood viscosity has been demonstrated as one of the hemorheological factors involved in the pathophysiology of VOC.[23]

The clinical phenotype of SCD in children from South-Western Nigeria is highly variable with the disease manifesting very early and about 10% having severe disease. Sociodemographic characteristics appear to have little influence on the development of SCD complications among our patients. AVN, transient aplastic crisis, nephropathy, priapism, gallstone, and chronic leg ulcers are less commonly seen.

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