Haematological Profiles of Children with Sickle Cell Anaemia in Steady State and Vaso-Occlusive Crisis: A Comparative Study

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ABSTRACT

Background: Sickle cell anaemia (SCA) is a major health problem in many parts of the world particularly in Sub-Saharan African countries with Nigeria having the highest disease burden. The disorder is characterised by chronic haemolytic process; with subsequent marrow hyperactivity resulting in higher levels of leucocytes and platelet counts in SCA patients compared to normal population. **Objectives**: To compare the haematological profiles (leucocyte counts, absolute neutrophil count, platelet counts, haemoglobin concentration and haematocrit level) of SCA children in steady state and in vaso-occlusive crisis aged one year to 17 years as well as compare them to age- and gender-matched children with haemoglobin genotype AA. **Methodology**: A cross-sectional study was conducted among 50 children with SCA grouped into subjects in steady state (36) and those having vaso-occlusive crisis (14) and age- and gender- matched controls (50) with haemoglobin genotype AA. Physical examination of the participants was conducted and blood samples collected for haematological tests. Data analyses were carried out using SPSS statistical package version 21. P value ≤ 0.05 set as significant level. **Results**: The leucocyte count, neutrophil count and platelet counts of children with SCA were higher (particularly for those in vaso-occlusive crisis) than matched controls (P-value < 0.05) whereas the haemoglobin concentration and haematocrit level were lower among children with SCA compared to the controls (P-value < 0.01). There was no statistically difference when compare these parameters among SCA in steady or in vaso-occlusive crisis. **Conclusion**: Strategies targeting on reduction of leucocyte and platelet count as well as improving the haemoglobin concentration could reduce the disease severity and improve wellbeing of children with SCA.

Keywords: Haematologic parameters, Sickle cell anaemia, Steady state, Vaso-occlusive crisis.

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INTRODUCTION

Sickle cell anaemia (SCA) is an autosomal recessive disorder of haemoglobin synthesis. It results from a point mutation in the β-globin chain where valine replaces glutamic acid at 6th position of the chain to form sickle haemoglobin.[1,2] The sickle haemoglobin has the unique property of polymerizing into long fibres when deoxygenated, thereby decreasing red cell deformability leading to cell membrane damage.[1,2,3] Red blood cells (RBCs) containing sickle haemoglobin become rigid, elongated and sickle-shaped with low oxygen concentration.[1,2,3]

Sickle cell anaemia is prevalent among people from sub-Saharan Africa, South America, the Caribbean, Central America, Saudi Arabia, India and Mediterranean countries.[1,4,5] It occurs more often in malaria endemic region where sickle cell trait is presumed to confer protection against severe forms of *Plasmodium falciparum* malaria.[1,5] Currently, Nigeria has the highest burden[4,5] of SCA disease globally with about 150,000 Nigerian children born annually with SCA.[4,5,6,7]

The intracellular polymerization of sickle haemoglobin is the primary event and hallmark of the disease.[8.9.10] This depends on the amount of oxygen carried by each RBC; factors such as high altitude, high temperature, exercise, acidosis, dehydration and low oxygen tension promote polymerization of the red cell. Polymerization and cell membrane deformability promotes vaso-occlusion of the microcirculation as well as haemolysis.[9] Haemolysis leads to hyperactivity of the marrow in response to the anaemia resulting to activation and increased production of other cell lines such as reticulocyte, leucocyte and platelets.[9,10,11,12,13] These cells clog microcirculation perpetuating the vaso-occlusive events[9,10,11,12,13]. In the long run, this marrow hyperactivity results to distortion of the bone architecture with subsequent bone conditions as seen in SCA patients.

Past studies had demonstrated increased levels of leucocyte and platelet counts in SCA patients compared to individuals with Hb AA and lower levels of haemoglobin concentration and haematocrit levels in SCA patients in relation to their counterparts with haemoglobin phenotype AA.[13,14,15,16,17,18] Most of these studies are done in adult population with few involving paediatric population.[13,14,15,16,17] Moreso, these studies focused attention among SCA subjects in steady state.[13,16,18] Haematological profiles of children with SCA has not been extensively studied in south-east Nigeria in the recent years particularly as it regards vaso-occlusive crisis. Thus, there is need to relate the haematological parameters of SCA patients with their crises particularly vaso-occlusive crisis; which is the commonest crisis in this group of subjects.

This study aimed to compare the haematological profiles (total leucocyte counts, absolute neutrophil count, platelet counts, haemoglobin concentration and haematocrit level) of SCA children in steady state and in vaso-occlusive crisis aged one year to 17 years as well as compare them to age- and gender-matched children with haemoglobin phenotype AA.

METHODOLOGY

The study was carried out at Paediatric Haemato-Oncology unit of Nnamdi Azikiwe University Teaching Hospital (NAUTH), Nnewi, Anambra State. Nnamdi Azikiwe University Teaching Hospital is one of the two tertiary, and the only Federal government owned health institution in the state. It provides primary, secondary and tertiary healthcare services to the people living in Nnewi and environs. Nnewi is a commercial city, located in Nnewi North Local Government Area of Anambra State.[19] The residents of Nnewi are predominantly Igbos, mainly traders and civil servants.

Study Population

A comparative prospective cross-sectional study was conducted among SCA children and age- and gender- matched counterparts with haemoglobin phenotype AA. The subjects were one year to 17 years old known SCA patients in vaso-occlusive crisis or in steady state seen in emergency room or Paediatric Haemato-Oncology Clinic of the institution. Steady state was in accordance with

Ballas and co-workers[20] definition with respect to the following criteria; non–intake of antibiotics in the preceding 3 weeks, absence of vaso-occlusive crisis and inter-current illness (such as infection) in the preceding 4 weeks, and no blood or blood product transfusion in the preceding 4 months. Vaso-occlusive crisis defined as new onset of pain in the extremities, back, abdomen or chest, lasting more than 4 hours that led to an unscheduled clinic or emergency room visit and required hospitalization, which could only be explained by SCD.[21]

The controls were age- and gender- matched non-SCA subjects whose haemoglobin phenotypes are HbAA and who were recruited from Children Out-Patient Clinic of the institution. Subjects with fever (temperature of 38 °C and above),[22] with clinical presentation suggestive of chronic disease such as diabetes, hypertension, renal disease as well as subjects with other forms of haemoglobinopathies or traits (HbSC, HbAS) were excluded from the study.

Sample size was calculated with the formula for comparative study

$$n = \frac{2\,(Z_{\alpha} + Z_{1-\beta})^{2}\sigma^{2}}{(\mu_1 - \mu_2)^2}$$

Where n= minimum sample size in the 2 groups

Z_{α}= the standard normal deviation set at 95% confidence interval (1.96)

$Z_{1-\beta}$ = the standard normal deviation corresponding to a power of 90% (1.28)

$\boldsymbol{\sigma}$ = standard deviation from previous study (0.10)[11]

$\mu_1 - \mu_2$= degree of accuracy desired set at half of $\boldsymbol{\sigma}$ (0.05)

Therefore the minimum sample size was 84 subjects for both Hb SS and Hb AA in ratio of 1:1.

To adjust for 10% attrition, using the formula

N = n/1-q

Where N = final sample size

n = initial calculated sample size

q = proportion of attrition at 10%

A minimal sample size of 94 subjects (47 Hb SS subjects and 47 Hb AA controls) will be used for the study.

Ethical Consideration

Ethical clearance was obtained from the Ethics Committee of Nnamdi Azikiwe University Teaching Hospital, Nnewi (Ref no. NAUTH/CS/66/VOL.10/2017/10). Written Informed consent was obtained from the subjects' parents/caregivers while informed assent was obtained from subjects aged 7 years old and above. Those who met the inclusion criteria were recruited in the study.

Data Collection Procedure

This study lasted for a period of 5 months from July 2019 to November 2019. A semi-structured interviewer administered pre-tested questionnaire was administered in respect of each child to the parent/caregiver by the researcher after obtaining informed consent (and assent where applicable). Information about the patient's socio-demographic data namely age, gender, parents' highest level of education and occupations and relevant medical history including history of vaso-occlusive crisis, past blood transfusion and previous admission were obtained. The parental level of education and occupation were used to calculate the socio-economic status using the classification proposed by Oyedeji.[23] For each of the subjects, axillary temperature was measured by using clinical mercury in glass thermometer.

Two millilitres of venous blood were collected from each subject after observing universal precaution and were transferred into the ethylenediaminetetraacetate (EDTA) bottle for haemoglobin phenotype (for controls) and haematological indices - haemoglobin (Hb) estimation, haematocrit level, leucocyte and neutrophil counts, and platelet counts. The blood samples were submitted to the haematology department of the institution within 2 hours of collection and analysed within 24 hours of submission. Automated haematology analyser (Mythic 22 AL Automatic Haematology Analyser Orphee, Switzerland) which uses the principle of aperture impedance, was used to analyse the haematological parameters. The phenotypes of the matched controls were determined using the alkaline cellulose acetate electrophoresis instrument at pH of 8.6. All the haematological investigations were carried by the Laboratory Scientists in the

Haematology Department of the institution. The sample bottles were coded to minimize bias and as a routine in the department, the haematology auto-analyser was subjected to periodic quality checks including manual verifications.

Data Analyses

The data obtained were entered, assessed for error and validated, then analysed using IBM SPSS statistics software version 21. Numeric variables (age and haematological parameters) were expressed as mean ± standard deviation. Student's t-test was used to compare the mean values of SCA subjects in steady state and SCA subjects in vaso-occlusive crisis. Analysis of variance (ANOVA) was used to compare the difference among mean values of SCA subjects in steady state, SCA subjects in vaso-occlusive crisis and HbAA controls. The association between categorical variables (gender and socioeconomic class) was assessed using chi square. P-values of ≤ 0.05 were considered as statistically significant for all the analyses.

RESULTS

A total of 110 participants were screened and recruited into the study. Of these, 10 participants were excluded for not meeting the inclusion criteria and clotted samples (5 controls were HbAS and 5 SCA subjects' haematological parameters could not be assessed because of clotted blood samples and were lost to follow up). Therefore, 100 subjects were analysed comprising 50 SCA subjects (36 in steady state and 14 in vaso-occlusive crisis) and 50 HbAA controls. The mean ages of all SCA subjects and that of HbAA matched controls were 9.4 years ± 5.1 years and 8.9 years ± 4.7 years respectively (P = 0.93). There were 54 males and 46 females giving a male to female ratio of 1.2: 1 (P = 0.66). However, there was significant difference in the distribution of study subjects across the three socio-economic subgroups with nearly half (43%) and just above a quarter (26%) belonging to the middle and lower socio-economic classes respectively (P < 0.01). (Table 1)

Table 1: Socio-demographic characteristics of the study subjects

Variable	HbSS-ST (n =36) (%)	HbSS-VOC (n=14) (%)	HbAA (n=50) (%)	Total (n=100) (%)	χ^2	*P* value
Age group (years)					1.858	*0.932*
1 – 5	10 (27.8)	5 (35.7)	15 (30.0)	30 (30.0)		
6 -10	12 (33.3)	4 (28.6)	15 (30.0)	31 (31.0)		
11-15	10 (27.8)	2 (14.3)	13 (26.0)	25 (25.0)		
≥ 16	4 (11.1)	3 (21.4)	7 (14.0)	14 (14.0)		
Gender					0.828	*0.661*
Female	18 (50.0)	5 (35.7)	23 (46.0)	46 (46.0)		
Male	18 (50.0)	9 (64.3)	27 (54.0)	54 (54.0)		
Socioeconomic class					29.683	*0.000**
Upper	2 (5.6)	1 (7.1)	28 (56.0)	31 (31.0)		
Middle	20 (55.6)	8 (57.1)	15 (30.0)	43 (43.0)		
Low	14 (38.9)	5 (35.7)	7 (14.0)	26 (26.0)		

**Statistically significant (P ≤ 0.05), χ^2 = chi square test, HbSS-ST = SCA subjects in steady state, HbSS-VOC = SCA subjects in vaso-occlusive crisis, HbAA = HbAA controls*

Selected haematological parameters of SCA subjects (in steady state and in vaso-occlusive crisis) and matched controls are shown in table 2. Except for haemoglobin concentration and haematocrit level which was lower among SCA subjects both in steady state and in vaso-occlusive crisis compared to

matched controls, all the other haematological parameters (total leucocyte counts, absolute neutrophil counts and platelets counts) were higher in SCA subjects compared to HbAA matched controls ($P < 0.01$). A sub-analysis of these parameters based on gender showed a similar result. (Table 3) There is no statistically significant difference in the haematological profiles of SCA subjects in steady state and vaso-occlusive crisis. (Table 4)

Table 2: Haematological profile of study participants according to the study groups

Variable	Hb SS-ST n = 36	Hb SS-VOC n = 14	Hb AA n = 50	F	*P* value
Hb Concentration (g/dl)					
Mean ± SD	7.5 ± 0.8	7.4 ± 1.1	11.7 ± 1.0	229.822	0.000*
Haematocrit (%) Mean ± SD	22.4 ± 2.5	23.2 ± 3.6	35.2 ± 3.1	225.695	0.000*
Leucocyte count (x 10^3/µl) (Mean ± SD)	12.8 ± 3.2	12.9 ± 5.9	6.3 ± 2.6	45.625	0.000*
Absolute Neutrophil count (x 10^3/µl) (Mean ± SD)	4.7 ± 2.1	5.9 ± 3.5	2.4 ± 1.4	21.153	0.000*
Platelet count (x 10^3/µl) (Mean ± SD)	345.8 ± 111.1	315.7 ± 152.7	272.1 ± 75.1	5.539	0.005*

**Statistically significant, F = ANOVA, HbSS-ST = SCA subjects in steady state, HbSS-VOC = SCA subjects in Vaso-occlusive crisis, HbAA = HbAA controls, SD = standard deviation, Hb = haemoglobin*

Table 3: Haematological profile of study participants based on gender

Variables	Female (n = 46)					Male (n= 54)				
	HbSS-ST n = 18	HbSS-VOC n = 5	HbAA n = 23	F	*P*-value	HbSS-ST n = 18	HbSS-VOC n = 9	Hb AA n = 27	F	*P*-value
Hb Concentration (g/dl) Mean ± SD	7.5 ± 0.5	7.4 ± 1.3	11.5 ± 1.3	95.618	0.000*	7.6 ± 1.1	7.4 ± 1.1	11.8 ± 0.9	138.996	0.000*
Haematocrit (%) Mean ± SD	22.5 ± 1.9	23.0 ± 3.9	34.7 ± 3.7	85.648	0.000*	22.4 ± 2.9	23.3 ± 3.7	35.5 ± 2.4	130.104	0.000*
Leucocyte count (x 10^3/µl) (Mean ± SD)	12.1 ± 2.7	15.5 ± 6.0	6.1 ± 2.4	30.956	0.000*	13.4 ± 3.6	11.5 ± 5.6	6.4 ± 2.7	21.627	0.000*
Absolute Neutrophil count (x 10^3/µl) (Mean ± SD)	4.5 ± 1.7	6.6 ± 2.7	2.3 ± 1.9	13.430	0.000*	4.8 ± 2.5	5 5 ± 3.9	2.5 ± 1.1	8.890	0.000*
Platelet count (x 10^3/µl) (Mean ± SD)	340.3 ± 120.4	273.2 ± 220.7	281.1 ± 80.5	1.490	0.237	351.3 ± 104.2	339.3 ± 108.5	264.4 ± 70.9	5.826	0.005*

**Statistically significant, F = ANOVA, HbSS-ST = SCA subjects in steady state, HbSS-VOC = SCA subjects in Vaso-occlusive crisis, HbAA = HbAA controls, SD = standard deviation, Hb = haemoglobin*

Table 4: Comparison of the haematological profiles SCA in steady state and vaso-occlusive crisis

Variable	HbSS-ST n = 36	HbSS- VOC n =14	t-Test	*P*- value
Hb Concentration (g/dl) Mean ± SD	7.5 ± 0.8	7.4 ± 1.1	0.340	0.738
Haematocrit (%) Mean ± SD	22.4 ± 2.5	23.2 ± 3.4	-0.704	0.490
Leucocyte count (x 10 ^{3}/µl) (Mean ± SD)	12.8 ± 3.0	12.9 ± 5.6	-0.110	0.914
Absolute Neutrophil count (x 10 ^{3}/µl) (Mean ± SD)	4.7 ± 2.1	5.9 ± 3.5	-1.222	0.239
Platelet count (x 10 ^{3}/µl) (Mean ± SD)	345.8 ± 111.1	315.7 ± 152.7	0.772	0.444

t-Test = student t-test, HbSS-ST = SCA subjects in steady state, HbSS-VOC = SCA subjects in Vaso-occlusive crisis, SD = standard deviation, Hb = haemoglobin

DISCUSSION

The study was carried out among children with SCA either in steady state or in vaso-occlusive crisis and was compared with their age- and gender- matched counterparts as controls. It was observed that majority of children with SCA belonged to middle and low socioeconomic class compared to the controls. This is in affirmation with previous studies[24,25] including a systematic review done by da Silva de Jesus *et al* [24] which showed that children with SCA are mainly from middle and low socioeconomic class and have more impact of the disease than otherwise. The explanation for this discrepancy in socioeconomic status among children with SCA seen in this study could be as a result of low educational attainment in their parents, poverty and poor health seeking behaviour that usually characterized this population of people and lack of knowledge of haemoglobin phenotype of their parents prior to their union. Thus, children with SCA belonging to this low socioeconomic class may have more impact of the disease than otherwise. Therefore, there is more need for focused and intense public health awareness, screening and policies among the populace to minimize the effect of the disease in our community and the nation.

The haematological parameters among SCA subjects and their HbAA matched controls showed higher values of haemoglobin concentration and

haematocrit level for matched controls than for SCA subjects confirming partly (other factors, not explored in this study, may also contribute) the fact that lower haemoglobin concentrations are the expected consequences of chronic haemolysis.[1,2,10,26] In addition, there were observed significant increases in the leucocyte and absolute neutrophil counts as well as the platelet counts among SCA subjects particularly those in vaso-occlusive crisis when compared to HbAA matched controls. This reinforces the role of leucocytes and platelets in the pathophysiological mechanisms underlying the disease processes.[9,10,26,27]

The study was similar to that of Antwi-Boasiako *et al,* who reported lower values of haemoglobin concentration, haematocrit and red cell count in Ghanaian patients with sickle cell disease (HbSS and HbSC) compared to their controls (HbAA) ($P < 0.001$).[17] They also observed higher white cell and platelet counts in these sickle cell disease patients than in controls ($P < 0.001$). This significant variation in haematological parameters affects those with vaso-occlusive crisis more compared to sickle cell disease patients in steady state. This may be explained by a higher prevalence of infections, haemolysis and red cell sequestration during or precipitating vaso-occlusive crisis. Other studies in the past reported similar findings.[13,14,15,16,17,18,28]

The difference in haematological parameters of SCA subjects in steady state and in vaso-occlusive crisis was not statistically significant. However, there may be some clinical implications such as increase

cellular dehydration and viscosity (evidenced by slight increase in haematocrit level observed among SCA subjects in vaso-occlusive crisis). The haematocrit level is expected to mirror the haemoglobin level except in conditions such as dehydration and blood loss. The higher level of leucocyte and absolute neutrophil count among SCA subjects in vaso-occlusive crisis may also increase risk of infection and/or activation of pro-inflammatory cells during and/or precipitating vaso-occlusive crisis.

Antwi-Boasiako *et al* observed an elevated WBC counts and platelet counts in SCD patients in vaso-occlusive compared to their counterparts in steady state which is similar to this study.[17] However, the observed higher level of haemoglobin level and haematocrit in SCD patients in steady state compared to those in vaso-occlusive crisis in their study was not seen in the present study. This disparity could be as a result of different study populations used in the studies; while they studied both adults and children, our study involved only paediatric subjects. The findings in this study were similar to that of Abubakar *et al* in Zaria, Nigeria who also noted the paradoxical relationship between haemoglobin concentration and haematocrit level.[28] The haematocrit level was higher in SCA subjects in vaso-occlusive crisis compared to those in steady state whereas the haemoglobin concentration was higher in SCA subjects in steady state compared to SCA subjects in vaso-occlusive crisis. Perhaps, it could be as a result of dehydration or influence of outliers in haematocrit level in lower range of normal among the SCA subjects in steady state compared to those in vaso-occlusive crisis. However, this similarity in our study and that of Abubakar calls for further studies to illuminate on the relationship between haemoglobin concentration and haematocrit level because it could be a reflection of cellular dehydration that promotes vaso-occlusive phenomena seen in SCA.

CONCLUSION

Children with SCA have lower levels of haemoglobin concentration and haematocrit percent compared to children with haemoglobin phenotype AA. However, they have higher values of leucocyte and neutrophil count as well as higher platelet count compared to their age- and gender- matched counterparts with haemoglobin phenotype AA. Majority of the children with SCA were from less favored socioeconomic families and this may impact on the morbidity and mortality of the disease. Strategies targeting on reduction of leucocyte and platelet count as well as improving the haemoglobin concentration could prevent the severity of the disease and improve well-being of children with SCA.

Limitation

The haemoglobin phenotypes of the cases (children with SCA) and controls (children with Hb AA) were diagnosed by haemoglobin electrophoresis using alkaline buffer; as such the possibility of Sβ-thal which could impact on haematological parameters could not be ruled out. There is no facility in researcher's centre to confirm the diagnosis.

REFERENCES

1. Adekile AD, Adeodu OO, Adegoke SA. Haemoglobinopathies. In: Azubuike JC, Nkanginieme KEO, (eds). Paediatrics and child health in a tropical region. 3rd ed. Lagos, Nigeria.: Educational Printing and Publishing; 2016. p. 1051–1065.
2. DeBaun MR, Frei-Jones MJ, Vichinsky EP. Sickle Cell Disease. In: Kliegman RM, Stanton BF, St Geme JW, Schor NF, Behrman RE (eds). Nelson Textbook of Pediatrics. 20th ed. Philadelphia: Elsevier Saunders; 2016. p. 2336–2344.
3. Ingram VM. Sickle Cell Anemia Hemoglobin: The molecular biology of the first "molecular disease" - The crucial importance of serendipity. *Genetics*. 2004;167:1–7.
4. Piel FB, Hay SI, Gupta S,Weatherel DJ, Williams TN. Global burden of sickle cell anaemia in children under five, 2010-2050: Modelling based on demographics, excess mortality,and interventions. *PLoS Med*. 2013;10: e1001484.

5. World Health Assembly, 59. Sickle-cell anaemia: Report by the Secretariat. *World Health Organization*, 2006 Apr 24 [cited 2020 Aug 31] https://iris.who.int/handle/10665/20890
6. World Health Organization. Sickle cell disease prevention and control. Nigeria; 2015. https://apps.who.int/gb/ebwha/pdf_files/wha59/a59_9-en.pdf
7. Inusa BP, Daniel Y, Lawson JO, Dada J, Mathews CE. Sickle cell disease screening in Northern Nigeria: The Co-existence of β-thalassemia Inheritance. *Pediat Ther*. 2015; 5:262.
8. Odievre M-H, Verger E, Silva-Pinto AC, Elion J. Pathophysiological insights in sickle cell disease. *Indian J Med Res*. 2011; 134:532–537.
9. Kato GJ, Hebbel RP, Steinberg MH, Gladwin MT. Vasculopathy in sickle cell disease: biology, pathophysiology, genetics, translational medicine and new research directions. *Am J Hematol*. 2009;84:618–625.
10. Kato GJ, Steinberg MH, Gladwin MT. Intravascular hemolysis and the pathophysiology of sickle cell disease. *J Clin Invest*. 2017;12:750–760.
11. El- Ghamrawy MK, Hanna WM, Abdel-Salam A, El-Sonbaty MM, Younes ER, Adel A. Oxidant-antioxidant status in Egyptian children with sickle cell anaemia: a single center based study. *J Pediatr (Rio J)*. 2014;90:286–292.
12. Barbu EA, Mendelsoh L, Samsel L, Thein SL. Pro-inflammatory cytokines associated eith NETosis during sickle cell vaso-occlusive crisis. *Cytokine*. 2020; 127: 154933
13. Ahmed AE, Ali YZ, Al-Suliman AM,Albagshi JM, Salamah MA, Elsayid M, *et al*. The prevalence of abnormal leukocyte count and its predisposing factors in patients with sickle cell disease in Saudi Arabia. *J Blood Med*. 2017; 8:185-191
14. Obeagu EI, Ogbuabor BN, Ikechukwu OA, Chude CN. Haematological parameters among sickle cell anaemia patients in steady state and haemoglobin genotype AA individuals at Micheal Okpara University of Agriculture, Umudike, Abia State, Nigeria. *Int. J.Curr.Microbiol. App.Sci*. 2014;3:1000-1005
15. Akinbami A, Dosunmu A, Adediran A, Oshinaike O, Adebola P, Arogundade O. Haematological values in homozygous sickle cell disease in steady state and haemoglobin phenotype AA controls in Lagos, Nigeria. *BMC Research Notes*. 2012; 5:396.
16. Mombo LE, Mabioko-Mbembo G, Bissrye C, Mbacky K, Thiam F, Edou A. Haematological values in steady state sickle cell anaemia patients and matched haemoglobin AA controls in rural area of Eastern Gabon. *Nigerian Postgrad. Med. J*. 2019; 26: 13-17
17. Antwi-Boasiako C, Ekem I, Abdul-Rahman M, Sey F, Doku A, Dzudzor B, *et al*. Hematological parameters in Ghanaian sickle cell disease patients. *J Blood Med*. 2018; 9:203-209
18. Aliu R, Iliya J, Quadri OR, Ibrahim OR, Daniel E. Haematological profile of children with sickle cell anaemia in steady state. *Cureus*. 2020; 12: 1-6
19. National Bureau of Statistics. Official Gazette 2006 National Population census [Internet]. 2006. [cited 2020 Aug 31] https://archive.gazettes.africa/archive/ng/2009/ng-government-gazette-dated-2009-02-02-no-2.pdf
20. Ballas SK. More definitions in sickle cell disease: Steady state v base line data. *Am J Hematol.* 2012;87:338.
21. Ballas SK, Lieff S, Benjamin LJ, Dampier CD, Heeney MM, Hoppe C, *et al*. Definitions of the phenotypic manifestations of sickle cell disease. *Am J Hematol.* 2010;85:6–13.
22. Nield LS, Kamat D. Fever. In: Kliegman RM, Stanton BF, St. Geme JW, Schor NF, Behrman RE, eds. Nelson Textbook of Pediatrics. 20th ed. Philadelphia: Elsevier Saunder; 2016. p. 1277–1279.
23. Oyedeji GA. Socio-economic and cultural background of hospitalised children in Ilesha. *Nigeria Journal of Paediatrics*. 1985; 12: 111-

117.
24. Jesus ACDS, Konstantyner T, Lobo IKV, Braga JAP. Socioeconomic and nutritional characteristics of children and adolescents with sickle cell anaemia: a systematic review. *Rev.Paul. Pediatri.* 2018;36:491-499
25. Animasahun BA, Temiyre EO, Ogunkunle OO, Izuora AN, Njokanma OF. The influence of socioeconomic status on the hemoglobin level and anthropometry of sickle cell anaemia patients in steady state at the Lagos University Teaching hospital. *Niger J Clin Pract*. 2011;14:422-427
26. Chirico EN, Pialoux V, Lyon D, Lyon CB. Role of oxidative stress in the pathogenesis of sickle cell disease. *IUBMB Life*. 2012;64:72–80.
27. Potoka KP, Gladwin MT. Vasculopathy and pulmonary hypertension in sickle cell disease. *Am J Physiol Lung Cell Mol Physiol*. 2015;308:L314–324.
28. Abubakar Y, Ahmad HR, Faruk JA. Hematological parameters of children with sickle cell anemia in steady and crisis states in Zaria, Nigeria. *Ann Trop Pathol*. 2019; 10:122-5

Authors' Contributions

CMU: conceptualization and design, definition of intellectual content, literature search, data acquisition, data and statistical analysis, manuscript preparation, manuscript review.

CEE: conceptualization and design, definition of intellectual content, literature search, manuscript editing and review, supervisor

HCO: definition of intellectual content, literature search, data acquisition, data and statistical analysis, manuscript editing and review, supervisor

CAE: data and statistical analysis, manuscript editing and review

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