Original Article

Hematological Parameters of Children with Sickle Cell Anemia in Steady and Crisis States in Zaria, Nigeria

Yakubu Abubakar, Hafsat Rufa'i Ahmad, Jamilu Abdullahi Faruk

Department of Paediatrics, Haematology/Oncology Unit, Ahmadu Bello University/Teaching Hospital, Zaria, Kaduna State, Nigeria

Abstract

Background: Sickle cell anemia (SCA) is the most common and severest form of sickle cell disease. It affects about 3% of the Nigerian population with a high mortality in children. Hematological parameters are routinely used in the monitoring of SCA patients and might vary in crisis and steady states. **Aims and Objectives:** This study was aimed at comparing the hematological parameters of SCA patients in steady state with those in hemolytic and vaso-occlusive crisis states. **Methodology:** It was a cross-sectional study carried out at the pediatric outpatient clinic of a tertiary hospital in North West Nigeria. We recruited 170 SCA patients in steady state or in crisis state. Five milliliters of blood sample was collected for full blood count analysis using the Sysmex Xt 2000i automated hematology analyzer. **Results:** Hemoglobin (Hb) and hematocrit (HCT) levels for SCA patients in steady state were 8.28 ± 1.64 g/dl and 21.8 ± 4.04% while in vaso-occlusive crisis (VOC) state were 7.81 ± 1.37 g/dl and 22.05 ± 1.37% and those with hemolytic crisis were 4.45 ± 0.12 and 13.35 ± 0.67, respectively. Total white blood cell (WBC) count in steady and VOC states was 14.51 ± 5.21 × 10^9/l and 17.46 ± 5.26 × 10^9/l, respectively, while those in hemolytic crisis had WBC of 14.92 ± 5.82 × 10^6/l. ANOVA test was 0.0001, 0.0001, and 0.03, respectively, which indicates a statistically significant difference between the groups. The mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH), and mean corpuscular hemoglobin concentration (MCHC) in steady state were 76.67 fl ± 9.02, 27.18 pg ± 4.36, and 35.17 g/dl ± 4.25, while in VOC state, they were 74.88 fl ± 11.60, 27.24 pg ± 3.70, and 35.49 g/dl ± 1.42 and, in anemic crisis state, they were 76.63 ± 11.74, 26.71 ± 3.78 and 35.03 ± 1.20, respectively. **Conclusion:** Hematological parameters were lower during crisis states, although most of these were not significantly different from those in steady state apart from the WBC count, Hb, and HCT. Therefore, routine monitoring of hematological parameters should remain an important component in the management of SCA children.

Keywords: Crises, hematological parameters, sickle cell anemia, steady state

Received on: 30-06-19 **Review completed on:** 08-09-19 **Accepted on:** 16-09-19 **Published on:** 06-12-19

Introduction

Sickle cell disease (SCD) is a condition resulting from the inheritance of abnormal allelomorphic genes controlling the formation of the beta (β)-chains of hemoglobin (Hb) at least one of which is the sickle gene.[1] The homozygous state, HbSS, termed sickle cell anemia (SCA) is the most common and severest form of SCD.[2] About 5% of the world's population carry the gene responsible for sickle hemoglobinopathies. Nigeria has the highest burden of the disease in the world with over 150,000 children born every year with SCA.[3] The homozygous state is found in about 3% of the Nigerian population,[4,5] but a prevalence of 11.87% of homozygous state was reported in the Kano metropolis and its suburbs in northern Nigeria.[6] The clinical presentation of SCA is variable with multisystemic manifestation. Children with SCA experience alternating periods of apparent good health (steady state) and acute exacerbation of symptoms (crisis state) as well as development of chronic complications.[7] The hematological parameters in these periods vary and at the same time provide evidence-based management information for the diagnosis, treatment, monitoring, and prognostication. The importance of some of the steady-state hematological values such as Hb concentration, white blood cell (WBC) counts, and platelet (PLT) counts in prediction of clinical severity as well

Address for correspondence: Dr. Yakubu Abubakar, Department of Paediatrics, Haematology/Oncology Unit, Ahmadu Bello University/Teaching Hospital, Zaria, Kaduna State, Nigeria.
E-mail: ayboku2@gmail.com

Access this article online

Quick Response Code:

Website: www.atpjournal.org

DOI: 10.4103/atp.atp_22_19

How to cite this article: 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.

as management of SCA has been documented.[7] This study, therefore, aimed to compare the hematological parameters of SCA patients in steady state with those in hemolytic and vaso-occlusive crisis states.

Methodology

This was a cross-sectional study involving 170 known SCA patients either in steady or crisis state attending the pediatric sickle cell clinic in a tertiary hospital in North West Nigeria. The patients were between the ages of 6 months and 12 years. The study was conducted from June to December 2015 after obtaining ethical approval from the health research ethics committee of the hospital. Informed written consent of the parents or caregivers and assent from older children (7–12 years) were also obtained.

The children were recruited consecutively. The inclusion criteria were a diagnosis of SCA through cellulose acetate Hb electrophoresis, while those excluded were patients who had a blood transfusion during the preceding 3 months. Patients in steady state were defined as the absence of infection or acute clinical symptoms or crisis for at least 3 months, whereas a patient in crisis state was defined as a child with SCA who developed a sudden adverse change in the course of the disease with the development of new signs and symptoms.[8,9]

All patients had blood specimens collected using standard techniques.[10] Five milliliters of venous blood was collected into commercially prepared concentrations of ethylenediaminetetraacetic acid bottles. Each sample was mixed gently and thoroughly to prevent cell lysis and ensure anticoagulation. Hb concentration, hematocrit (HCT), red blood cell (RBC) concentration, mean corpuscular hemoglobin (MCH), Mean corpuscular volume (MCV), MCH concentration (MCHC), WBC, and platelet (PLT) parameters were estimated using Sysmex Xt 2000i automated hematology analyzer.[11] The WBC differentials are displayed as lymphocytes, granulocytes, and mixed differentials (MID) which represent monocytes, basophils, and eosinophils. Reticulocyte (RETIC) count was also done using standard guidelines.[12] Corrected reticulocyte percentage and reticulocyte production index were calculated using the following formulae, respectively,

$$\text{Corrected reticulocyte percentage} = \text{reticulocyte percentage} \times \frac{\text{actual haematocrit}}{\text{Normal hematocrit}(45)}$$

$$\text{Reticulocyte Production index}\,(\text{RPI}) = \frac{\text{Corrected reticulocyte percentage}}{\text{Normal hasmatocrit}(45)}$$

Data were analyzed using the statistical software EPI Info 3.5.3 version (Developed by Centers for Disease Control (CDC), Atlanta, Georgia (USA)). Results were presented in prose and tables. Student's *t*-test and ANOVA test were used to compare normally distributed continuous variables; $P < 0.05$ was considered statistically significant.

Results

A total of 170 children with diagnosis of SCA were recruited after fulfilling the inclusion criteria. Table 1 shows that 91 (53.5%) patients were male, whereas 79 (46.5%) were female. The mean age of the patients was 5.7 ± 3.3 years. The age range was 6 months to 12 years. In addition, 136 (80%) patients were in steady state, whereas 6 (3.5%) and 28 (16.5%) were in hemolytic crisis and vaso-occlusive crisis (VOC) states, respectively. There were four boys and two girls with hemolytic crisis, whereas 15 boys and 13 girls had VOC, respectively.

Table 2 shows the hematological parameters of the study patients segregated by gender. Males had lower Hb, HCT, MCHC, and RBC, whereas other parameters were above the values for the females but no significant statistical differences in all the hematological parameters between the sexes of children.

Table 3 compares the hematological parameters of the patients in steady, hemolytic, and vaso-occlusive crisis states. There was a significant difference in total WBC count, Hb and HCT levels as well as the reticulocyte index between the patients. Interestingly, the HCT was higher in VOC state compared with the steady state, even though the Hb was higher in the steady state. Other parameters showed no significant variations.

Discussions

The study recorded low HCT and Hb levels among the study patients in general, but it was lower among males compared to females. This is not surprising from the present study given that there were more males with hemolytic crises. However, there was no statistically significant difference between the sexes. This preponderance of anemia among males contrasts to the findings of Iheanacho who reported higher Hb among males even though it was also not statistically significant too.[7]

The observed HCT was higher in VOC state compared with the steady state, even though the Hb was higher in the steady-state group. This is rather paradoxical, as it is expected that the HCT should mirror the Hb. Perhaps, the HCT in the steady state was influenced by extreme values or outliers in the lower ranges of normal. There was no statistical significance in the observed differences.

Table 1: Age distribution of sickle cell anemia patients

Age (years)	SCA patients (n=170)		Total, n (%)
	Females, n (%)	Males, n (%)	
0-4	36 (21.2)	36 (21.2)	72 (42.3)
5-9	31 (18.2)	37 (21.8)	68 (40.0)
≥10	12 (7.1)	18 (10.6)	30 (17.7)
Total	79 (46.5)	91 (53.5)	170 (100.0)

SCA: Sickle cell anemia

Table 2: Mean values of hematological parameters based on gender

Parameters	SCA			*t*	*P*
	Overall	Males	Females		
WBC	15.06±5.14	14.83±5.93	14.30±4.01	0.19	0.85
Lym	44.51±12.70	47.88±15.57	45.65±13.32	1.0	0.32
Gran	47.09±12.26	45.04±16.45	44.05±13.49	0.4	0.67
MID	7.17±2.27	7.82±2.77	7.04±2.08	2.7	0.4
Hb (g/dl)	7.77±1.64	7.64±1.77	7.90±1.50	1.1	0.20
HCT (%)	21.83±4.04	21.73±4.23	21.93±3.85	0.5	0.64
MCV fl	76.67±9.02	77.76±8.73	75.29±9.19	0.92	0.35
MCH pg	27.18±4.36	27.52±4.80	26.82±3.84	1.79	0.07
MCHC g/dl	35.15±4.26	34.90±5.63	35.40±1.92	1.03	0.30
RBC	2.90±0.71	2.83±0.69	2.98±0.71	0.75	0.45
PLT ($\times 10^9$/l)	409.22±145.54	409.44±150.04	408.98±141.77	0.02	0.98
RETIC count	2.18±1.07	2.19±1.09	2.16±1.05	0.18	0.85
RETIC index	0.57±0.34	0.58±0.34	0.57±0.35	0.19	0.85

Lym: Lymphocyte, Gran: Granulocyte, MID: Mixed differential, WBC: White blood cell, Hb: Hemoglobin, HCT: Hematocrit, MCV: Mean corpuscular volume, MCH: Mean corpuscular hemoglobin, MCHC: Mean corpuscular hemoglobin concentration, RBC: Red blood cell, PLT: Platelet, RETIC: Reticulocyte, SCA: Sickle cell anemia

Table 3: Analysis of variance of hematological parameters in steady and crisis states

Variables	Steady (*n*=136)	Hemolytic crisis (*n*=6)	VOC (*n*=28)	ANOVA
WBC ($\times 10^9$/l)	14.51±5.21	14.92±5.82	17.46±5.26	0.03*
Lym	44.57±12.59	55.73±11.39	41.77±12.56	0.05
Gran	47.14±12.24	37.53±10.83	48.85±12.12	0.12
MID	7.16±2.23	5.58±2.51	7.57±2.35	0.15
PLT ($\times 10^9$/l)	409.22±145.54	320.33±125.59	383.93±175.18	0.29
RBC	2.90±0.71	3.05±0.82	2.95±0.67	0.08
Hb (g/dl)	8.28±1.64	4.45±0.12	7.81±1.37	0.0001*
HCT (%)	21.8±4.04	13.35±0.67	22.05±1.37	0.0001*
MCV (fl)	76.67±9.02	76.37±11.74	74.88±11.60	0.66
MCH (pg)	27.18±4.36	26.71±3.78	27.24±3.70	0.96
MCHC (g/dl)	35.17±4.25	35.03±1.20	35.49±1.42	0.92
RDW	24.54±6.40	25.77±8.71	24.76±10.05	0.91
RETIC count	2.67±1.07	2.23±1.03	2.65±1.18	0.62
RETIC index	0.57±0.34	0.63±0.41	0.82±0.59	0.01*

Lym: Lymphocyte, Gran: Granulocyte, MID: Mixed differential, ANOVA: Analysis of variance, WBC: White blood cell, Hb: Hemoglobin, HCT: Hematocrit, MCV: Mean corpuscular volume, MCH: Mean corpuscular hemoglobin, MCHC: Mean corpuscular hemoglobin concentration, RBC: Red blood cell, PLT: Platelet, RETIC: Reticulocyte, RDW: Red cell distribution width, VOC: Vaso-occlusive crisis, *statistically significant

The RBC was lower in males and can be easily assumed to be the result of more males having hemolysis in the study. In addition, the MCV and MCH were higher in the males which might lead to the speculation that the hemolysis placed additional demands on folate supply, hence giving rise to larger erythrocytes which were mirrored in the raised MCV. However, this is purely an assumption and cannot be substantiated by the present study design. From this point, it is also possible to extrapolate why the MCHC will be lower in males, as it is derived from the MCV and MCH.

WBC count was also high among the patients which were comparable to the findings in other studies.[13-16] The high WBC count among the patients may be due to reasons suggested by Akinola *et al*. "that subclinical VOC in the steady state may generate a covert inflammatory response leading to the release of cytokine mediators some of whose main function is increased neutrophil production by the bone marrow."[17,18] The WBC level found among the SCA patients with VOC was significantly higher than those in the steady states in this study which was similar to the findings by Omoti.[9] However, the differential WBC counts showed no significant difference between the patients in steady and the crisis states, which is contrary to the findings by Omoti. This probably might be due to the observed pattern of rise in the differential counts, as shown in Table 3, whereby lymphocytes were higher in hemolytic states, while granulocytes and MID were higher in vaso-occlusive states.

Red cell distribution width, which is a measure of erythrocyte anisocytosis, was significantly raised in the patients. This is in agreement with previous studies which showed that SCA is associated with marked anisocytosis.[9,19] This may be because,

with more rapid erythropoiesis, cells at different stages of maturation with certainly different sizes are released into the peripheral circulation.

Platelets and leukocyte counts recorded in this study were high. Other studies similarly reported high values.[9,19,20] The thrombocytosis and leukocytosis demonstrated in this study were also noted in the children with SCA in the study by Akinbami *et al*.[20] A negative feedback effect on erythropoietin production in SCA patients could be responsible for the thrombocytosis. Redistribution of the white cells between the marginal and circulating pools, pain, nausea and vomiting, anxiety, and autosplenectomy has been reported to cause leukocytosis in the absence of infection.[21,22] It is recognized that thrombocytosis is associated with anemia of chronic disease and several types of anemia.[21] Except for levels of Hb, HCT, and the RETIC index levels that were significantly different between patients, other hematological parameters were not significantly different.

Conclusion

The study found a lower Hb in VOC patients compared to steady state, with a difference of about 0.5 g/dl, and this difference is further accentuated in the hemolytic crisis group up to 3 g/dl. In addition, WBC was higher in VOC and hemolytic crisis compared to steady-state patients.

Therefore, it is recommended to routinely monitor the hematological parameters in the management of SCA children and develop individualized treatment protocols based on patients' baseline steady-state parameters.

This study is limited in its scope, in that only children with hemolytic and vaso-occlusive crises were enrolled during the study period. As such, it cannot be generalized to all sickle cell crisis states.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

References

1. Fleming AF, editor. Definitions and abbreviations. In: Sickle Cell Disease, A Handbook for the General Clinician. Edinburgh: Churchill livingstone; 1982. p. 17.
2. Adeodu OO, Alimi T, Adekile AD. A comparative study of perception of sickle cell anaemia by married Nigeria rural and urban women. West Afr J Med 2000;19:1-5.
3. Okpala I, editor. Epidemiology, genetics and pathophysiology of SCD. In: Practical Management of Haemoglobinopathies. Oxford: Blackwell; 2004. p. 20-5.
4. World Health Organization. Prevalence of Sickle Cell Anaemia. Agenda item 11.4. World Health Organization; 2006.
5. Adekile AD, Adeodu OO. Haemoglobinopathies. In: Azubuike JC, Nkanginieme KE, editors. Paediatrics and Child Health in Tropical Region. Owerri: African Educational Services; 2007. p. 373-90.
6. Mustapha O, Abubakar F. Study of the prevalence of sickle cell disease in Kano metropolis and its suburbs in Northern Nigeria. Niger J Basic App Sci 2001;10:219-25.
7. Iheanacho OE. Haematological parameters of adult and paediatric subjects with sickle cell disease in steady state in Benin city, Nigeria. Int Blood Res Rev 2015;3:171-7.
8. Konotey-Ahulu FI. The sickle cell diseases. Clinical manifestations including the "sickle crisis". Arch Intern Med 1974;133:611-9.
9. Omoti CE. Haematological values in sickle cell anaemia in steady state and vaso-occlusive crises in Benin, Nigeria. Ann Afr Med 2005;4:62-7.
10. Bain BJ, Lewis SM, Imelda B, editors. Basic haematology techniques. In: Dacie and Lewis Practical Haematology. Philadelphia: Churchill Livinstone; 2007. p. 25-57.
11. Kobe J. Operator's Manual. XT-2000i Automated Hematology Analyzer. Sysmen Corporation; 2004.
12. Prchal JT. Production of erythrocytes. In: Lichtman MA, Kipps TJ, Seligson U, Kaushansky K, Prchal JT, editors. Williams Hematology. New York: McGraw-Hill; 2010.
13. Emmanuelchide O, Charle O, Uchenna O. Hematological parameters in association with outcomes in sickle cell anemia patients. Indian J Med Sci 2011;65:393-8.
14. Abdullahi SU, Hassan-Hanga F, Ibrahim M. Ultrasonographic spleen size and haematological parameters in children with sickle cell anaemia in Kano, Nigeria. Niger Postgrad Med J 2014;21:165-70.
15. Rao SS, Goyal JP, Raghunath SV, Shah VB. Hematological profile of sickle cell disease from South Gujarat, India. Hematol Rep 2012;4:e8.
16. Girei AI, Alao OO, Joseph DE, Damulak DO, Orkuma J, Bawat EB. Haematological profile of SCA in children with human papiloma virus B19 infection in Jos. J Clin Med Res 2010;2:152-5.
17. Akinola NO, Stevens SM, Franklin IM, Nash GB, Stuart J. Subclinical ischaemic episodes during the steady state of sickle cell anaemia. J Clin Pathol 1992;45:902-6.
18. Leikin SL, Gallagher D, Kinney TR, Sloane D, Klug P, Rida W, *et al.* Mortality in children and adolescents with sickle cell disease. Cooperative study of sickle cell disease. Pediatrics 1989;84:500-8.
19. Ajay WM, Priyanka AB, Ruchir K, Komal P. Haematological indices and electrolyte status in SCD at rural hospital in central Maharashtra. Int J Med Sci Public Health 2014;3:1410-12.
20. Akinbami A, Dosunmu A, Adediran A, Oshinaike O, Adebola P, Arogundade O, *et al.* Haematological values in homozygous sickle cell disease in steady state and haemoglobin phenotypes AA controls in Lagos, Nigeria. BMC Res Notes 2012;5:396.
21. Milhorat AT. Leucocytosis during various emotional state. Arch Neurol Psychiatry 1942;47:779.
22. Olopoenia L, Frederick W, Greaves W, Adams R, Addo FE, Castro O, *et al.* Pneumococcal sepsis and meningitis in adults with sickle cell disease. South Med J 1990;83:1002-4.