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Original Article

Haematological Profile of Children with Sickle Cell Anaemia in Crises and Steady State: A Comparative Study in A Tertiary Hospital, North-Eastern Nigeria

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ABSTRACT

Introduction: Sickle cell anaemia (SCA) is an inherited, most severe, and commonest form of sickle cell disease that results from the β-globin gene mutation. Complications of SCA are mostly dependent on the activation of blood indices. This study is aimed at evaluating haematological parameters needed for monitoring sickle cell anaemia children.

Materials and Methods: This was a comparative cross-sectional study conducted in a tertiary hospital where 198 sickle cell children were recruited using convenience sampling technique. The data was analysed using SPSS version 23.0. The complete blood count parameters of sickle cell anaemia children in crisis and steady states were compared. Haemoglobin (Hb), haematocrit, White blood cell (WBC), Mean corpuscular volume (MCV), Mean corpuscular haemoglobin (MCH), mean corpuscular haemoglobin concentration (MCHC) and platelet (Plt) were determined. Independent T-test and ANOVA were used to summarise the continuous variables. A p-value<0.05 was considered statistically significant.

Results: The mean Hb, MCV & MCH were significantly lower in children with crises compared with the steady state (p= <0.001, <0.001 and 0.046). The mean WBC was 20.58 ± 9.91 in crises and 14.29 ± 4.47 in steady state (p=<0.001). The Hct was lower in crises (21.76 ± 4.62) compared with steady state (22.41 ± 3.52) (p= 0.269) and the Plt was higher in crises (426.52 ± 219.67) compared with steady state (391.46 ± 182.63/mm^3) (p=0.224).

Conclusion: Haemoglobin and Hb-dependent haematological indices in sickle cell anaemia were lower in crisis states especially in haemolytic crisis while WBC and platelets were higher. Close monitoring of Complete Blood Count, rather than the usual Hb value only, is highly necessary for SCA children with haemolytic crises.

KEYWORDS: Sickle Cell Anaemia, Children, Steady State, Crisis State, Haematological Profile,

INTRODUCTION

Sickle cell anaemia (SCA) is one of the commonest genetic disorders globally and in Sub-Sahara Africa, in particular, where more than two-thirds of the global cases are found[1]. Nigeria, the most populous black nation, has the highest burden of SCA where more than 150,000 children with SCA are born yearly, accounting for half of the global cases and a prevalence of 20 per 1000 births[1].

Sickle cell anaemia has multisystemic manifestation[2]. These manifestations, although continuous, are sometimes covert (steady state) when the patient is in a state of apparent good health and other times overt (crises) when an infectious or non-infectious trigger exacerbates the symptoms[3]. Among these crises, vaso-occlusive and anaemic crises are the commonest manifestations occurring in about 50% of the sickle cell anaemia children and usually cause hospital admission,

organ failures and death[4]. In sub-Saharan Africa, mortality of children with SCA has been shown to be as high as 50-90% in children less than 5 years of age[5]. This sickle cell disease-associated mortality translates to 5-10% of overall under-5 mortality. The mortality of sickle cell anaemia children in Nigeria is comparably higher than in other countries. Children with sickle cell anaemia have 116 deaths per 1000 persons-year before age 5[6]. Different haematological indices have been shown to characterise the steady and crisis states. These clinical, state-dependent values have a significant impact on clinical manifestations, morbidity and mortality, treatment, and prognosis. Interrogation and knowledge of these differential haematological parameters will enhance the high index of suspicion, early diagnosis and rapid treatment, especially in settings where the disease is endemic such as Nigeria[3]. This study aims to determine and compare the haematological parameters in children in steady and crisis states.

MATERIAL AND METHODS

Study setting

The study was conducted at the sickle cell disease centre of the Federal Teaching Hospital, Gombe (FTHG), North-East Nigeria. The FTHG is a tertiary health centre with a sickle cell centre, one of the six sickle cell centres spread across the six geopolitical zones in Nigeria. The hospital receives referrals from various secondary health facilities within and outside the state. The clinic has an average clinic attendance of 35 patients weekly.

Study Design

Hospital-based comparative study

Study Population

Sickle cell anaemia children aged 1-18 years attending sickle cell anaemia clinic at FTHG

Inclusion Criteria

1. Children aged 1-18 years who were on follow-up at the sickle cell clinic in FTHG, in steady state (defined as the absence of fever and crisis in the previous four weeks or more in a child who was not on any medication other than routine folic acid and prophylactic antimalarial drug) were recruited[7].
2. Children aged 1-18 years who were on follow-up at the sickle cell clinic in FTHG, in a crisis state (described as a sudden adverse change in the pattern of disease manifesting as new symptoms and signs) were also recruited [8-9].

Exclusion Criteria

1. Children aged 1-18 years who were on hydroxyurea as it alters the steady-state haematological indices in SCA.
2. Children aged 1-18 years who had received blood transfusion in the last one month (because of reduced red blood cell survival in sickle cell anaemia children).

Sample Size Determination

The minimum sample size was calculated using the formula for comparison of two groups at a single point in time [10].

$$n = \frac{[Z_{\alpha/2} + Z_{\beta}]^2 \times [P_1 (1 - P_1) + P_2 (1 - P_2)]}{[P_1 - P_2]^2}$$

Following sample size determination, the subjects with crises were recruited consecutively using the convenience sampling method in the sickle cell clinic. Corresponding subjects (SCA children) in steady states were then also recruited consecutively using the convenience sampling method until the sample size was reached.

Data Collection Method

A semi-structured interviewer administered questionnaire was used in obtaining data from the respondents. The researcher met with the staff of the sickle cell clinic one week prior to the onset of data collection during which information about the study was given. This was followed by weekly recruitment of children who met the inclusion criteria having obtained the informed consent. Well-labelled Ethylene diamine tetra acetic acid bottles were used to obtain 5-ml of venous blood samples from the participants. Hb, Hct, WBC, MCV, MCH, MCHC, and Plt were determined using combined automation-manual method using Sysmex XN-550 Five parts Haematology Analyser.

Data Analysis

All data generated was processed and analysed using statistical software, IBM SPSS version 23.0 (IBM, Armonk, NY). Socio-demographic data was presented as percentages, while quantitative data were described using means and standard deviations. Chi-square test was used to determine any association between certain socio-demographic variables while t-test and ANOVA were used to determine any significant difference between the independents and dependent variables. A confidence interval of 95% was used in this study and a p-value <0.05 was considered statistically significant.

Ethical Consideration:

Ethical clearance was obtained from the ethics and research committee of Federal Teaching Hospital, Gombe. Verbal/written consent for the study was obtained from parents while assent was obtained from children aged seven years and above.

RESULTS

Of the total 198 children recruited for the study, (Ninety-nine in steady state and ninety-nine in crises) all were interviewed with a response rate of 100%. The mean age of the respondents was 8.44±5.13. Those within the age group 15 years and above were the least (15.1%) group,

Table 1: Socio-Demographic Characteristics of Participants in Steady and Crisis State

Variables Age (years)	Steady state (N=99) n (%)	Crisis state (N=99) n (%)	X^2	P value
<5	27 (46.6)	31 (53.4)	5.719	0.126
5-9	28 (47.5)	31 (52.5)		
10-14	23 (45.1)	28 (54.9)		
>15	21 (70.0)	9 (30.0)		
Mean age	9.10±5.31	7.78±4.88		
Sex				
Male	53 (52.5)	48 (47.5)	0.503	0478
Female	46 (47.4)	51 (52.6)		
Socio-economic status				
Low	75 (56.4)	58 (43.6)	7.173	0.028
Middle	18 (40.0)	27 (60.0)		
High	6 (30.0)	14 (70.0)		

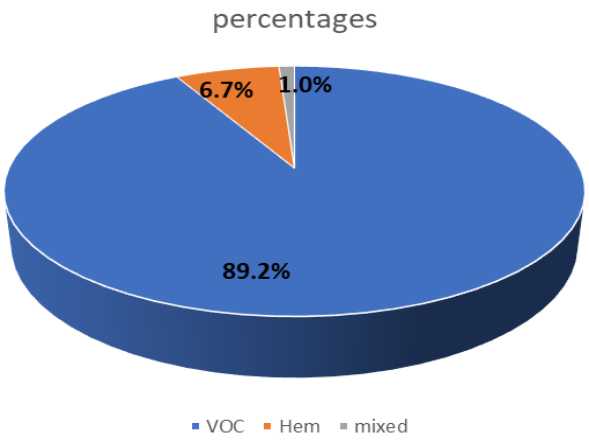

Figure 1: Types of sickle cell crises

Table 2: Haematological parameters in crisis and steady states

variables	Steady State	Crisis	P value
Hb (g/dl)	7.88±1.27	7.03±1.56	<0.001*
Hct (%)	22.41±3.52	21.76±4.62	0.269
WBC (x 10^9/l)	14.29±4.47	20.58±9.91	<0.001*
Platelet (x 10^9/l)	2.54±0.22$^+$	2.57±0.22$^+$	0.224$^+$
MCV (fl)	81.26±7.14	79.20±9.50	0.046*
MCH (pg)	28.63±2.90	26.51±4.32	<0.001*
MCHC (g/dl)	3.56±0.05$^+$	3.59±0.804$^+$	0.112$^+$

*Significant P values; $^+$Log-transformed (normalised) values

Table 3: Haematological Parameters in Different Crisis and Steady-State

variables	Steady-state	VO Crisis	Hem crisis	P value
Hb	7.88±1.27	7.08±1.50	6.09±1.52	<0.001*
Hct	22.41±3.52	21.91±4.29	19.00±7.81	0.099
WBC	14.29±4.47	20.15±9.50	26.16±13.99	<0.001*
Plt	2.54±0.22$^+$	2.58±0.23$^+$	2.49±0.87$^+$	0.558$^+$
MCV	81.26±7.14	78.46±8.76	88.96±13.81	0.001*
MCH	28.63±2.90	26.25±4.18	29.96±5.06	<0.001*
MCHC	3.56±0.05$^+$	3.51±0.264$^+$	3.49±0.47$^+$	0.371$^+$

Hb: Haemoglobin; Hct: Haematocrit; *Significant p values; $^+$Log-transformed (normalised) values

more than half (51.0%) of the respondents were males and majority (67.2%) belong to the low socio-economic group. (Table 1) Among the 99 participants with sickle cell crises, 91 (89.2%) had vaso-occlusive crisis (VOC), 7 (6.7%) had haemolytic crisis and 1 (1.0%) had mixed crises, Figure 1. The general haematological parameters in sickle cell anaemia children with crisis and steady state. The Hb, MCV and MCH were significantly lower in crisis state, p <0.001, 0.046, <0.001 respectively while WBC was significantly higher in crisis state, p < 0.001.(Table 2) The specific haematological parameters

in sickle cell anaemia children in different crisis states compared with steady state. (Table 3)

DISCUSSION

The children with SCA were mostly from families with low socio-economic class in this study. This may be a result of their low literacy, and thus inadequate information about the need for genotype compatibility checks before marriage among would-be parents. This finding is similar to a study by Thales Allyrio et al.[11] underscoring the need for increased counselling among parents who are of low socio-economic status. It might also be due to the cultural practice of consanguineous marriage whereby the first and second cousins intermarriages are preferred with no premarital genotype check among these individuals as noted by Ibrahim et al.[12]

The mean age of children with SCA in crises was lower than those in steady state, albeit non-significant statistically. This may be because children with pains and/or other acute symptoms are more likely to present in the hospital early compared with those in a steady state who may have minimal or no complaints. Red blood cell indices (Hb and Hct) were generally lower in the haemolytic crisis state compared with the VOC and steady state. This may be due to the accentuation of chronic haemolysis that characterises sickle cell anaemia during the haemolytic crisis leading to lower Hb and Hct. This could also be related to the depletion of iron stores during the haemolytic crisis [13-14]. During the haemolytic crisis, as the red blood cells get destroyed by various mechanisms, the iron stored in the body is mopped up to produce more red blood cells to replace the lost cells. This may also be due to the reduced response of bone marrow of sickle cell anaemia patients to erythropoietin [15].

In haemolytic crisis, the degree of anaemia is more, causing more blunted response to erythropoietin. The anaemia in a crisis state may also be attributed to the elaboration of toxins and cytokines that attack the red blood cells. The Hb and Hct are also lower in the VOC compared with the steady state. Whereas this is similar to the report by Timothy et al.[16] and Kenechukwu et al. [17], it is in contrast with the report by Abubakar et al. [18], Antwi-Boasiako et al. [19], and Omoti CE et al.[7] who reported higher Hb and Hct values in VOC. This disparity is intriguing as it shows that changes in Hb and Hct in VOC is multifactorial. Haemoglobin (Hb) and haematocrit (Hct) are higher when VOC is heralded by intravascular dehydration and thus haemoconcentration as explained by Antwi et al. [19] and Omoti et al.[7], but are reduced in situations devoid of dehydration.

The value of Hb and Hct has also been shown to be dependent on the phase of VOC where Hb is increased in phase 1 but decreased in phase 2 [20,21]. It is thus pertinent to know that the changes in Hb and Hct in VOC are multifactorial. The MCV and MCH were lower in VOC compared with the steady state. This is similar to finding by Kenechukwu et al.[17], Abubakar et al. (18) and Antwi et al.[19]. Higher values of MCV and MCH were, however, reported by Omoti et al[7]. The MCV and MCH were higher in haemolytic crisis than both VOC and steady state. This may be explained by the folate deficiency that accompanies haemolysis. As the red cell is destroyed, bone marrow attempts to produce more RBC and thus folate is used up resulting in increased MCV and MCV. Although Abubakar et al reported different finding, small sample size (6 haemolytic crises VS 136 steady state) was a draw back to his study.

The WBC was higher in VOC and haemolytic crises than in steady state. This is similar to the findings of several studies[7, 17-19]. This can be explained by increased inflammatory biomarkers that herald VOC and haemolysis in children with SCA. Thus, the use of WBC as a biomarker of VOC in previous studies[22,23]. This is clinically significant in early diagnosis of silent VOC, such as acute chest syndrome that may surreptitiously lead to death. The platelet count was higher in VOC than both haemolytic crisis and steady state. This may be because platelet is an acute phase reactant and has a tendency to increase in the presence of inflammatory markers as obtained in VOC.

CONCLUSION

Vaso-occlusive crisis is generally associated with lower red blood cell indices (Hb, Hct, MCV, MCH) and high WBC and platelets while Haemolytic crisis is mainly associated with lower HB, Hct but higher MCV MCH, platelet and WBC. These indices may be used as early bio-markers of occult sickle cell anaemia crises to aid early diagnosis and prompt treatment before the overt clinical manifestation and decompensation. Complete blood count should be routinely done to children with sickle cell anaemia to aid early diagnosis sub-clinical crises and prompt intervention

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