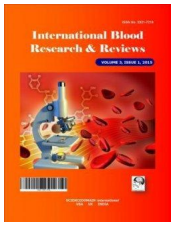

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Haematological Parameters of Adult and Paediatric Subjects with Sickle Cell Disease in Steady State, in Benin City, Nigeria

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Author's contribution

The sole author designed, analyzed and interpreted and prepared the manuscript.

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ABSTRACT

Background: Sickle cell disease (SCD) remains a major health burden in Sub-Saharan Africa and the management requires regular monitoring of the patients. The monitoring includes routine assessment of haematological parameters and any deviation can best be appreciated when steady state values are previously known. This study evaluated the patients with SCD in steady state to determine certain haematological parameters (particularly the full blood count values).
Methods: This is a cross-sectional study. One hundred and forty-three (known) SCD subjects in steady state and thirty controls (HB phenotype AA) had their full blood count parameters evaluated using haematology auto analyser – white blood cell (WBC), granulocyte (GRA) and platelet (PLT) counts as well as haemoglobin concentration (HB), mean cell volume (MCV) and mean cell haemoglobin (MCH). The participants were regrouped into adult and paediatric groups and their results analysed accordingly.
Results: The adult SCD patients had their mean haematological values as follows: HB 7.7±2.5 g/L, MCV 77.5±19.3 fl, MCH 25.1±6.5 pg, WBC 12.0±5.9x10^9 /L and PLT 306.6±169.3x10^9 /L. Their paediatric counterparts had the following mean values: HB 6.9±1.3 g/L, MCV 77.4±11.0 fl, MCH 24.6±3.7 pg, WBC 16.0±6.9x10^9 /L and PLT 329.1±101.9x10^9 /L. The adult patients had

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significantly higher HB ($p<0.05$) and lower WBC ($p<0.05$) than the paediatric patients.
Conclusion: This study has therefore provided some steady state haematological values of both paediatric and adult SCD patients in our locality and could be useful in establishing reference values.

Keywords: Sickle cell disease; steady state; haematological parameters; adult and paediatric.

1. INTRODUCTION

Sickle cell disease (SCD) is an inherited chronic condition that arises from a point mutation in the DNA coding for the synthesis of b-globin chain. It results in the production of sickle haemoglobin which has a high tendency to polymerise and deform red cells, leading to chronic haemolysis [1]. Sickle cell disease is primarily a red cell disorder but significant changes are observed in other haematological parameters such as white cells and platelets which play important roles in pathophysiology of the disease and in prediction of outcome [2]. The SCD patients experience alternating periods of apparent good health (steady state) and acute exacerbation of symptoms (crisis) as well as development of chronic complications. The haematological parameters in these periods vary but at the same time provide evidence-based management information for diagnosis, treatment, monitoring and prognostication. Although the haematological parameters of SCD patients vary significantly from those of normal HbAA individuals, these patients are able to adapt to their steady state haematological values and remain apparently healthy. The importance of some of the steady state haematological values such as Haemoglobin (HB) concentration, white blood cell (WBC) and platelet (PLT) counts in prediction of clinical severity as well as management of SCD has been documented [3,4]. Lower steady state HB is associated with higher risk of stroke [5] whereas higher values are reported to have higher rates of severe pain [6]. Furthermore, red cell transfusions beyond the steady state HB may increase blood viscosity [7] with attendant consequences such as worsening of vaso-occlusion and osteonecrosis. High WBC count (above 11 x 10^9 /L) [4] is associated with SCD complications including cerebrovascular accidents.[5] Some researchers have also shown that lowering the WBC count through the use of drugs such as Hydroxyurea improves the clinical outcome of these patients [8]. Other parameters for assessment include the red cell indices such as MCV, MCH and mean cell haemoglobin concentration (MCHC) which are useful in detecting co-existing causes of anaemia in the patients. Over the years several modalities of treatment of SCD such as blood transfusion, haematinics and hydroxyurea have been used and these modify the haematological parameters of these patients. Knowledge of the steady state haematological values in these patients becomes an important asset for the managing physician.

Several works [4,9,10] on related topic have been carried out in our locality but many did not study the adult and paediatric groups separately, despite the fact that some of the haematological parameters vary normally with age. Moreover the most recent similar study 9 in our immediate environment was carried out about a decade ago. Meanwhile there has been some improvement in access to medical care, socioeconomic development and education over the years; [1,12] a phenomenon which may impact the haematological values in patients with SCD [13]. The aim of this study therefore, is to determine the haematological parameters in paediatric and adult patients with SCD (in our locality) who are in steady state, as well as to compare these values with those of normal HbAA controls. This could provide reference values for the management of these patients and also reveal any deviation from earlier reports as a result of changes in treatment and socioeconomic factors on the parameters.

2. METHODOLOGY

This is a cross-sectional (case-control) study on sickle cell disease patients (in steady state) who attend clinics at the University of Benin Teaching Hospital (UBTH) and the Sickle Cell Centre in Benin City, Edo state, Nigeria. The controls were recruited from healthy staff and children of the staff of the hospital, whose HB phenotypes were AA. Steady state was defined by the absence of clinical event in the preceding three weeks as well as blood transfusion in the preceding three months [14]. Subjects who are up to eighteen years of age were taken as adults and others included in the paediatric age group. Haemoglobin phenotypes of subjects had been previously determined by cellulose acetate haemoglobin electrophoresis at pH 8.6, using tris-buffer. Subjects who had conditions that could alter the haematological values were

excluded. These conditions include: transfusion in the preceding three months, pregnancy and renal failure.

The study was approved by the hospital ethics and research committee and informed consent obtained from the study participants and/or parents (where applicable).

2.1 Procedure

For each subject, the venepuncture site was carefully cleaned with methylated spirit and two and a half millilitres (2.5 ml) of venous blood collected (into commercially prepared ethylene di-amine tetra-acetic acid, EDTA, bottle) from the ante-cubital vein using plastic syringe. Full blood count: haematocrit, haemoglobin concentration and total white cell and platelet counts were obtained from the EDTA sample, using automated blood cell counter (PCE-210N, Erma Inc, Tokyo, Japan; 2012. A three-part haematology autoanalyzer that measures blood cells using the principle of electric resistance, and colorimetry for haemoglobin). The procedure was done in the main haematology laboratory, UBTH. Well mixed blood sample was aspirated, by letting the equipment sampling probe into the blood sample and then pressing the start button. Approximately 20 ul of blood was aspirated by the auto analyzer; after about 30 seconds the results of the full blood count parameters were displayed and subsequently printed out. The parameters collated included: white blood cell (WBC), granulocyte (GRA), platelet (PLT) counts, haemoglobin (HB) concentration, mean cell volume (MCV) and mean cell haemoglobin (MCH).

2.2 Statistical Analysis

Data were analyzed using SPSS version 16.0 (Statistical Package for Social Sciences). The means, ranges and standard deviations (S.D) of the haematological values in the patients and in controls were calculated. Values in the patients were compared with values in controls using the student t-test. The p-value <0.05 was considered to be statistically significant.

3. RESULTS

A total of 143 cases and 30 controls were enrolled. The cases consisted of 73 (51.0%) males and 70 (49.0%) females, while controls were made up of 17 (56.7%) males and 13 (43.3%) females. There were 75 (52.4%) adult and 68 (47.6%) paediatric cases as well as 15 (50%) adult and 15 (50%) paediatric controls. The mean ages for the adult and paediatric SCD subjects were 27.9±9.1 and 8.5±4.4, respectively (as shown in Table 1).

The haematological values in SCD subjects and controls are shown in Tables 2 and 3. The SCD subjects had significantly higher mean WBC, GRA and PLT counts but lower HB than their respective controls ($p<0.05$). The adult SCD patients had their mean haematological values as follows: Haemoglobin concentration (HB) 7.7 ±2.5g/L, mean cell volume (MCV) 77.5±19.3 fl, mean cell haemoglobin (MCH) 25.1±6.5 pg, white blood cell count (WBC) $12.0\pm5.9\times10^9$ /L, granulocyte count (GRA) $7.3\pm4.4\times10^9$ /L and platelet count (PLT) $306.6\pm169.3\times10^9$ /L. Their paediatric counterparts had the following mean values: HB 6.9±1.3 g/L, MCV 77.4±11.0 fl, MCH 24.6±3.7pg, WBC $16.0\pm6.9\times10^9$ /L, GRA $8.7\pm5.2\times10^9$ /L and PLT $329.1\pm101.9\times10^9$ /L.

The haematological values in adult and paediatric subjects were compared in Table 4. The adult patients had significantly higher HB ($p<0.05$) and lower WBC ($p<0.05$) than the paediatric patients. The comparison of the haematological parameters in male and female subjects is depicted in Tables 5 and 6. This revealed no statistically significant difference between males and females ($p>0.05$), for all the values tested.

Table 1. Demographic parameters of SCD subjects and controls

Adult	**Subjects (n=75)**	**Control (n=15)**
Sex	Frequency (%)	Frequency (%)
Male	38 (50.7%)	9 (60%)
Female	37 (49.3%)	6 (40%)
Mean age (years ±2SD)	27.9±9.1	28.2±6.6
Paediatric	**Subjects (n=68)**	**Control (n=15)**
Sex	Frequency (%)	Frequency (%)
Male	35 (51.5%)	8 (53.3%)
Female	33 (48.5%)	7 (46.7%)
Mean age (years ±2SD)	8.5±4.4	9.4±4.1

Table 2. Haematological parameters of adult SCD subjects and controls

Variable	Subjects (n=75)	Control (n=15)	p-value
WBC ($x10^9$ /L ±2SD)	12.0±5.9	5.6±1.5	<0.001
GRA ($x10^9$ /L ±2SD)	7.3±4.4	2.8±1.0	0.001
HB (g/dl ±2SD)	7.7±2.5	14.1±1.8	<0.001
MCV (fl ±2SD)	77.5±19.3	80.2±6.5	0.595
MCH (pg ±2SD)	25.1±6.5	27.7±2.5	0.135
PLT ($x10^9$ /L ±2SD)	306.6±169.3	199.2±58.6	0.018

KEY: WBC- white blood cell count; GRA-granulocyte count; PLT-platelet count; HB-haemoglobin concentration; MCV-mean cell volume; MCH-mean cell haemoglobin

Table 3. Haematological parameters of paediatric SCD subjects and controls

Variable	Subjects (n=68)	Control (n=15)	p-value
WBC ($x10^9$ /L ±2SD)	16.0±6.9	5.5±1.1	<0.001
GRA ($x10^9$ /L ±2SD)	8.7±5.2	2.7±0.8	<0.001
HB (g/dl ±2SD)	6.9±1.3	12.7±0.7	<0.001
MCV (fl ±2SD)	77.4±11.0	73.7±4.2	0.204
MCH (pg ±2SD)	24.6±3.7	25.6±2.2	0.315
PLT ($x10^9$ /L ±2SD)	329.1±101.9	249.9±52.0	0.005

Table 4. Comparison of the haematological parameters of adult and paediatric SCD subjects

Variable	Adult (n=75)	Paediatric (n=68)	p-value
WBC ($x10^9$ /L ±2SD)	12.0±5.9	16.0±6.9	**<0.001**
GRA ($x10^9$ /L ±2SD)	7.3±4.9	8.7±5.2	0.105
HB (g/dl ±2SD)	7.7±2.5	6.9±1.3	**0.027**
MCV (fl ±2SD)	77.5±19.3	77.4±11.0	0.990
MCH (pg ±2SD)	25.1±6.5	24.6±3.7	0.548
PLT ($x10^9$ /L ±2SD)	306.6±169.3	329.1±101.9	0.345

Table 5. Haematological parameters of adult male and female SCD subjects

Variable	Male (n=38)	Female (37)	p-value
WBC ($x10^9$ /L ±2SD)	13.1±5.9	10.9±5.8	0.111
GRA ($x10^9$ /L ±2SD)	8.1±4.8	6.6±4.9	0.198
HB (g/dl ±2SD)	7.8±2.6	7.6±2.6	0.710
MCV (fl ±2SD)	74.1±2.1	80.0±1.8	0.130
MCH (pg ±2SD)	24.0±7.0	26.2±5.8	0.142
PLT ($x10^9$ /L ±2SD)	324.4±190.1	288.3±145.3	0.359

Table 6. Haematological parameters of paediatric male and female SCD subjects

Variable	Male (n=35)	Female (33)	p-value
WBC ($x10^9$ /L ±2SD)	16.1±6.7	15.8±7.3	0.884
GRA ($x10^9$ /L ±2SD)	9.7±6.0	7.7±3.9	0.128
HB (g/dl ±2SD)	7.0±1.0	6.9±1.5	0.723
MCV (fl ±2SD)	75.5±1.1	79.5±1.1	0.136
MCH (pg ±2SD)	24.3±3.8	24.8±3.7	0.565
PLT ($x10^9$ /L ±2SD)	330.5±109.1	327.6±95.2	0.908

4. DISCUSSION

Haematological parameters in SCD patients have been widely studied in our locality but the need to establish paediatric values as distinct from adult values has not been appreciated despite the effect of age on some of the haematological values. This work was therefore carried out in an attempt to fill in the gap. A review of the sex and age distribution in this

study revealed that males were only slightly more than females in both paediatric and adult groups; just as there was no significant difference in their mean ages. It is worthy of note that the mean age for the adult cases is higher compared to 23.69±10.94 years reported by Omoti [9] several years ago. Akinbami [10] in a more recent study in Lagos had a mean age of 23.79±7.81 years in a work that also lumped both adult and paediatric cases together.

The SCD patients have chronic haemolysis, [1] low erythropoietin response [15] and shortened red cell survival which explains the low HB observed in the SCD subjects of this study. However, a more detailed analysis revealed a higher mean HB in the adult subjects; in line with previous finding that haemoglobin concentration increases with age. [16] The mean HB for the paediatric patients (6.9±1.3 g/dl) was in agreement with Akodu's [17] work in Lagos and close to that observed by Abbas [18] in Sudanese children. On the other hand, the adult patients had a mean HB which corresponded with mean HB of 7.54±2.26 g/L observed by Omoti, [9] in a work whose subjects were predominantly adults (mean age of 23.69 years). Despite the low HB level, the patients enjoy apparent good health as they have adapted to this anaemic state. Nevertheless it has been reported that SCD patients with lower steady state HB may have higher risk of complications such as stroke [5].

The findings of low MCV and MCH in SCD patients by other researchers [9,10] were similarly observed in the SCD patients; although the differences were not statistically significant when compared to controls. The mean MCV and MCH values in the paediatric patients were lower than 84 ±16fl reported by Abbas [18] in his study population. These observations may reflect a background iron deficiency in the SCD patients in our environment; although iron deficiency anaemia is expected to be uncommon due to chronic haemolysis with increased iron turnover and higher rate of blood transfusion in SCD patients. This present study also observed low MCV and MCH in both paediatric groups (SCD and control); a phenomenon which may be related to increased iron demand for growth in children. Akodu [17] reported identical values in their SCD group whereas their control group had lower values. Adeyemo [19] in another related research in Lagos noted low MCV and MCH, but equally revealed a high frequency of HB variants (such as beta thalassaemia trait) co-existing with SCD in their study population. Thalassaemia is a known cause of low MCV and MCH; hence the need to screen and determine its contribution to the observed values.

The WBC and GRA counts for the adult SCD patients were comparable to the findings in a previous study [9] whereas their paediatric counterparts had a higher mean count. A similar study on Sudanese children showed a much higher mean WBC ($21.7\pm10.3x10^9$/l) [18]. The higher values of WBC and GRA counts for the SCD patients (with respect to their control group) is consequent upon the persistent low grade inflammation and a shift of granulocytes from the marginated to the circulating compartment [20]. The observation of a higher mean WBC and GRA counts in the paediatric SCD subjects may require further investigation to ascertain if it is due to subclinical infection since the children are known to have higher incidence of infections [21]. However hydroxyurea, a drug with the capacity to lower WBC count [22], is administered more on adult SCD patients in our environment and may affect the WBC values in these patients. Nonetheless, high WBC is associated with poor clinical phenotype in SCD [4,5,23], thus such patients may benefit from hydroxyurea therapy [22].

The mean platelet count of the SCD patients were higher than those of their control group as expected, due to the decrease or absent splenic sequestration of platelets [24]. The increase in erythropoietin (which has structural homology with thrombopoietin [25,26] as a result of anaemia in SCD patients may also contribute to the high platelet count observed in the SCD subjects (compared to controls). The observation was in agreement with several other reports [9,10,18]. The value for the paediatric patients was equally comparable to the 319.2 x 10^9/L reported by Abbas [18]. Their adult counterparts had relatively lower mean platelet count (although the difference was not statistically significant); an observation which conforms with normal finding of decreasing platelet count with increase in age [27] as a result of decreasing thrombopoietin levels [28]. Furthermore, the greater frequency of hydroxyurea administration in our adult SCD patients may contribute to this observation. Hydroxyurea has been reported to lower platelet count in SCD patients [22].

5. CONCLUSION

This study has therefore provided some steady state haematological values of both paediatric

and adult SCD patients in our locality and could be useful in establishing reference values. The low MCV and MCH in SCD patients require further investigation in order not to miss a growing iron deficiency in a group of patients known to be otherwise prone to iron overload.

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COMPETING INTERESTS

Author has declared that no competing interests exist.

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