Original Article

Steady state hemoglobin concentration and packed cell volume in homozygous sickle cell disease patients in Lagos, Nigeria

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Abstract

Background: Sickle cell disease is a genetic disorder of hemoglobin causing myriad of pathology including anemia. The purpose of this study was to evaluate the baseline values of steady state hemoglobin and packed cell volume as a guide to managing the early recognition of hemolytic crises in sickle cell anemia.

Methods: A cross-sectional study was conducted among the sickle cell patients attending the Sickle Cell clinic of Lagos State University Teaching Hospital, Ikeja. A blood sample of 4.5 ml blood was collected from each participant for hemoglobin concentration and packed cell volume. All blood samples were also screened for HIV and hemoglobin phenotypes were done using cellulose acetate hemoglobin electrophoresis at pH 8.6.

Results: A total of 98 subjects in steady state were recruited, consisting of 53 (54.1%) females and 45 (45.9%) males. The overall means were 7.92±1.49 and 24.46±4.76; a female mean of 7.73±1.45; 23.89±4.60, and a male mean of 8.14±1.54 and 25.14±4.91 were obtained for hemoglobin and packed cell volume, respectively. Sixty – nine of the 98 (70.40%) subjects have been previously transfused with blood.

Conclusion: The mean hemoglobin concentration and packed cell volume in males was higher than females. The overall mean was lower than what was expected for age and sex. Over two-third of sickle cell anemia population had been transfused.

Keywords: Homozygous sickle cell disease, Steady state, hemoglobin concentration, packed cell volume.

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Sickle cell disease is a genetic disorder of hemoglobin, glutamine is substituted for valine at position six of the beta-hemoglobin chain. The substitution of glutamine, a positively charged amino acid for a neutral amino acid valine results in the formation of hemoglobin S and causes a variety of pathological conditions that affect the hemoglobin concentration and the packed cell volume of the individual. Hemoglobin S result from the substitution of an unusual form of hemoglobin in the red cells and interfering oxygenation and subsequent sickling of red cells and hemolysis. The repeated sickling and unsickling damages the red cell membrane leading to irreversibly sickled red cells even when the oxygen pressure is increased. The resulting hemolysis consequent to the damaged red cell membrane may occur intravascularly or extravascularly (1-3).

Extravascular hemolysis occurs by phagocytosis of red cells that have undergone sickling and physical entrapment of rheologically compromised red cells (4-6). Increased susceptibility to mechanically induced cell fragmentation has been documented in vitro and in sickle cell patients undergoing vigorous exercise (3).

Degree of hemolysis is inversely related to hemoglobin concentration and packed cell volume in sickle cell anemia patients.

Numerous factors affect hemolysis in sickle cell anemia, percentage of irreversible sickle cell is of greatest significance (7). The degree of hemoglobin polymer formation calculated from the mean corpuscular hemoglobin concentration, and the relative proportion of hemoglobin fractions, also correlated closely with the severity of hemolysis (8, 9).

Majority of the sickle cell patients are relatively stable much of the time and are said to be in a steady state because they achieve a steady state level of fitness. The steady state may be periodically interrupted by hemolytic crises which may be acute and fatal.

The early recognition of hemolytic crises and subsequent clinical assessment of sickle cell anemia are greatly facilitated by familiarity with the patients' steady state hemoglobin and packed cell volume. Knowledge of the baseline values of steady state hemoglobin and packed cell volume in sickle cell patients serves as guide to clinicians managing sickle cell anemia. The need to study the pattern of steady state hemoglobin and packed cell volume cannot be overemphasized.

Methods

A cross-sectional study was conducted amongst the sickle cell patients attending the Sickle Cell clinic of Lagos State University Teaching Hospital, Ikeja from September to December 2011 after obtaining approval from the institution's Ethics and Research Committee. Written and verbal consents were obtained from each participant. The participants were asked to fill structured questionnaires including demographic information, history of previous blood transfusion and surgery, previous history of crises, date of last crises, cigarette and alcohol intake. Inclusion criteria were patients with hemoglobin phenotype SS, no history of crises in the past 3 months established by a careful history and complete physical examination, no previous history of surgery, no history of blood transfusion in the past 3 months. Exclusion criteria were history of blood transfusion in the past 3 months, hemoglobin phenotype SC patients, previous history of surgery, and HIV infected patients.

Collection of Samples: A blood sample of 4.5 mls was collected into ethylenediaminetetraacetic acid (EDTA) anticoagulant bottle for full blood count analysis done on the same day of collection using Sysmex KN-21N, (manufactured by Sysmex corporation Kobe, Japan) a three-part auto-analyzer able to run 19 parameters per sample including hemoglobin concentration, packed cell volume, red blood cell concentration, mean corpuscular hemoglobin, mean cell volume, mean corpuscular hemoglobin concentration, white blood cells and platelet parameters. Well mixed blood sample was aspirated by letting the equipment sampling probe into the blood sample and then pressing the start button. Approx. 20 µl of blood was aspirated by the auto-analyzer. Result of analysis is displayed after about 30 secs. A printout copy of result is released on the thermal printing paper.

All blood samples were also screened for HIV using determine rapid kit, and hemoglobin phenotypes of all participants were done using cellulose acetate hemoglobin electrophoresis at pH 8.6.

Statistical Analysis: Data were analyzed using SPSS version 16.0 (Statistical Package for Social Sciences, Inc., Chicago, Ill). The descriptive data were given as means ± standard deviation (SD).

Independent t–test was used to test the significance of the differences between mean values. The Pearson chi square test was used for analytic assessment and the differences were considered to be statistically significant when the p value obtained was< 0.05.

Results

A total of 98 subjects in steady state were recruited, consisting of 53 (54.1%) females and 45 (45.9%) males (table 1). The minimum age was 13 and maximum of 44 years with a mean of 24.08 ±7.84. Majority of them, 69 of 98 (70.4%) had been previously transfused with blood while 29 (29.6%) gave no history of blood transfusion (table 1).

Most of them (57.1%) had hemoglobin between 7-10 g/dl and 63.3% had packed cell volume between 20-30%. Only 11.2% had hemoglobin greater than 10 g/dl and 12.2% had packed cell volume greater than 30%. While 31 (31.6%) had hemoglobin less than 7 g/dl and 24 (24.5%) had packed cell volume between 13-20% (table 2).

Thirty-three males out of 45 (73.33%) had been previously transfused while only 12 of 45 (26.7%) had no previous history of blood transfusion.

Mean Hb level in males was 8.14±1.54 and in females was 7.73±1.45 (p=0.8). The mean PCV in males was 25.1±4.9 and in females was 23.9±4.6 (p=0.6) (table 3).

Table 1. Mean, range, PCV, Hb concentration, and age according to sex and history of blood transfusion

	Past history of transfusion		No past history of transfusion	
	Male	Female	Male	female
Number	33	36	12	17
Age, mean (range)	23.29±6.97 (13-43)	26.64±9.27 (14-44)	21.00±6.63 (13-32)	21.94±5.44 (15-3)
PVC, mean (range)	25.71±4.94 (13.1-36.6)	24.46±5.27 (15.2-35.8)	22.78±4.26 (15.1-27.8)	23.02±2.39 (18-27.4)
Mean Hb	8.31±1.52 (4.7-11.8)	7.87±1.62 (5-11.2)	7.42±1.47 (4.6-9.1)	7.42±0.89 (5.7-9.2)

PCV=Packed cell Volume, Hb=haemoglobin Concentration

Table 2. Univariate analysis of haemoglobin concentration and packed cell volume

	Male	Female	Total
Age mean±SD (range)	22.8±6.8 (13-43)	25±8.4 (14-44)	24.8±7.8) (4.6±11.8)
Hb mean±SD (range)	8.1±1.5 (4.6-11.8)	7.7±1.4 (5-11.2)	7.9±1.49 (13.7-36.6)
PCV, mean±SD (tange)	25.1±4.99 (13.7-36.6)	8.9±4.6 (15-2-35.8)	24.4±4.7 (13-7-36.6)

Table 3. Bivariate analysis of haemoglobin concentration and packed cell volume

	Blood transfusion		Pvalue
	Yes(n=69)	No(n=26)	
Hgb			
High	10	0	
Low	20	10	0.143
Moderate	39	16	
PCV			
Low	16	8	
Moderate	42	18	0.160
Normal	11	0	

Discussion

Blood transfusion in sickle cell anemic patients serves two major functions, namely increasing oxygen-carrying capacity of blood and replacing the abnormal red cells with the normal, thus alleviating symptoms and preventing complications (10-12). Over 70% of the patients recruited for this study had previous history of blood transfusion. This highlights the fact that blood transfusion practice is common in sickle cell anemia population and almost all adult patients may have been multiply transfused. However, this study did not show a statistically significant correlation between previous history of blood transfusion and hemoglobin concentration/packed cell volume. About 60% of the patients had hemoglobin concentration between 7-10 g/dl and packed cell volume between 20-30%. A female and a male mean

obtained for hemoglobin and packed cell volume in this study fell short of hemoglobin concentration and packed cell volume expected amongst healthy Nigerian adults for males and females, respectively (13).

The increased rate of hemolysis associated with sickle cell anemia patients could account for these lower values. There is also a blunted response to erythropoietin secretion in sickle cell anemia, the rate of increase is not proportional to the degree of anemia (14). This may be due to right-shifted hemoglobin dissociation curve seen in sickle cell disease (15).

An average of 10% of the patients had hemoglobin concentration over 10 g/dl and packed cell volume over 30%.Variations in the severity of sickle cell disease between individuals usually defy explanation. Some factors known to ameliorate severity include the presence of high concentration of erythrocyte hemoglobin F, which disrupts the polymerization of deoxy-Hb-S, possession of senegal haplotype, compared with the Central Africa Republic and the benin haplotypes (16-18).

No clear explanation exists for the differences in average severity between the haplotypes. The rate of hemolysis is also lower in people who possess two-gene deletion alpha-thalassemia (19). The mechanism by which alpha-thalassaemia ameliorates hemolysis is unknown. These are individually and synergistically associated with reduced hemolysis in sickle cell anemia and higher hemoglobin concentration and packed cell volume.

The means hemoglobin concentration and packed cell volume obtained in this study were similar to values obtained amongst the sickle cell disease patients in previous studies in Nigeria (20-22). These values were expected considering the degree of chronic hemolysis. Most patients have adapted to their severity of anemia, there is therefore no clinical benefit to treat anemia with blood transfusion. On the contrary, raising the packed cell volume to over 30% can increase blood viscosity, which increases with high packed cell volume, causing increased time during which the cells remain in the low oxygen tension regions of the circulation, and worsen the sickling propensity (23).

Expectedly, the mean hemoglobin concentration and packed cell volume for males were higher than those for the females. Increased erythropoesis due to androgens in males, and low iron or blood loss in females during menstruation may be responsible for higher levels of hemoglobin levels and erythrocyte count in males. Reference ranges for erythropoietin are however, not different between the sexes (24). A negative feedback effect on erythropoietin production in males resulting in lower erythropoietin levels will have been expected because of the androgen effect. This indicates that females have better tissue oxygenation for a given hemoglobin level and more efficient tissue red cell delivery. However, like a similar study amongst Nigerian children this study did not show a significant value when the means of hemoglobin concentration and packed cell volume were compared between the males and females (25). When hematological profile of Nigerian sickle cell disease patients in unsteady and steady state were compared, higher percentage of derangement was obtained amongst those in unsteady state (26).

In summary the mean hemoglobin concentration and packed cell volume in males were higher than females. The overall means were lower than that expected amongst healthy Nigerian adults. Over 70% of sickle cell anemia population has been transfused.

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