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Evaluation of Iron Status in Adult Sickle Cell Anaemia Patients in Zaria, North Western Nigeria

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Abstract

This is a case-controlled study designed to evaluate iron status of adult sickle cell anaemia patients and to compare findings with vaso-occlusive crises in sickle cell anaemia. One hundred and one (101) subjects aged 18-46 years participated in this study and these participants were divided into thirty five (35) sickle cell anaemia subjects in stable state (SS), thirty five (35) sickle cell anaemia subjects with history of vaso-occlusive crises (VOC) in the last preceding three months and thirty one (31) apparently healthy subjects (Hb AA) as control subjects (C) were recruited into the study using simple random sampling. Approximately 4 ml of venous blood samples was collected from each subject into a plain tube, allowed to clot and serum sample separated from it was analysed for serum iron, ferritin, total iron binding capacity (TIBC) and percentage transferrin saturation. The haemoglobin electrophoresis was determined using the alkaline cellulose acetate electrophoresis method Serum iron was analysed using atomic absorption spectrophotometer (AAS). Serum ferritin was determined using Ferritin Enzyme Immunoassay (Genway). TIBC was done using Ferene method and percentage transferrin saturation (%TFS) was derived from serum iron and TIBC. The mean values of serum iron and ferritin were significantly lower (P=0.00, P=0.00) respectively in SCA subjects compared with control. However, there was no significance difference in the mean values of TIBC and %TFS between SCA subject and control (P=0.56, P=0.14) respectively. There was significant difference in the mean values of serum iron and ferritin between SCA in stable state and control subjects (P=0.00, P=0.00) respectively. Also, there was significant difference in the mean values of serum iron and ferritin between SCA subjects with vaso-occlusive crises and control subjects (P=0.00, P=0.00) respectively. However, the comparison of the mean values of TIBC and %TFS between SCA in stable state and control subjects did not show any significance difference (P=0.56, P=0.33) respectively. Also, the mean values of TIBC and %TFS between SCA with vaso-occlusive crises and control subjects did not show any significant difference (P=0.88, P=0.37) respectively. The mean values of serum iron, ferritin, TIBC and %TFS between SS and VOC did not show any significant difference (P=1.00, P=0.99, P=0.79, P=0.97) respectively. The outcome of this work show reduced serum iron and ferritin levels in SCA subjects. Periodic assessment of iron status is therefore suggested in the monitoring and management of sickle cell anaemia.

Keywords: Sickle cell anaemia; Steady state; Vaso-occlusive crises; Serum iron; Serum ferritin; Haemolytic process.

Introduction

Sickle cell anemia is a genetic disorder that is caused due to the inheritance of a mutant gene that encodes haemoglobin S (HbS) [1]. This abnormal HbS is formed when glutamic acid is replaced with valine in the sixth position of β-globin chain [2]. The b-globin chain is made up of 146 amino acids and the fault occurs at the sixth position [3]. An individual who inherits this gene from both parents suffer from sickle cell anaemia [4]. The clinical manifestations of this disorder is often referred to as crises [5]. These crises could be aggravated by factors such as infections, extremes of temperature and stress [6-8]. Vaso-occlusive crises (VOC) is defined as the occurrence of pain in the extremities, back, abdomen, chest, or head that lasts two or more hours [9]. VOC is the hallmark of sickle cell anaemia and it is responsible for most hospital admissions [10].

Sickle cell anaemia may lead to various acute and chronic complications with high mortality rate [11]. The main symptoms of this disorder includes increased susceptibility to infection, anaemia, pains and crises due to the polymerization of HbS molecules and irreversible sickling of red blood cells leading to vaso-occlusion [12]. Sickle cell anaemia is a public health problem in Africa than any other continent in the world and it affects about 2% of Nigerian population [13].

Iron plays a central role in erythropoiesis and many other intracellular processes in all the tissues of the body [14]. Although iron is an important element required by the human body, the control of this necessary but potentially toxic substance is an important aspects of human health and disease [15]. Iron deficiency leads to decrease in the amount of red blood cells or haemoglobin [16]. Iron overload on the other hand leads to toxicity and cell death via free radical formation and lipid peroxidation [17].

Iron deficiency or overload, complicating SCA, is likely to worsen the clinical state of the disease (14). Thus iron haemostasis requires tight regulation [18]. Recently, serum ferritin is considered as an effective indicator of the iron status of the body [19]. Serum iron, serum ferritin, percentage transferrin saturation and total iron binding capacity constitute indices of iron status in SCA subjects [20].

Study design

This is a case-controlled study conducted in haematology clinic of Ahmadu Bello University teaching (ABUTH) Zaria, North Western Nigeria. One hundred and one (101) subjects aged 18-46 years participated in this study and these subjects were divided into thirty five (35) confirmed sickle cell anaemia subjects in stable state (SS), thirty five (35) sickle cell anaemia subjects with history of vaso-occlusive crises (VOC) in the last three months and thirty one (31) apparently healthy subjects (Hb AA) as control subjects (C). Only confirmed HbSS adult subjects without history of blood transfusion in the last preceding three months and were on routine drugs (folic acid and paludrine) in haematology clinic in ABUTH, Zaria were included in this study. Subjects that were on iron drugs, had blood transfusion in the last three months were not included from the study. Ethical approval was obtained from health and research ethics committee of ABUTH, Zaria and informed consent was obtained from each participant. Approximately 4ml venous blood was collected from each participant into a plain container and was allowed to clot after which the serum was separated and kept at -20°C. The serum was analysed for serum iron, ferritin and TIBC.

Laboratory Methods

Haemoglobin electrophoresis was done using alkaline cellulose acetate electrophoresis method [21]. Serum iron estimation was done using flame atomic absorption spectrophotometer [22]. Serum ferritin was determined by ferritin enzyme immunoassay (Genway). Total iron binding capacity (TIBC) was determined using direct Ferene method and percentage transferrin saturation (%TFS) was derived from serum iron and TIBC.

Statistical analysis

Data generated was analysed using SPSS (version 17). Comparison between groups was done using ANOVA and Post Hoc and a P value of <0.05 was considered statistically significant.

Results

Table 1 shows the demographic pattern of the study subjects. The 101 subjects comprising of 35 HbSS subjects in SS, 35 HbSS subjects with VOC and 31 apparently healthy Hb AA subjects as controls (C). There were more females 54 (53%) than males 47 (47%). The overall mean age for SS group was 23.94 ± 5.83 years; VOC was 24.63 ± 6.63 years and control 25.55 ± 5.33 years. Also, the overall mean weight of SS was 53.49 ± 8.79 kg, VOC was 50.57 ± 6.99 kg and control was 58.19 ± 7.55 kg. The result shows a significant difference in the sex and weight of SCA subjects when compared with control subjects (p=0.00 and p=0.00) respectively. However, no significant difference was observed in the mean age of SCA subjects when compared with control subjects (P=0.71).

Table 1 The demographic pattern of the studied subjects.

Group	SS (n=35)	VOC (n=35)	C (n=31)	p value
Age (years)	23.94 ± 5.87	24.63 ± 6.63	25.55 ± 5.33	0.71
Gender				
Male	11	12	21	0.00*
Female	24	23	10	
Weight (kg)	53.49 ± 8.79	50.57 ± 6.99	58.19 ± 7.55	0.00*

*=significant at P<0.05, SS=Steady state, VOC=Vaso-occlusive crises, C=Control

In **Table 2**, the SCA group had significantly lower (P=0.00) iron and ferritin mean values than the controls. However, the mean values of TIBC and % TFS of SCA group did not show any significant difference when compared with control (P=0.56 and P=0.14) respectively. Also the mean values of TIBC and %TFS between SS and VOC did not any significant difference (P=0.79 and P=0.97) respectively. In comparing SS with VOC groups, the mean values of iron and ferritin showed no significant difference (P=1.0, P=0.99) respectively. However, the comparison of the mean values of TIBC and %TFS between SS and control subjects, between VOC and control subjects did not show any significant difference(P=0.56, P=0.33, P=0.88 and P=0.37) respectively.

Discussion

The life expectancy of SCA subjects is short [23] but with elaborate and comprehensive laboratory monitoring and management, SCA subjects can have a much longer life expectancy. Females might have longer life expectancy of 48-58 years than men with 42-53 years [23]. There were more females 54 (53%) than males 47 (47%) in this study. The weight of SCA subjects was significantly lower when compared with control. This might be due to chronic complications associated with sickle cell anaemia. However, there was no significant difference in the mean age of SCA subjects and control subjects. The peak age of the subjects in this study is the

fourth decade. This is because the study was carried out among adult SCA subjects.

Although iron is an important element required by the human body, the control of this necessary but potentially toxic substance is an important aspects of human health and disease [15]. In this study, serum iron was significantly lower in sickle cell anaemia subjects when compared with control subjects and this agrees with studies conducted by Olivieri [24], Akinsegun [25] and Olaniyi et al. [26]. This is based on the fact that excessive amount of iron is lost in sickle cell anaemia patients due to haemolysis associated with the condition [27].

Table 2 Serum iron, ferritin, TIBC and percentage transferrin saturation (% TFS) of SCA compared with control group.

Group	Iron (µg/dl)	Ferritin (µg/dl)	TIBC (µg/dl)	TFS (%)
SS (n=35)	150.75 ± 18.55	94.22 ± 1.69	80.157 ± 2.98	8.61 ± 2.29
VOC (n=35)	150.79 ± 19.58	94.36 ± 10.77	389.634 ± 7.38	38.72 ± 2.17
C (n=31)	166.33 ± 19.03	105.73 ± 12.14	394.713 ± 8.92	40.74 ± 7.96
F (P) value	7.16 (0.00)*	11.71 (0.00)*	0.59 (0.56)	2.03 (0.14)
SS vs VOC P-value	1	0.99	0.79	0.97
SS vs C P-value	0.00*	0.00*	0.56	0.33
VOC vs C P-value	0.00*	0.00*	0.88	0.37

*=significant at P<0.05, SS=Steady state, VOC=Vaso-occlusive crises, C=Control

This study showed that serum ferritin value was significantly reduced in sickle cell anaemia subjects when compared with control subjects. This is contrary to findings of Akinsegun et al. [25], Akodu et al. [28] and Ikusemoro et al. [29]. The lower body stores of ferritin among SCA subjects especially, might be explained by increased mobilization and utilization of ferritin-iron from the stores to erythropoietic precursors in the bone marrow to meet increased demand for new red blood cells production in SCA subjects as a result of chronic haemolytic/ hyper haemolytic process.

The SCA subjects displayed a grossly normal values of TIBC and percentage TFS. TIBC increases when iron stores decreases and percentage transferrin saturation is abnormal when iron stores is completely reduced [30].

Although the mean values of serum iron, ferritin, TIBC and percentage transferrin saturation was slightly higher in SCA subjects with VOC than SCA subjects in SS, the result was not statistically significant. This might be due to increased haemolysis in SCA subjects with VOC. The lack of significant difference between SCA subjects with VOC and SCA subjects in stable state might be explained by increased mobilization and utilization of ferritin-iron from the stores to erythropoeitic precursors in the bone marrow to meet the increased need for the production of new red blood cells caused by chronic haemolytic process in SCA subjects. None of the parameters studied can be used as a sensitive marker of VOC in sickle cell anaemia subjects. This is contrary to report by Olaniyi et al. [26] where it was posited that %TFS may be used as a sensitive marker of VOC in SCA subjects.

Conclusion

Interpretation of iron status of sickle cell anaemia patients remained a difficult task due to chronic inflammatory and haemolytic processes associated with this condition. In this study, reduced serum iron and ferritin values was observed in SCA subjects. Periodic evaluation of iron status of sickle cell anaemia patients is suggested in the monitoring and management of SCA subjects.

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