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Trace Elements Deficiency in Patients with Homozygous Sickle Cell Disease

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Authors' contributions

This work was carried out in collaboration between all authors. Author JKN originated the Concept, designed experiments and collected data. Authors MS and CD performed critical reviews of the manuscript. Authors CEO, AI and CA performed the data analysis and wrote the first draft. All authors approved of the final manuscript.

Original Research Article

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ABSTRACT

Aim: The serum trace elements statuses of sickle cell patients attending at General Hospital Owerri, Nigeria were investigated to determine whether or not the serum levels of these elements were normal.
Materials and Methods: One hundred confirmed sickle cell patients (HbSS) age 5–30 years were selected. One hundred normal subjects (HbAA) age 5–30 years were used as control.
Results: The levels of trace elements were significantly decreased in sickle cell anemia ($p<0.05$), except copper, when compared with the control.
Conclusion: The result suggests, but not conclusively, that supplementation of sickle cell

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patients with food and drug containing trace elements might be helpful, particularly if diminished mineral levels predispose patients to crises.

Keywords: Trace elements; deficiency; homozygous sickle cell disease.

1. INTRODUCTION

Sickle cell disease (SCD) is an inherited disorder caused by the substitution of valine for glutamic acid at the sixth position in β-chain of the hemoglobin molecule [1,2]. Individuals with sickle cell disease possess high level of sickle cell hemoglobin [3,4,5].

Sickle cell disease is a significant cause of morbidity and mortality among black individuals and descendant of Africans [6]. The prevalence of SCD is very high in central Africa, Mediterranean region, Eastern countries and in certain part of India [7]. Nigeria still remains among the country with high prevalence. Life expectancy is shortened with studies reporting an average life expectancy of 42 and 48years for male and female respectively [8].

Although sickle cell disease is present from birth, symptoms are rare before the age of 3 to 6 months since a large percentage of hemoglobin is of the fetal type (HbF). As more Hbs replaces HbF in the subject, the main symptoms: episode of anemia, pains and infections and associated crisis begins to manifest due to irreversible sickling of the erythrocytes when Hbs molecule polymerizes invariably leading to vasoocclusion in the small capillary [9].

Patients with sickle cell disease are liable to increased oxidative stress [10], particularly during vasoocclusive crises and acute chest pain [11]. Several aspects of the abnormalities in sickle cell disease are thought to result from the oxidative stress of red blood cells (RBCs), white blood cells and endothelial cells and activation of platelets [12]. Oxidative stress represents the imbalance between enhanced generation of reactive oxygen species and low cellular content of antioxidants [13,14]. Antioxidants are substances that may protect cells against the effect of free radicals. Free radicals can damage cells and may play a role in heart disease, cancer and sickle cell disease [15]. Sickle cell disease is emerging as an important model of oxidative stress. The peculiar structural features of HbS also make them susceptible to oxidant assault [16]. In an earlier study of Jyoti et al and coworkers [17], the prooxidant and antioxidant status in patients with sickle cell disease were assessed. On the whole, available reports suggest that sickle cell HbS erythrocytes are susceptible to damage caused by endogenous free radicals [18].

Trace elements are essential inorganic molecules found in minute quantities of milligram or microgram per kilogram of body weight. Trace elements include zinc, copper, selenium, chromium and magnesium [19]. People with sickle cell disease suffer from deficiency of many micronutrients. However, maintaining the membrane integrity and trace elements are important in SCD. The disruption of membrane integrity arises from fragility, dehydration as well as increased production of reactive oxygen species [20]. These metabolic changes lead to depletion of trace elements required for proper cell function in sickle cell disease [21]. The global use of micronutients in health care system has taken central stage due to the realization of their importance in the understanding of this disease [22].

This study was embarked upon to evaluate status of trace elements in sickle cell disease patients. Since monitoring of these biochemical parameters is an important guide to some

disease conditions, this study was equally undertaken so that the knowledge gained from the research work may suggest a better understanding and diagnosis of sickle cell disease.

2. MATERIALS AND METHODS

One hundred patients HbSS diagnosed by haemoglobin electrophoresis [1] (50 males and 50 females) aged 5-30 years were selected for the study. One hundred HbAA normal subjects (50 males and 50 females) were used as control. In all subjects, 5ml of venous blood was collected into a non-anticoagulated tube. The samples were spun in a Wisterfuge (model 684), centrifuge at 1000g for 10minutes and the serum collected into a clean dry bijou bottle. The trace elements were estimated.

Trace elements (copper, zinc, chromium, magnesium and selenium) levels were determined by atomic absorption spectrophotometer technique as described by Kaneko [23].

The results were expressed as mean ± standard deviation. The statistical evaluation of data was performed by using student t-test. The level of significance was $P<0.05$.

The study was approved by the hospital ethics board and informed consent was obtained from all patients.

3. RESULTS AND DISCUSSION

The level of zinc, chromium, magnesium and selenium were significantly decreased in HbSS and HbSS-crisis when compared with the control, while copper was increased when compared with the control ($P<0.05$) (Table 1).

Table 1. Trace elements levels in sickle cell anemia and control

PARAMETERS	HbAA	HbSS	HbSS-crisis
Copper (μ/L)	62.34±2.02	68.09±1.52	68.16±1.62*
Zinc (μ/L)	136.21±4.65	113.71±2.54*	114.1±3.08*
Chromium (μ/L)	64.84±3.12	60.34±3.58*	59.68±3.73*
Magnesium (μ/L)	13.771±0.69	10.72±1.21	10.74±1.02*
Selenium (μ/L)	67.42±1.35	60.69±3.12	59.87±3.7*

**Significantly different from control at P<0.05*

Sickle cell disease is a heritable disease for which no cure has been found. It is characterized by inflammation vasoocclusion, anemia and increased energy demand [24]. However, the understanding of the full mechanism of sickle cell disease is incomplete. Haemolysis leads to loss of hemoglobin which in turn leads to depletion of essential antioxidants and trace elements required for proper cell function.

In this study, it was observed that some trace elements in sickle cell disease subjects which are important in red blood cell maintenance, body growth and development were significantly decreased when compared with HbAA. Specifically, the level of serum zinc in sickle cell patients was significantly depleted when compared with the control ($P<0.05$). The significantly low level of zinc is consistent with Hasanato [25], who related zinc deficiency in sickle cell disease to manifestations such as growth retardation, hypogonadism in males, hyperammonemia, abnormal dark adaptation and cell mediated immune disorder. Zinc

deficiency can also be the result of the adverse effect of hydroxyurea which increase zinc excretion [26,27]. Zinc deficiency in patients with sickle cell anemia probably due to continuous hemolysis, has been reported by several studies with strong indications that zinc deficiency is linked with impaired T-helper functions, cell mediated immunity and reduced interleukin-2 production as well as increase of bacterial infection, vasoocclusive crises, frequently hospital admissions and growth retardation[28]. The low concentration of magnesium has been noted in sickle cell disease subject when compared with the control ($P<0.05$). This probably contributes to red blood cell dehydration and a concomitant increase in the symptoms of sickle cell disease. This study is in agreement with the work of Defrancheschi et al*,* [29]. Sickle RBCs (red blood cells) are fragile and dehydrated. It has been shown that magnesium is not only useful in reducing the painful episode in SCD subjects but also affects the hydration of RBC. Hence low level of magnesium in SCD patient may not be beneficial.

Likewise, the level of chromium among SCD subjects was significantly depleted when compared with the control ($P<0.05$). The involvement of chromium in SCD subjects is not clearly defined but chromium is known to potentiate insulin action by acting as a cofactor in the initial reaction of insulin sensitive cell membrane [30]. In SCD subjects, there is an increased energy demand, which activates more chromium for carbohydrates metabolism. This will lead to decreased level of chromium in SCD subjects as reported in this study.

Furthermore, it was observed from this study that serum selenium level was significantly decreased when compared with the control ($P<0.05$). Selenium plays an important role as a cofactor for the reduction of antioxidant enzyme such as glutathione peroxidase, an enzyme which helps react with potentially harmful oxidizing agents in substances like hemoglobin. High levels of glutathione function in the blood are linked with longevity. Deficiency of selenium may be associated with the mortality in sickle cell disease [31].

On the other hand, it was observed that the level of copper in sickle cell patients was significantly elevated. This is in line with Idonije et al*.* [21], but in contrast with Fashiola et al*.* [24]. Therefore the depleted level of some trace elements in sickle cell disease may contribute to worsening cases of sickle cell crisis.

4. CONCLUSION

It is quite obvious that the levels of many trace elements are deficient in homozygous sickle cell. Hence, supplementing individuals with sickle cell disease with food or drug containing trace elements to enhance their quality of life.

CONSENT AND ETHICAL APPROVAL

All authors declare that informed consent was obtained from the patients for publication of this research work. We certify that we have participated sufficiently in the intellectual content, conception and design of this work or the analysis and interpretation of the data, as well as the writing of the manuscript, to take public responsibility for it and have agreed to have our name listed as a contributor.

We believe the manuscript represents valid work. Neither this manuscript nor one with substantially similar content under our authorship has been published or is being considered

for publication elsewhere. We certify that all the data collected during the study is presented in this manuscript and no data from the study has been or will be published separately.

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COMPETING INTERESTS

Authors have declared that no competing interests exist.

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