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SERUM TRACE ELEMENTS PICTURE IN SICKLE CELL ANAEMIA: A COMPARATIVE STUDY OF HBSS AND HBAA INDIVIDUALS AT A TEACHING HOSPITAL IN SOUTHWEST NIGERIA

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Abstract

Background: Sickle cell anemia (SCA) is a chronic hemoglobinopathy associated with oxidative stress and altered trace element metabolism. This study evaluates the levels of key trace elements in SCA patients and their potential clinical implications. **Methods:** A cross-sectional comparative study was conducted at Ekiti State University Teaching Hospital. A total of 111 participants, including 74 SCA patients (37 in steady state and 37 in crises) and 37 age- and sex-matched healthy controls (HbAA), were recruited. Serum copper, zinc, magnesium, selenium, and chromium levels were measured using validated spectrophotometric and colorimetric methods. Data were analyzed using SPSS version 20, with statistical significance set at $p \leq 0.05$. **Results:** SCA patients had significantly higher mean serum copper levels than controls ($p < 0.001$), while zinc, magnesium, selenium, and chromium levels were significantly lower ($p < 0.001$). Correlation analysis revealed a significant negative correlation between copper and zinc ($r = -0.875$, $p < 0.001$) and positive correlations between zinc and magnesium ($r = 0.925$, $p < 0.001$), selenium ($r = 0.94$, $p < 0.001$), and chromium ($r = 0.918$, $p < 0.001$).**Conclusion:** This study highlights significant trace element imbalances in SCA patients, suggesting potential micronutrient deficiencies. Further research is needed to assess the clinical impact and potential benefits of targeted nutritional interventions in SCA management.

Keywords: *Sickle Cell Anaemia, Trace Elements, Serum Levels, Comparative Study, Nigeria.*

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Introduction

Sickle cell anaemia (SCA) is a hereditary haemoglobinopathy characterized by the production of abnormal haemoglobin S (HbS), leading to chronic haemolytic anaemia, vaso-occlusive crises, and multiorgan complications (Inusa et al., 2019). It is a significant public health concern, particularly in sub-Saharan Africa, where Nigeria bears the highest burden, with an estimated 150,000 children born annually with the disease (Ojewunmi, 2017). The disorder manifests with recurrent painful episodes, increased susceptibility to infections, and progressive organ damage, severely impacting the quality of life of affected individuals (Pecker & Little, 2018). Beyond the physical burden, SCA poses substantial mental, social, and economic challenges to patients, their families, healthcare systems, and the nation at large (Alabi et al., 2023).

Micronutrient imbalance, particularly trace element deficiency, has been implicated in the pathophysiology of SCA (Khan et al., 2016; Ohemeng & Boadu, 2018). Trace elements, such as zinc, copper, iron, selenium, and magnesium, play crucial roles in enzymatic functions, immune responses, and the regulation of oxidative stress (Qureshi et al., 2005). Studies have reported altered levels of these elements in individuals with SCA, contributing to increased oxidative stress, poor immune function, and disease severity (Gueye Tall et al., 2020; Pavan et al., 2024). For instance, zinc deficiency has been associated with increased frequency of infections and delayed wound healing, while copper imbalance may exacerbate oxidative damage (Gammoh & Rink, 2017). However, despite existing evidence on trace element abnormalities in SCA, findings have been inconsistent, and there is a paucity of data, particularly in the Nigerian population (Ali, 2022; Onukwuli et al., 2018).

Several gaps remain in our understanding of the serum trace element profile in SCA, especially in comparison to healthy individuals (HbAA); while some studies suggest that trace element supplementation could improve clinical outcomes in SCA patients, there is limited research on the specific deficiencies prevalent in different populations and their correlation with disease severity (Obeagu et al., 2024; Okocha et al., 2017). Furthermore, the influence of genetic, dietary, and environmental factors on trace element homeostasis in SCA remains poorly understood (Ohemeng & Boadu, 2018). Addressing these knowledge gaps is essential for developing targeted nutritional and therapeutic interventions.

The objective of this study is to assess the serum trace element profile in individuals with SCA (HbSS) compared to healthy controls (HbAA) at a teaching hospital in southwest Nigeria. The study aims to determine the levels of key trace elements and evaluate their potential role in disease progression and complications. The findings of this study are expected to provide valuable insights into the role of micronutrient status in SCA management. Identifying specific trace element deficiencies could guide nutritional supplementation strategies to improve patient outcomes. Additionally, the study could contribute to policy recommendations for routine micronutrient assessment and intervention in SCA management, ultimately reducing disease burden and enhancing the quality of life for affected individuals.

Methodology

This descriptive cross-sectional comparative study was conducted among sickle cell anaemia (SCA) patients and healthy controls at the Departments of Chemical Pathology and Haematology Clinic of Ekiti State University Teaching Hospital, Ado-Ekiti, Nigeria. The study population comprised confirmed HbSS adult patients attending the sickle cell clinic and healthy HbAA individuals who served as controls. Participants included HbSS adult patients in either a steady state or those who had experienced crises in the preceding three months, as well as healthy individuals with the HbAA genotype.

Individuals were excluded from the study if they were on hydroxyurea therapy, iron supplementation, or were unwilling to participate. Additionally, SCA patients presenting with febrile illness, a history of blood transfusion within the previous three months, chronic blood transfusion, or those on trace element or antioxidant supplementation were also excluded.

A total of 111 participants, aged 18-46 years, were recruited. This included 74 SCA patients, with 37 in steady state and 37 who had experienced crises in the last three months, as well as 37 age- and sex-matched healthy HbAA individuals serving as controls. Control samples were obtained from medical students. Participants were recruited consecutively, and structured questionnaires were administered to gather relevant data. Before participation, informed consent was obtained from all individuals. The study protocol was approved by the Ethics Committee of Ekiti State University Teaching Hospital, with approval code EKSUTH/2023/12/003, dated 06/12/2023.

Laboratory investigations included haemoglobin genotype determination using cellulose acetate electrophoresis at an alkaline pH of 8.6. Serum levels of trace elements such as copper, zinc, and magnesium were analyzed using a colorimetric method with commercial kits from Fortress Diagnostics Ltd, Antrim, UK. Selenium and chromium levels were measured using the Buck 210/211 Atomic Absorption Spectrophotometer (Buck Scientific Inc., USA). For these analyses, five milliliters of venous blood were collected aseptically from each participant. The blood samples were allowed to clot at room temperature and subsequently centrifuged at 3000 rpm for five minutes. The serum was then separated into labelled plain dry specimen containers and stored at -20°C until analysis.

Statistical analysis was performed using SPSS version 27 (SPSS Inc., Chicago, IL, USA). Descriptive statistics, including means and standard deviations, were computed for the data collected. Group comparisons were conducted using independent sample t-tests and analysis of variance (ANOVA). A p-value of ≤ 0.05 was considered statistically significant.

Results

Demography and clinical data of the participants

Seventy-four HbSS patients and thirty-seven age and gender matches HbAApatients were recruited and studied between May to August 2024. There were 41 males and 70 females.

There was no significant difference in the gender distribution between the participants and the control group. The age of the study population was between 18 and 46 years, with a mean age (24.94 ± 4.25. The mean age of HbSS participants (24.94 ± 4.25) and controls was similar (24.27 ± 4.32).

Table 1 shows the demography and clinical data of the participants. The 111 participants consisted of 37 HbSS in steady state (SS), 37 HbSS with crises, and 37 HbAA as controls. HbSS in steady state comprised 14 males and 23 females, those in crises comprised 13 males and 24 females, and the control group comprised 14 males and 23 females, giving a total of 41 males and 70 females. The overall mean age of HbSS was 24.94 ± 4.25; those in crises were 23.89 ± 3.91, and the control 24.27 ± 4.32. Also, the overall mean weight of HbSS was 47.43 ± 2.18, those in crises were 45.95 ± 1.73, and the control was 52.08 ± 5.36.

Table 1: Demography and clinical data of the participants

	HbSS (Total)	HbSS (Steady State)	HbSS (Crisis)	HbAA (Control)	Total
No of participants	27 M, 47 F	14 M, 23 F	13 M, 24 F	14 M, 23 F	41 M, 70 F
Age range (years)	15–46	15–46	15–46	15–46	15–46
Mean age (years)	24.94 ± 4.25	24.94 ± 4.25	23.89 ± 3.91	24.27 ± 4.32	-
Mean weight (kg)	47.43 ± 2.18*	7.43 ± 2.18	45.95 ± 1.73	52.08 ± 5.36	-

*Significantly different from HbAA (control) at $p<0.05$.

Effect of age and body weight on participants in the study

Table 2 shows the one-way ANOVA effect of age and body weight on participants in the study. As shown in the table, there was no statistically significant difference in the mean ages of the groups, as indicated by the between-group sum of squares of 4.108, the F-value of 0.118, and the p-value of 0.888. In contrast, the body weight between-group sum of squares was 758.000, with a highly significant p-value of less than 0.001 and an F-value of 31.205. This suggests that the groups' mean body weights varied statistically significantly. Although there was no discernible difference in age between the groups, there were notable variations in body weight.

Table 2:One-Way ANOVA analysis

Parameter	Source	Sum of Squares	df	Mean Square	F	Sig.
Age	Between Groups	4.108	2	2.054	0.118	0.888
	Within Groups	1872.973	108	17.342		
	Total	1877.081	110			
Body Weight	Between Groups	758.000	2	379.000	31.205	<0.001
	Within Groups	1311.730	108	12.146		
	Total	2069.730	110			

Trace element levels of participants in the study

The trace element levels of HbAA, HbSS, and Crisis participants are shown in Table 3. HbSS participants (in steady and crises) had significantly high mean serum copper (32.14±5.39) (45.08±3.09) compared with the control (17.80±2.08). The serum zinc (8.50±1.27), magnesium (10.16±0.41), selenium (61.32±1.27), and chromium (60.64±0.53) were lower in the Hbss compared to the control. There was a slight difference in the mean values of Cu, Zn, Se, Cr, and Mg of the HbSS and those in crises.

Table 3: Trace Element Levels in Sickle Cell Anemia and Control

Parameters	HbAA (Control)	HbSS	Crisis	p-value
Magnesium (mmol/L)	13.99±0.70	10.16±0.41*	8.04±0.45*	<0.001
Chromium (µg/L)	64.66±0.82	60.64±0.53*	59.02±0.52*	<0.001
Selenium (µg/L)	67.32±0.60	61.32±1.27*	59.26±0.55*	<0.001
Copper (mmol/L)	17.80±2.08	32.14±5.39*	44.91±3.21*	<0.001
Zinc (mmol/L)	18.49±2.19	8.50±1.27*	6.26±0.33*	<0.001

Significantly different from control at P<0.05

Correlation analysis of the participants' trace elements in the serum

Table 4 shows the correlation analysis of the participants' trace elements in the serum. Significant negative correlations were observed between copper and zinc (r -0.875 and P = (<0.001). Also, significant positive correlations were observed between magnesium and zinc (r = 0.925) and P = (<0.001. Significant positive correlations were observed between selenium and zinc (r = 0.94 and p <0.001). Also, there is a significant positive correlation between chromium and zinc. (r= 0.918 and p<0.001)

Table 4. Correlation analysis between trace elements in the serum of the participants

Trace element	Correlation Coefficient (r)	P-Value	Significant
Cu and Zn	-0.875	<0.001	Significant (*)
Mg and Zn	0.925	<0.001	Significant (*)
Se and Zn	0.940	<0.001	Significant (*)
Cr and Zn	0.918	<0.001	Significant (*)

Significantly different from control at P<0.05

Discussion

The study revealed that there was no significant difference in the gender distribution between HbSS and HbAA participants, with 41 males and 70 females across both groups. The mean age of the study population was 24.94 ± 4.25 years, with no significant difference between the HbSS participants (24.94 ± 4.25) and controls (24.27 ± 4.32). This finding aligns with

previous studies by Adegoke et al. (2018), which reported similar demographic distributions among SCA patients and controls in Nigeria (Nwabuko et al., 2022; Olaniyi et al., 2014).

The study found that HbSS patients had lower body weight compared to controls, with those in crises exhibiting the lowest mean weight (45.95 ± 1.73 kg) compared to those in steady state (47.43 ± 2.18 kg) and controls (52.08 ± 5.36 kg). This trend is consistent with findings by Olaniyi et al. (2019), who reported significantly lower BMI and body weight in SCA patients compared to HbAA controls, attributing it to chronic haemolysis, increased metabolic demand, and malnutrition (Olaniyi et al., 2014).One-way ANOVA analysis was conducted to examine the effect of age and body weight among study participants. The results showed no statistically significant difference in the mean ages across the groups, as indicated by a between-group sum of squares of 4.108, an F-value of 0.118, and a p-value of 0.888. This suggests that age distribution was comparable across HbSS and HbAA participants, aligning with findings by Sharma et al. (2017), who reported similar age homogeneity in SCA studies(Garadah et al., 2015).

In contrast, there was a statistically significant variation in body weight across the groups. The between-group sum of squares was 758.000, with a highly significant p-value of <0.001 and an F-value of 31.205. This confirms that body weight differences among the groups were not due to chance, with HbSS participants, especially those in crises, having significantly lower body weight compared to the control group. This aligns with the findings of Garadah et al. (2015), who reported that SCA patients often exhibit lower body mass due to increased metabolic demands and chronic anaemia (Garadah et al., 2015).These results highlight the necessity of targeted nutritional interventions for SCA patients, particularly those prone to crises, to improve overall health outcomes. Analysis of trace elements in the study participants showed significant differences between HbSS patients (both steady-state and crisis) and HbAA controls. The mean serum copper levels were significantly elevated in HbSS patients (32.14 ± 5.39 µg/dL in steady state and 45.08 ± 3.09 µg/dL in crises) compared to controls (17.80 ± 2.08 µg/dL). Elevated copper levels in SCA patients have been previously documented by Lang et al. (2014), who suggested that increased copper levels could be linked to oxidative stress and inflammatory responses during haemolysis and crises.

Conversely, serum levels of zinc (8.50 ± 1.27 µg/dL), magnesium (10.16 ± 0.41 µg/dL), selenium (61.32 ± 1.27 µg/L), and chromium (60.64 ± 0.53 µg/L) were significantly lower in HbSS patients compared to controls. Zinc deficiency in SCA patients has been well-documented, with studies by Livingstone (2015) indicating that chronic haemolysis and increased urinary excretion contribute to low zinc levels, potentially exacerbating immune dysfunction and delayed wound healing (Livingstone, 2015). Similarly, selenium and chromium deficiencies have been linked to impaired antioxidant defense mechanisms, which could worsen oxidative stress in SCA patients (Delesderrier et al., 2019).A slight difference in the trace element levels was observed between HbSS patients in steady state and those in crises, with crisis-state patients exhibiting marginally higher copper levels and slightly lower zinc, selenium, and magnesium levels. These findings further reinforce the role of oxidative

stress and metabolic dysregulation in SCA pathophysiology, underscoring the need for micronutrient supplementation as a potential therapeutic intervention.

Table 4 presents the correlation analysis of the participants' trace elements in the serum. A significant negative correlation was observed between copper and zinc, suggesting an inverse relationship between these two elements. Conversely, significant positive correlations were noted between magnesium and zinc, selenium and zinc, and chromium and zinc. These findings indicate a strong interdependence among zinc, magnesium, selenium, and chromium levels in the serum, which may have implications for trace element metabolism in individuals with sickle cell anaemia. Similar trends have been reported in previous studies, underscoring the importance of maintaining adequate trace element balance in these patients. (Delesderrier et al., 2019; Livingstone, 2015).

This study has some limitations that may introduce bias or imprecision. Selection bias is a concern, as participants were drawn from a single tertiary hospital, limiting broader applicability. Measurement bias may also be present due to the inherent limitations of the methods used to assess trace element levels. Additionally, unaccounted confounding factors, such as dietary intake and environmental exposure, could have influenced the results. The cross-sectional design further restricts causal inferences, as it only captures data at a single time point. Despite these limitations, the study provides valuable insights into trace element imbalances in sickle cell disease. However, its generalizability remains limited, necessitating further studies in diverse populations.

This study has several strengths that enhance its reliability and contribution to knowledge. First, it employs a **comparative cross-sectional design,** allowing for direct evaluation of trace element differences between sickle cell patients and healthy controls. The inclusion of **age- and sex-matched controls** minimizes demographic confounders, improving result validity**.** Additionally, **strict eligibility criteria**, such as excluding patients on hydroxyurea or recent transfusions, reduce potential confounding effects on trace element levels. The use of **validated laboratory methods**, including atomic absorption spectrophotometry and colorimetric assays, ensures precise measurement of serum trace elements. Furthermore, ethical approval and informed consent procedures reinforce the study’s adherence to research ethics. Despite its limitations, the study provides valuable data on trace element imbalances in sickle cell disease, highlighting potential areas for further research and clinical interventions. These strengths enhance the study’s credibility and its potential contribution to understanding micronutrient dynamics in sickle cell patients.

Conclusion

This study highlights significant trace element imbalances in sickle cell anaemia patients, with elevated copper levels and reduced zinc, magnesium, selenium, and chromium compared to healthy controls. These findings suggest potential micronutrient deficiencies that may contribute to disease pathology. While the study’s strengths enhance its reliability, limitations such as selection bias and cross-sectional design should be considered. Further longitudinal and interventional studies are needed to explore the clinical implications of these

trace element variations. Addressing these deficiencies through targeted nutritional interventions may improve disease management and overall health outcomes in sickle cell patients.

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