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The Complex Interactions Between Micronutrients, Iron Overload, and Health Outcomes in Iraqi Thalassemia Patients

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Abstract Patients with thalassemia face a heightened risk of mineral deficiency due to elevated oxidative stress and the effects of iron chelation therapies. The Objective of the Study:- investigate the impact of iron overload on the variations in micronutrient levels in patients diagnosed with significant β-thalassemia. This case-control study is from August 2024 to December 2024. The study involved 100 participants, 50 of whom had significant β-thalassemia (25 males and 25 females) and 50 healthy controls (25 males and 25 females), aged 19 to 25. The ferritin, iron, and micronutrients were employed to conduct assays using the COBAS diagnostic test system. The results were calculated as the mean and standard error, presented in the format mean±standard error. A one-way analysis of variance (ANOVA) was employed to assess the data, with statistical significance determined at $p<0.05$ to find noteworthy differences. The results illustrated increased in zinc, magnesium, and manganese inpatient group when compared with control group. Unlike that copper, and calcium decrease significantly in patient group when compared with control group [1].

Key Words Macronutrients, Manganese and Copper

INTRODUCTION

Beta thalassemia is a hereditary hematological condition characterized by inadequate or aberrant production of globin chains, resulting in diminished hemoglobin levels in erythrocytes and the occurrence of anemia [1]. The direct effect is an imbalance in the synthesis of α and β globin chains, leading to anemia due to ineffective erythropoiesis and hemolysis [2]. The homozygous state results in severe anemia, requiring frequent blood transfusions that cause iron accumulation. This subsequently leads to problems including diabetes mellitus, hypoparathyroidism, hypothyroidism, hypogonadism, heart dysfunction, and liver fibrosis [3]. Patients with thalassemia face a heightened risk of mineral deficiency due to elevated oxidative stress and the effects of iron chelation therapies. Thalassemia consequences encompass growth and developmental delays, cardiomyopathy, endocrinopathies, and osteoporosis. Minerals may serve a specific function in preventing these complications. This review presents an overview of essential minerals such as zinc (Zn), copper (Cu), selenium (Se), magnesium (Mg), and calcium (Ca) in patients with thalassemia major. We also emphasize that certain complications of thalassemia may arise from an increased demand for minerals or a deficiency of these minerals [4,5]. Additionally, iron overload contributes to oxidative stress through the excessive generation of free radicals, changes in serum element levels, and variations in antioxidant enzyme activity [6]. Considering that elements operate as activators and/or inhibitors in the human body and are vital for various biochemical activities, it is imperative to evaluate and monitor serum levels of these elements before and during the treatment of major β-thalassemia [7]. Serum concentrations of elements may also contribute to the early detection of this condition. There has been less emphasis on the atypical distribution or accumulation of elemental concentrations in the body, except iron, inside organs and biological fluids [8]. Because elements can either activate or inhibit biochemical processes in the body and play a key role in many others,

it is important to find out and keep an eye on the blood levels of these elements before and during treatment for major β-, Serum levels of elements may also aid in the early diagnosis of this illness [8,9]. Thus far, minimal focus has been directed toward elemental concentrations in the body, aside from iron, that are irregularly distributed or aggregated in organs and biological fluids [6].

The aim of study

This study aimed to investigate the role of iron overload on the variations in micronutrient levels in patients diagnosed with significant β-thalassemia.

MATERIAL AND METHOD

Subjects

Al-Shams Medical Laboratory in Diyala Governorate conducted this case-control study from August 2024 to December 2024. The study involved 100 participants, 50 of whom had significant β-thalassemia (25 males and 25 females) and 50 healthy controls (25 males and 25 females), aged 19 to 25.

Inclusion criteria

Patients aged 19-25 years with a confirmed diagnosis of β-thalassemia major who underwent blood transfusions one times per month to keep Hb 10 mg/dl were included in the study.

Recessive iron chelating

Criteria for exclusion

Patients with current infections who had a splenectomy.
patients don't take iron chelating

Methods

A blood sample of 4 ml was collected from each participant participating in this investigation under stringent aseptic conditions. The blood samples were meticulously transferred into gel tube containers specifically suited for the measurement of various factors. The containers were subsequently utilized to perform assays using the COBAS diagnostic test system, a product developed and marketed by Roche Diagnostics. This method ensured accurate and reliable testing of the collected samples for the required parameters during the study.

Statistical examination

The statistical analysis of continuous variables was conducted using SPSS software version 20 (SPSS Inc., Chicago, IL, USA). The results were calculated as the mean and standard error, presented in the format Mean±standard error. A one-way analysis of variance (ANOVA) was employed to assess the data, with statistical significance determined at $p<0.05$ to find noteworthy differences.

RESULTS

Table 1 illustrated serum ferritin and iron, the level of serum ferritin and iron increased significantly in patients' group (555.12±11.50 and 235.25±23.76 µg/dL) when compared with control group (48.20±2.27 and 70.58±1.63 µg/dL) (Figure 1).

Heterogeneous anechoic area

The statistical analysis illustrated increased in zinc, magnesium and manganese inpatient group (99.50±0.50 µg/L, 2.31±0.04 mg/dl and 11.92±0.54 ng/ml, 1 respectively) when compared with control group (88.60±0.62 µg/L, 1.86±0.02 mg/dl and 2.74±0.07 ng/ml, respectively) p-value 0.000 (Figure 2). Unlike that copper and calcium decrease significantly in patient group (81.62±0.49 µg/L and 9.23±0.13 mg/dl) when compared with control group (117.80±2.29 µg/L and 8.51±0.04 mg/dl) p-value 0.000 (Table 2, Figure 3).

DISCUSSION

This study revealed that thalassemic patients display increased zinc levels and diminished copper levels. Thalassemia major is a severe form of beta thalassemia, requiring patients to receive regular blood transfusions and chelation therapy for survival [1]. Increased zinc concentrations in thalassemia patients may result from various factors related to the disease and its management.

This can lead to enhanced zinc absorption; nevertheless, individuals with thalassemia frequently get numerous blood transfusions, resulting in iron overload. Administer iron chelators such as deferoxamine, deferasirox, or deferiprone to mitigate this patient's condition. These chelators may also bind additional trace elements, such as copper, resulting in an imbalance in trace element homeostasis and a relative elevation in zinc levels [10]. Copper is recognized as an essential trace element, present in minimal concentrations in

Table 1: Descriptive and statistical test of ferritin and iron between groups

Parameters	Normal rang	Control Mean±SE	Patients Mean±SE	ANOVA p-value
Ferritin	20.0-300.0 µg L^{-1}	48.20±2.27	555.12±11.50	0.000
Iron µg dL^{-1}	59-158 µg dL^{-1}	70.58±1.63	235.25±23.76	0.000

Table 2: Descriptive and statistical test of micronutrients between groups

Parameters	Normal rang	Control Mean±SE	Patients Mean±SE	ANOVA p-value
Zinc	70-115 µg L^{-1}	88.60±0.62	99.50±0.50	0.000
Copper	80.0-140.0 µg L^{-1}	117.80±2.29	81.62±0.49	0.000
Calcium	8.60-10.40 mg dL^{-1}	9.23±0.13	8.51±0.04	0.000
Magnesium	1.6-2.6 mg dL^{-1}	1.86±0.02	2.31±0.04	0.000
Manganese	4.7-18.3 ng mL^{-1}	2.74±0.07	11.92±0.54	0.000

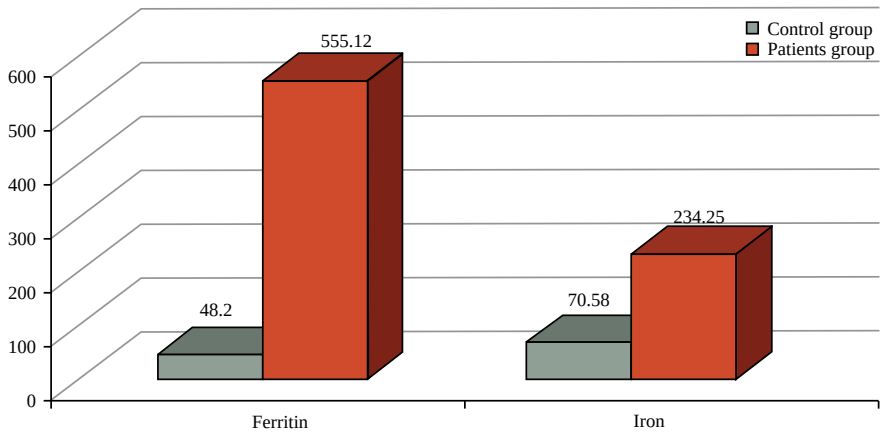

Figure 1: Ferritin and iron in increased in patients with β-thalassemia

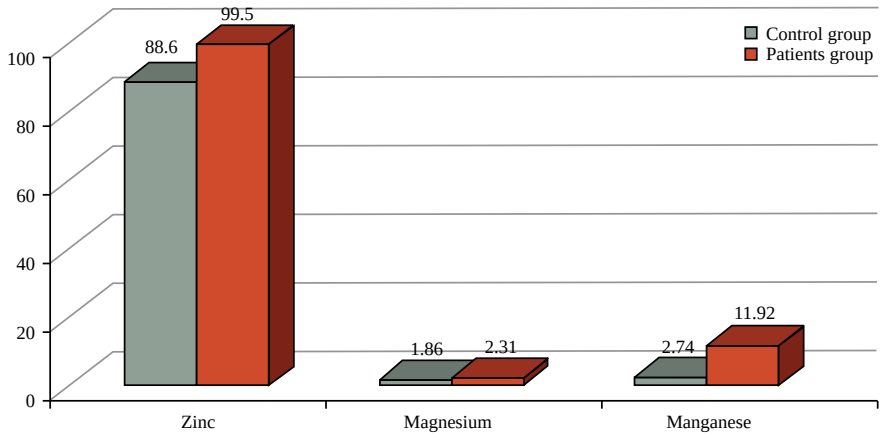

Figure 2: Zinc, magnesium and manganese increased in patients with β-thalassemia

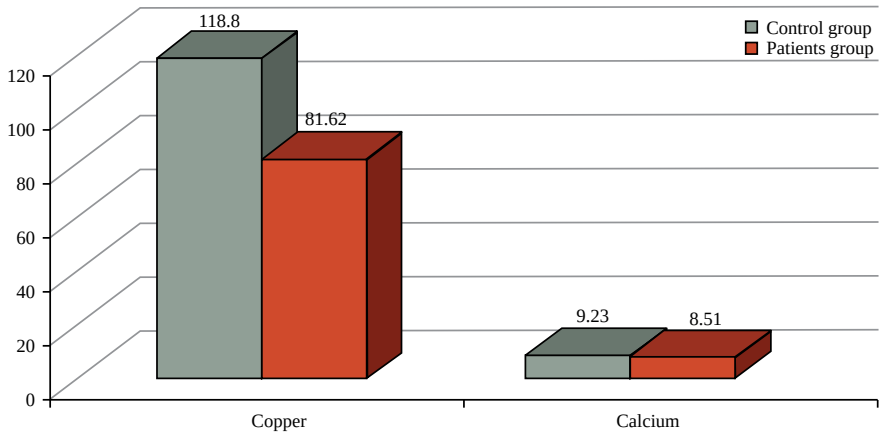

Figure 3: Copper and calcium decreased in patients with β-thalassemia

various cells and organs. The liver and brain contain the highest concentrations of copper [11]. Copper functions as a cofactor for several crucial enzymes, known as copper enzymes, such as tyrosinase, dopamine beta-hydroxylase, lysyl oxidase, cytochrome c oxidase and Cu-Zn superoxide dismutase [12]. Patients exhibited significantly decreased

calcium levels compared to the control group. This is due to hypoparathyroidism in thalassemic patients, leading to hypocalcemia. Aleem et al. and Hamidieh et al. demonstrated that hypoparathyroidism occurs in thalassemic patients receiving regular blood transfusions [13,14]. In this study, the serum magnesium and manganese levels in the patient group were statistically higher than those in the control group. However, the concentrations of magnesium and manganese in both the control and patient groups remained within the normal range.

CONCLUSIONS

This study emphasizes the changes in trace element concentrations in thalassemic patients, namely the increase in serum zinc levels and the decrease in copper levels. These alterations are intricately linked to the recurrent blood transfusions and iron chelation therapy necessary for managing their illness. The chelators employed in these therapies, including deferoxamine, deferasirox, and deferiprone, serve a dual function by alleviating iron overload and affecting the homeostasis of other vital trace elements, such as copper. Comprehending these imbalances is essential for enhancing the management of thalassemia. Consistent monitoring and personalized supplementation approaches for trace elements can alleviate potential difficulties and improve the quality of life for those affected.

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