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ORIGINAL ARTICLE

Status of Vitamin D and Evaluation of Growth Parameters Seen in the Children Suffering from Thalassemia Major

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ABSTRACT

Objective: The objective of this research is to evaluate the growth metrics, as well as the levels of calcium, vitamin D, and phosphorus, in children diagnosed with beta-thalassemia major (BTM) who are undergoing treatment with packed red cell transfusions and chelation therapy.

Study design: An analytical cross-sectional study

Place and duration This study was conducted in Hamdard College of Medicine and Dentistry Karachi from March 2022 to March 2023.

Methodology: In this study, 80 patients diagnosed with BTM, aged between 3 and 16 years, were meticulously compared to 80 children serving as the control group. The control group was selected to match the patients in terms of both sex and age. The study involved conducting anthropometric measurements and determining the serum levels of phosphorus, calcium, and vitamin D (specifically 25-hydroxycholecalciferol) for all the participants, both patients and controls.

Results: Among the patients in our study, 49% exhibited short stature, and 47% were identified as underweight. Additionally, 43% of the patients had a low Body Mass Index (BMI). The mean total serum calcium level was measured at 6.5 ± 1.3 mg/dl, and the 25-hydroxycholecalciferol (25-OH Vit D) level was recorded at 10.5 ± 4.7 mcg/dl for our BTM patients group. In comparison, the control group had significantly higher mean levels of serum calcium (10.3 ± 1.1 mg/dl) and vitamin D (40.4±12.4 mcg/dl). The comparison of each shows statistical significance (P< 0.001).

Conclusion: Children diagnosed with BTM commonly experience delays in growth and irregularities in metabolism, highlighting the crucial need for therapy. The observed metabolic disturbances are likely a result of iron overload and inadequate nutritional support. These factors underscore the significance of implementing appropriate treatments and nutritional strategies to address the health challenges faced by these children.

Keywords: Calcium, Thalassemia major, Vitamin D deficiency, Growth, children

INTRODUCTION

Thalassemia is an inherited condition that impacts the synthesis of hemoglobin chains due to gene mutations that lead to different deficiencies in globin chain production. As a consequence, there is a decrease or even complete absence of specific globin chains that result in ineffective erythropoiesis and eventually cause anemia [1]. BTM typically becomes apparent between 4 to 6 months old children because the safeguarding effect of hemoglobin-F at the time of birth diminishes during the first year [2]. The manifestations include anemia-related symptoms like lethargy, pallor, organomegaly, and failure to thrive [3]. In cases presenting later, signs of extramedullary hematopoiesis may arise, such as hepatosplenomegaly, skull bossing in the frontal region, thinning of the cortices of long bones, widening of diploic spaces and widening of medullary spaces [4].

BTM represents a significant public health concern in the region under study. It is thought to be a common genetically determined hemolytic anemia [5]. A high rate of carriers can be attributed to a considerable prevalence of consanguineous marriages, which leads to the accumulation of deleterious genes. Untreated or partially treated children with thalassemia major typically have a life expectancy extending to their first two decades [6].

The main treatment for BTM is transfusions of blood. This help to replace the erythrocytes that are not being produced properly. The goal of blood transfusions is to raise hemoglobin concentration to 13-14 g/dl and maintain it up to 9-10 g/dl afterwards [7]. Many patients require transfusions every 2 to 4 weeks, starting at one year of age. However, frequent blood transfusions can lead to iron overload. Iron overload can cause a number of serious health problems, such as hypoparathyroidism, hemosiderosis, diabetes mellitus, hypogonadism, and many other endocrine abnormalities. To prevent iron overload, people with thalassemia may need to take iron chelation therapy [8]. This treatment removes excess iron from the body. There are a number of different iron chelation medications available, and the best choice for a particular patient will depend on their individual circumstances. In addition to blood transfusions along with iron chelation therapy, BTM patients may also need to take supplements of folic acid to help build erythrocytes. The treatment of thalassemia is complex and requires careful monitoring by a healthcare team. However, with proper treatment, people with thalassemia can live long and healthy lives [9].

Multiple studies have shown that children and young adults with BTM have a higher growth incidence and endocrine abnormalities. Additionally, previous research has found that patients with BTM have abnormal serum levels of calcium, vitamin D, and phosphorus [10].

This research aims to fill the existing knowledge gap and shed light on the health conditions and nutritional status of these children, providing valuable insights into their medical management and overall well-being.

METHODOLOGY

We conducted this study including 80 patients with BTM aged 3 years to 16 years. The participants were randomly selected. The diagnosis of BTM was made based on standard criteria. All participants in the study had been receiving packed red cell transfusions every one to two months from a very early age. This was done to maintain hemoglobin levels up to 9 g/dL or above. Additionally, they were all undergoing chelation therapy with deferoxamine, which was infused subcutaneously at doses of 30-50 mg/kg for 8 to 12 hours every night, at least 5 nights a week.

We excluded individuals detected with Hypersplenism, other types of chronic hemolytic anemia, malnutrition-related diseases, or feeding difficulties from the study. Patients who were receiving steroid therapy were also excluded. For the control group, we included 80 healthy children of similar age and gender having good

nutritional health and no feeding difficulties or malnutrition. Neither the cases nor the control group received any supplements containing calcium, phosphorus, or vitamin D.

A thorough history was taken and comprehensive clinical examinations were conducted for both groups. Anthropometric measurements, such as gender, age, height, weight, and Z-score, were meticulously recorded for both groups. The BMI was calculated and the standard BMI ranges were used to categorize participants into normal, underweight, and overweight groups. Precise measurements were taken using a scale for weight. The height was measured in centimeters using height gauges. It is important to note that all measurements were consistently taken by the same individual to ensure accuracy and reliability.

To evaluate the growth and development of the participants, a software program was used that integrated the raw data on gender, age, sex, height, and weight. With this software, we computed various nutritional status indices, including Z-score, weight-for-age, weight-for-height, and height-for-age. This comprehensive approach enabled us to thoroughly assess the growth patterns and nutritional status of all the participants in the study.

Optimal vitamin D levels are indicated by concentrations greater than 30 ng/mL (75 nmol/L). If the vitamin D concentration falls within the range of 20-30 ng/mL (50-75 nmol/L), it is considered as vitamin D insufficiency. However, when the Vitamin D level falls below 20 ng/mL (50 nmol/L), it indicates vitamin D deficiency. These defined ranges allow us to categorize the vitamin D status of the study participants and evaluate its potential impact on their overall health and well-being. The data was carefully observed and analyzed in the IBM SPPS version 26.

RESULTS

The mean age of the participants in the study was 7.45 ± 4.8 years. The mean age of the patients in the control group was 7.78 ± 4.6 years. The mean body height and weight of the patients [(97 ± 87 cm) and (14.56 ± 9.1 kg), respectively] were significantly lower when compared to the controls [(120 ± 26 cm) and (27.1 ± 18 kg), respectively]. The differences were statistically significant with P<0.001 for both height and weight.

Among the patients, 49% were classified as short, defined by having a height z-score below -2, whereas only 2% of the control group exhibited this characteristic (P<0.001). Additionally, 47% of the patients were found to be underweight. Furthermore, 43% of the patients had an abnormal BMI, with a BMI below 18.5, indicating that they were underweight. No significant correlations were observed between growth retardation and factors such as gender, anemia, and the amount of transfused iron load.

These findings indicate that the thalassemic patients in the study display growth-related abnormalities, including short stature and underweight status when compared to the control group. Such outcomes emphasize the importance of monitoring and addressing the growth parameters in children with BTM to ensure their overall health and well-being.

Table 1: Demographic data of patients in both groups

Variables	Case	Control	P-value
Age (years)	7.45 ± 4.8	7.78 ± 4.6	--
Height in cm	97 ± 87	120 ± 26	<0.001
Weight in kg	14.56 ± 9.1	27.1 ± 18	<0.001

The mean total serum calcium level was measured at 6.5 ± 1.3 mg/dl, and the 25-hydroxycholecalciferol level was recorded at 10.5 ± 4.7 mcg/dl for our BTM patients group. These values were found to be significantly lower than the control group in which patients had significantly higher mean levels of serum calcium (10.3 ± 1.1 mg/dl) and vitamin D (40.4 ± 12.4 mcg/dl). The differences between the patient and control groups were statistically significant, with P< 0.001 for both calcium and vitamin D levels.

Only 9% of the BTM patients had a normal vitamin D concentration, while 37% were found to have vitamin D deficiency, and the remaining 54% had vitamin D insufficiency. This indicates a notable prevalence of inadequate vitamin D levels among the patients.

Regarding serum phosphorous concentration, no significant difference was observed between the BTM patients (3.3 ± 0.7 mg/dl) and the controls (3.2 ± 0.7 mg/dl). There was no significant correlation found between the vitamin D concentration and factors such as gender, age, anemia, and the amount of transfused iron load in the patients. The results highlight the presence of significantly lower serum calcium and vitamin D concentration in BTM patients compared to the controls, which can be attributed to the underlying condition and its management.

Table 2: Laboratory findings in both groups

Serum levels	Case	Control	P-value
Phosphorus (mg/dl)	3.3 ± 0.7	3.2 ± 0.7	--
Calcium (mg/dl)	6.5 ± 1.3	10.3 ± 1.1	<0.001
Vitamin D (pg/ml)	10.5 ± 4.7	40.4 ± 12.4	<0.001

DISCUSSION

Patients with BTM are prone to a diverse range of complications, including growth impairment, endocrinopathy, and metabolic abnormalities. These complications arise due to the underlying pathophysiology of the condition, characterized by the reduced or absent synthesis of one or more protein chains, leading to an inefficient process of erythropoiesis and chronic hemolytic anemia [11, 12].

In our research, we found that the mean height of the BTM patients in our study was notably lower than that of the control group. Additionally, 49% of the BTM patients were classified as having short height, defined by a height z-score below -2. These findings are consistent with previous studies that have also reported a high incidence of short stature among individuals with BTM. The study conducted by Hashemi et al. revealed that 65.71% of thalassemic patients had height measurements falling below the fifth percentile for their age and sex. This means that a significant proportion of individuals with thalassemia in their study exhibited growth impairment and were shorter than what is considered typical for their age and gender. [13]

According to the research conducted by Chekir et al., their patients with beta-thalassemia major (BTM) exhibited a height lateness of 7.14%. This finding suggests that a considerable percentage of their BTM patients had growth delays and were shorter than what would be expected for their age and gender. Height lateness refers to the difference between a patient's actual height and the expected height for their age and gender. A height lateness of 7.14% indicates a significant deviation from the typical growth trajectory. [14]

In our study, it has been seen that the average serum concentration of Vitamin D was significantly lesser in BTM patients compared to the control group. Moreover, among the thalassemic patients, 37% were diagnosed with vitamin D deficiency, and 54% had vitamin D insufficiency. These findings underscore the prevalence of inadequate vitamin D levels in thalassemic patients and highlight the importance of addressing this issue to optimize their health and well-being. The results of our study are consistent with those reported by Vogiatzi et al., who found that 12% of thalassemic patients were vitamin D deficient, and 69.8% had insufficient levels. Similarly, another study on an Iranian population found that 37.2% of thalassemic patients had vitamin D deficiency. The lower levels of vitamin D observed in thalassemic patients can be attributed to various factors, including hepatic dysfunction, chronic inflammation, iron overload, and other disease-related processes that may hinder the normal metabolism and synthesis of vitamin D. Vitamin D deficiency can have significant health implications, including impaired bone health, compromised immune function, and an increased risk of various chronic diseases. Given the high prevalence of vitamin D deficiency and

insufficiency in thalassemic patients, regular monitoring of vitamin D levels and appropriate supplementation, if necessary, is crucial for their optimal health and management. Addressing vitamin D status can play a pivotal role in improving bone health and overall health outcomes for individuals with thalassemia [15].

In our study, we did not observe any significant difference in serum phosphorus levels between thalassemic patients and the control group. These findings are in line with other studies that also reported no significant variation in phosphorus levels between patients and controls. On the other hand, there have been other reports suggesting that serum phosphorus levels in thalassemic patients were significantly higher than those in the control groups. This discrepancy in findings could be attributed to various factors, including the sample size, demographics, and the specific characteristics of the thalassemic population under investigation. The normal range of serum phosphorus in thalassemic patients, as observed in our study, indicates that the kidneys are functioning effectively in maintaining appropriate phosphorus levels in the blood. However, it is essential to interpret these results in the context of the individual patient's overall health and medical history. As with any research, it is essential to consider the limitations and variations in the data when interpreting study findings. Additional research and larger sample sizes may be necessary to further explore the relationship between serum phosphorus levels and thalassemia, potentially shedding more light on the underlying mechanisms and implications for patient care [16, 17].

CONCLUSION

Patients diagnosed with BTM frequently encounter growth delay as well as metabolic irregularities, underscoring the significance of prompt therapeutic interventions. The observed metabolic disturbances are likely influenced by iron overload and insufficient nutritional support. Early interventions and appropriate treatments are crucial in addressing the health challenges faced by these children and improving their overall well-being. The presence of these growth deficits and metabolic issues is often attributed to factors like iron overload and inadequate nutritional support. The chronic anemia and ineffective erythropoiesis in BTM lead to chronic hypoxia, which can impede normal growth and development in affected children. Additionally, iron overload resulting from frequent blood transfusions and ineffective erythropoiesis can cause damage to various organs, including the endocrine glands, leading to hormonal imbalances that further contribute to growth impairment and other metabolic abnormalities.

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