Research article

Hypoparathyroidism due to iron overload in beta-thalassemia patients

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ABSTRACT

Introduction and Aim: Beta-thalassemia is a genetic blood condition characterized by a lack of or abnormal globin chain synthesis, resulting in low hemoglobin levels needing repeated blood transfusions. Iron overload and skeletal issues are frequently observed in beta-thalassemia patients. The current study aims to assess the bone status of beta-thalassemia major patients who are on treatment with repeated blood transfusion and compare it to thalassemia patients who do not require blood transfusion.

Material and Methods: In this case-control study, conducted between December 2021 and April 2022 at Al-Shams Medical Laboratory, Diyala Governorate, 150 subjects were included consisting of 100 thalassemia patients and 50 healthy individuals.

Results: This study revealed that in patients with minor and moderate thalassemia, the levels of red blood and white blood cells considerably increased. Additionally, both minor and major thalassemia patients had significantly higher platelet counts, and a considerably higher iron and ferritin levels. PTH, vitamin D, calcium, and calcium phosphate levels all significantly decreased in major thalassemia patients when compared to patients with moderate thalassemia and the control group, however phosphorus levels sharply increased.

Conclusion: Patients with significant thalassemia have an unstable bone profile and hence, regular bone profile monitoring is recommended. In addition, such individuals are also advised to take calcium and vitamin D supplements and receive strong nutritional support.

Keywords: Hypoparathyroidism; iron overload; beta thalassemia.

INTRODUCTION

Beta (β)-thalassemia is a genetic blood condition characterized by a lack of or abnormal globin chain synthesis, resulting in low hemoglobin levels in red blood cells and anemia (1). Iron overload from the homozygous state's severe anaemia, which necessitates frequent blood transfusions, leads to endocrine complications such as hypothyroidism, hypogonadism, diabetes, hypoparathyroidism, liver disorders, and fibrosis (2,3). The mainstay of treatment for severe Beta-thalassemia major and intermediate is regular blood transfusions (packed red cells infusion), with the aim of maintaining haemoglobin levels above 10 g/dl (4). Bone disease is a leading cause of morbidity and mortality. Skeletal problems such as osteopenia, scoliosis, osteoporosis, spinal deformities, rickets, nerve compression, and spontaneous fractures are frequently observed in transfusion-dependent thalassemia patients (5). Repeated blood transfusions result in iron accumulation in the parathyroid gland, resulting in hypoparathyroidism. According to some studies, some thalassemic patients receiving regular packed red cell infusions develop hypoparathyroidism, especially after the age of ten (6). In the past, the pathogenesis of bone disease in Beta thalassemia patients prior to transfusions was mainly attributed to inadequate erythropoiesis, which led to bone marrow hyperplasia (7). Recently, molecular techniques have been used to diagnose hereditary disorders such as CML (8) and adenocarcinoma (9, 10). Therefore, polymerase chain reaction is advocated for (β)-thalassemia diagnosis. However, this study aimed to evaluate the bone status of Beta thalassemia Major patients who required repeated frequent blood transfusions in comparison to thalassemia patients who do not require blood transfusion.

MATERIALS AND METHODS

Subjects

The present case-control study was conducted from December 2021 to April 2022 at Al-Shams Medical Laboratory in Diyala Governorate, Iraq. The study included 150 subjects comprising of 100 β thalassemia patients and 50 healthy individuals (controls) aged between 18-30 years.

Inclusion criteria

Patients (21 male and 29 female) with a confirmed diagnosis of β-thalassemia minor and patients (18 male and 32 female) with a confirmed diagnosis of β-thalassemia major.

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Exclusion criteria

Patients with any infection and splenectomies were excluded. Five ml of a venous blood sample was collected from each patient involved in study, of which 1.8 mL was transferred to an EDTA tube and used for complete blood count. Remaining blood was transferred to a gel tube for further estimation of parathyroid hormone, calcium, phosphorus, vitamin D, alkaline phosphorus, iron, and ferritin levels. The serum was obtained from the blood samples after centrifugation at 2500g for 15 minutes. An Automated Hematology Analyzers XT2000 I (Sysmex, Japan) was used to measure the haematological parameters in the whole blood. The serum vitamin D and PTH levels were assessed using an automated quantitative COBAS C311 test (Roche, Germany) the remaining parameters were assessed by using an automated quantitative COBAS e411 test (Roche, Germany).

Statistical analysis

SPSS ver. 20 software (SPSS, Inc., Chicago, IL, USA) was used to analyze the data obtained. The mean and standard error was calculated and expressed as the mean ± standard error. The statistical analysis was performed using the student’s one-way analysis of variance (ANOVA) test. P ≤ 0.05 was measured to indicate a statistically significant difference.

RESULTS

The general characteristics of the study subjects are given in Table 1. In total 150 individuals included were divided into three groups comprising of healthy individuals as controls (n=50); β-thalassemia major (n=50) and β-thalassemia minor (n=50) patients.

The statistical analysis showed the red blood cells count and white blood cells count levels increased significantly in patients with minor (5.34 ± 0.03 x 10⁹/L, and 7.75 ± 0.02 x 10⁹/L, respectively) and major β-thalassemia (5.85 ± 0.01 x 10⁹/L, and 10.80 ± 0.01 x 10⁹/L, respectively) when compared with control groups (4.62 ± 0.02 x 10⁹/L, and 7.00 ± 0.01 x 10⁹/L) respectively. Also, platelets count increased significantly in patients with β-thalassemia minor (252.80 ± 6.78 x 10⁹/L) and β-thalassemia major (310.95 ± 0.18 x 10⁹/L) β-thalassemia when compared with control groups (178.05 ± 0.18 x 10⁹/L). Hemoglobin and hematocrit reduced significantly in patients with β-thalassemia minor (9.70 ± 0.10 g/L, and 31.72 ± 0.01%, respectively), and β-thalassemia major (7.00 ± 0.01 g/L, and 22.50 ± 0.03% respectively) when compared with the control group (13.50 ± 0.11 g/L, and 41.40 ± 0.23 %, respectively) (Table 2).

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Groups</th>
<th>Mean ± Std. Error</th>
<th>ANOVA P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>RBC</td>
<td>Control</td>
<td>4.62 ± 0.02</td>
<td>&lt;0.000</td>
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<tr>
<td></td>
<td>β-thalassemia Minor</td>
<td>5.34 ± 0.03</td>
<td></td>
</tr>
<tr>
<td></td>
<td>β-thalassemia Major</td>
<td>5.85 ± 0.01</td>
<td></td>
</tr>
<tr>
<td>Hb</td>
<td>Control</td>
<td>13.50 ± 0.11</td>
<td>&lt;0.000</td>
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<tr>
<td></td>
<td>β-thalassemia Minor</td>
<td>9.70 ± 0.10</td>
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<td></td>
<td>β-thalassemia Major</td>
<td>7.00 ± 0.01</td>
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<tr>
<td>HCT</td>
<td>Control</td>
<td>41.40 ± 0.23</td>
<td>&lt;0.000</td>
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<tr>
<td></td>
<td>β-thalassemia Minor</td>
<td>31.72 ± 0.01</td>
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<tr>
<td></td>
<td>β-thalassemia Major</td>
<td>22.50 ± 0.03</td>
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<tr>
<td>WBC</td>
<td>Control</td>
<td>8.65 ± 0.01</td>
<td>&lt;0.000</td>
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<tr>
<td></td>
<td>β-thalassemia Minor</td>
<td>7.75 ± 0.02</td>
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<tr>
<td></td>
<td>β-thalassemia Major</td>
<td>10.80 ± 0.01</td>
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<tr>
<td>Plat</td>
<td>Control</td>
<td>178.05 ± 0.18</td>
<td>&lt;0.000</td>
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<tr>
<td></td>
<td>β-thalassemia Minor</td>
<td>252.80 ± 6.78</td>
<td></td>
</tr>
<tr>
<td></td>
<td>β-thalassemia Major</td>
<td>310.95 ± 0.18</td>
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</tbody>
</table>

The statistical analysis showed the iron and ferritin level increased significantly in patients with β-thalassemia minor (31.59 ± 0.36 µmol/L and 100.40 ± 4.22 mg/dL, respectively) and β-thalassemia major (80.47 ± 0.10 µmol/L, and 2120 ± 425.91 mg/dL, respectively) β-thalassemia when compared with control groups (8.14 ± 0.15 µmol/L and 40.10 ± 3.86 mg/dL respectively) Table 3.

The statistical analysis showed in PTH, Vitamin D, and calcium in β-thalassemia major (12.50 ± 1.19 pg/L, 14.25 ± 0.50 ng/mL and 6.25 ± 0.02 mg/dL respectively) and β-thalassemia minor (40.75 ± 1.19 pg/L, 14.25 ± 0.50 ng/mL, and 8.15 ± 0.05 mg/dL respectively) when compared with control groups (40.10 ± 0.15 pg/L, 54.56 ± 0.29 ng/mL and 9.25 ± 0.02 mg/dL respectively). Phosphorus levels increased in patients with β-thalassemia major (6.75 ± 0.02 mg/L) when compared with patients with β-thalassemia minor (3.45 ± 0.02 mg/L) and control group (2.70 ± 0.01 mg/L; Table 4).

Table 2: Hematological parameters and their levels for each group

<table>
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<th>Parameters</th>
<th>Groups</th>
<th>Mean ± Std. Error</th>
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<td>Iron</td>
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<td>Ferritin</td>
<td>Control</td>
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<td>100.40 ± 4.22</td>
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<tr>
<td></td>
<td>β-thalassemia Major</td>
<td>2120 ± 425.91</td>
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</table>
DISCUSSION

According to the different forms of thalassemia and the degree of anaemia, the haematological parameters of thalassemia patients typically vary. However, all kinds of thalassemia frequently exhibit microcytosis (11). The low levels of hemoglobin and hematocrit values and increased red blood cell counts in cases of β-thalassemia major and minor seen in this study agrees with findings of previous studies (12, 13). The pathophysiology of the disease results in rise in red blood cells because an excess in globin chain precipitates erythroid precursors and RBC, leading to inefficient erythropoiesis, which causes increased RBC production to compensate for anemia (14).

Patients with thalassemia have an increase in white blood cells, which can be seen as stippling or ragged inclusion bodies in the red blood cells (15, 16). In this investigation, high serum ferritin and iron levels were found in β-thalassemia patients which is consistent with findings by Katsanos et al., (17, 18) who reported that all β-thalassemia patients had elevated serum ferritin levels. All human tissues are harmed by excess iron, which makes people with -thalassemia and other iron-overload disorders, like endocrine difficulties, more likely to suffer from morbidity and mortality (19).

Results in this study showed reduced levels of PTH, calcium and vitamin D, and an increase in phosphorus level, indicative of bone defects in β-thalassemia major patients. Calcium is a vital mineral in the human body, as it aids in bone mineralization (20). When paired with calcium, phosphorus has the greatest impact on bone growth and development, and osseous tissue accounts for 85% of the body’s total phosphorus (21). Osteoporosis, osteopenia, skeletal deformities, bone pain, scoliosis, nerve compression, and spontaneous pathological fractures are a few of the skeletal issues that can occur in transfusion-dependent thalassemia patients (22). The anterior pituitary is particularly vulnerable to iron buildup, which prevents hormone emission and causes a variety of endocrine dysfunctions. These endocrinological manifestations include hypoparathyroidism, hypothyroidism or growth failure, and gonadal damage. According to several studies, the prevalence of hypoparathyroidism ranges from 4 to 40 percent (23). Patients with thalassemia frequently have hypoparathyroidism due to an excess of iron in the body (24) and decreased PTH levels (25) and suggested that hypoparathyroidism seen in these patients is due to inappropriate use of chelation therapy. Patients with significant thalassemia have lower levels of vitamin D, and this lower level has been linked to vitamin D malabsorption and inadequate dietary consumption. Research has also hypothesized that 25-OH-D insufficiency could be caused by excessive hepatic iron rather than endocrine tissue failure (26).

CONCLUSION

Patients with thalassemia major usually have a bone profile that is clearly unstable. For these patients, aggressive dietary support and calcium/vitamin D supplementation are particularly advised. Regular bone profile monitoring is also indicated.

CONFLICT OF INTEREST

Authors declare no conflicts of interest.

REFERENCES


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