Original Article

Metabolic Abnormalities in Patients with Beta Thalassemia Major

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ABSTRACT

Objective: To assess the metabolic abnormalities in patients with beta thalassemia major.

Methodology: It was a cross-sectional study conducted at Department of Pathology in collaboration with Department of Orthopedic Surgery, Sharif Medical and Dental College, Lahore. Thirty diagnosed patients of beta thalassemia major of age 5-11 years were included in this study by random sampling technique. All the patients were transfused regularly and were taking desferrioxamine. Complete blood counts, serum ferritin, liver function tests, corrected serum calcium, serum phosphorus, serum vitamin D and parathyroid hormone levels were measured.

Results: The study included 30 patients of beta thalassemia major with the mean age of 11.45±5.1 years. Eighteen patients were males and 12 were females. Serum ferritin was significantly raised in all patients. Hypophosphatemia, hypocalcemia and 25-OH vitamin D deficiency were found in 11%, 74% and 71% thalassemic patients respectively. Hypoparathyroidism was seen in 11.6% patients whereas hyperparathyroidism was observed in 9.1% patients.

Conclusion: Metabolic abnormalities including hypoparathyroidism, hypocalcemia, hypophosphatemia and vitamin D deficiency occurs in patients with thalassemia major.

Keywords: *Beta thalassemia major. Ferritin. Desferrioxamine. Osteoporosis.*

INTRODUCTION

Thalassemia is the most common inherited hemoglobinopathy worldwide. The most prevalent type of thalassemia in Pakistan is beta thalassemia.[1] Each year almost 70,000 infants are born with beta thalassemia throughout the world. It is prevalent in all Mediterranean countries, Southeast Asia, India, Central America, Africa and the Middle East. It was estimated that 5000-9000 children are born with β thalassemia major in Pakistan every year and carrier rate is 5-7%.[1,2] It is an autosomal recessive genetic disorder and is characterized by severe hemolytic anemia associated with skeletal abnormalities. Patients with beta thalassemia major require regular blood transfusions and present with growth failure, osteopenia and fractures.[3] Thalassemia used to be a fatal disorder but with regular blood transfusions and iron chelation therapy life expectancy of these patients is prolonged. Despite all therapeutic advancements, secondary hemochromatosis is still a major challenge.[4]

Bone disease is an important cause of morbidity in thalassemic patients. Various skeletal abnormalities including osteoporosis, osteopenia, rickets, scoliosis, spinal deformities, nerve compression and spontaneous fractures are seen in these patients.[5] Several factors can cause osteopenia in these patients such as bone marrow expansion due to ineffective erythropoiesis and thinning of adjacent bone, delayed puberty and hypogonadism.[6] Several endocrine disorders occur in patients with beta thalassemia major.

Hemochromatosis is the leading cause of endocrine abnormalities.[7] It decreases mineral deposition and causes accumulation of iron in the osteoblasts that result in osteopenia. Osteoporosis and decreased bone mineral density have also been reported in thalassemic patients. Sex hormones play an important role in bone metabolism. Hypogonadism and delayed puberty are involved in early development of osteoporosis. Secondary endocrinopathies such as growth hormone deficiency, hypo/hyperparathyroidism and diabetes mellitus are also seen in these patients.[8,9]

The prevalence of beta thalassemia major is high in Pakistan and it is associated with significant morbidity. Bone and endocrine complications are highly prevalent in thalassemic patients. The underlying cause of the bone disease is attributed to several factors including ineffective erythropoiesis, bone marrow expansion, calcium & vitamin D deficiency, metabolic dysfunctions due to iron overload and reduced physical activity. Regular monitoring, treatment and follow-up of the patients are required to prevent these complications. Early recognition of metabolic abnormalities leads to successful management of patients. So, this study was planned to assess the metabolic abnormalities in patients with beta thalassemia major.

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METHODOLOGY

It was a cross-sectional study conducted at Department of Pathology in collaboration with Department of Orthopedic Surgery, Sharif Medical and Dental College, Lahore. With the approval by the ethics committee of the institution, 30 diagnosed patients of beta thalassemia major of age 5-11 years were included in this study by random sampling technique. All the patients were transfused regularly and were taking desferrioxamine. The diagnosed patients of heart, kidney, liver, thyroid disease or diabetes mellitus were excluded from the study. The blood sample of the patients was taken by using aseptic techniques. Complete blood counts, serum ferritin, liver function tests, corrected serum calcium, serum phosphorus, serum vitamin D and parathyroid hormone levels were measured. Complete blood count was performed by Sysmex-1000. Serum ferritin, serum vitamin D levels and intact parathyroid hormone were measured by chemiluminescence method. Liver function tests, serum calcium and serum phosphorus were performed on automated chemistry analyzer Selectra.

STATISTICAL ANALYSIS

The analysis of the data was carried out by using Statistical Package for Social Sciences (SPSS) version 23. Mean & SD was calculated for all quantitative study variables. Frequency and percentages were estimated for qualitative variables. Comparison of categorical data was carried by Chi-square test. A p-value of <0.05 was considered as statistically significant.

RESULTS

The study included 30 patients of beta thalassemia major with the mean age of 11.45±5.1 years. Eighteen patients were males and 12 were females. The mean hemoglobin level of the patients was 7.9±2.1g/dL and hematocrit was 25.2±4.9%. Serum ferritin level was 4810±3219ng/mL. Total bilirubin was 1.6±0.7mg/dL. Serum AST and ALT were 65.5±39.5u/L and 73.7±68.0µ/L respectively. Level of alkaline phosphatase was 365±65UL/L. Results of all laboratory parameters are shown in table 1.

Hypophosphatemia, hypocalcemia and 25-OH vitamin D deficiency were found in 11%, 74% and 71% thalassemic patients respectively. Hypoparathyroidism was seen in 11.6% of patients.

The study parameters were compared and no significant correlation was found between the study variables.

Table 1: Mean values of study variables

Variable	Mean±SD	Reference range
Hemoglobin (g/dL)	7.9±2.1	12–16
Serum ferritin (ng/mL)	4810±3219	20–200
Total bilirubin (mg/ dL)	2.1±0.7	0.3–1.2
Serum AST (µ/L)	65.5±39.5	<40
Serum ALT(µ/L)	73.7± 68.0	7–56
Alkaline phosphatase (UL/L)	365±65	<500
Serum Phosphorus (mg/ dL)	2.3±2.5	2.5–4.5
Corrected Serum Calcium (mg/ dL)	7.9±0.6	8.6–10.2
Parathyroid Hormone Level (pg/mL)	15.5±7.5	12–50
Serum Vitamin D (ng/mL)	21.1±10.6	>30

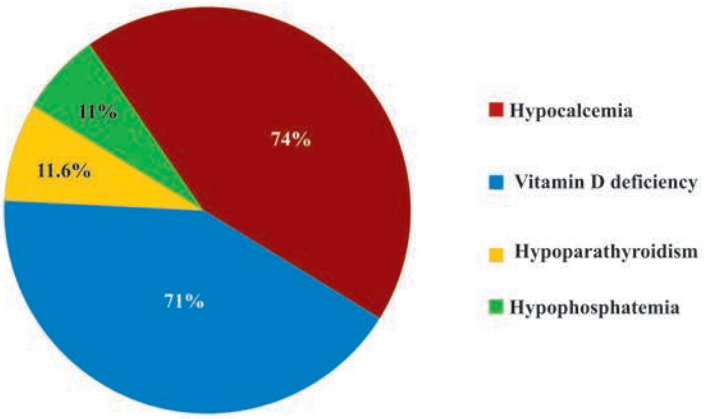

Figure 1: Metabolic abnormalities in the patients with beta thalassemia major

DISCUSSION

Beta thalassemia causes various hematological, endocrinal and skeleton complications. Osteopenia, osteoporosis and spontaneous fractures are the most common skeleton complications. The iron accumulation in anterior pituitary decreases hormonal emission, leading to various endocrine dysfunctions. The metabolic abnormalities include hypoparathyroidism, hypocalcemia, hypophosphatemia and vitamin D deficiency.[10,11]

Our results showed that ferritin levels are raised in these patients. Elevated serum ferritin levels were reported in many other studies due to repeated blood transfusion, which leads to iron overload.[12,13]

We found that serum alkaline phosphatase was not increased in study participants, which indicates the decreased osteoblastic activity of bone. This may occur due to iron accumulation in the osteoblasts. Another study conducted by Stefano et al. showed that alkaline phosphatase did not show significant change from baseline.[4]

Serum vitamin D levels were decreased in 71% patients enrolled in our study. Similar results were found in other studies.[1,9,14] Another study conducted in Italy showed vitamin D deficiency in 9.6% thalassemic patients.[15] Vitamin D deficiency in thalassemic patients is multifactorial. It may occur due to decreased dietary intake, malabsorption or iron overload in the liver which may lead to defective hydroxylation of vitamin D.[1,17]

Our results showed that hypoparathyroidism was seen in 11.6% patients. Low levels of parathormone are sequel of iron overload. Early iron chelation can prevent development of hypoparathyroidism.[10] A study conducted in Southern Pakistan showed the prevalence of hypoparathyroidism in 13.8% patients.[1] Another study conducted in Pakistan found that hypoparathyroidism was present in 40% of patients.[18] A study conducted in Oman showed hypoparathyroidism in 19% thalassemic.[19]

The corrected calcium level was low in our study population. We found hypocalcemia in 74% thalassemic patients. Comparable results were found in other studies conducted in Iran, Saudi Arabia and the USA.[8,20,21] Hypocalcemia occurs in these patients due to hemosiderosis and desferrioxamine therapy. On the contrary, some studies conducted on thalassemic patients showed no significant decrease in calcium levels.[4,22]

We found hypophosphatemia in 11% patients whereas in 89% thalassemic patients serum phosphorous level was within normal range. Another study conducted in Southern Pakistan showed that only 13.8% of patients had hypophosphatemia.[1] Similar results were revealed by other studies conducted in different countries.[4,23] A study conducted in Turkey showed hyperphosphatemia in thalassemic patients.[9] Significantly high serum phosphorus levels were reported in other studies.[24,25]

Endocrine abnormalities like hypogonadism, delayed puberty and diabetes mellitus are commonly seen in thalassemia patients. Osteoporosis leading to fractures is a common bone complication of thalassemic patients. It occurs due to decreased bone formation and increased bone resorption. Iron overload and malnutrition are associated with increased rates of osteoporosis in these patients.[4] Calcium, phosphorous and vitamin D in sufficient amounts are required for bone growth and development. Hypoparathyroidism can also lead to hypocalcemia and osteoporosis. All these factors observed in this study showed that these patients are at risk of developing osteopenia and osteoporosis. **High prevalence of endocrine and metabolic complications among thalassemic patients signifies the importance of therapeutic interventions.** However, further studies are required with a larger sample size and follow-up of the patients.

CONCLUSION

Metabolic abnormalities including hypoparathyroidism, hypocalcemia, hypophosphatemia and

vitamin D deficiency occurs in patients with thalassemia major. Hypocalcemia is the most common metabolic derangement.

RECOMMENDATIONS

Regular monitoring of biochemical profile and treatment with nutritional supplementation like calcium and vitamin D are recommended in thalassemic patients. So that skeleton complications can be prevented in these patients.

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