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Serum calcium and serum phosphate levels in transfusion dependent beta thalassemia

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Abstract

Background: Patients with transfusion dependent beta thalassemia with severe anemia require regular blood transfusion to improve quality of life. This can lead to iron overload which might cause various complications including hypocalcaemia.

Objective: To estimate the serum calcium and phosphate levels in transfusion dependent beta thalassemia patients. **Methods:** This cross-sectional study was conducted in the Department of Physiology, Dhaka Medical College, Dhaka from July 2016 to June 2017. After fulfilling the ethical aspect, a total number of 60 subjects were selected with the age ranging from 5 to 25 years. Among them, 40 transfusion dependent beta thalassemia patients were selected as the study group and 20 age and sex matched apparently healthy individuals were considered as control group for comparison. The study population were selected from Thalassemia foundation hospital, Dhaka. These serum calcium and phosphate levels were estimated by autoanalyzer. For statistical analysis, unpaired Student's 't' test, Chi-square test were performed as applicable. **Results:** In this study, serum calcium level were significantly ($p < 0.001$) lower and serum phosphate level were significantly ($p < 0.001$) higher in transfusion dependent beta thalassemia patients as compared to healthy controls. In addition, 67.5% thalassemia patients had hypocalcemia (calcium level < 8.5 mg/dl) and 85% of thalassemia patients had hyperphosphatemia (phosphate level > 4.7 mg/dl). **Conclusions:** This study concludes transfusion dependent beta thalassemia patients have low calcium level and high serum phosphate level which should be monitored to avoid complications related to hypocalcaemia and hyperphosphatemia.

Key words: Iron overload, hypocalcaemia, transfusion dependent beta thalassemia.

Introduction

“**T**halassemia” name is derived from the Greek words “thalassa” means sea and “haema” means blood. It is a heterogeneous family of inherited disorders in which there are defective synthesis of α or β globin subunits of hemoglobin A and accordingly termed as Alpha (α) or beta (β) thalassemia^{1,2,3}. Currently, thalassemia has been classified into Transfusion dependent thalassemias (TDTs) and Non-transfusion dependent thalassemias depending on requirement of regular blood transfusion to survive^{3, 4}.

World Health Organization data shows that about 3% populations are carriers of beta thalassemia and about 4% populations are carriers of Hb-E in Bangladesh⁵.

The accumulation of excess α-globin chains in erythroid precursors due to impaired biosynthesis of the α-globin chains in Beta thalassemia major and HbE thalassemia leading to red blood cells destruction by oxidative means. All these changes result in ineffective erythropoiesis, hemolysis and anemia and associated with increased mortality from congestive cardiac failure or other complications of chronic anemia within few years of life. But this scenario has been changed after treatment started with combination of transfusion and chelation therapy⁶⁻¹⁰.

Despite chelation therapy, repeated blood transfusions may cause iron overload in body which in turn lead to increased load of reactive oxygen species. This increased oxidative stress may damage parathyroid glands in addition to other organs or tissues may cause hypoparathyroidism and hypocalcemia^{11, 12}.

Calcium and phosphate are major minerals essential for bone rigidity. In addition they exert important role in muscle function, nerve impulse transmission, intracellular signaling, various glandular secretion. Parathyroid hormone is the main regulatory hormone for calcium homeostasis^{13, 14}. The physiologic balance of phosphate is maintained by coordinated interactions of the small intestine, bone,

parathyroid gland and kidney. Functional impairment of any of these organs can lead to abnormal phosphate level^{15, 16}.

Earlier reports showed lower serum calcium level and higher phosphate level in thalassemia patients than controls¹⁷⁻¹⁸. In addition, correlation of increased calcium level with increased serum ferritin level was also reported¹⁹.

It is evident from these previous studies that iron overload due to repeated blood transfusion in thalassemic patients may be attributed to altered calcium and phosphate level in these patients. Though few studies investigated serum calcium and phosphate level in transfusion dependent Thalassemic patients but the volume of data is inadequate to reach a solid conclusion. So, the present study has been designed to reveal the serum calcium and phosphate levels in these patients. The observations may facilitate prevention of transfusion related complication of patients of transfusion dependent beta thalassemia patients.

Method

This cross sectional study was conducted in the Department of Physiology, Dhaka Medical College, Dhaka from July 2016 to June 2017 after approval from the ethical review committee from this institute. Forty transfusion dependent beta thalassemia patients aged 5 to 25 years were enrolled from Thalassemia foundation hospital, Dhaka and 20 age and sex matched apparently healthy individuals were selected as control. Informed written consent was taken from the participants after proper briefing about the nature, purpose and benefit of the study. Before taking blood, detailed family and medical history were taken. Anthropometric measurement of the subjects was done and blood pressure was measured. With aseptic precaution, 4 ml of venous blood was collected from ante-cubital vein by a disposable plastic syringe and serum was prepared and sent to lab for estimation serum calcium, phosphate levels by auto analyser. All the parameters were expressed as mean ± SD. Unpaired Student ‘t’ test and Chi-Square test were performed as applicable. P value < 0.05 was

accepted as level of significance. Statistical analyses were performed by using a computer based statistical program SPSS (Statistical package for social science) Version 22.0.

Results

General characteristics of the subjects of both groups are presented in Table I. Mean weight and BMI were significantly lower in thalassemia patients and other variable were not statistically different in both groups. Table II showed significantly lower serum calcium level and higher serum phosphate level in thalassemia patients than controls. This study showed that 67.5% thalassemia patients had serum calcium level < 8.5 mg/dl (Figure 1) and 85% thalassemia patients had phosphate level > 4.7mg/dl (Figure 2).

Table I: General characteristics of the subjects in both groups (N=60)

	Control (n ₁ =20)	Thalassemia pts (n ₂ =40)
Age (years)	14.45±6.52	13.36±5.02
Male	11 (55.0%)	27 (67.5%) ^b
Female	9 (45.0%)	13 (32.5%) ^b
Height (cm)	141.15±18.37	134.75±14.43
Weight (kg)	40.10±12.48	29.45±10.37**
BMI (kg/m ²)	19.58±1.46	15.90±2.49***
SBP (mm ofHg)	102.00±15.08	97.13±15.68
DBP (mm ofHg)	58.75±14.13	58.50±14.64

Data were expressed as mean ± SE. Statistical analysis was done by Unpaired Student's 't' test and Chi square test.

=p<0.01, *=p<0.001.

Table II: Serum calcium and serum phosphate levels of the subjects of both groups (N= 60)

Outcome measures	Control (n=20)	Thalassemia patients (n=40)
Serum Calcium (mg/dl)	9.04±0.51	6.90±2.17***
Serum Phosphate (mg/dl)	4.08±1.40	6.01±1.38***

Data were expressed as mean ± SE. Statistical analysis was done by unpaired Student t < test.*** = p<0.001

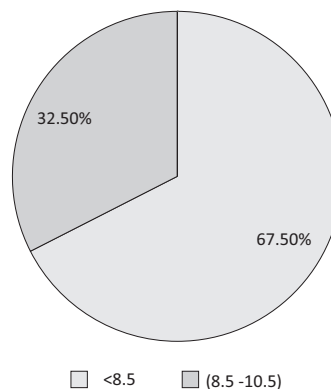


Figure 1: Frequency distribution of serum calcium level in thalassemia patients (n=40)

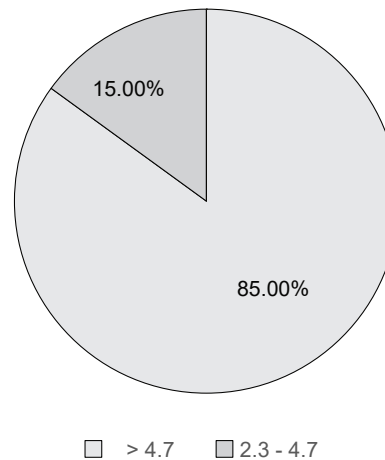


Figure 2: Frequency distribution of serum phosphate level in thalassemia patients (n=40)

Discussion

The present study was undertaken to assess serum calcium and phosphate levels in transfusion dependent beta thalassemia. In this study, the mean serum calcium level was significantly decreased in transfusion dependent beta thalassemia patients than that of controls. Similar types of observations were reported by some researchers²⁰⁻²². However, some researchers found no change in serum calcium level in beta thalassemia patients. This dissimilarity in findings might be due to variation in nutritional status in study group²³.

In the present study, the mean serum phosphate level was increased in transfusion dependent beta thalassemia patients than that of controls and the result was statistically significant. This finding was in agreement with others²⁴⁻²⁵. Again, some investigators found no change in serum phosphate level in beta thalassemia patients. This dissimilarity in findings might be due to variation in nutritional status in study group²³. Further more, the present results suggested greater percentage of Thalassemia patients were affected with hypocalcemia and hyperphosphatemia indicating their impaired of parathyroid function.

Several studies have suggested that parathyroid gland damage occurs in transfusion dependent beta thalassemia may be due to oxidative stress caused by iron overload. In these patients, excess iron following repeated blood transfusion deposited in various organ including parathyroid gland. These excess iron generate large number of reactive oxygen species (ROS) via Fenton Cs reaction and Haber - Weiss reaction. Reactive oxygen species (ROS) are capable of causing oxidative damage to macromolecules leading to lipid peroxidation, DNA damage and causes damage to parathyroid gland^{26, 27}.

Again Intracellular iron regulates number of transferrin receptor and serum ferritin levels by interfering the translation of mRNA. When intracellular iron level increase, it stimulates translation of ferritin mRNA and causes degradation of transferrin receptor mRNA. So, there are increase in serum ferritin level and decrease in number of transferrin receptor. As transferrin receptor decrease, excess iron binds with other blood component, leading to formation of plasma non-transferrin bound iron (NTBI). It is potentially toxic and contribute to generation of ROS leading to parathyroid gland damage. As a result decreased serum calcium and increased serum phosphate levels^{28- 30}.

Conclusions

After analyzing the results of the study, it may be concluded that lower serum calcium level and higher serum phosphate levels and impaired parathyroid may occur in transfusion dependent beta thalassemia patients. Therefore, estimation of these parameters in transfusion dependent beta thalassemia patients might be useful for early detection of hypocalcaemia and proper management of hypocalcemia to prevent its complication.

Conflict of interest None.

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