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Relationship between serum ferritin and parathyroid function in adult male patients with transfusion dependent thalassemia

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Abstract

Background: Thalassemia is a genetic disorder of defective hemoglobin synthesis. In transfusion dependent thalassemia (TDT), iron overload is caused by repeated blood transfusion for a long time. This increased iron is deposited in body tissue and may lead to endocrine dysfunction. **Objective:** To evaluate the relationship between serum ferritin and parathyroid dysfunction in adult male patients with TDT. **Methods:** It was a cross sectional study which was conducted from March 2018 to February 2019 in the Department of Physiology, Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka. For this study, 35 TDT male patients aged 18 to 40 year, were considered as study group and 35 age and sex matched apparently healthy subjects were considered as control group. The outpatient department of Hematology and Transfusion Medicine was the point of collection of study group. Parathyroid function was assessed by plasma intact para thyroid hormone (iPTH), serum total calcium and serum inorganic phosphate. Plasma iPTH and serum ferritin levels were estimated by Electrochemiluminescence Immunoassay method using automated analyzer. Serum total calcium and serum inorganic phosphate levels were estimated by colorimetric method using automated analyzer. Independent sample t test and Pearson's correlation coefficient (r) test were applied for statistical analysis using SPSS version 16. **Results:** In this study, serum ferritin level was significantly ($p < 0.001$) higher in patients with TDT than that of healthy control. Correlation analysis showed negative correlation of serum ferritin with plasma iPTH and

serum corrected calcium and positive correlation with serum inorganic phosphate in patients with TDT. Among them correlation with serum corrected calcium and inorganic phosphate were statistically significant ($p < 0.05$). **Conclusion:** This study concluded that TDT may be associated with elevated iron status which is inversely related with parathyroid function.

Key words: Thalassemia, parathyroid hormone, ferritin, calcium, phosphate.

Introduction

Thalassemia is the most common inherited disorder in the world. It is an autosomal recessive disorder characterized by ineffective erythropoiesis and hemolytic anemia.[1-4] It is a single gene disorder in which there is defective synthesis of alpha or beta globin chain of hemoglobin.[5-7] Data published by World Health Organization (WHO) showed that beta thalassemia is carried by about 3% population and Hb-E is carried by about 4% population in Bangladesh. Approximately 6000 children are born with thalassemia in Bangladesh per year.[6,8]

In patients with TDT, iron overload is caused by repeated blood transfusion and increased gastrointestinal iron absorption due to ineffective erythropoiesis and anemia.[9,10] Circulating transferrin becomes saturated by this excess iron resulting in the emergence of non-transferrin bound iron (NTBI). These NTBI species are taken up by liver, spleen, endocrine organs and myocardium by tissue specific L-type voltage dependent calcium channel and deposited within the cell as hemosiderin and ferritin. Ferritin is the storage form of iron in the tissue and provides a reserve; so that iron becomes readily available for synthesis of Hb and other heme proteins. Ferritin consists of a protein shell of 24 subunits surrounding an iron core. This stored iron is shielded from body fluids and thus is unable to cause oxidative damage, as would occur if it were in a free ionic form.[11] Reactive oxygen species (ROS) such as superoxide anion (O_2^-), hydroxyl radical ($OH^\cdot$), singlet oxygen and hydrogen peroxide (H_2O_2) are produced by NTBI.[12] There are some protective systems in our body eg. enzymatic and non-enzymatic antioxidant systems; scavenge these ROS. Tissue damage of various systems occurs by oxidative stress when production of ROS exceeds the capacities of protective systems.[4, 13-15]

Endocrine dysfunction is a common complication in TDT due to iron overload which is associated with Hypoparathyroidism.[12,16-20] One study showed that there is a negative correlation between serum ferritin and iPTH[13]. This study is not conclusive at all to describe the relationship between serum ferritin and parathyroid dysfunction. Again this study was performed in both genders. But gender variation of this correlation is also important in TDT patients. Therefore, this study has been designed to assess the relationship between serum ferritin and parathyroid dysfunction in adult male patients with TDT.

Methods

Design Setting and participants

It was a cross sectional study which was conducted from March 2018 to February 2019 in the Department of Physiology, BSMMU, Dhaka. this study, 35 TDT male patients aged 18 to 40 year, were selected as study group by consecutive sampling. The outpatient department of Hematology and Transfusion Medicine was the point of collection of study group. The patients receiving regular blood transfusion for at least 5 years were included.

For comparison 35 age and sex matched apparently healthy subjects were considered as control group and was collected by personal contact.

Exclusion criteria

The exclusion criteria was thyroidectomy, malignancy, acute illness, taking nutritional supplement like multivitamins, calcium and vitamin D (within 120 days), malabsorption syndrome, renal insufficiency.

Data collection

After enrollment, informed written consent was taken from all subjects. Detail family, socioeconomic, medical history was taken and thorough physical examination was done and documented in a preformed data schedule. Anthropometric measurements including height and weight of the subjects were recorded and BMI was calculated. Parathyroid function was assessed by plasma iPTH, serum total calcium and serum inorganic phosphate. The total calcium level was corrected for albumin.[21] Serum creatinine was analyzed to exclude renal insufficiency. Under aseptic precaution six ml of fasting venous blood was collected. Serum ferritin and plasma iPTH levels were estimated by Electrochemiluminescence Immunoassay method using automated analyzer. Serum total calcium, serum inorganic phosphate, serum albumin and serum creatinine levels were estimated by colorimetric method using automated analyzer.

Statistical analysis

Data was expressed as mean±SE. Independent sample t test and Pearson's correlation coefficient (r) test were applied for statistical analysis using SPSS version 16.

Results

In this study, age of both groups was almost similar and statistically no significant difference was observed. BMI was significantly ($p< 0.001$) lower in TDT compared to control (Table I). In addition, significantly ($p< 0.001$) higher serum ferritin and serum inorganic phosphate levels and) lower plasma iPTH and serum corrected calcium levels in TDT than that of control has been published in our previous article.[1]

Correlation analysis showed negative correlation of plasma iPTH and serum corrected calcium (Figure 1, 2) and positive correlation of serum inorganic phosphate with serum ferritin (Figure 3) in patients with TDT. Among them correlation with serum corrected calcium and inorganic phosphate were statistically significant ($p < 0.05$).

Table I: Age and BMI levels in both groups (N=70)

Parameters	TDT (n=35)	Control (n=35)
Age (Year)	26.23 ± 1.23	27.31 ± 1.11
BMI (kg/m^2)	17.14 ± 0.33***	22.1 ± 0.48

Data are expressed as mean±SE. Statistical analysis was done by independent sample t test. TDT – Transfusion dependent thalassemia, BMI – Body mass index, ***p ≤0.001.

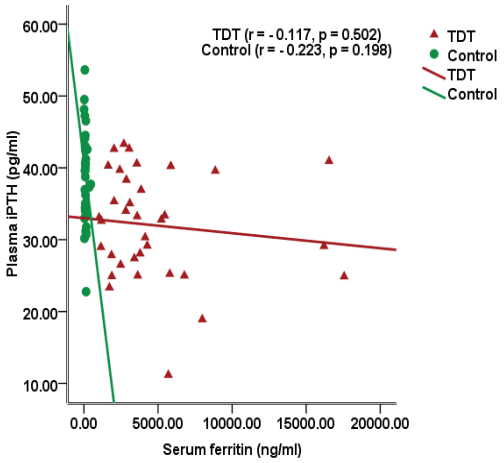

Figure 1: Negative correlation of plasma Intact parathyroid hormone (iPTH) with serum ferritin in Transfusion dependent thalassemia (TDT).

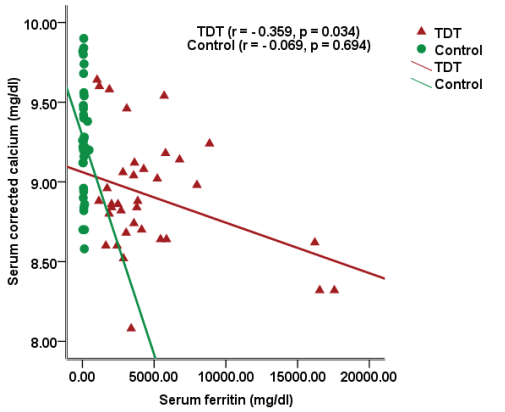

Figure 2: Significant negative correlation of serum corrected calcium with serum ferritin in Transfusion dependent thalassemia (TDT).

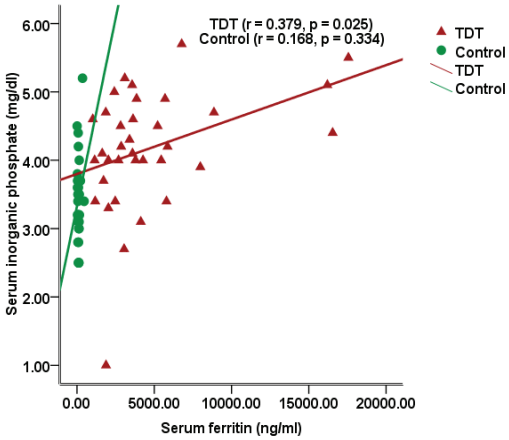

Figure 3: Significant positive correlation of serum inorganic phosphate with serum ferritin in Transfusion dependent thalassemia (TDT).

Discussion

The present study observed the relationship of parathyroid dysfunction with serum ferritin in adult male patients with TDT. This study published association of higher serum ferritin and inorganic phosphate and lower plasma iPTH and serum corrected calcium levels with male TDT[1] which agree to others but in both male and female. [12, 16-20,]

To explore further relationship between iron overload in TDT patients and Parathyroid dysfunction correlation analysis of plasma iPTH and serum corrected calcium with serum ferritin showed inverse relationship, whereas serum inorganic phosphate showed direct relationship with serum ferritinin TDT. One study published significant negative correlation of serum ferritin with plasma iPTH.[13] These results affirm the attenuation of Parathyroid gland in TDT. It has been suggested that due to repeated blood transfusion excess iron is deposited in all organs including the parathyroid glands. The excess iron leads to generation of ROS which causes oxidative stress.[15] The ROS causes peroxidation of membrane lipids yielding peroxides, which are themselves unstable and reactive; propagating an autocatalytic chain reaction. These reactions ultimately result in cellular mitochondrial, lysosomal and sarcolemmal membrane damage.[4, 21, 22] When these events of oxidative damage occur in the cell of parathyroid gland; decrease synthesis and secretion of PTH occurs resulting in defective calcium and phosphate homeostasis. So, it can be stated that parathyroid glandular damage may be caused by iron overload.

Conclusion

This study concluded that TDT may be associated with elevated iron status which is inversely related with parathyroid function. So, regular monitoring of serum ferritin, plasma iPTH, serum total calcium and serum inorganic phosphate may be helpful for early prediction of any abnormality.

Ethical consideration

This study was approved by Institutional Review Board of BSMMU, Dhaka.

Conflict of interest

Authors of this study have no conflict of interest.

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