Serum Calcium, Phosphate and Ferritin Level in Adult Male Patients with Transfusion Dependent Thalassemia

SFH Urmi¹, S Begum², FT Munira³, KC Das⁴

Abstract:
Thalassemia is an inherited blood disorder characterized by decreased hemoglobin production resulting in anemia. Patients with transfusion dependent thalassemia (TDT) develop iron overload due to regular blood transfusion. This excess iron is deposited in the tissue and causes organ failure which may lead to hypocalcaemia and hyperphosphatemia. This study was done to measure serum total calcium, serum inorganic phosphate and serum ferritin levels in adult male patients with TDT. This cross sectional study was carried out from 01 March 2018 to 28 February 2019 in Bangabandhu Sheikh Mujib Medical University, Dhaka. Thirty five consecutive male patients with TDT of 18 to 40 year were selected from the outpatient department (OPD) of Transfusion Medicine and Hematology. For comparison, 35 age matched apparently healthy male subjects were selected on the basis of selection criteria. Serum total calcium, serum inorganic phosphate, serum ferritin, serum albumin, serum alkaline phosphatase and serum creatinine levels were measured by colorimetric method using automated analyzer. For statistical analysis independent sample t-test was done using SPSS version 16. Serum total calcium level was significantly (p<0.001) lower, serum inorganic phosphate and serum ferritin level was significantly (p<0.001) higher in patients with TDT than that of healthy control. In addition, 1 (2.86%) TDT patient had hypocalcaemia and 12 (34.29%) had hyperphosphatemia. In conclusion of this study, serum total calcium level decreased and serum inorganic phosphate and serum ferritin level increased in patients with TDT.

Key words: Transfusion dependent thalassemia, Calcium, Phosphate, Ferritin.

Introduction:
Thalassemia is a set of heterogeneous, recessive genetic disorder of hemoglobin synthesis. It is characterized by complete absence or reduced synthesis of alpha or beta globin chains which leads to ineffective erythropoiesis and hemolytic anemia. The name thalassemia is derived from two Greek words “thalassa” and “haema”, which means sea and blood respectively. It is an autosomal recessive disorder where deletion or point mutation occurs in alpha or beta globin gene on chromosome 11 (beta) and 16 (alpha). A World Health Organization (WHO) data shows that about 4% population are carrier of beta thalassemia in Bangladesh. Approximately 6000 children are born with thalassemia in our country per year. Worldwide about 150 million people are affected with β-thalassemia.

Patients with transfusion dependent thalassemia (TDT) receive regular blood transfusion to maintain normal hemoglobin level, which causes accretion of excess iron in the body. Excess iron leads to increase saturation of circulating transferrin, resulting in the emergence of non-transferrin bound iron (NTBI). NTBI generates reactive oxygen species (ROS) which induce oxidative stress. This oxidative stress may damage parathyroid glands in addition with other organ and may cause hypocalcaemia and hyperphosphatemia.

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Calcium is a major mineral of our body which is essential for bones and teeth. Moreover calcium plays an important role in muscle contraction, transmission of nerve impulse, hormonal secretion, intracellular signaling and blood clotting. Phosphorus is another essential mineral; usually found as phosphate in the body. Phosphate plays an important role in energy production as component of ATP. It is a component of DNA and RNA which carry genetic information and help in protein synthesis. Phosphate is also present in cAMP and 2, 3-diphosphoglycerate. Ferritin binds with iron and stores excess iron within the cell. Ferritin synthesis is regulated by intracellular iron through interaction with iron responsive element (IRE) and iron regulatory protein (IRPs); acting as intracellular iron sensor. Excess iron causes inactivation of IRPs which induces a rapid increase in ferritin mRNA translation and increase ferritin synthesis.

Some analysts reported that, serum calcium level significantly reduced and serum phosphate and serum ferritin levels significantly increased in TDT. All these variables were studied in both male and female in other studies. But gender variations of these variables are important in TDT patients. Therefore, this cross sectional study has been planned to evaluate these variables in male TDT patients.

Materials and Methods:
This cross sectional study was done from 01 March 2018 to 28 February 2019 in Bangabandhu Sheikh Mujib Medical University, Dhaka. The protocol of this study was granted by Institutional Review Board (IRB), BSMMU. For this study, 35 TDT male patients of 18 to 40 year were enlisted from the OPD of Hematology and Transfusion Medicine of BSMMU. For comparison, 35 age matched apparently healthy male subjects were selected. For sample collection consecutive sampling technique was used. All the selected patients were receiving regular blood transfusion at least for about 5 years. Patients with acute illness, on nutritional supplement like multivitamins, calcium and vitamin D (within 120 days), thyroidectomy, malabsorption syndrome, renal insufficiency, malignancy, taking any drug which affect calcium level were excluded from this study. Anthropometric measurements including height and weight of the subjects were taken and BMI was calculated. Under aseptic precaution 6 ml of fasting venous blood was collected from ante-cubital vein. Serum total calcium, inorganic phosphate, ferritin, albumin, alkaline phosphatase and creatinine were estimated using colorimetric method. The total calcium level was corrected for albumin. For statistical analysis independent sample t test was done.

Results:
In this study, both groups were matched for age and serum albumin. BMI was significantly (<0.001) lower and serum ALP level was significantly (<0.001) higher in TDT than that of control (Table-I).

<table>
<thead>
<tr>
<th>Parameters</th>
<th>TDT (n=35)</th>
<th>Control (n=35)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (Year)</td>
<td>26.23±1.23</td>
<td>27.31±1.11</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>17.14±0.33***</td>
<td>22.1±0.48</td>
</tr>
<tr>
<td>Serum albumin (gm/dl)</td>
<td>4.33±0.09</td>
<td>4.46±0.05</td>
</tr>
<tr>
<td>Serum ALP (U/L)</td>
<td>103.31±8.86***</td>
<td>69.03±2.10</td>
</tr>
</tbody>
</table>

Data were expressed as mean±SE. Statistical analysis was done by independent sample t-test. BMI= Body mass index, ALP= Alkaline phosphatase, TDT= Transfusion dependent thalassemia. ***p<0.001.

Serum corrected calcium level was significantly (p<0.001) lower and serum inorganic phosphate and serum ferritin levels were significantly (p<0.001) higher in TDT than that of control (Table-II).

<table>
<thead>
<tr>
<th>Parameters</th>
<th>TDT (n=35)</th>
<th>Control (n=35)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Corrected calcium (mg/dl)</td>
<td>8.91±0.06***</td>
<td>9.26±0.06</td>
</tr>
<tr>
<td>Inorganic phosphate (mg/dl)</td>
<td>4.18±0.15***</td>
<td>3.45±0.10</td>
</tr>
<tr>
<td>Serum ferritin (ng/ml)</td>
<td>4743.71±707.45***</td>
<td>109.65±14.71</td>
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</table>

Data were expressed as mean±SE. Statistical analysis was done by independent sample t-test. TDT= Transfusion dependent thalassemia. ***p<0.001.

Again, hypocalcaemia was found in 1 (2.86%) and hyperphosphatemia was found in 12 (34.29%) of TDT patients. No hypocalcaemia but 1(2.86%) subject was found with hyperphosphatemia in control group (Table-III).
Table III: Distribution of patients according to frequency distribution of hypocalcaemia and hyperphosphatemia in both groups (N=70)

<table>
<thead>
<tr>
<th>Parameters</th>
<th>TDT (n=35)</th>
<th>Control (n=35)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypocalcaemia (&lt;8.1 mg/dl)</td>
<td>01 (2.86)</td>
<td>00 (00)</td>
</tr>
<tr>
<td>Hyperphosphatemia (&gt;4.5mg/dl)</td>
<td>12 (34.29)</td>
<td>01 (2.86)</td>
</tr>
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</table>

Data were expressed as no. (%). TDT= Transfusion dependent thalassemia.

Discussion:

Present study assessed serum total calcium, serum inorganic phosphate and serum ferritin levels in adult male patients with TDT. The result of this study showed serum total calcium level was significantly lower in TDT patients than that of control. Again, serum inorganic phosphate and serum ferritin levels were significantly higher in TDT patients than that of control. Similar findings were reported in TDT patients by some other researchers. Iron overload is attributed with TDT due to frequent blood transfusion. This excess iron causes increase saturation of transferrin. The iron binding capacity of circulating transferrin is exceeded with increasing severity of iron overload, resulting in the emergence of non-transferrin bound iron (NTBI). NTBI give rise to ROS, such as hydroxyl radical (OH·), superoxide anion (O2·-), hydrogen peroxide (H2O2) and singlet oxygen which cause oxidative stress. The ROS yields peroxides by peroxidation of membrane lipids. Peroxides are reactive and unstable; propagating an autocatalytic chain reactions. These reactions ultimately result in mitochondrial, sarcosomal and lysosomal membrane damage. So, it can be stated that iron overload causes organ damage by oxidative stress in TDT patients.

The physiologic balance of calcium and phosphate is maintained by bone, kidney and intestine in coordination with parathyroid gland. Previous studies suggested that parathyroid glandular damage occurs due to iron overload in TDT patients. As a result hypocalcaemia and hyperphosphatemia occurs.

Conclusion:

From the results of this study, it may be concluded that, serum total calcium level decreased and serum inorganic phosphate and serum ferritin levels increased in TDT patients. Regular follow up of serum total calcium, inorganic phosphate and serum ferritin should be done, so that early measures can be taken in case of any abnormality.

Reference:


