Assessment of Vitamin D levels and Parathyroid Hormone levels in children with Beta Thalassemia major, and to compare their respective values with age and sex matched controls

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Abstract: Beta Thalassemia major (thalassemia) is a heterogeneous inherited disorder of haemoglobin synthesis¹. There is ineffective erythropoiesis and anaemia². Regular blood transfusions and chelation therapy has noticeably prolonged survival in thalassemic patients³ however they suffer growth, multiple endocrine and metabolic abnormalities. There is gross derangement of Calcium homeostasis in multi-transfused thalassemic patients. Both defective syntheses of 25 OH vitamin D (25OH D) and/or hypoparathyroidism are seen in these patients, which negatively affects their bone metabolism⁴. Sixty Beta Thalassemia children (cases) and an equal number of age, sex matched apparently healthy children (controls) were included in this study. After recording of history and thorough clinical examination blood samples from cases and controls were collected and tested for Vitamin D level, Serum Parathyroid level. Results were compared with age specific normal values. It was observed that Vitamin D levels were significantly deficient (66.67%) in thalassemic patients than controls (P value<.0001). Only 16.6% cases were having sufficient Vitamin D levels in comparison to 30% control. Most of the children cases and controls had insufficient vitamin D levels but it was far more in thalassemic children. There was no significant difference in the median PTH levels in cases (31.15) and controls (29.1) (P value 0.902).

I. Introduction

In India Beta Thalassemia affects over 1 lakh people and more than 8000 thalassemic children are born every year¹. Thalassemia is a heterogeneous inherited disorder of haemoglobin synthesis². There is ineffective erythropoiesis and anaemia. Beta-thalassemia major usually presents at 4 - 6 months of life, following weaning of protective effect of high Hb F concentration at birth. Most patients require blood transfusion every 2-4 weeks commencing at around 1 year of age².

Regular blood transfusions and chelation therapy have noticeably prolonged survival in thalassemic patients. Despite a significant increase in the lifespan of these patients, they suffer from multiple abnormalities probably due to iron overload, including endocrinial abnormalities such as hypogonadism, diabetes mellitus, hypothyroidism and hypoparathyroidism³. It is observed that calcium homeostasis is grossly deranged in β-thalassemic multi-transfused patients. Defective synthesis of 25 OH vitamin D (25OH D) and/or hypoparathyroidism are seen in these patients which negatively affects their bone metabolism⁴. There is paucity of data in Indian population regarding the Vitamin D level and Parathyroid hormone levels in Beta-Thalassemia children. This prompted us to plan a study aiming to assess various parameters including, Vitamin D, Parathyroid hormone(PTH), Calcium, Alkaline Phosphatase(ALP), and Phosphorous levels in these children receiving regular packed red cells transfusion and chelation therapy.

II. Materials and methods

The present case-control study was conducted in Department of Paediatrics, at Dr.Baba Saheb Ambedkar Medical College and Hospital, during the period of August 2015 to November 2016.

The study was approved by the scientific and ethical committee of the Institute.

Sixty Beta Thalassemia children (cases) in the age-group of 1 to 12 years and an equal number of age, sex matched apparently healthy children (controls), were included in this study, after informed consent of parents/guardians. Healthy controls were children coming to hospital for minor illnesses and immunisations.

After recording of complete history and clinical examination on a predesigned Performa, blood samples from both cases and controls, were collected in Serum Separator Tubes (SST) and processed at the
designated testing facility, maintaining strict cold chain during transportation. All blood samples were tested for Vitamin D levels, Serum Parathyroid levels, Serum Calcium, Serum Phosphorous, and Serum Alkaline Phosphate (ALP).

The assays for Serum parathyroid hormone(PTH) levels and Serum 25 hydroxyvitamin D were measured by Chemiluminescence immunoassay(CLIA) using Beckman coulter machine BECKMAN ACCESS2 and serum calcium levels, were measured by ARSENAZO 3 method, phosphate levels by Phosphomolybdate enzyme method and Serum alkaline phosphatase(ALP) were measured by Para-Nitro Phenyl Phosphate AMP method using OLYMPUS AU400.

Data was compiled in MS Excel sheet. Statistical testing was conducted with the Statistical Package for the Social Science system SPSS 20.0. For all statistical tests, a p value less than 0.05 was taken to indicate a significant difference.

### III. Results

The study included 60 Beta-thalassemia major children (cases) and 60 normal healthy children (controls).

**Table no 1.** Shows the descriptive characteristics and laboratory parameters.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Cases (mean value)(60)</th>
<th>Controls (mean value)(60)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>5.52 +/- 2.89</td>
<td>5.73 +/- 3.32</td>
<td>0.91</td>
</tr>
<tr>
<td>Sex</td>
<td>M:F 44:16</td>
<td>M:F 36:24</td>
<td>0.121</td>
</tr>
<tr>
<td>ALP (IU/L)</td>
<td>256.08 +/- 98.18</td>
<td>208.62 +/- 104.66</td>
<td>0.006</td>
</tr>
<tr>
<td>PHOSPHATE (MG/DL)</td>
<td>5.28 +/- 0.67</td>
<td>4.82 +/- 0.85</td>
<td>0.002</td>
</tr>
<tr>
<td>CALCIUM (MG/DL)</td>
<td>9.49 +/- 0.55</td>
<td>9.11 +/- 0.75</td>
<td>0.002</td>
</tr>
<tr>
<td>25 OH VITAMIN D (NG/ML)</td>
<td>19.73 +/- 17.85</td>
<td>25.75 +/- 11.63</td>
<td>0.002</td>
</tr>
<tr>
<td>PTH (PG/ML)</td>
<td>39.31 +/- 40.14</td>
<td>33.94 +/- 22.95</td>
<td>0.902</td>
</tr>
</tbody>
</table>

The study showed significantly deficient Vitamin D levels in cases alongside with significantly higher phosphate levels and ALP levels than controls. The Calcium levels and PTH levels were not significantly different in both the groups.

**Graph no 1:** Showing distribution of cases and controls on the basis of Vitamin D levels. Vitamin D levels were significantly deficient (66.67%) in cases than in controls. Only 16.6% cases were having sufficient Vitamin D levels in comparison to controls (30%). The mean value of vitamin D levels in cases was (19.73 ± 17.85ng/ml), as compared to controls (25.75 ± 11.63ng/ml).
IV. Discussion

Our study showed that there was significant Vitamin D deficiency in cases as compared to controls, which is in concurrence with many earlier studies mentioned below in Table no 2.8,9,10,11,12.

Table no 2: Depicting studies showing status of Vitamin D in Beta Thalassemic Children

<table>
<thead>
<tr>
<th>STUDIES</th>
<th>DEFICIENT (%)</th>
<th>INSUFFICIENT (%)</th>
<th>P-VALUE</th>
</tr>
</thead>
<tbody>
<tr>
<td>PRESENT STUDY</td>
<td>66.67</td>
<td>15.00</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Fahim FM(2013)</td>
<td>37</td>
<td>54</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Safai F(2012)</td>
<td>45.5</td>
<td>24.7</td>
<td>&lt;0.002</td>
</tr>
<tr>
<td>Wood JG(2008)</td>
<td>54.16</td>
<td>41.16</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Isik P(2014)</td>
<td>78.2</td>
<td>-</td>
<td>&lt;0.002</td>
</tr>
<tr>
<td>Nakavachara(2013)</td>
<td>89.9</td>
<td>-</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Singh K(2012)</td>
<td>80.67</td>
<td>-</td>
<td>&lt;0.01</td>
</tr>
</tbody>
</table>

Low serum 25-OH Vitamin D levels can be attributed to malabsorption of Vitamin D as well as hepatic dysfunction, which also leads to defective hydroxylation of vitamin D resulting in its paucity. Some researchers have attributed the etiology of Vitamin D deficiency to hepatic iron overload. In our study, Vitamin D deficiency was recorded in more than 80% of cases. Multiple factors have been attributed to growth faltering in Thalassemia, some of which like Vitamin D deficiency can be easily monitored and corrected.

Table No 3: Showing Median Vitamin D levels and Parathyroid Hormone levels in cases and controls in present study:

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Case (Median)</th>
<th>Controls (Median)</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vitamin D (ng/ml)</td>
<td>12.85</td>
<td>24.6</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Parathyroid Hormone</td>
<td>39.31</td>
<td>33.94</td>
<td>0.902</td>
</tr>
</tbody>
</table>

There is gross deficiency of Vitamin D in cases. Serum PTH levels were not significantly different between cases (39.31 pg/ml) and controls (33.94 pg/ml). In different previous studies the incidence of hypoparathyroidism varies from 0% to 22.5% of patients, although overt hypoparathyroidism is very rare and even subtle abnormalities are not well established in these cases. Majority of cases of hypoparathyroidism in Beta-Thalassemic children were seen in second decade of life. Parathyroid hormone levels is chiefly regulated by alteration in calcium levels in the body along with Calcitonin. Vitamin D directly affects calcium absorption and its excretion. Hence, it is suggested that supplementation with Vitamin D and Calcium would greatly help in normalisation of function of parathyroid gland and serum parathyroid hormone levels.

In the present study, the serum level of calcium was found in eucalcmic range in both the groups. In literature, many studies have shown serum calcium level in thalassemic children to vary from hypocalcemia to hypercalcemia with no consensus. Normal serum calcium levels in this study can be explained, as in young children, during early stages of Vitamin D deficiency, decreased intestinal calcium absorption leads to moderate and/or intermittent increase of PTH and also stimulates the production of 1,25Dihydroxy Vitamin D that increases calcium absorption from the gut, and ensures maintenance of normal serum calcium concentration, important for adaptive stage.

The phosphate levels were found to be significantly high in cases (5.3 mg/dl) in comparison to controls (4.8 mg/dl) and these results were in agreement to various previous studies. ALP levels in our study were found statistically significantly high in cases than in controls. It basically represents the presence of high bone turnover rate in the cases.

V. Conclusion & Recommendations

We conclude that Vitamin D deficiency is significantly prevalent even among apparently healthy children in our country but it is far more in children affected by B-thalassemia, probably because of iron overload following repeated blood transfusions. Hence, it is suggested that Vitamin D supplementation in these children must be started early in life.

Due to very high prevalence of Vitamin D deficiency in these children, it would be a very cost effective therapy to supplement adequate vitamin D to all children with thalassemia major, even where the facilities for its estimation are not available. Therapy is relatively easier and with no adverse effects if instituted properly under medical supervision.

Supplementation with vitamin D in these children would also help in normalisation of various other growth markers such as calcium, phosphorous and ALP, as they are directly affected by vitamin D activity.
Assessment of Vitamin D levels and Parathyroid Hormone levels in children with Beta Thalassemia major, and to compare their respective values with age and sex matched controls.

We should try to screen all B-thalasemic children for parathyroid hormone abnormalities at regular intervals especially from the end of first decade of life, so as to detect early alterations, if any and treat the same.

References


Dr VINEET POPLI Corresponding Author “Assessment of Vitamin D levels and Parathyroid Hormone levels in children with Beta Thalassemia major, and to compare their respective values with age and sex matched controls.”IOSR Journal of Dental and Medical Sciences (IOSR-JDMS), vol. 17, no. 3, 2018, pp 60-63.