Study of Vitamin D Levels in Thalassemia Major Patients in Children

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Abstract

Introduction: Thalassemia is an inherited disorder of hemoglobin synthesis. Regular blood transfusions and chelation therapy have noticeably prolonged survival in thalassemic patients.[¹] 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 hypoparathyroidism.[²] The pattern of levels of vitamin D levels among the patients with thalassemia major undergoing repeated blood transfusions remain unexplored. Very few studies have been undertaken among Indian population.

Methodology: It is a prospective study and was conducted at St George hospital, Mumbai, on diagnosed patients of thalassemia major admitted to the pediatric wards. Duration of the study was 3 months and 36 patients were included.

Inclusion Criteria

1. All admitted patients of thalassemia major aged 12 years and below.

Exclusion Criteria

1. Chronic hemolytic anemia apart from thalassemia major
2. Those that was very sick
3. Those suffering from malnutrition
4. Those who were on supplementation of calcium, phosphorus and vitamin d.

Patients who were willing to participate and sign the inform consent were enrolled in the study. Serum 25 hydroxyvit D levels were done using CLIA.

Results: The mean age of the studied thalassemia patients was 8.76 ± 3.7 years with no gender preponderance. Mean (SD) Vitamin D levels was 16.26 ±8.75 and was found to be statistically significant (p<0.001).

Conclusion: It is evident from the present study that the levels of vitamin D are deficient among β-thalassemia major patients on repeated blood transfusion. The deficiencies may be due to iron overload or due to nutritional deficiency. Frequent monitoring and supplementation in deficient states is recommended.

Keywords: Beta Thalassemia major, Vitamin D levels.
Introduction
In India, Beta Thalassemia affects over 1 lakh people and more than 8000 thalassemic children are born every year.\(^1\) Thalassemia is a heterogeneous inherited disorder of hemoglobin synthesis due to mutations of the globin gene, leading to various degrees of quantitative defect in globin production and reduced synthesis or complete absence of one or more of the globin chains, resulting in ineffective erythropoiesis and anemia. Beta-thalassemia major (BTM) usually presents at 4 - 6 months of life, due to the protective effect of high hemoglobin F concentration at birth that slowly declines through the first year of life. The mainstay of treatment of severe β thalassemia is regular blood transfusion with an attempt to maintain hemoglobin levels greater than 10g/dl.

Inspite of optimal management, children with transfusion-dependent beta thalassemia have poor bone health.\(^2\) Osteoporosis is found in 40-80 % of well –treated thalassemic patients.\(^3-5\) The pathogenesis of low bone mass is multi-factorial and includes defective synthesis of 25 OH vitamin D (25OH D) and/or hypoparathyroidism, effect of iron chelators, nutritional deficiency, direct iron toxicity and progressive marrow expansion.\(^6-9\)

Materials and Methods
A prospective study was conducted in the department of pediatrics, St George hospital Mumbai. The study was conducted on diagnosed patients of thalassemia major admitted to the pediatric wards. Duration of the study was 3 months. Taking into consideration of availability of patients within data collection period, a total of 36 children, diagnosed with β thalassemia major were enrolled in the study.

All the necessary information regarding the study was explained to the parents and informed written consent was taken from the parents who were willing to participate in the study. After obtaining written informed consent in local vernacular language, the patients who were fulfilling the inclusion criteria were included in the study.

Inclusion Criteria
1. All admitted patients of thalassemia major aged 12 years and below.

Exclusion Criteria
1. Chronic hemolytic anemia apart from thalassemia major
2. Those who were very sick
3. Those suffering from malnutrition
4. Those who were on supplementation of calcium, phosphorus and vitamin D.

Serum 25 hydroxyvit D levels were done using CLIA (Chemiluminiscence immunoassay).

Statistical Analysis
All the data collected were entered in to a spread sheet on Microsoft office Excel Sheet and then transferred to SPSS IBM version 21.0 for analysis. Significance of p value was taken as p<0.001.

Results and Observation
The mean age of the studied thalassemia patients was 8.76 ± 3.7 years with no gender predilection. Mean (SD) Vitamin D levels was 16.26 ±8.75. As per Indian pediatric population, Vitamin D concentrations of >20 ng/mL (50 nmol/L) are considered as sufficient, between 12-20 ng/mL (30-50 nmol/L) as insufficient and <12 ng/mL (<30 nmol/L) as deficient \(^{15,16}\) as shown in figure 1 and table 1.

Table no. 1

<table>
<thead>
<tr>
<th>Range of Vitamin D levels(ng/dl)</th>
<th>Interpretation</th>
<th>Frequency (n=36)</th>
<th>Chi square</th>
<th>P value</th>
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</thead>
<tbody>
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<td>&lt;12</td>
<td>deficient</td>
<td>12</td>
<td>166</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>12–20</td>
<td>insufficient</td>
<td>16</td>
<td>.0384</td>
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</table>
Mean (SD) Vitamin D levels was 16.26 ±8.75. The cut off vitamin D deficiency is 20ng/ml. Similar lower Vitamin D deficiency was found in other studies as well. Fahim M et al in their study reported that vitamin D levels are 10.4±4.6mcg/dl.[10] In our study, it is found that 77.7 % patients had vitamin D levels lower than required, out of which 33 % had vitamin D in deficiency range and 44.4% in insufficiency range. This was found to be significant with p value <0.001. In the study conducted by Vogiatzi et al, it was seen that 12 % of thalassemia patients were Vitamin D deficient and 69.8 % had insufficient levels.

Several studies have reports low Vitamin D levels in thalassemia patients.[10-14] These were attributed to hepatic dysfunction, geographical attitude and dysfunctions of endocrine tissues.[12] Some researchers have attributed the etiology of Vitamin D deficiency to hepatic iron overload[9]. This shows that thalassemics are at a greater risk for vitamin D deficiency and hence require a greater need for Vitamin D supplementation.

Conclusion and Recommendations
We can conclude that the levels of vitamin D are deficient among β-thalassemia major patients on repeated blood transfusion. Hence, it is important to emphasize that treatment of thalassemia patients with aggressive nutritional support which include fortified cereals, fortified milk and supplementation with vitamin D are highly recommended. 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. We should try to screen all B-thalasemic children for parathyroid hormone abnormalities, calcium, and phosphorus levels as well.

References
2. NR Thiagarajan, Cg Delhi Kumar, Jayaparakash Sahoo And Sriram Krishnamurthy. Effect of Vitamin D and Calcium Supplementation on Bone Mineral Content in Children with Thalassemia. Indian Pediatrics VOLUME 56: APRIL 15, 2019


