### **Original Research Article**

DOI: http://dx.doi.org/10.18203/2349-3291.ijcp20190694

# Study of serum calcium, phosphorus and vitamin D status in multitransfused $\beta$ -thalassemia major children and adolescents of Jharkhand, India

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Received: 28 October 2018 Accepted: 13 December 2018

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#### **ABSTRACT**

**Background:** The pattern of levels of calcium, phosphorous and vitamin D levels among the patients with thalassemia major undergoing repeated blood transfusions remain unexplored. Only very few studies have been undertaken among Indian population. The present study was an attempt to determine the levels of calcium, phosphorous and vitamin D levels among thalassemia major patients undergoing repeated multiple transfusions.

**Methods:** In a prospective observational study, 65 patients suffering from  $\beta$ -thalassemia major, aged 2-18 years, having undergone regular blood transfusion and chelation therapy, were evaluated for the levels of serum calcium, phosphorus and vitamin D and the values were compared to the standard values of the same.

**Results:** The mean values of serum calcium  $(6.72\pm0.66)$ , phosphorous  $(5.51\pm1.07)$  and vitamin D  $(13.12\pm2.9)$  were significantly lower in our patients as compared to that of standard population values, the difference in each being statistically significant (p<0.05).

Conclusions: It is evident from the present study that the levels of calcium, phosphorous and vitamin D are deficient among  $\beta$ -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: Calcium, Hypoparathyroidism, Iron overload, Phosphorus, Thalassemia major, Vitamin D

#### INTRODUCTION

Beta thalassemia is one of the most common inherited single gene disorders caused by about 200 mutations in the beta globin genes. In beta thalassemia where there is no or reduced production of beta globin chains, the alpha chain production will continue to occur. This increased synthesis of alpha chains makes the developing erythrocytes more fragile leading to early damage, ineffective erythropoiesis and anemia. In southern asia, the prevalence of  $\beta$  thalassemia has been reported to be

from as low as 2% to as high as 28% in various studies.  $^{1\text{-}3}$  The mainstay of treatment of severe  $\beta$  thalassemia is regular blood transfusion with an attempt to maintain hemoglobin levels greater than  $10g/dl.~\beta\text{-}$  thalassemia major patients present within the first year of their life and require regular, lifelong blood transfusions for correction of anemia. These frequent transfusions lead to iron overload which itself is fatal by the second decade of life. With the advent of chelation therapy, the survival of thalassemia major patients has increased, and they are entering even into third and fourth decades of life.

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Inspite of chelation therapy, iron overload related complications like endocrinopathies are still occurring. Thus, there might be other mechanisms too responsible for these problems. Common endocrine disorders reported in  $\beta$ -thalassemia major patients are short stature, hypogonadism, hypoparathyroidism, hypothyroidism and diabetes mellitus. Many studies have been done on endocrine disorders including hypoparathyroidism in thalassemia patients and frequency reported varies from center to center, but largest study so far done included 1861 patients from 25 centers and showed that 3.6%  $\beta$ -thalassemia major patients had hypoparathyroidism. Limited studies have also shown that supplementation with vitamin D and calcium improves serum calcium status.  $^4$ 

The pattern of levels of calcium, phosphorous and vitamin D levels among the patients with thalassemia major undergoing repeated blood transfusions remain unexplored. Very few studies have been undertaken among Indian population.

The present study was an attempt to determine the levels of calcium, phosphorous and vitamin D levels among thalassemia major patients undergoing repeated multiple transfusions.

#### **METHODS**

The study was carried out as a prospective observational study conducted in department of pediatrics, Rajendra Institute of Medical Sciences, Ranchi, Jharkhand, India from April 2016 to September 2017. Taking into consideration of availability of patients within data collection period, a total of 65 children and adolescent with diagnosed with  $\beta$  thalassemia major were enrolled in the study. As the study participants who were admitted for blood transfusion between April 2016 to September 2017 were included, a consecutive sampling method was followed.

All the necessary information regarding the study was explained to the parents of infants. 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

- All children and adolescent between age 2 and 16 years of age
- Diagnosed as β-thalassemia major by HPLC/ hemoglobin electrophoresis
- Those who had >20 packed cell transfusions
- Those who were on regular iron chelation therapy
- Those children and adolescent who were admitted for blood transfusion between April 2016 and September 2017.

#### Exclusion criteria

- Age <2 years or >16 years
- Chronic hemolytic anaemia apart from β-thalassemia major
- Poor compliance to packed cell transfusion and iron chelation therapy
- Those who were very sick patients
- Those who were suffering from malnutrition
- On any calcium, phosphorus or vitamin-D containing preparations.

Serum calcium will be estimated using Arsenio iii complex method (spectrophotometry). Serum phosphorus by molybdate method (spectrophotometry). Serum levels of vitamin D by CMIA (chemiluminescent microparticle immunoassay).

#### Statically analysis

All the data collected were entered in to a spread sheet on Microsoft office Excel Sheet and later transferred to SPSS IBM version 21.0 for analysis. Data analysis was done with Statistical Package for Social Sciences (SPSS IBM) version 21.0. Students t-test for comparison of means was used. Significance of p value was taken as p<0.05.

#### **RESULTS**

Most of the participants were of the age 6-10 years (50.8%) and majority were male (61.5%). Mean (SD) of calcium was  $(6.72\pm0.66)$ , mean phosphorous value is  $(5.51\pm1.07)$  respectively.

Table 1: Age group of study participants (n=65).

Age group (in years)	Number of study participants	Percentage
2-5	25	38.5
6-10	33	50.8
11-16	7	10.8
Total	65	100

Mean (SD) Vitamin D levels was  $(13.12\pm2.9)$ . The cut off vitamin D deficiency is 30 ng/ml. On comparing serum calcium and phosphorus levels of present study participants with standard values  $(10.2\pm1.8)$  mg/dl,  $(3.2\pm0.4)$  mg/dl respectively for children in India, results obtained are as shown below.

**Table 2: Gender distribution of study participants.** 

Gender of study participants	Number of study participants	Percentage
Male	40	61.5
Female	25	38.5
Total	65	100

Table 3: Mean values of serum calcium, phosphorus and vitamin D.

Serum values	Mean±SD	Standard values±SD
Total Calcium (gm/dl)	6.72±0.66	10.2±1.8
Phosphorous (gm/dl)	5.51±1.07	3.2±0.4
Vitamin D (ng/ml)	13.12±2.90	24.2±4.1

Likewise, authors compared vitamin D levels of present study participants with standard values of vitamin D (24.2±4.1) in india among pediatric population.

Table 4: Comparison of mean calcium, phosphorus and vitamin d levels with standard values.

Parameter	Calcium levels	Phosphorous levels	Vitamin D levels
Difference	3.510	2.000	11.170
Standard error	0.233	0.146	0.544
95% CI	3.0521-3.967	1.285-4.567	10.10-12.2
T-statistic	15.041	13.726	20.52
DF	1058	1058	558
P value	P<0.0001	P < 0.0001	P < 0.0001

Hence, authors find that the alteration in serum levels of calcium, phosphorus and vitamin D in multi-transfused  $\beta$  Thalassemia major children and adolescents is statistically significant when compared with standard values.

#### **DISCUSSION**

Mean (SD) of calcium was 6.72±0.66, mean phosphorous value is 5.51±1.07. In a previous study done reported that the study results were frequency of hypocalcemia was 49% in their study. Hyperphosphatemia was associated with 53% of hypocalcemia patients. Mean serum calcium was 8.46±0.94mg/dl while mean phosphate level was 5.33±0.77mg/dl in the subjects. <sup>1</sup>

Low serum calcium is very prevalent in transfusion-dependent beta thalassemia major patients in our set up possibly due to poor chelation as was confirmed by present study where 49% of patients had hypocalcemia. Lower calcium and higher phosphate levels was also reported from another study.<sup>5</sup> Similar value of serum calcium (6.6±1.2mg/dl) was found in a study done by Fahim M et al.<sup>6</sup>

In a study done by Chakandi T et al, reported that among patients with thalassemia on repeated transfusion presented with low calcium, high phosphorous due to hypoparathyroidism.<sup>7</sup>

Mean (SD) vitamin D levels was 13.12±2.90. The cut off of vitamin D deficiency is 30ng/ml. The mean (SD)

vitamin D level was lower than the cut off taken. Similar lower Vitamin D deficiency was found in other studies as well. This is similar to a study finding of Fahim M et al, who reported that vitamin D levels are 10.4±4.6mcg/dl.<sup>7</sup>

In a study done by Safari F et al, found that vitamin D deficiency and vitamin D insufficiency were observed in 45.5% and 24.7% of patients, respectively. They also reported that nearly 80% of patients had low bone mineral density.<sup>8</sup>

A review done reported that Vitamin D deficiency and insufficiency is found to be high in thalassemic patients in many countries despite the presence of good sunshine and routine prescription of 400-1,000IU vitamin D per day.<sup>9</sup>

#### **CONCLUSION**

It is evident from the present study that the levels of calcium, phosphorous and vitamin D are deficient among  $\beta$ -thalassemia major patients on repeated blood transfusion.

Hence, frequent monitoring of serum levels of calcium, phosphorous and vitamin D levels has to be done for all the  $\beta$ -thalassemia major patients receiving repeated multiple transfusion along with regular supplementation of calcium and vitamin D in patients who are found to be deficient. Monitoring of PTH for screening of hypoparathyroidism has also to be undertaken for patients with thalassemia receiving repeated multiple transfusions.

Funding: No funding sources Conflict of interest: None declared Ethical approval: Not required

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Cite this article as: Ahmed Z, Pushpanjali, Kausar MS, Sinha D. Study of serum calcium, phosphorus and vitamin D status in multitransfused  $\beta$ -thalassemia major children and adolescents of Jharkhand, India. Int J Contemp Pediatr 2019;6:598-601.