VITAMIN D STATUS IN CHILDREN WITH THALASSAEMIA IN NORTH EAST INDIA

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ABSTRACT

BACKGROUND

The aim of the study was to determine the frequency of vitamin D deficiency and insufficiency in children with thalassaemia who were on regular blood transfusion.

MATERIALS AND METHODS

Total 25 children were included in this retrospective study in the age group of 2-14 years with confirmed diagnosis of thalassaemia syndrome. They were on regular blood transfusion every 3-4 weeks and they had serum ferritin >1000 µg/L irrespective of chelation therapy. Serum level of calcium, phosphorous, alkaline phosphatase, serum ferritin and 25OH vitamin D were estimated.

RESULTS

Out of 25 patients, 6 (24%) showed sufficient amount of vitamin D, 6 (24%) showed insufficiency, 10 (40%) showed deficiency and 3 (12%) showed severe deficiency. Children with vitamin D deficiency showed high level of serum ferritin level. Severe vitamin D deficiency was seen when number of transfusions were >20.14 children showed abnormal vitamin D level when their serum ferritin level was between 1000-2000 ng/dL. There was no association between use of iron-chelating agent, duration of their use and nutritional status with vitamin D level.

CONCLUSION

In regularly transfused thalassaemic children, vitamin D insufficiency and deficiency were common and they need frequent monitoring for early detection and management.

KEYWORDS

Vitamin D, Calcium, Phosphorous, Thalassaemia, Paediatrics.

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BACKGROUND

Vitamin D is essential for absorption of dietary calcium and phosphorous, which in turn promotes growth and mineralisation of bone.[1] Those children with thalassaemia are prone to develop bone disease, which causes high morbidity in them. They develop osteoporosis, rickets, scoliosis, spinal deformities, nerve compression and fractures.[2,3] Thalassaemia are a group of hereditary disorders of Haemoglobin (Hb) where there is quantitative and qualitative abnormal production or structure of Hb molecule leading to anaemia.[4] The clinical spectrum varies from asymptomatic carrier state to more serious state, which require regular blood transfusions.[5]

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As these children need regular blood transfusion, they are susceptible to iron overload, which leads to impaired calcium homeostasis in these children. Because of this, they develop both defective synthesis of 25OH vitamin D (25OHD) and/or hypoparathyroidism, which negatively affect their bone metabolism.[6] Apart from musculoskeletal problems like osteoporosis, pathological fractures, muscle weakness, vitamin D deficiency may lead to diabetes, adrenal insufficiency, allergy and myelofibrosis.[7,8,9] In addition to the disease process, high dose of iron chelation therapy to overcome iron overload may also contribute to osteopenia and osteoporosis.[10]

Prevalence of vitamin D deficiency is reported to be high in these children. In North American, Thalassaemia Clinical Research Network found that 12.8% children out of 361 patients with thalassaemia had 25OHD concentration less than 27 nmol/L and 82% had less than 75 nmol/L regardless of thalassaemia syndrome.[11] Singh K et al in their study from North India showed 80% prevalence of vitamin D deficiency in thalassaemia patients.[12] As many cells have vitamin D receptors, its deficiency leads to several clinical and biochemical abnormalities. So, it is important to measure the vitamin D level in regularly transfused children with

thalassaemia and in case of any abnormalities in its level, they need supplementation of vitamin D.[13]

AIMS AND OBJECTIVES

The aim of this retrospective study was to determine the status of vitamin D level in children with thalassaemia who are on regular blood transfusion.

MATERIALS AND METHODS

This retrospective study was done at Department of Paediatrics, Jorhat Medical College and Hospital. Those children with confirmed diagnosis of thalassaemia syndrome (including beta-thalassaemia, E-beta thalassaemia, thalassaemia intermedia) between the age group of 2-14 years attending the thalassaemia clinic under Department of Paediatrics for regular blood transfusion at an interval of 3-4 weeks interval were included using inclusion and exclusion criteria.

As a part of standard treatment protocol calcium, phosphorus, alkaline phosphatase, 25OH vitamin D, serum ferritin and thyroid function test were routinely done in these children on regular blood transfusions in the thalassaemia clinic. Nutritional statuses of these children were recorded using weight for age, weight for height and body mass index in the clinic.

Inclusion Criteria

1. Children with serum ferritin >1000 ng/dL, irrespective of chelation therapy.
2. Children with >10 blood transfusions.

Exclusion Criteria

1. Children on antiepileptic drugs, oral calcium and vitamin D supplementation.
2. Children with infection.
3. Children with chronic use of systemic corticosteroids.

Recorded data from thalassaemia clinic regarding age, gender, duration of diagnosis, number of blood transfusion since diagnosis, duration of chelation therapy, if any, and serum level of calcium, phosphorous, alkaline phosphatase, ferritin and 25OH vitamin D were analysed in this study. Recorded nutritional statuses of the cases were assessed using WHO reference chart.

Vitamin D was estimated using ELISA technique, while serum Ca, phosphorus and alkaline phosphatase were estimated by Arsenazo III method, photometric UV method and orthophosphoric-monoester phosphohydrolase method, respectively. Serum ferritin was estimated by enzyme-linked fluorescent immunoassay.

Serum level of 25 (OH) D<10 ng/dL is considered as severe deficiency. The values between 10-19.99 ng/dL will be accepted as deficiency and levels between 20 and 29.99 ng/dL as insufficiency.[7] Nutritional status of the cases were assessed using weight for height in children less than 6 years of age and Body Mass Index (BMI) in children more than 6 years of age and interpretation was done using WHO reference charts.

Data were analysed by MS Excel and SPSS software version 23. We used paired t-test, unpaired t-test and ANOVA test to find out the significance test for normally distributed variables. Categorical data were analysed using chi-square test. P value <0.05 was considered to be statistically significant for 95% confidence interval.

RESULTS

Total 25 regularly transfused children in the age group between 2-14 years were included out of which 10 were girls and 15 were boys in different age groups. Table 1 shows the age and gender wise distribution of vitamin D status among these children, which was statistically significant (p <0.0224). 6 (24%) children showed sufficient amount of vitamin D level, 6 (24%) children showed insufficiency, 10 (40%) showed deficiency, while 3 (12%) children showed severe deficiency of vitamin D. Deficiency of vitamin D was maximum in the age group of 6-10 years.

Table 2 shows the serum calcium, phosphorous, alkaline phosphatase and serum ferritin in relation to vitamin D level. Serum calcium and phosphorous showed decreasing trend with increased severity of vitamin D deficiency. Those children with vitamin D deficiency showed high level of serum ferritin level (2002.60±959.72) compared to those with sufficient level of vitamin D (1366.98±208.67).

Table 3 shows the various parameters in relation to serum ferritin level. Those children with serum ferritin more than 2000 ng/dL, they had low level of serum calcium, phosphorous and alkaline phosphatase level compared to those with ferritin level between 1000-2000 ng/dL. Phosphorous level showed statistically significant difference between the two group (p<0.0393). Those with serum ferritin between 1000-2000 ng/dL, total 14 children showed abnormal vitamin D level, while 5 children showed abnormal vitamin D level when ferritin level was more than 2000 ng/dL, which was statistically significant (p<0.0345).

Table 4 shows that the serum calcium level decreased with increasing number of transfusion while phosphorous and alkaline phosphatase showed increasing trend with increased number of transfusion, although they were not statistically significant. Out of 16 children who received more than 20 blood transfusions, 10 children showed abnormal vitamin D level. 7 children out of 9 children showed abnormal vitamin D level when the number of transfusion was 10-20. Three children showed severe deficiency in this study and these 3 children were in the more than 20 blood transfusion received group.

Table 5 shows the vitamin D status in relation to chelation therapy. Total 16 children received chelation therapy. 7 children showed abnormal level of vitamin D when duration of chelation was between 6 months to 2 years while 4 children showed abnormal vitamin D level when duration of chelation was less than 6 months. 8 children who received no chelation therapy showed abnormal level.

Table 6 shows the various parameters in relation to nutritional status. Out of 9 children in malnourished group, 6 children showed abnormal vitamin D level and 12 children out of 16 with normal nutrition showed abnormal level,

which was not statistically significant. Calcium level in 6-14 years age group showed statistically significant difference between malnourished group and those with normal nutrition.

Vitamin D Status	2-5 Years		6-10 Years		11-15 Years		Total (25)	P Value
	Males	Females	Males	Females	Males	Females		
Sufficiency	3		2	1			6	0.0224 <0.05
Insufficiency	2	1	2		1		6	
Deficiency		1	4	4		1	10	
Severe Deficiency			1			2	3	

Table 1. Age and Gender Wise Status of Vitamin D

Parameters	Vitamin D Sufficient (6)	Vitamin D Insufficiency (6)	Vitamin D Deficiency (10)	Severe Deficiency of Vitamin D(3)	P Value
Calcium	8.90±0.296	8.81±0.117	8.78±0.181	8.87±0.115	0.6821
Phosphorous	6.68±1.313	5.42±0.563	5.24±1.225	5.33±1.504	0.0925
Alkaline phosphatase	519±128.89	447±134.08	363.90±129.20	429.33±85.42	0.1546
Serum ferritin level	1366.98±208.67	1507.48±191.46	2002.60±959.72	1725.73±751.96	0.0563

Table 2. Different Parameters According to Vitamin D Status

Parameters	Serum Ferritin Level		
	1000-2000 (20)	>2000 (5)	P value
Calcium	8.84±0.214	8.76±0.114	0.4324
Phosphorous	5.85±1.003	4.58±1.73	0.0393
Alkaline phosphatase	445.40±140.49	362.60±82.65	0.2231
Vitamin D level			
Sufficient (6)	6		0.0345
Insufficient (6)	6		
Deficiency (10)	6	4	
Severe deficiency (3)	2	1	

Table 3. Various Parameters and Vitamin D Status According to Serum Ferritin Level

Parameters	10-20 (9)	>20 (16)	P Value
Calcium	8.84±0.174	8.831 ±0.212	0.9148
Phosphorous	5.49±0.59	5.66±1.484	0.7467
Alkaline phosphatise	431.11±142.73	448.19±122.57	0.7552
Vitamin D			
-Sufficiency	2	6	0.1655
-Insufficiency	3	3	
-Deficiency	4	4	
-Severe deficiency		3	

Table 4. Various Parameters and Vitamin D Status According to Number of Blood Transfusion

Parameters	On Chelation (16)			No Chelation (9)	P Value
	<6 Months	6 Months to 2 Years	P value		0.2110
Vitamin D			0.166		
-Sufficient	1	4		1	
-Insufficient	2	1		3	
-Deficiency	1	4		5	
-Severe deficiency	1	2			

Table 5. Vitamin D Status According to Chelation or Not

Vitamin D Level	Weight for Height			BMI (6-14 Years)		
	Malnutrition (2)	Normal (5)	P Value	Malnutrition (7)	Normal (11)	P Value
Sufficient	1	3	0.3599	2	1	0.3437
Insufficient		2		1	2	
Deficiency	1			3	6	
Severe Deficiency				1	2	

Table 6. Vitamin D Level according to the Nutritional Status

DISCUSSION

In our study, we found that out of 25 children, 19 children showed abnormal level of vitamin D level, out of which, 6 (24%) children showed insufficiency, 10 (40%) children showed deficiency, while 3 (12%) children showed severe deficiency. Maximum deficiency was noted in the age group of 6-10 years. Albayrak C et al reported that 36% children with severe deficiency, 43% with deficiency and 14% with insufficient amount of vitamin D level in their study.[13] Fahim FM et al found that 37% thalassaemic children suffered from vitamin D deficiency.[14] Malabsorption of vitamin D and inadequate nutrient intake may contribute to the low level of vitamin D in thalassaemic children.[15]

Those children with vitamin D deficiency showed high level of serum ferritin level than those with sufficient level of vitamin D, which was similar to the finding of Albayrak C et al.[13] We found a statistically significant correlation between increased level of serum ferritin and abnormal vitamin D level. Similar finding was reported by Zoga J et al and Tantawy AA et al.[16,17] 10 children showed abnormal vitamin D level when number of transfusion was more than 20. Out of these 10 children, 3 showed severe deficiency. This may result from increased blood transfusions in them leading to iron over load, which in turn leads to defective hydroxylation of vitamin D in liver resulting in low level of vitamin D level.[14,18] Iron deposition may lead to skin hyperpigmentation and dark colour skin decreases vitamin D conversion by sun light.[7,8]

There was no association between use of iron chelating agent and duration of their use with vitamin D ($p>0.2$) in our study. Zoga J et al found similar findings in their study.[16] On the other hand, Perrotta S et al reported that high dose of iron chelation therapy with deferoxamine leads to osteopenia and osteoporosis as it causes deficiency of vitamins and minerals like vitamin D and zinc, which affect the bone health.[10,19]

There was no statistically significant relation between nutritional status and vitamin D level in our study. Other contributing factor like iron overload as indicated by high serum ferritin level because of frequent blood transfusion may contribute to the abnormal level of vitamin D in the study group.

CONCLUSIONS

The thalassaemic children suffer from significant bone disease because of increased frequency of vitamin D deficiency and insufficiency in them. Early detection and treatment of vitamin D deficiency in thalassaemic children with nutritional support and supplementation with vitamin D will help to prevent such complication in them. To achieve this, they need regular monitoring of vitamin D level particularly those with high serum ferritin level and those with high number of blood transfusions.

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