
Review Article

Study of vitamin D status and bone age in children with Thalassemia major

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ABSTRACT:

Objectives: To study Vitamin D levels and bone age estimation in patients with thalassemia major and to correlate various factors associated with short stature, Vitamin D deficiency and bone age difference.

Study Design: Prospective observational study

Setting: Thalassemia clinic, Civil hospital, Ahmedabad

Subjects and intervention: Total 84 patients with Beta-thalassemia major less than 12 years of age during 1 month period were included after taking informed consent.

Study period: 15 October 2016 to 15 November 2016

Results: Out of 84 patients 34 patients had Vitamin D deficiency (<20ng/ml), 34 patients had short stature and 24 patients with bone age >36 months had age >10 years. Vitamin D levels <30ng/ml is associated with ferritin level >2500(mcg/l)(OR=2.23 p=0.02 95%CI). Age >10 year (OR=7.7 P=0.0001 95%CI) and ferritin >2500mcg/l (OR=1.9 P=0.1 95%CI) are associated with bone age difference >36 months. Increased S.ALP (OR=1.1 P=0.02 95%CI) and ferritin levels >2500 mcg/l (OR:3.6 P=0.0056 95% CI) are associated with short stature.

Conclusion: Vitamin D and calcium supplementation along with disciplined transfusion and chelation regimen can likely prevent or delay late complications like short stature, osteoporosis in thalassemia patients.

Key words: Thalassemia, Vitamin D, Bone age, Ferritin

INTRODUCTION:

Thalassemia is a disease of the blood in which there is increased destruction (hemolysis) of the red cells. Thalassemia major is severe form in which the patient needs regular blood transfusions in order to survive while thalassemia minor an asymptomatic carrier state with patients of thalassemia intermedia in between. [1]

Certain communities in India, like Punjabis, Gujarati, Sindhis and Bengalis, are more commonly affected with beta thalassemia, the incidence varying from 1 to 17% [2].

Estimation that the prevalence of pathological hemoglobinopathies in India is 1.2/1,000 live births [3], and with approximately 27 million births per year [4] this would suggest the annual birth of 32,400 babies with a serious hemoglobin disorder Vitamin D deficiency and bone age difference frequently present in children with thalassemia major despite regular multiple blood transfusions and optimal chelation. There is a scarcity of Indian studies in children <12 years of age regarding vitamin D levels and bone age in Thalassemia major.

METHODOLOGY:

This prospective observational study was conducted at the Pediatric Thalassemia Clinic of Civil Hospital Ahmedabad during 15 October 2016 to 15 November 2016. The inclusion criteria were Patients with thalassemia major less than 12 years of age and patients receiving regular blood transfusion and chelation. We excluded patients >12 years of age. We performed physical examination, serum ferritin measurement, and bone age examination. A child was diagnosed as short stature if the height was below third percentile on National Center for Chronic Disease Prevention and Health Promotion (CDC) 2000 curve. [5] Normal level of vitamin D is defined as a 25-OH Vit D concentration greater than 30 ng/mL (75 nmol/L). Vitamin D insufficiency is defined as a 25-OH Vit D concentration of 20-30 ng/mL (50-75 nmol/L). Vitamin D deficiency is defined as a 25-OH Vit D level less than 20 ng/mL (50 nmol/L). Serum ferritin level was examined by ECLIA methods. Bone age was reviewed from hand radiograph (including wrist), based on Greulich and Pyle's Radiographic Atlas of Skeletal Development. [6] The chronological age was subtracted with the bone age result to get the bone age difference. The bone age difference was then classified into two groups: >36 months and <36 months. The

association between each variable was analyzed with odd's ratio.

RESULTS:

Out of total 84 patients 40 (47%) were male and 44 (52%) were female. Mean age of starting blood transfusion was 13.5± 6(months),mean age of starting of iron chelation therapy was 4.5± 3.2(years),mean pretransfusion Hb in last year was 9.3±2.8(g/dl),mean Ferritin levels was 2486±1856 (µg/l) and mean total years of blood transfusion were 6.4±3.4. . Out of 84 patients 24 were in < 5 year age group,24 patients in 5-10 year age group while 38 patients in >10 year age group. 12(14%) of our patients had normal (>30ng/ml) Vitamin D 34(40%) had Vitamin D deficiency(<20 ng/ml) and the rest 38(48%) had vitamin D insufficiency(20-30ng/ml).

Table 1: Vitamin D and S.ferritin levels

	Vitamin D deficiency /insufficiency	Normal vitamin D levels	Total
Ferritin >2500	38	4	42
Ferritin <2500	34	8	42
Total	72	12	84

Out of 72 patients with Vitamin D <30ng/ml 38(52%) have ferritin >2500(µg/l) (OR=2.23 P=0.220 95%CI) and 15(35%) have age <5 years (OR=0.18 P=0.01 95%CI).

Table 2:Bone age levels and ferritin

	Bone age difference >36 months	Bone age difference <36 months	Total
Ferritin >2500	24	17	41
Ferritin <2500	13	18	31
	37	35	72

From 72(86%) patients with bone age deficit , 34(44%) had bone age difference >36 months from that 28(75%) were >10 years of age.(OR=4.5 P=0.001 95%CI)and 24(64%) patients have ferritin >2500(µg/l)(OR=1.9 P= 0.1 95%CI).

Table 3: Complication and age wise distribution.

Complication	Prevalence	<5 year	5-10 year	>10year
Short stature	34	6	18	10
Vitamin D deficiency/insufficiency	72	19	11	4
Bone age difference >36 months	37	3	6	28

Table 4: Short stature and vitamin D

	Short stature	Normal stature	Total
Vitamin D deficiency	20	14	34
Normal vitamin D levels	14	36	50
Total	34	50	84

Out of 34(40%) patients with short stature 20(58%) had vitamin D deficiency(OR:3.6 P=0.0056

95% CI) and 12(35%) has increased alkaline phosphatase (OR: 1.1 P=0.7 95%CI).

High mean ferritin levels, Mean age at iron chelation started, and total years of blood transfusion

correlated significantly with Short stature & bone age difference >36 months.

DISCUSSION:

Out of 84 patients 34 patients had Vitamin D deficiency(<20ng/ml), 34 patients had short stature and 24 patients with bone age >36 months had age>10 years.

Vitamin D levels <30ng/ml is associated with ferritin level >2500(mcg/l)(OR=2.23 p=0.02 95%CI)

Age>10 year(OR=7.7 P=0.0001 95%CI) and ferritin >2500mcg/l (OR=1.9 P=0.1 95%CI)are associated with bone age difference>36 months.

Increased S.ALP(OR=1.1 P=0.02 95%CI) and ferritin levels>2500 mcg/l (OR:3.6 P=0.0056 95% CI)are associated with short stature.

High mean ferritin levels,High mean age at iron chelation started and total years of blood transfusion correlated significantly with short stature and bone age difference >36 months.

Vitamin D deficiency with increased S.ALP is more prevalent in >10 years age group where as Vitamin D insufficiency with hypocalcaemia present more in 5-10 year age group.Increased alkaline phosphatase and Hypocalcaemia can be used to predict Vitamin D deficiency in centers where tests for vitamin D can't be done.Short stature, Vitamin D deficiency and bone age difference known to have multiple causes. Evaluating and Excluding all those was not possible.Most patients were on Calcium supplementation. So actual deficiency can be greater.There are several factors that influences serum ferritin level, such as acute infection due to bacterial or virus, or vitamin C deficiency. More iron overload leads to more severe bone disturbance. Other studies also found that bone age disturbance in patients with thalassemia is caused by iron overload. [7] Study that observed the association between serum ferritin level and growth retardation in thalassemic patients showed that mean serum ferritin level in group with short stature is higher than in those with normal stature. [8] Other studies showed Subjects with

bone age difference <36 months mostly had serum ferritin level <5,000 ng/dL, while most subjects with bone age difference >36 months had serum ferritin level =5,000 ng/dL. [9]

CONCLUSION:

Vitamin D and calcium supplementation along with disciplined transfusion and chelation regimen can likely prevent or delay late complications like short stature, osteoporosis in thalassemia patients

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