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Assessment of Vitamin D Status and Growth Parameters in Thalassemia Major Patients

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Abstract:
Background: *Vitamin D deficiency and insufficiency has been frequently reported in thalassemic patients in many countries despite the presence of good sunshine. Adequate circulating level of vitamin D is essential for optimal skeletal growth and reducing fracture risk.*
Objective: *To assess Vitamin D, Calcium, Phosphorus status and growth parameters in thalassemia major patients*
Methodology: *This study, a hospital based case control study was conducted from January 2016 to December 2016 in Department of Paediatrics and Neonatology, Rajendra Institute of Medical Sciences, Ranchi. In this study, 60 patients of beta thalassemia major (aged from 8 months to 12 years) were compared with 60 sex and age matched children serving as control group. Anthropometric measurement, serum level of calcium, phosphorus and vitamin D (25 hydroxy cholecalciferol) were estimated for all patients & controls.*
Results: *25 hydroxy vitamin D deficiency was present in 82% of the patients and in 47% of the controls. Difference in mean vitamin D levels between cases and controls was statistically significant ($p<0.05$). Weight and body mass index were also significantly lower ($p<0.05$) in cases.*
Conclusion: *Thalassemia is associated with increased prevalence of 25 hydroxy vitamin D deficiency which may be responsible for poor growth and quality of life in these children. Monitoring and maintaining normal serum level of 25-OH vitamin D through oral intake of vitamin D and early correction of Vitamin D deficiency by oral or parenteral use of vitamin D may significantly improve bone mineral deposition and improved quality of life in these children.*
Keywords: *Thalassemia, 25 hydroxy vitamin D, Calcium, Growth*

I. Introduction

Thalassemias are the most common genetic disorder worldwide. In India, over 40 million people carry genes for beta thalassemia.[1] The thalassemias are heterogeneous group of disorders with genetically determined reduction in rate of synthesis of one or more types of globin chains of haemoglobin (alpha or beta chains).[2] The high mortality and morbidity in patients of thalassemia is the consequence of iron overload. Iron overload occurs mainly due to repeated blood transfusions and other factors other factors like increased gastrointestinal absorption, ineffective erythropoiesis, lack of physiologic mechanism to excrete excess iron.

The survival of patients with thalassemia major has progressively improved with advances in therapy; however osteoporosis and cardiac dysfunction still remain frequent complications. Adequate circulating levels of vitamin D are essential for optimal skeletal health and reducing fracture risk. Vitamin D is critical for calcium homeostasis and for mineralization of the skeleton, especially during periods of rapid growth, namely infantile and pubertal growth periods.

Vitamin D is transported to the liver and hydroxylated to 25-OH vitamin D, additional hydroxylation to 1,25 dihydroxy vitamin D3 takes place in the kidney. The major circulating metabolite of vitamin D is serum 25-OH vitamin D3[3]. It is the best indicator of vitamin D status and reflects levels from dietary intake and synthesis in the skin[4]. Levels 20 ng/ml are generally considered deficient; levels 21-29 ng/ml are considered insufficient.[5] Both defective synthesis of 25-OH vitamin D and/or hypoparathyroidism have been described in thalassemic patients and negatively affect their bone metabolism and optimal growth.[6]

II. Methodology

This case control study was carried out after obtaining clearance from the ethical committee of the institute. An informed written consent was taken from all the patients and controls prior to the study and they were briefed about the study in the language they understood. This study included 60 confirmed cases of thalassemia diagnosed on the basis of HPLC (High Performance Liquid Chromatography) of age group 8 months to 12 years attending inpatient and outpatient ward, Department of Paediatrics and Neonatology, Rajendra Institute of Medical Sciences, Ranchi, during the period of January 2016 to December 2016 were

randomly selected. Cases with other concomitant disease affecting vitamin D levels and calcium metabolism e.g. chronic kidney disease, celiac disease, protein energy malnutrition grade 3 and 4, chronic liver disease were excluded from the study. 60 healthy children with comparable age and sex were included to serve as control group. All cases and controls were not receiving calcium and vitamin D containing preparations. Detailed history and thorough clinical examination was done for each case and control included in the study. Anthropometric measurements of patients and controls included age, sex, weight, height and Z score were recorded. Body mass index (BMI) was calculated as kg/m2 (Normal BMI = 18.5–24.9, underweight = BMI <18.5 and Overweight BMI = 25–29). Weight was measured in kg (to the nearest 100 grams) using an electronic digital scale. Height was measured in cm (measured to the nearest mm). Laboratory tests included Serum calcium, phosphorus, 25-OH vitamin D level estimation done by chemiluminescence assay. Normal level of vitamin D is defined as a 25-OH Vit D concentration of >30 ng/mL. Vitamin D insufficiency is defined as a 25-OH Vit D concentration of 20-30 ng/mL. Vitamin D deficiency is defined as a 25-OH Vit D level <20 ng/mL. Statistical Package for Social Sciences (SPSS) program version 20 was used for data analysis. P value of 0.05 or less was considered significant.

III. Result

Demographic variables: In this study, out of 60 thalassemia patients, 42 were males and 18 females. The mean age of in this group was 8.43 + 3.72. In the control group, 42 males and 18 females were studied. The mean age in control group was 8.27 + 4.14.

The mean height of cases and controls was 118.41 ± 35.176 cm and 126.57 ± 29.133 cm respectively. Difference was statistically not significant (p>0.05). There was statistically significant difference (P<0.05) between the mean weight of cases (21.46 + 13.85) kg and controls (28.57 + 12.66) kg. Also there was significant difference (P<0.05) between the mean BMI of cases (16.37 + 1.75) kg/m^2 and controls (19.66 +1.23) kg/m^2.

TABLE 1: Demographic Parameters in the Thalassemia Patients and Controls

Variable	Cases	Controls	Significance
Age (years)	8.43 + 3.72	8.27 + 4.14	P value >0.05
Height (cm)	118.41 ± 35.176	126.57 ± 29.133	P value >0.05
Weight (kg)	21.46 + 13.85	28.57 + 12.66	P value <0.05
BMI (kg/m^2)	16.37 + 1.75	19.66 +1.23	P value <0.05

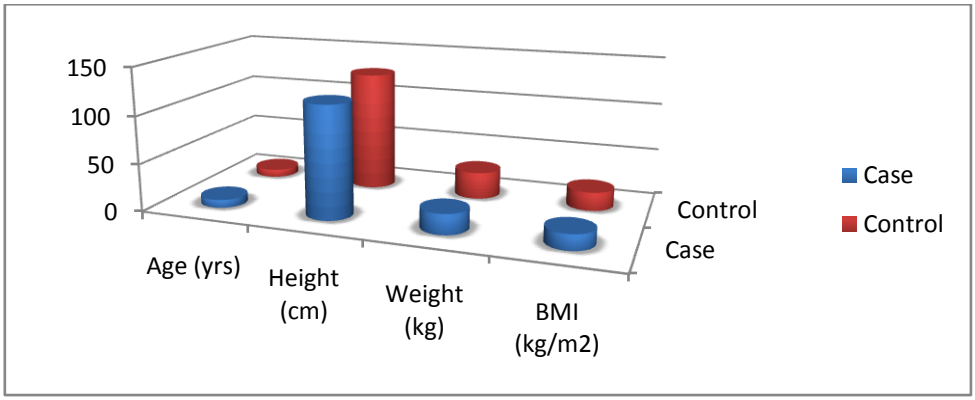

FIG 1: Demographic Variables in cases and controls

Biochemical parameters: The mean level of serum Calcium in cases and controls was 8.2 + 1.7 mg/dl and 8.7 + 2.3 mg/dl respectively. Difference was statistically not significant (P value>0.05). There was no statistically significant difference (P> 0.05) in mean level of serum phosphorus of cases (4.8 + 0.9) mg/dl and controls (4.5 + 0.7) mg/dl. There was significant difference (P<0.05) in the mean level of 25- OH Vitamin D in cases (12.3 + 7.8) ng/ml and controls (32.4+ 10.3) ng/ml. 41% of the thalassemia patients had Vitamin D deficiency (25- OH Vit D< 20 ng/ml) as compared to 19% in controls. 46% of cases were found to be Vitamin D deficient (25- OH Vit D = 20-30 ng/ml) as compared to 34% in controls. Only 13% of cases had adequate Vitamin D level (> 30 ng/ml) as compared to 47% in controls. No significant correlation was found between 25-OH Vit D level with age and sex.

Table 2: Biochemical parameters in the Thalassemia cases and controls

Variables	Case	Control	Significance
Serum Calcium (mg/dl)	8.2 + 1.7	8.7 + 2.3	P>0.05
Serum Phoshorus (mg/dl)	4.8 + 0.9	4.5 + 0.7	P>0.05
25 hydroxy Vitamin D (ng/ml)	12.3 + 7.8	32.4+ 10.3	P<0.05

Table 3: Level of Vitamin D in cases and controls

25-OH VITAMIN D LEVEL	Cases	Controls
Deficiency (< 20ng/ml)	41%	19%
Insufficiency (20- 30 ng/ml)	46%	34%
Normal (>30 ng/ml)	13%	47%

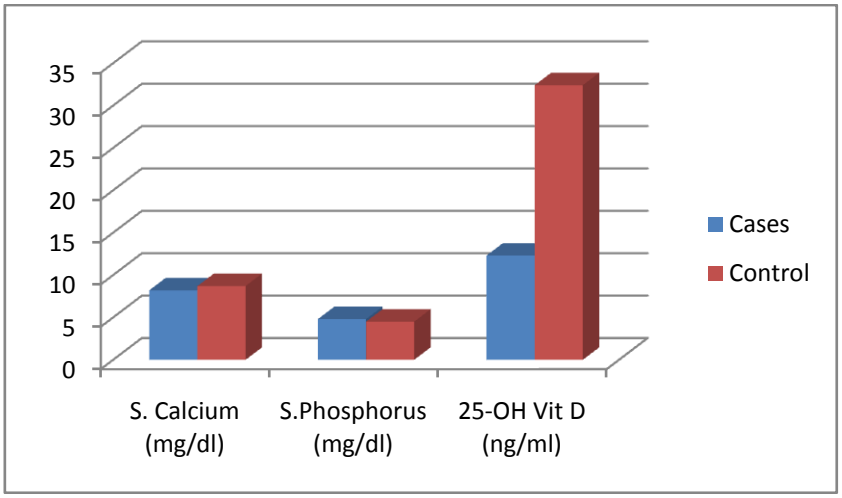

FIG 2: Biochemical parameters in Cases and Controls

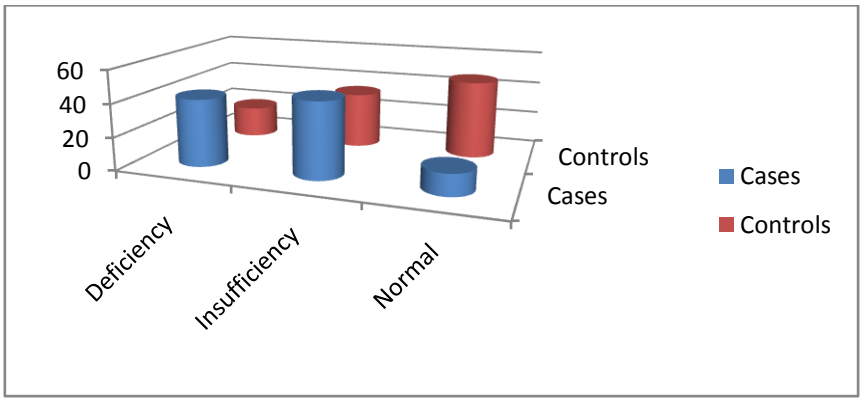

FIG 3: Level of 25-OH Vitamin D (ng/ml) in Cases and Controls

IV. Discussion

Thalassemia patients are subjected to variety of complications like growth impairment, endocrinopathies, metabolic derangements. Adequate circulating levels of vitamin D are essential for optimal skeletal health and reducing fracture risk. Regarding Body Mass Index (BMI) and weight, there was significant difference in the mean weight and BMI of thalassemia patients to that of controls (Table: 1). Similar findings were reported by other workers. Hashemi et al[7] reported underweight in 45.71% and low body mass index in 18.6% of their patients with B thalassemia major. Jain et al[8] found 20% were underweight. Shamshirsaz et al[9] reported a low body weight compared to controls and Chekir et al[10] reported weight lateness in their patients by 14.28%. However, few reports also stated there was no significant difference between cases and controls. There was no significant difference in the mean height of cases and controls. However, many reports are there having significant difference in height of cases and controls.

Growth failure is common in patients with thalassemia. However, growth failure is multifactorial in thalassemia, related to chronic hypoxia due to chronic anemia, chelation toxicity, low serum zinc level, hepatic iron overload with hepatic dysfunction and iron associated endocrinopathies such as hypogonadism, hypothyroidism, and growth hormone deficiency. Regarding serum calcium there was no significant ($p>0.05$) difference between cases and controls (Table2). Similar result was seen by Mahachoklertwattana P et al[11], Di Stefano M et al[12], Eren E et al[13]. However some workers found hypocalcemia in their thalassemic patients. They explained their results by the presence of iron overload and haemosiderosis resulting in endocrinopathies.

Regarding phosphorous level; there was no significant difference between patients and controls (Table 2). These results were in agreement with studies reported that phosphorous levels were within the normal range in patients compared to controls.

The mean serum level of 25-OH Vit D was significantly lower in our thalassemic patients than in controls. 41% had vitamin D deficiency, 46 % had vitamin D insufficiency and only 13% had normal Vit D level. Rashid merchant et al[14] found vitamin D deficiency in 62% Indian thalassemia major children and suggested that vitamin D deficiency was due to nutritional deficiency and defective hydroxylation of vitamin D in liver due to hemochromatosis as all children had high serum ferritin levels [25]. Vogiatzi et al[15] reported that 12% of thalassemic patients were vitamin D deficient and 69.8% had insufficient levels. Another study on Iranian population found that 37.2% of thalassemic patients had vitamin D deficiency. Low vitamin D concentrations have been reported previously in thalassemia patients by many authors. 25- OH Vitamin D deficiency in thalassemia patients is most likely due to hepatic dysfunction which lead to defective hydroxylation of vitamin D and so decreased serum 25-OH Vitamin D level. Hepatic dysfunction is as a result of iron overload in the liver rather than the dysfunctions of endocrine tissues. So, individuals with thalassemia are at a greater risk for vitamin D deficiency and therefore have a greater need for vitamin D supplementation.

V. Conclusion

Vitamin D deficiency is highly prevalent in thalassemia major patients due to iron overload and poor nutritional support. This may be responsible for decreased bone mineral accretion and growth failure. So, monitoring of 25 hydroxy Vitamin D level in these patients and timely therapeutic interventions for correction of Vitamin D either oral or parenteral is recommended. It may significantly improve bone mineral accretion, optimal growth, prevent bone disease and improve quality of life in these children.

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