Section: Paediatrics

Research

PREVALENCE OF HYPOPARATHYROIDISM IN CHILDREN WITH BETA THALASSEMIA MAJOR AND ITS ASSOCIATION WITH SERUM FERRITIN

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Abstract

Background: With the advances in the understanding of pathophysiology and therapeutic modalities of beta thalassemia, there has been a significant improvement in the management and the life expectancy of the patients with TDT. This has translated into new complications being identified that are associated with increasing age. Endocrine complications are amongst the most common complications attributed to iron overload and inadequate chelation. These include hypogonadism, delayed puberty, growth retardation, hypothyroidism, hypoparathyroidism and adrenal dysfunction. This study was aimed to assess the frequency of hypoparathyroidism in Thalassemia major patients attending our thalassemia care centre. **Materials and Methods:** The study was conducted over a period of 1 year and patients of 1 to 18 years of age, ferritin level > 1000 ng/dL and greater than 10 blood transfusions were recruited in the study. A total of 164 patients were studied. Parathyroid hormone levels were estimated by ELISA kit. Serum Ferritin, calcium and phosphorous levels were also estimated. **Result:** Mean parathyroid hormone levels in hypo-parathyroid patients was 25.7 ng/mL and it was 31.9 ng/mL in patients with normal parathyroid hormone status with a significant difference between the two groups (p value 0.018).Mean age of hypo-parathyroid patients was 14.2 years while as mean age in patients with normal parathyroid status was 12.9 years with no significant difference between the two groups. Hypo-parathyroidism was reported in 11 (17.18%) patients, including 8 subclinical (72%) and 3 (28%) overt cases. Mean Calcium level in hypo-parathyroid thalassaemic patients was 7.4 while it was 8.9 in thalassaemic patients with normal parathyroid levels (p value-0.019). Mean Serum ferritin levels in patients with hypoparathyroidism was 3631.5 ng/mL and it was 2698 ng/mL in patients with normal parathyroid levels. it showed significant association with p value of <0.001. **Conclusion:** Hypoparathyroidism is not uncommon in patients with transfusion-dependent thalassemia treated with suboptimal iron chelation and it shows significant association with serum ferritin levels.

INTRODUCTION

Thalassemia syndromes are one of the most common monogenetic diseases distributed worldwide. They are a group of hereditary blood disorders which result from a defect in the synthesis of either alpha or beta globin chains. Due to this defect, there is an imbalance in the ratio of alpha and beta chains resulting in ineffective erythropoiesis and a chronic haemolytic anaemia. Based on the severity of the phenotype, beta-thalassemia is divided into two groups: transfusion dependant thalassemia (TDT) and non-transfusion dependent thalassemia (NTDT).[1] With the advances in the understanding of pathophysiology and therapeutic modalities of beta thalassemia, there has been a significant improvement in the management and the life expectancy of the patients with TDT. This has translated into new complications being identified that are associated with increasing age. Endocrine complications are amongst the most common complications attributed to iron overload and inadequate chelation. These include hypogonadism, delayed puberty, growth retardation, hypothyroidism, hypoparathyroidism and adrenal dysfunction.[2]

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In the present study, we aimed to assess the frequency of hypoparathyroidism in TM patients attending our thalassemia care centre.

MATERIALS AND METHODS

The study population included TM patients, admitted to the care centre of department of paediatrics, Government Medical College Jammu, India. The study was conducted over a period of 1 year from May 2020 - April 2021. Patients of 1 to 18 years of age, ferritin level > 1000 ng/dL and greater than 10 blood transfusions were recruited in the study. A total of 164 patients were studied. The study was conducted according to the ethical standards of the committee on publication ethics (COPE) and was approved by the ethics committee of government medical college Jammu.

In addition to demographic details, general physical examination and anthropometric measurements, parathyroid hormone levels were estimated by ELISA kit. Serum calcium and phosphorous levels were also estimated. Hypoparathyroidism was diagnosed in patients with a low serum level of calcium, accompanied by increased serum phosphorus and reduced PTH levels; the normal range of PTH was 3.1 - 40 pg/mL.

RESULTS

A total of 64 Thalassemia Major patients were recruited in this study, including 43 (56.7.1%) males and 21 (43,2%) females. Mean parathyroid hormone levels in hypo-parathyroid patients was 25.7 ng/mL and it was 31.9 ng/mL in patients with normal parathyroid hormone status with a significant difference between the two groups (p value 0.018).It is shown in figure 2.Mean age of hypo-parathyroid patients was 14.2 years while as mean age in patients with normal parathyroid status was 12.9 years with no significant difference between the two groups. The age distribution of the patients is shown in [Table 1]. Hypo-parathyroidism was reported in 11 (17.18%) patients, including 8 subclinical (72%) and 3 (28%) overt cases. Mean Calcium level in hypo-parathyroid thalassaemic patients was 7.4 while it was 8.9 in thalassaemic patients with normal parathyroid levels (p value-0.019). It is shown in [Figure 1]. Mean Serum ferritin levels in patients with hypoparathyroidism was 3631.5 ng/mL and it was 2698 ng/mL in patients with normal parathyroid levels. it showed significant association with p value of <0.001. it is shown in [Table 2 and Figure 3]. All the patients were on oral chelation therapy with deferasirox or deferiprone. All patients were on regular blood transfusion therapy.

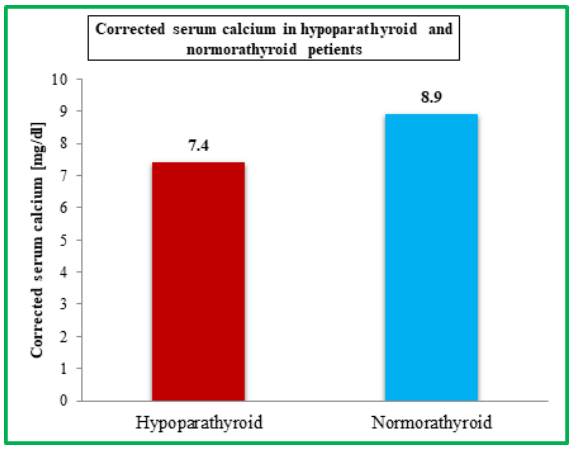

Figure 1: Corrected Serum calcium levels in study patients

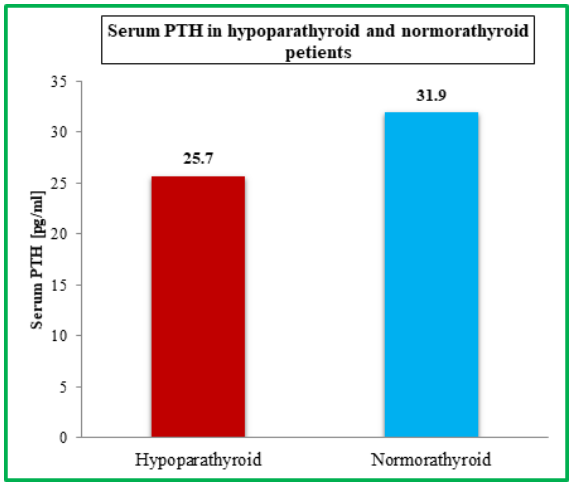

Figure 2: Serum PTH levels in study patients

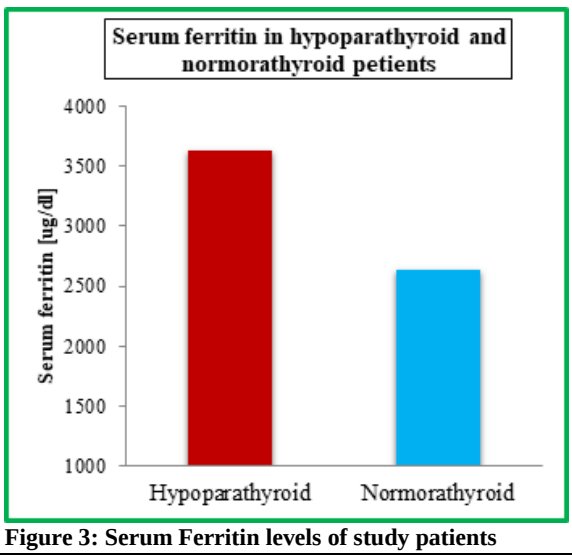

Figure 3: Serum Ferritin levels of study patients

Table 1: Age distribution of hypo-parathyroid and normo-parathyroid patients

Age (Years)	N	Mean	SD	Range	P-value
Hypo parathyroid	11	14.2	2.35	4-18 years	0.234
Normo-parathyroid	53	12.9	3.41	2-15 yeas	

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Table 2: Biochemical parameters in hypo-parathyroid and normo-parathyroid patients

Parameter	Hypo-parathyroid [n=11]		Normo-parathyroid [n=53]		P-value
	Mean	SD	Mean	SD	
Corrected serum calcium [mg/dl]	7.4	1.29	8.9	1.98	0.019*
Serum phosphorus [mg/dl]	4.8	1.54	5.1	1.28	0.497
Serum creatinine [mg/dl]	0.47	0.237	0.43	0.319	0.695
Serum PTH [pg/ml]	25.7	6.74	31.9	7.83	0.018*
Serum 25 OH-D [ng/ml]	28.9	5.83	27.4	5.17	0.395
Serum ferritin [ug/dl]	3631.5	439.7	2638.7	297.5	<0.001*

*Statistically Significant Difference (P-value<0.05)

Statistical Methods

The recorded data was compiled and entered in a spreadsheet (Microsoft Excel) and then exported to data editor of SPSS Version 20.0 (SPSS Inc., Chicago, Illinois, USA). Continuous variables were expressed as Mean±SD and categorical variables were summarized as frequencies and percentages. Graphically the data was presented by bar diagrams. Student's independent t-test or Mann-Whitney U-test, whichever feasible, was employed for comparing continuous variables. Chi-square test or Fisher's exact test, whichever appropriate, was applied for comparing categorical variables. A P-value of less than 0.05 was considered statistically significant.

DISCUSSION

Symptomatic hypoparathyroidism i.e. symptomatic hypocalcaemia without elevated serum parathyroid hormone (PTH)] in patients with thalassemia is relatively rare. Asymptomatic mild hypocalcaemia without elevated PTH, which is considered hypoparathyroidism, may be more common but under-recognized.[3] Regular red blood cell transfusions and iron chelation therapy to remove excess iron introduced with transfusions are the standard therapeutic interventions in thalassemia. Despite early establishment of chelation therapy, elevated ferritin is commonly due to iron overload from multiple blood transfusions; and in the long term may lead to cardiac, hepatic, or endocrine dysfunctions.[4] As the survival of the Transfusion dependent Thalassemia patients improved with modern management, most patients suffer from at least one endocrine complication, the most common being hypogonadotropic hypogonadism, Type 1 Diabetes, impaired glucose tolerance, Hypoparathyroidism, subclinical hypothyroidism, overt hypothyroidism, central hypothyroidism and growth hormone deficiency are other common endocrine complications. Even some can have multiple endocrine complications simultaneously.[2] Oxidative damage by reactive oxygen species (ROS) is responsible for endocrine organ damage in patients with thalassemia. ROS generation is caused due to iron overload and chronic hypoxia resulting from chronic anaemia.[1]

This study found a significant difference between serum ferritin levels of hypoparathyroid and other thalassemia patients with normal parathyroid status. However, studies conducted by Angelopoulos NG et al found no significant association of serum ferritin in the prediction of the development of HPT, as no significant differences have been reported in serum ferritin level in patients with HPT in the background of thalassemia in many studies.[5] The prevalence of hypoparathyroidism was 17% in this study. This is in line with previous studies of Mostafavi et al with 22.7 % prevalence.[6] Adil et al,[7] conducted a study that reported hypoparathyroidism in 35.3% of thalassaemic patients double than our study. Other factors, such as individual susceptibility to iron toxic effects and the haematological phenotype of the disease might play some roles in the development of Hypoparathyroidism.[8]

CONCLUSION

Hypoparathyroidism was not uncommon in patients with transfusion-dependent thalassemia treated with suboptimal iron chelation.

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