Original Research Article

Study on correlation of Serum ferritin levels with serum calcium, phosphate and parathormone levels in patients with β-thalassemia major receiving blood transfusion

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Abstract

Introduction:Thalassemia is a heterogeneous family of inherited disorders of hemoglobin synthesis. The combination of transfusion and chelation therapy has dramatically extended the life expectancy of thalassemia patients, but with complications like hypocalcaemia. The present study was undertaken to estimate serum calcium, phosphate and parathormone levels in patients with β- thalassemia who are receiving repeated blood transfusion and to correlate them with serum ferritin levels.**Method:**Hospital based study conducted at S. Nijalingappa Medical College and Hanagal Shri Kumareshwar hospital, Bagalkot. The study period was from 2015 to 2016. During study period, 53 beta thalassemia major cases were fulfilling inclusion criteria were investigated. Serum calcium level was determined by OCPC method, serum phosphate levels by ammonium molybdate method. And chemiluminescent immunoassay (CLIA) method used to estimate the parathormone levels.**Result:**The study consisted of 32 (60.4%) males and 21 (39.6%) females. Among 53 transfusion dependent children studied, the mean age is 5.249 years. There is a negative correlation between serum ferritin and serum calcium as well as, parathyroid hormone which is statistically significant (p value <0.005).There is a positive correlation between serum ferritin and serum phosphate and ALP which is statistically significant (p <0.005).**Conclusion:** Thalassemia is a genetic disorder, which should be diagnosed as early as possible, regular blood transfusion in order to sustain a good growth and prevent stunting.

Key words: Beta- thalassemia major; serum calcium; serum phosphate; serum ferritin

Introduction

Thalassemia is a heterogeneous family of inherited disorders of hemoglobin synthesis. It is characterized by the complete absence or reduced synthesis of one or more types of globin chains[1].

Thalassemias,autosomal recessive disorders, are among the most prevalent genetic and major hemoglobin disorders globally. In Southern Asia, the prevalence of β thalassemia has been reported to be from as low as 2 % to as high as 28% in various studies[2].

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Phenotypes are variable, ranging from severe anemia to clinically asymptomatic individuals[3].Although blood transfusions are important for patients with anemia, chronic transfusions inevitably lead to iron overload as humans cannot actively remove excess iron. The cumulative effects of iron overload lead to significant morbidity and mortality, if untreated. A unit of red blood cells transfused contains approximately 250 mg of iron, while the body cannot excrete more than 1 mg of iron per day[4]. In 1988, de Virgiliis et al. reported the occurrence of a growth disturbance associated with radiologic changes in the long bone metaphyses in patients with thalassemia major treated with hyper transfusion and chelation [5].

Hypoparathyroidism is thought to be a rarer complication, usually, but not always, accompanied by hypocalcemia[6,7]. However, hypoparathyroidism may cause various neurological manifestations, including tetany, seizures, carpopedal spasms, and paresthesia, and little is known about these associated complications in thalassemic patients [8,9].

Nevertheless, data on the prevalence of parathyroid dysfunction in these patients are still discordant[6,10]. Early detection and the implementation of an appropriate transfusion regimen and chelation therapy are essential for proper management.

Patients with beta-thalassemia major are prone for hypoparathyroidism; an irreversible and preventable disorder caused by iron overload[11].

This condition is asymptomatic in most β thalassemia patients, with hypocalcemia usually only detected during routine laboratory examinations[12].

The previous studies have shown that iron overload due to repeated blood transfusions in thalassemia patients may result in changes in calcium and phosphate levels in these patients. Although several studies have examined calcium and phosphate levels in transfusion-dependent patients with thalassemia, the amount of data is insufficient to reach strong conclusions.

So, the present study has been undertaken to estimate serum calcium, phosphate, alkaline phosphatase and parathormone levels in patients with β-thalassemia who are receiving repeated blood transfusion and to correlate them with serum ferritin levels.

Methods

This prospective study was conducted in the Department of Paediatrics, SNMC & HSK Hospital and Research centre Bagalkot from 2015 to 2016 after taking approval from the review board of Institutional Ethical Clearance committee.

Inclusion criteria: Patients diagnosed with β-thalassemia major by electrophoresis, Receiving repeated blood transfusion, Serum ferritin levels more than 1000 ng/ml.

Exclusion criteria : Poor compliance for blood transfusion,On any drug which affect the calcium level, Having renal disease, Malabsorption syndrome, Rickets Guardians of the patients who were selected for the study were explained about the study procedure and a written consent was taken. History of the patients was taken in detail. They were examined for the signs like chvostek sign and trousseau sign and also their anthropometry was done.Patients diagnosed with β-thalassemia major, who are receiving regular blood transfusion, were selected for the study. Informed written consent was taken. 4ml venous blood was taken, 2 ml in plain bulb and 2 ml in EDTA bulb. EDTA bulb is sent for hemogram.Serum is separated from the sample of plain bulb with the ERBA CHEM-5 v2 plus semiautoanalyzer. Serum calcium and serum phosphate are analyzed by commercially available kit method. Serum calcium will be estimated using o-Cresolphthalein (oCPC method).

Ammonium molybdate method will be employed to estimate serum phosphate levels. And chemi-luminescent immunoassay (CLIA) method was used to estimate the parathormone levels. Data were entered in MS Excel and analyzed in SPSS Version 22.

Descriptive statistics like percentage for the qualitative data and mean, standard deviation for quantitative data were applied. Karl Pearson‘s correlation was applied to determine correlation between variables. P – value less than 0.05 was considered as statistically significant.

Results

Table 1:Basic characteristics

Characteristics	Number	Percentage
Age		
<1	5	9.4
1-5	28	52.8
6-10	14	26.4
11-14	6	11.3
Gender		
Male	32	60.4
Female	21	39.6
Age at diagnose (in months)		
≤ 3	9	17.0

4-6	29	54.7
7-9	10	18.9
10-12	5	9.4
Number of transfusions		
≤ 25	12	22.6
26-50	13	24.5
51-75	8	15.1
76-100	8	15.1
>100	12	22.6
Frequency of transfusion (in days)		
15	8	15.1
30	45	84.9

Among 53 transfusion dependent children studied, majority i.e. 28 (52.8%) of the children belonged to the age group of 1-5 years. The maximum age studied was 14 years of age. Among the cases studied, the mean age was found out to be 5.249 years. The study consisted of 53 thalassemia patients among which, 32 (60.4%) were males and 21 (39.6%) females. Maximum number of cases i.e. 29 (54.7%) were diagnosed at the age of 4-6 months.These transfusion dependent children studied had mean number of transfusion of 68.11. Among the thalassemia patients studied, majority of them i.e. 45 (84.9%) needed packed red blood cells transfusion every 30 days. Whereas, very few i.e. 8 (15.1%) children required transfusion every 15 days.

Table 2 : Laboratory evaluation of the children

	Number	Percentage
Serum Calcium (mg/dl)		
<8.5	36	67.9
8.5-10.5	16	30.2
>10.5	1	1.9
Serum Phosphorous		
<2.5	1	1.9
2.5-4.5	28	52.8
>4.5	24	45.3
PTH		
<10	29	54.7
10-65	23	43.4
>65	1	1.9
Serum alkaline phosphatase		
44-147	9	17.0
>147	44	83.0

Children with serum ferritin more than 1000 were studied, among which the maximum serum ferritin level observed was 3657 and mean level of 1971.15 with standard deviation of 725.60. The serum calcium levels studied ranged from 6.30 mg/dl to 11.50 mg/dl. The mean value of serum calcium level was found to be 8.28 $\pm$ 0.89 mg/dl. In the present, majority of children are having less serum calcium (67.9%).The serum phosphate levels of the cases studied ranged from 2.40 mg/dl to 6.40 mg/dl. The mean value of serum phosphate level was found to be 6.40 $\pm$ 0.80 mg/dl. Majority of children are having more serum phosphate level (45.3%).The serum PTH levels of the cases studied ranged 5.40 to 105 ng/L. The mean value of serum phosphate level was found to be 14.96 $\pm$ 15.49 ng/L. Majority of children are having less serum PTH level (54.7%).The serum ALP ranged from 106 U/L to 289 U/L with the mean value of 166.789 U/L. Majority of children are having more serum ALP level (83%).

Table 3 : Correlation of serum ferritin level with Serum Calcium, Serum Phosphate, alkaline phosphatase and parathormone levels in patients with β-thalassemia

	Correlation coefficient (r-value)	p-value
Serum Calcium	-0.724	<0.001
Serum Phosphate	0.496	<0.001
PTH	-0.571	<0.001
ALP	0.706	<0.001

There was a negative correlation between Serum Ferritin and Serum Calcium that means if Serum Ferritin increases then Serum Calcium is decreased. There was a positive correlation between Serum Ferritin and Serum phosphate in turn it indicates that Serum Ferritin increases then Serum phosphate is also increased. There was a negative correlation between Serum Ferritin and Serum PTH levels .that means if Serum Ferritin increases then Serum PTH is decreased. There was a positive correlation between Serum Ferritin and ALP in turn it indicates that Serum Ferritin increases then ALP is also increased.

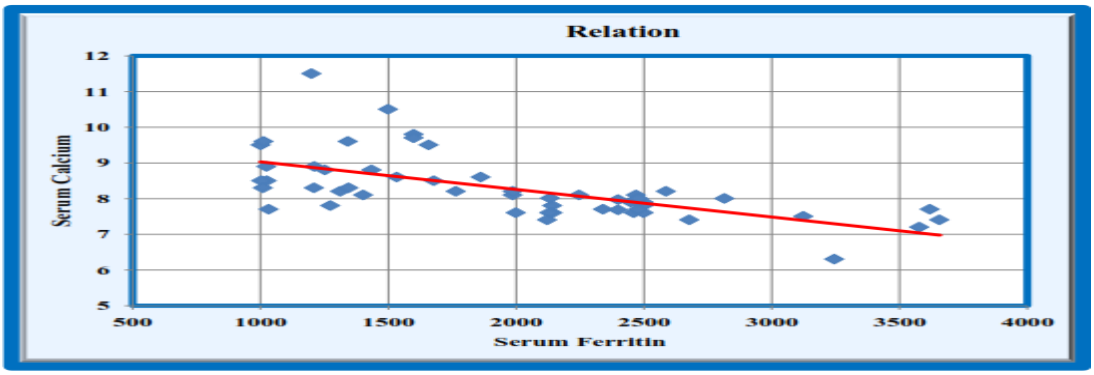

Fig 1: Correlation of serum ferritin level with Serum Calcium

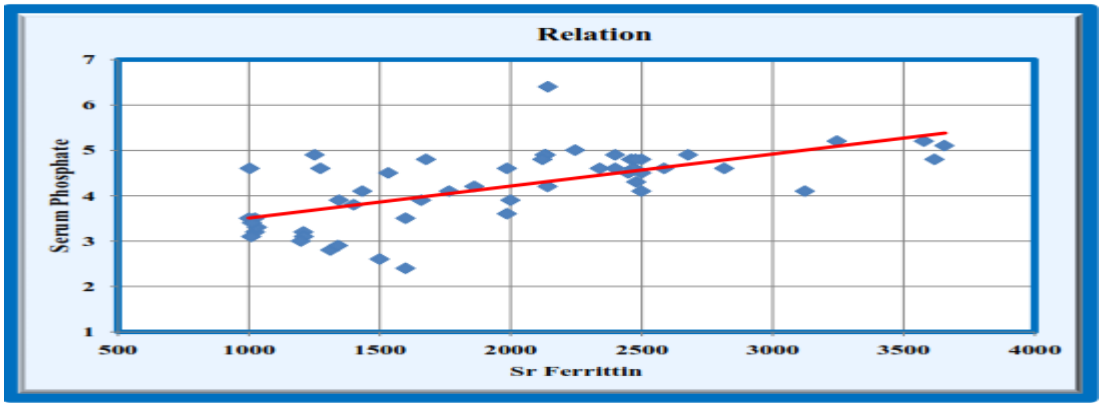

Fig 2: Correlation of serum ferritin level with Serum Phosphate

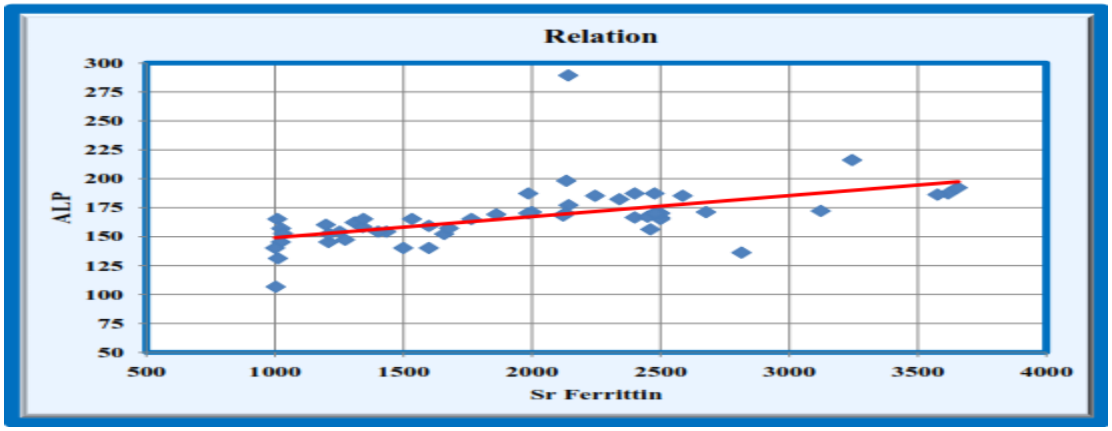

Fig 3: Correlation of serum ferritin level with Alkaline phosphatase

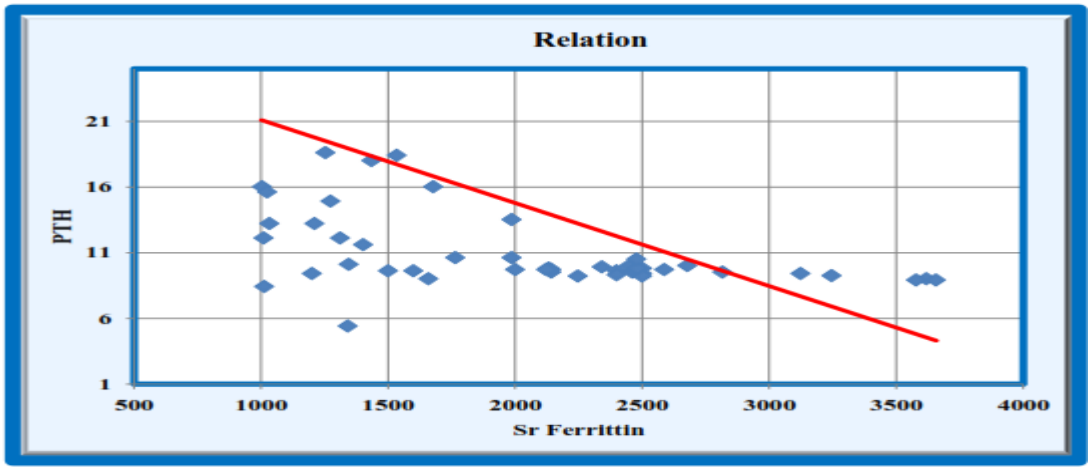

Fig 4: Correlation of serum ferritin level with Parathormone levels

Discussion

The present study is a hospital based prospective study involving β – thalassemia major children to study the correlation between serum ferritin and the serum calcium, phosphate and parathormone levels in patients with β-thalassemia major receiving blood transfusion.The age group of patients in the present study was between 1-5 years, with the mean age being 5.249± 3.4562 years, comparable with other study with mean age 6.35 ± 2.27 years[2]. The reason for current male preponderance in Indian studies could be attributed to the Indian society where the female children are neglected. There is no reason for the male preponderance in thalassemia major. Findings of present study was comparable with study done by George (60%) and Choudhary VP (54.9%)[13,14].In this study the majority of the cases i.e 54.7% was diagnosed at the age of 4-6 months. β thalassemia major manifests very early childhood with pallor being predominant with in the first year of life.Lokeshwar MR, et al states that transfusion to be given at the interval of 2-4 weeks[15]. In the present study, it was observed that majority of the thalassemia patients i.e. 84.9% needed transfusion every 30 days (4 weeks) whereas, only 15.1% of them needed transfusion for every 15 days (2 weeks).Aleem AA, et al in their study observed ionized calcium levels in thalassemia patients and found the levels low, ranging from 1.58mmol/L – 2.04 mmol/L and a mean value of 1.88mmol/L[16]. Hagag AA, et al also studied about the ionized calcium levels in β-thalassemia patients and concluded that the ionized calcium levels were as low as 0.60-1.23 mmol/L with a mean value of

0.96±0.13[17]. In the present study, patients with β- thalassemia have low serum calcium levels ranging from 6.30-11.50 mg/dl and a mean value of 8.28±0.89 mg/dl.Findings of the present study was comparable with studies done by Goyal M with 8.42±0.32, Modi AS with 8.37±0.20[1,18].In the present study, serum phosphate levels were observed to be ranging from 2.40-6.40mg/dl with the mean value of 4.19± 0.80 which was found to be increased. This suggests that serum phosphate levels were found to at the higher level of the normal range. Findings of the present study was comparable with the study done by Modi AS with 4.87 ± 0.37, Angelopoulos NG with 4.87 ± 1.39 [18,19]. In the present study parathormone levels (14.96 ± 15.49) were found to be low which was also seen in studies done by Goyal M,et al (32.2 ± 0.96) and Angelous NG,et al. (10.48±4.46), whereas Basha KP, et al study did not find any clear relation between serum ferritin and serum PTH[1,19,20].Goyal M, et al in their case control study studied the alkaline phosphatase levels in the thalassemia major patients who received blood transfusion and compared with the normal children. They found the levels of ALP in patients to be 7.67± 0.85 (KA U/L)[1]. In the present study, the mean value of ALP is found to be increased. Basha KP, et al in their study observed that there is no clear relationship between HPT and serum ferritin levels[20]. Aleem A, et al studied about hypocalcemia due to hypoparathyroidism in thalassemia major patients and found out that, there was no consistent relationship between serum ferritin and degree of hypocalcemia[16].In the present study, it is found that there is significant negative correlation between serum ferritin and serum calcium that means if serum ferritin increases then serum calcium is decreased.Data regarding correlation between serum ferritin and serum phosphate is unavailable. In the present study, significant positive correlation was found which means if serum ferritin is increased, then serum phosphate is also increased.In this study, a significant negative correlation with p value <0.001 was found between serum ferritin and parathyroid hormone levels which indicate that if serum ferritin increases, the parathyroid hormone levels decrease.In the study conducted by Hagag AA, et al observed a significant negative correlation between serum ferritin and serum parathyroid hormone levels[17].Basha KP et al observed that there is no clear relationship between HPT and serum ferritin levels. Whereas in Italian study conducted by the department of pediatrics, observed 24 cases of HPT in beta thalassemia major. HPT is thought to be mainly the consequence of iron deposition in the parathyroid glands. The age of their patients when HPT was diagnosed ranged from 11 to 24 years (mean 16.5 years). Their serum ferritin levels ranged from 810 to 15,200 ng/mL (mean 3,772 ng/mL). The severity of HPT varied widely[20].

Conclusion

From the present study, it was noted that, Thalassemia is a genetic disorder, which should be diagnosed as early as possible, regular blood transfusion in order to sustain a good growth and prevent stunting, screened for HIV, HCV and HBsAg every 6 months since they are very much liable to get the infections through blood, monitored for serum ferritin levels in order to look for iron overload and its complications, calcium supplementation in order to avoid hypocalcaemia and require yearly monitoring of PTH levels.

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