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Original Article

Correlation of Serum Ferritin with Age and Growth in Thalassemia Major Children

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Abstract

Background: *Thalassemia is the most prevalent single gene defect in human beings worldwide. Repeated blood transfusions along with chelation therapy are mainstay of treatment in thalassemia patients. However, these recurrent blood transfusions along with inadequate chelation therapy results in iron overload. The study aimed to investigate the serum ferritin level in children with blood transfusion in thalassemia major patients and to know their correlation with age and growth.*

Materials and methods: *A cross-sectional analytical study was conducted including 79 children of thalassemia major in the age group of 5-12 years who were on regular blood transfusion and oral iron chelators from thalassemia unit of Chittagong Medical College Hospital. Serum ferritin was tested and their correlation with age and growth was assessed. Chi square was done to determine the correlation.*

Results: *The age of the patients ranged from 5 to 12 years and 45(56.9%) were males. The mean age at diagnosis of thalassemia was 10.7±4.2 months and mean number of transfusion was 90±29 and ranged between 40-140 transfusions. All of the children were on oral iron chelation therapy and the average age of initiation chelation therapy was 5.7±1.1 years. 64(81%) children had growth retardation. Mean serum ferritin level was 3740.7±2185.8 ng/ml and only 3.8% of the patients had serum ferritin level <1000 ng/ml.*

Conclusions: *This study concludes that serum ferritin is raised and positively correlated with age and growth in thalassemia major patients. So routine evaluation of serum ferritin tests may be advocated for thalassemic patients.*

Key words: Growth retardation; Serum ferritin; Transfusion dependent thalassemia.

INTRODUCTION

Thalassemia is a common genetic disorder. Beta thalassemia syndromes are inherited disorders characterized by a deficiency in the production of beta-globin chains resulting in ineffective erythropoiesis complicated by a lack of affinity of circulating haemoglobin F to 2,3-diphosphoglycerate.[1] Chronic blood transfusion is the mainstay of care for individuals with β-thalassemia major for preventing growth retardation, skeletal changes that result from the expansion of the bone marrow and development of masses from extramedullary hematopoiesis. In spite of that, repeated blood transfusion causes iron-overload that requires monitoring and management through long-term iron chelation therapy. With inadequate chelation therapy, cardiac arrhythmia, cardiomyopathy, and heart failure are the predominant causes of death, while endocrine abnormalities and chronic liver disease contribute significantly to morbidity and mortality.[2] The liver is the earliest site of iron deposition in transfusion-dependent thalassemia children and iron-induced liver injury is the commonest cause of morbidity. Iron overload occurs both in hepatocytes and reticuloendothelial cells. The iron induced liver injury is characterized by development of fibrosis and eventually cirrhosis.[2] The liver is the only site for ferritin and transferrin synthesis, as well as the primary organ for iron storage.[3] This

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iron burden is usually reflected by increased serum ferritin levels, the long-term control of which correlates with long-term survival. Estimation of serum ferritin concentration is the index of measuring total iron in the body.[4] In previous studies, a good correlation between serum ferritin and hepatic iron concentration has been reported in transfusion-dependent thalassemia patients.[5] It is possible that multiple serum ferritin measurements over time could be a valuable parameter in predicting complications of iron overload than a single liver biopsy as reported by Telfer.[6] Previous study from Bangladesh reported serum ferritin, bilirubin, Alanine Transaminase (ALT) Aspartate Transaminase (AST) Alkaline Phosphatase (ALP) were significantly higher in children with thalassemia than the healthy children and the parameter of iron overload and jaundice are correlated without any statistical correlation in children with thalassemia. Several studies conducted in Bangladesh and other countries investigated the correlations between serum ferritin levels with age and growth, but the results were inconsistent.[7] The effect of iron chelation therapy is also inconsistent in previous studies.[8] Moreover, there is a lack of local data regarding iron overload in thalassemia patients. Therefore, the present study aimed to see the association between serum ferritin level with age and growth in β-thalassemia major patients receiving treatment in a tertiary hospital in Chattogram, Bangladesh.

MATERIALS AND METHODS

This cross sectional study was done in Department of Biochemistry and Paediatrics of Chittagong Medical College Hospital from July 2022 to June 2023. 79 diagnosed cases of thalassemia major were included in the study by convenience sampling. Patients who received blood transfusion in last 15 days and with chronic diseases like tuberculosis, hepatitis B and malignancy were discarded from the study. Data were compiled and analysis was done by using SPSS version 23.

RESULTS

Table I Age and gender of the patients.(n=79)

Variables	Frequency	Percentage (%)
Age		
5 years	11	13.9
6 years	09	11.3
7 years	09	11.3
8 years	11	13.9
9 years	10	12.6
10 years	08	10.1
11 years	10	12.6
12 years	11	13.9
Mean age	8.5±2.4	
Gender		
Male	45	56.9
Female	34	43.0
Age at diagnosis		
Median (Range)	10.7±4.2	
<12 months	48	60.8
≥12 months	31	39.2

The study reveals that majority of the patients were in age of 5 years and 12 year. Among the patients 45(56.9%) were males and 34(43.0%) were females. The earliest age at diagnosis was 4 months in the study but in 39.2% of the cases diagnosis was made beyond one year of age. The mean age at diagnosis was 10.7±4.2 months (Table I).

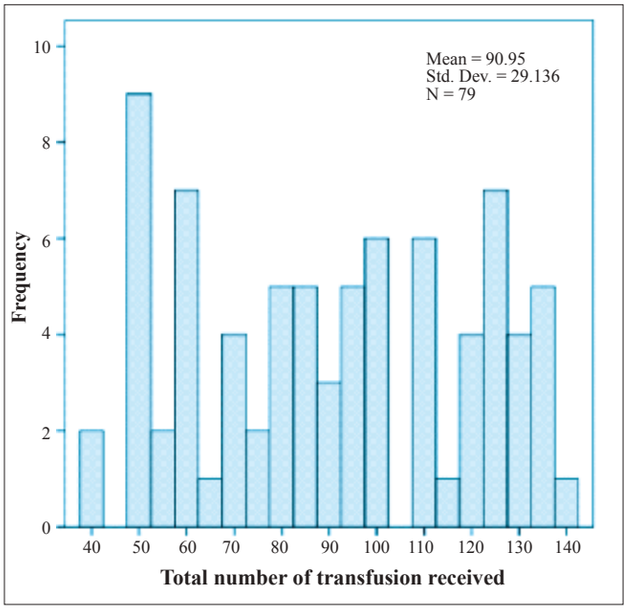

Figure 1 Total number of transfusion in the studied patients

The above figure shows that mean number of transfusion was 90±29 and ranged between 40-140 transfusions.

Table II Relation between age with number of transfusion required and serum ferritin level

Age group	No. of transfusion required (Mean± SD)	Serum ferritin level (Mean±SD)
5-7 years (29)	61.48+12.9	2748.14 ±1741.7
8-10 years (29)	95.39+15.45	3574.17±2002.5
11-12 years (21)	125.52±14.13	5041.24±2144.0
p value	0.001	0.001

*F test (Analysis of variance).

Above Tables shows that number of transfusion was higher in 12 years of children and significant association ($p<0.005$) between serum ferritin and age group indicating that as age was increased, the serum ferritin level was also increased.

Table III Serum ferritin level in the thalassemic patients

Serum ferritin	Frequency	Percentage
<1000ng/ml	3	3.8
1000-2999ng/ml	36	45.6
3000-5999ng/ml	24	30.4
6000 ng/ml	16	20.3
Mean±SD	3740.7±2185.8	
Range	109.0-9090.0	

Above Table depicts that mean serum ferritin level was 3740.7±2184.8ng/ml and only 3.8% of the patients had serum ferritin level <1000 ng/ml.

Table IV Distribution of the patients according to their Iron Chelation Therapy (ICT) characteristics

Variables	Frequency	Percentage
Age of ICT iniation, years		
Mean±SD		5.7±1.1
Range	2.1	8.0
Duration of ICT received, years		
Mean±SD		4.8+1.1
Range	1.3	7.3

The Table shows that all of the included children in this study were on oral iron chelation therapy. The average age of initiation chelation therapy was 5.7±1.1 years. The mean duration of chelation therapy was 4.8±1.1 years.

Table V Comparison of actual height and weight with expected height and weight of the patients

Observed mean (±SD) height, cm	Expected mean (±SD) height, cm	Mean (±SD) difference, cm	p value
121.5±12.2	129.3±13.69	7.7±5.1	<0.001
Observed mean (±SD) weight, kg	Expected mean (±SD) weight, kg	Mean (±SD) difference	p value
21.3±6.2	27.2±6.6	5.8±2.9	<0.001

SD: Standard Deviation, Independent sample t test.

Observed mean height of the children was 121.5±12.2 cm and the expected mean height was 129.3±13.69 cm, which indicated that patients were 7.7±5.1 cm shorter than their expected height. The difference was highly significant statistically (p<0.001). Observed mean weight of the children was 21.3±6.2 kg and the expected mean weight was 27.2±6.6 kg, which indicated that mean weight was 5.8±2.9 kg less than their expected mean weight. The difference was highly significant statistically (p<0.001).

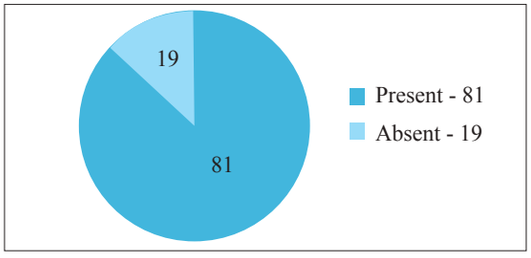

Figure 2 Proportion of the children with growth retardation

Out of 79 children, 64 (81%) children had growth retardation (Figure 2).

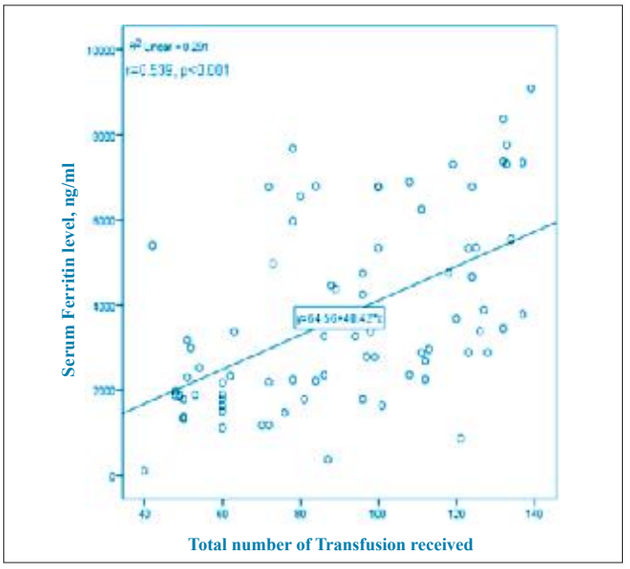

Figure 3 Scatter and dot plot showing correlation and regression line between total number of transfusion received and serum ferritin

The Figure reveals that there was a significant positive correlation between total number of transfusion received and serum ferritin level (Pearson correlation r=0.539, p<0.001).

DISCUSSION

Current study included the thalassemic children of 5 to 12 years of age. The mean age of the studied patients was 8.5±2.4. Male patients were predominant as males represented 45(56.9%) whereas females were 36(43.1%) of the total studied cases. The male to female ratio observed in the present study was also consistent with the values reported in previous studies carried out by Hossain in Bangladesh.[8] Previously, Tahura in her study found that, 1% β Thalassemia major children was diagnosed at less than 2 year of their age. In the current study, the mean age at diagnosis was 10.7±4.2 months, the earliest age at diagnosis was 4 months but in 39.2% of the cases diagnosis was made beyond one year of age.[9] All of the included children in the present study were on oral iron chelation therapy. The average age of initiation of chelation therapy was 5.7±1.1 years and the the average duration of chelation therapy was 4.8±1.1 years. Guidelines from the Thalassemia International Federation recommend that chelation therapy is initiated when serum ferritin levels reach ≥1000 ng/ml, which usually occurs after the first 10–20 transfusions or around 2–3 years of age.[10] The majority of the present studied cases were in the age group 5–7 years at the time of initiation of chelating agent therapy, which indicated that initiation of chelation therapy in the study center mostly started at much later ages comparable with the optimal age advised by the Guidelines. To determine the toxic level of iron, the critical values of serum ferritin varies from 1000-3000 µg/L in different studies and the standard values of serum ferritin level

have a very wide range in males (10-220 µg/L) and females (10-85 µg/L) in normal conditions.[11] In the current study, the average serum ferritin level (3740.7±2185.8 ng/ml) was considerably higher than its peak value (1000 ng/mL), showing that regularly transfused patients are in iron overload status. Iron levels and serum ferritin have a positive correlation and this findings is similar to another study by Riaz.[12] As the transfusion increased, serum iron level also increased. In this study there was a positive correlation between total number of transfusion received and serum ferritin level. Suman in his study found that, as soon as the serum ferritin level crosses the value of 1000 ng/ml and number of transfusions are more than 30, which is consistent with the current study.[13] In the present study, observed mean height and mean weight was significantly lower than the expected height and weight, respectively. The observed and expected difference of height and weight was found statistically significant ($p<0.001$). Growth retardation was present in 81% of the present studied children which was 100% in the study by Ali.[14] This indicates growth retardation is invariably present in all cases which is probably because many parents in this study followed advice of regular blood transfusion but properly not maintained. One of the important findings of the present study was the significant relation between growth retardation and serum ferritin level ($p<0.001$). Age, age at first transfusion, age of starting chelation and serum ferritin level were considered as positive predictors for nutritional status, whereas puberty, gender and fasting blood sugar as negative predictors in a previous study.[15] Sangha and her colleagues found that, out of 93 cases of transfusion dependent thalassemia cases, 44.1% cases were short statured and they observed a significant correlation between frequency of transfusion and the incidence of short stature.[16] The abnormalities in the present study indicates the need for further evaluation and improvement in the management of thalassemic patients in Bangladesh. The reasons are probably multiple transfusions, lower pre-transfusion hemoglobin level and inadequate chelation therapy, and severe anemia. Present study findings suggest that monitoring of serum ferritin level is important because they may reflect the severity of iron overload. The present study highlights the importance of prevention measures and timely diagnosis and management of iron overload in β-thalassemia major patients.

LIMITATION

The study had a small sample size that might not reflect the actual scenario of the generalization of the findings to the thalassemia population.

CONCLUSION

From present study it is concluded that there was a positive correlation between serum ferritin with growth retardation and age. As the age increases there is evidence of increased number of blood transfusion and increased serum ferritin. Moreover as age increases there is growth retardation. These results support the need for clinical evaluation of growth and serum ferritin level in beta-thalassemia major children.

RECOMMENDATION

Based on the study findings, it could be recommended that blood transfusion and serum ferritin level should be carefully monitored in patients with β-thalassemia major. Future prospective studies should be conducted to evaluate the effect of early and adequate chelation therapy on children with β-thalassemia major.

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DISCLOSURE

All the authors declared no competing interest.

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