

Growth pattern in thalassemic children and their correlation with serum ferritin

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ABSTRACT

Background: This study was conducted to determine the effects of iron overload on growth and correlation of serum ferritin and growth disorders in children with thalassemia. **Methodology:** It was a cross-sectional study conducted from January to June 2019 on 70 children age up to 18 years with transfusion-dependent thalassemia. Detailed history, demographics, anthropometric parameters, clinical and laboratory details were evaluated. Data was analyzed by statistical package of social sciences (SPSS) software. Logistic regression model was used to determine the correlation between serum ferritin with short stature. **Results:** It included 46 male and 24 female, of which 65.71% had short stature and 77% were underweight. The mean serum ferritin level was 1,560.9 µg/L, 45.71% have serum ferritin level >2,500 µg/L, and 65.71% had hemoglobin levels of 5–8 g/dL before transfusion. The receiver operating curve value of serum ferritin was 1,107 µg/L with respect to the incidence of short stature and there was significant correlation between serum ferritin level and the incidences of short stature ($P=0.001$). **Conclusion:** There was a significant correlation between serum ferritin level and growth disorders.

Keywords: Ferritin, growth, short stature, Thalassemia

Introduction

Thalassemia is prevalent in India.^[1] Around 3.4% are carrier and 7,000–10,000 born with thalassemia per year.^[2] In thalassemia, there is lifelong sequence of blood transfusions and chelation therapy leading to iron overload.^[3,4]

With treatment, life expectancy can be prolonged. However, growth retardation affects quality of life. Many factors including iron overload causes growth delay.^[5,6] High-serum ferritin leads to short stature.^[7] Very few studies have reported problem of growth delay; so, present study is undertaken to determine effects of iron overload on height, body mass index (BMI) and ferritin and to determine correlation of ferritin and growth disorders in these children.

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Methodology

A cross-sectional study was conducted on 70 children age up to 18 years (46 boys, 24 girls) with transfusion dependent thalassemia over a time period of 6 months from January 2019 to June 2019 after taking approval from ethics committee on 22 December 2018. Detailed history is evaluated. The following information is collected from medical records of the patients: demographics (age, gender, age at the time of diagnosis and at first transfusion), anthropometric parameters (weight, height, and BMI), and clinical details (blood transfusion history, last pretransfusion hemoglobin and last serum ferritin level). Serum ferritin is measured by chemi-luminescent micro-particle immunoassay.

Center of disease control and prevention (CDC) growth chart were used for boys and girls to assess their weight, height, and BMI percentiles. BMI is calculated as weight in kg/height

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in square meters. Short stature is defined as height less than 3rd percentile. Underweight is defined as BMI less than 5th percentile, overweight between 85th and 95th percentile and obese more than 95th percentile.

The inclusion criteria were children aged up to 18 years, diagnosed with thalassemia on the basis of hemoglobin electrophoresis or high-performance liquid chromatography and receiving blood transfusion regularly.

The exclusion criteria were children having congenital disease and chronic illness other than thalassemia (such as malignancy, tuberculosis, chronic hepatitis, congenital heart disease, chronic renal failure, epilepsy, and diabetes mellitus).

Data were collected, managed, edited, entered, and analyzed by statistical package of social sciences (SPSS) software. A descriptive analysis of all patients in the study was performed. Male: female ratio was also computed. The mean, median and range were calculated for various variables. Short stature was computed as per different study characteristics. Receiver operating curve was analyzed for ferritin level and short stature. The level of significance taken for all the statistical test was a *P* value of < 0.05.

Results

In total, 70 children of transfusion-dependent thalassemia were enrolled in the study, which included 46 males and 24 females over a time period of 6 months from January 2019 to June 2019. When we assessed the growth pattern of these children, we found that 46 children (65.71%) had short stature, which included 32 male and 11 female. Among 70 children, 77% were underweight and rest had normal BMI.

Mean serum ferritin in patients with height more than 3rd percentile was 1484.77 µg/L and in height less than 3rd percentile was 1600.74 µg/L. Mean serum ferritin in patients with normal BMI was 1,518.24 µg/L, in underweight it was 2,114.82 µg/L, in overweight it was 1,393.03 µg/L and in obese it was 1810.68 µg/L.

The serum ferritin level, hemoglobin level before transfusion, and transfusion frequency were evaluated in these children. The study revealed mean serum ferritin level was 1,560.9 µg/L, 45.71% have serum ferritin level >2,500 µg/L, 65.71% had hemoglobin level of 5–8 g/dL before transfusion, and 52.86% have transfusion frequency twice a month [Table 1].

On comparison of short stature with study characteristic like sex, age when first diagnosed, average hemoglobin before transfusion, frequency of transfusion, and serum ferritin level, we found a significant correlation between short stature and serum ferritin level (*P* < 0.05) [Table 2].

Receiver operating characteristics (ROC) curve was prepared to evaluate serum ferritin cut-off point and short stature

incidence [Figure 1, Table 3]. Serum ferritin cut off point was found to be 1,107 µg/L with respect to the incidence of short stature.

After obtaining the serum ferritin cut-off point, the subjects were divided based on serum ferritin cut-off point. It was analyzed in relation to the incidence of short stature and we observed a significant correlation between serum ferritin level and the incidence of short stature (*P* = 0.001) [Table 4].

The correlation of short stature with serum ferritin level and age was observed in Table 5 and we found a statistically significant correlation between serum ferritin level and short stature (*P* < 0.05), whereas it was not significant with age.

Discussion

Thalassemia poses a challenge to health and it drastically reduces the quality of life. However, with optimal treatment, the quality of

Table 1: Variables characteristics

Variable	N	Percentage (%)
Ferritin level(µg/L)		
Mean	1560.987	
Median	1212	
Range	9641.9(207-9848.9)	
<1000	16	22.85%
1000-2500	22	31.42%
>2500	32	45.71%
Hemoglobin level before transfusion(g/dl)		
<5	2	2.857%
5-8	46	65.71%
8-10	18	25.71%
>10	4	5.71%
Frequency of blood transfusion		
Once a month	25	35.71%
Twice a month	37	52.86%
Thrice a month	1	1.43%
Irregular	7	10%

Table 2: Short stature based on study characteristic

Characteristics	Short stature n=46	Normal Stature n=24	P value
Sex			0.347
Male	32	14	
Female	14	10	
Average hemoglobin level before transfusion			0.138
Mean	8.365	8.867	
Median	8.75	8.9	
Range	7.2(3.6-10.8)	5.5(6-11.5)	
Age when firstly diagnosed			0.417
<6 months	7	5	
6month-2year	28	15	
>2year	11	4	
Frequency of blood transfusion			0.412
Once a month	14	11	
Twice a month	25	12	
Thrice a month	1	0	
Irregular	6	1	
Ferritin level			0.006
Mean	1600.04	1203.83	
SD	615.37	432.14	

Table 3: Youden index

Youden index J	0.4764
Associated criterion	>1107
Sensitivity	93.48
Specificity	54.17

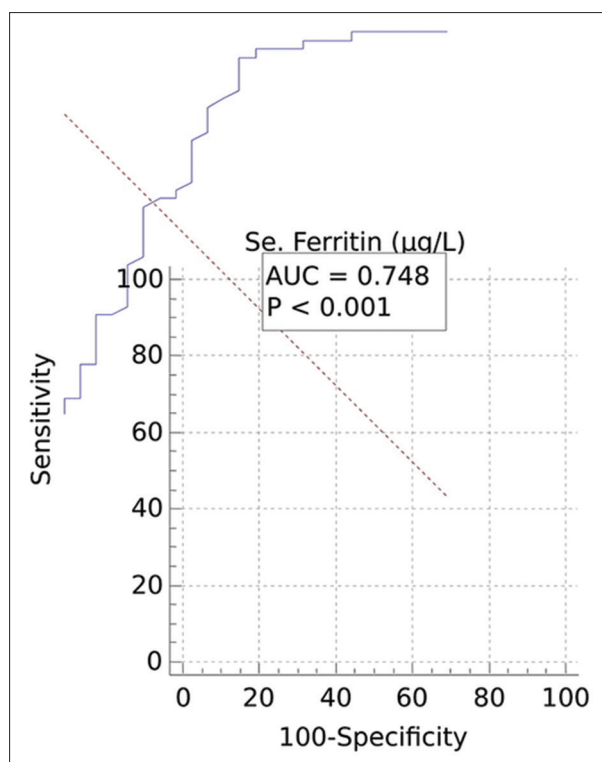


Figure 1: Receiver operating characteristic curve serum ferritin levels with short stature

life and life expectancy of these patients can be improved. Other factors in thalassemia that affect growth disorders are decreased level of pretransfusion hemoglobin, high-serum ferritin level, suboptimal use of iron chelator, and increasing age of thalassemic children. Thalassemic children grow normally in first decade of life but growth retardation occur after 10 years.^[8]

In total, 70 children of transfusion-dependent thalassemia were enrolled in this study, of which 65% were male and 35% female. The anthropometric data from this study demonstrated growth failure in transfusion-dependent thalassemia secondary to iron overload. As age advances, growth impairment increases. As per the growth pattern, we found that 65.71% were short statured and rest had normal height. The proportion of short stature in our study was similar to the previous studies of Jana *et al.*,^[9] Fadlyana *et al.*,^[10] and ParthaSarathiDas *et al.*,^[11] which discovered the incidence of short stature were 65.8%, 62%, and 67%, respectively. The cause of short stature in thalassemic children can be chronic anemia, hypersplenism, and folate deficiency.^[8] Nutritional status was assessed by BMI based on age and we found that 77% of these thalassemic children were underweight which was similar to study of ParthaSarathiDas *et al.*^[11] in which 70% were underweight. Bushra Moiz *et al.*^[12] also noted that 42% were malnourished and obesity was absent in thalassemic children. Yeni *et al.*^[13] found undernutrition in 29.4% and stunting in 58.5% of children. Similarly, Badiger S *et al.*^[14] also observed undernutrition and stunting amongst irregularly transfused thalassemic children. Along with this, they also observed pubertal delay in these children. The pathogenesis of growth failure in

Table 4: Analysis between the variables and short stature

Ferritin value	Short stature	Normal Stature	P value
≤1107 µg/L	3	13	0.001
> 1107 µg/L	43	11	

Table 5: Analysis between the variables and short stature (Logistic regression)

	B	S.E.	95% C.I. for EXP(B)	
			Lower	Upper
Age	-.064	.062	.830	1.060
Ferritin	-0.002	.001	0.996	0.999

thalassemia is multifactorial. One of the major factors is iron overload. Frequent blood transfusions can control hemoglobin level, but if serum ferritin levels are greater than the desired level, patient's physical growth can be affected.

Normal growth in thalassemic children can be attained if hemoglobin level is maintained in a range of 10–11 g/dL in first decade of life. In our study, 65.71% children had average hemoglobin level of 5–8 g/dL before transfusion this was almost similar to study of Fadlyana *et al.*^[10] In our study, we did not found any correlation between average hemoglobin level before transfusion and the incidence of short stature ($P = 0.138$). However, in contrast to our study, Al-Wataify,^[15] showed that the average hemoglobin level before transfusion was <9 g/dL which statistically increases the incidence of short stature. This may be due to lack of compliance to attend regular blood transfusion due to low socioeconomic status and less awareness about the disease in parents.

We found that 45.71% children had high-serum ferritin level. The results were much higher (77%) in study of Fadlyana *et al.*^[10] Serum ferritin value was statistically significant in short stature children ($P = 0.006$). Serum ferritin level is influenced by many factors, such as the age at presentation, the age when firstly transfused, and the age when firstly chelated, efficacy of the iron chelation drug, and its compliance. The stature of thalassemic children is associated with higher serum ferritin level.^[9]

In this study, we found a statistically significant correlation between serum ferritin level and the incidence of short stature ($P = 0.001$). This finding was similar ($P = 0.003$) to study of Fadlyana *et al.*^[10] The multivariate analysis to examine the variables showed that serum ferritin level influence the incidence of short stature in thalassemic children, whereas Fadlyana *et al.*^[10] showed that in addition to serum ferritin level, age also influence the incidence of short stature. Shalitin *et al.*^[16] observed that short stature occurred when serum ferritin level were >3,000 µg/L. High-serum ferritin level may cause growth retardation.^[10] In our study, we found a correlation between serum ferritin level and the incidence of short stature, which

was thought to be due to iron overload in endocrine glands producing growth disorders.

This study remains the first to be conducted in our region, which depicted about the growth pattern and its correlation with serum ferritin level. The limitation of this study was these children were not examined for their sexual development. Since hypogonadism is the major determinant of growth failure in beta thalassemia major, therefore, it leads to progression of growth stunting with advancing age. The effect of other factors such as hormonal status, endocrinopathies on growth and their exact association with serum ferritin level need to be assessed in a meticulous manner. This could not be done in this study due to the expensive cost of hormonal testing.

It is not only important to transfuse the packed red blood cells to maintain hemoglobin level for proper growth and development of the children affected with thalassemia but also it is of utmost importance for the primary care givers to monitor the iron status of these patients with the help of serum ferritin level. As high-serum iron and serum ferritin will be equally detrimental and will lead to growth faltering.

Hence to conclude, regular blood transfusions can maintain pretransfusion hemoglobin level, but if serum ferritin levels are higher than the desired level, patient's physical growth can be affected. There was significant correlation between serum ferritin level and short stature in thalassemic children. Thalassemia patients requiring regular blood transfusion need better strategies for removing excess iron from their body. Thus, along with maintaining hemoglobin level, it is important to have effective iron chelation therapy to minimize retardation of growth in patient with transfusion-dependent thalassemia.

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Conflicts of interest

There are no conflicts of interest.

References

1. Thacker N. Prevention of thalassemia in India. *Indian Pediatr* 2007;44:647-8.
2. Madan N, Sharma S, Sood SK, Colah R, Bhatia HM. Frequency of β thalassemia trait and other hemoglobinopathies in northern and western India. *Indian J Hum Genet* 2010;16:16-25.
3. Taksande A, Prabhu S, Venkatesh S. Cardiovascular aspect of Beta-thalassaemia. *Cardiovasc Hematol Agents Med Chem* 2012;10:25-30.
4. Rund D, Rachmilewitz E. Beta-thalassemia. *N Engl J Med* 2005;353:1135-46.
5. Spiliotis BE. β -Thalassemia and normal growth: Are they compatible. *Eur J Endocr* 1998;139:143-4.
6. Majmoodi Nesheli H, Farahanian E. Relation between bone mineral density and serum ferritin levels in patients with thalassemia major. *Caspian J Pediatr* 2016;2:158-63.
7. Hashemi A, Ghilian R, Golestan M, Ghalibaf M, Zare Z, Defghani MA. The study of growth in thalassemic patients and its correlation with serum ferritin level. *Iranian J Pediatr Hematol Oncol* 2011;1:147-51.
8. Borgna-Pignatti C, Gamberini MR. Complications of thalassemia major and their treatment. *Expert Rev Hematol* 2011;4:353-66.
9. Jana A, Gupta D, Bhattyacharyya M, Sarkar BN. Correlation between nutritional status and clinical parameters among thalassaemic patients - A study of West Bengal. *Hum Biol Revi* 2016;5:349-60.
10. Fadlyana E, Ma'ani F, Elizabeth M, Reniarti L. Correlation between serum ferritin level and growth disorders in children with thalassemia. *Am J Clin Med Res* 2017;5:31-5.
11. Das PS, Majumdar S. A study on growth parameters and clinical profile in children with thalassemia major. *IOSR J Dent Med Sci* 2019;18:25-30.
12. Moiz B, Habib A, Sawani S, Raheem A, Hasan B, Gangwani M. Anthropometric measurements in children having transfusion-dependent beta thalassemia. *Hematology* 2018;23:248-52.
13. Yeni H, Lubis G, Izzah A, Yani F. Relationship between serum ferritin and zinc levels in pediatric thalassemia major patients. *Pediatr Indones* 2019;59:144-9.
14. Badiger S, Barauh A. A study of growth pattern in regularly transfused thalassemic children of age group of 2 years to 12 years. *Int J Contemp Pediatr* 2019;6:1575-81.
15. Al-Wataify AS. Growth retardation among multi-transfused thalassemic patients in thalassemia center in Babylon Governorate. *Med J Babylon* 2012;4:815-23.
16. Shalitin S, Carmi D, Weintrob N, Philip M, Miskin H, Kornreich L, *et al.* Serum ferritin level as a predictor of impaired growth and puberty in thalassemia major patients. *Eur J Haem* 2005;74:93-100.