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Original Article

Correlation of Serum Ferritin Level and Number of Blood Transfusion in Thalassemic Patients

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ABSTRACT

Introduction: Thalassemia is a prevalent hereditary disorder of hemoglobin causing chronic anemia that necessitates regular blood transfusions. Unfortunately, these treatments often cause iron overload. In order to evaluate the accumulation of iron and adjust chelation therapy, it is necessary to monitor serum ferritin. The present study was conducted to determine the relationship between serum ferritin levels, transfusion frequency, and nutritional status of thalassemic children. **Methods & Materials:** This study was a cross-sectional study conducted in the Department of Pediatrics, Chittagong Medical College Hospital, Chittagong, over a period of six months from December 2013 to May 2014. The study population included 50 patients admitted to the Pediatrics Wards. **Result:** The study result indicated that patients who received transfusions more frequently recorded higher serum ferritin levels. The patients who were transfused at intervals of less than 1 month had the highest mean ferritin (4192.45 ng/mL), whereas those with intervals of over 2 months had the lowest mean ferritin (408.70 ng/mL), although most patients historically had transfusions every 1, 2 months. Serum ferritin levels did not show any significant correlation with weight for height, height for age, or weight for age, thus iron overload in this case was more linked to stunting and chronic malnutrition than to wasting. Almost half of the patients (46%) were severely stunted and 40% moderately stunted, with mean ferritin levels of 2542.13 ng/mL and 2689 ng/mL, respectively. On the other hand, the majority (88%) were nonwasted. **Conclusion:** The elderly patients received more blood transfusions and had higher levels of serum ferritin, with most of them having levels above 1000 ng/mL, which is an indication of severe iron overload. Higher levels of ferritin were strongly associated with stunting and chronic malnutrition, while wasting was uncommon.

Keywords: *Thalassemia, Blood Transfusion, Serum Ferritin*

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INTRODUCTION

Thalassemia is considered among the top inherited hemoglobin disorders globally and it is especially common in South and Southeast Asia, the Middle East, and the Mediterranean region. The most severe form beta thalassemia major, is due to a deficiency or absence of beta, globin chain synthesis, which results in ineffective erythropoiesis, chronic hemolytic anemia, and growth and developmental problems. Patients with transfusion, dependent thalassemia need to be given blood transfusions regularly and for their entire life to keep up their hemoglobin levels, to prevent the expansion of the bone marrow and to improve their quality of life [1,2]. Besides the fact that the transfusion is a life, saving procedure, it will still lead to iron overload as iron cannot be actively removed from the body since it has no physiological mechanism for active iron excretion. Each unit of concentrated red blood cells is estimated to have 200250 mg of iron. Thus, the excess iron from repeated transfusions gradually accumulates in such major organs as the liver, the heart, and the endocrine glands [3]. In addition, thalassemia, related ineffective erythropoiesis suppresses hepcidin secretion, resulting in increased intestinal iron absorption, which also exacerbates the systemic iron overload condition [4]. Without reassurance by iron chelation therapy, iron overload may cause serious complications such as hepatic fibrosis, cardiomyopathy, diabetes mellitus, hypogonadism, and growth retardation, which are still the leading causes of morbidity and mortality in thalassemic patients [5,6]. Hence, the evaluation of the bodys iron stores plays a very crucial role in the management of transfusion, dependent thalassemia. Among the different methods, serum ferritin measurement is the most common and feasible lab marker for total body iron load due to its low cost, easiness to get, and non, invasive character. Relative high serum ferritin concentration over time is mainly representative of the increased iron stores and thus, can be used to determine when to start and how to adjust chelation therapy [7]. Advanced methods such as MRI T2* are capable of quantifying the iron level in the organ with greater accuracy and they allow a more precise assessment of iron overload; however, these methods are not always accessible in many places with limited resources. Thus, serum ferritin is the main monitoring instrument in routine clinical practice, particularly in developing countries [8]. Even with different studies, it was found that serum ferritin levels have a positive relationship with the transfusion load such as the frequency and the total number of transfusions given. Patients who have received larger numbers of transfused blood units usually have much higher ferritin levels, which indicate that there is a progressively increasing amount of iron in the body over time [9]. Knowing this association well is quite helpful in clinical practice since it enables doctors to predict the extent of iron overload from the history of blood transfusions and to start iron chelation treatment on time so that irreversible damage to the organs can be avoided. On the other hand, serum ferritin is one of the markers of inflammation, and its concentration may go up in cases of infection, inflammation, or liver disease, which are some of the factors that can influence its reliability as a single test for determining iron overload [3]. Accordingly, it is essential to localize a patient population and study the correlation between serum ferritin levels and the number of blood transfusions in it, so that the issue of the clinical reliability of serum ferritin and its value as a monitoring parameter can be further resolved.

METHODS & MATERIALS

This study was a cross-sectional study conducted in the Department of Pediatrics, Chittagong Medical College Hospital, Chittagong, over a period of six months from December 2013 to May 2014. The study population included patients admitted to the Pediatrics Wards who met the inclusion criteria. A total of 50 consecutive cases of thalassemia were enrolled, comprising children aged 1–12 years diagnosed with beta-thalassemia major or transfusion-dependent Hb E beta-thalassemia, confirmed by hemoglobin electrophoresis, and receiving regular blood transfusions. Patients were excluded if they had received chelation therapy prior to inclusion, did not maintain a dietary chart for thalassemia, had previously received blood transfusions at an incompatible center, or exhibited signs of infection or inflammation such as hepatitis. Data were analyzed using SPSS version 15, applying appropriate statistical methods including Pearson's correlation coefficient, Spearman's rank-order correlation, and Student's t-test according to the nature of the variables. Frequencies and proportions were calculated for categorical variables, while means and standard deviations were determined for quantitative variables. A p-value of <0.05 was considered statistically significant. Ethical approval for the study was obtained from the relevant department and authority of Chittagong Medical College Hospital following the due procedure.

RESULTS

Out of 50 patients, 32 (64%) were male and 18 (36%) were female, with a male-to-female ratio of 1.77:1. The majority of patients, 35 (70%), had Hb E β-thalassemia (severe/transfusion dependent), while 15 (30%) had β-thalassemia major. Most patients were from rural areas (31, 62%) compared to urban areas (19, 38%). Regarding guardians' occupation, the largest group was in service (14, 28%), followed by day labor (11, 22%), business (11, 22%), farming (10, 20%), and others (4, 8%). In terms of socioeconomic status, most patients belonged to the middle class (27, 54%), followed by poor (20, 40%) and very poor (7, 14%), and no patient belonged to the rich category (*Table I*).

Table I
Socio-demographic and Clinical Characteristics of the Patients (*n* = 50).

Variable	Category	Frequency (n)	Percentage (%)
Gender	Male	32	64
	Female	18	36
Type of Thalassemia	Hb E β-thalassemia (severe/transfusion dependent)	35	70
	β-thalassemia major	15	30
Locality	Rural	31	62
	Urban	19	38
Guardian's Occupation	Service	14	28
	Day labor	11	22
	Business	11	22
	Farming	10	20
	Others	4	8
Socioeconomic Status	Middle class	27	54
	Poor	20	40
	Very poor	7	14
	Rich	0	0

The mean age of the patients was 8.16 ± 3.40 years, ranging from 1 to 12 years. The mean duration of illness was 5.44 ± 3.09 years, with a range of 1 to 12 years. The average age at first blood transfusion was 2.81 ± 2.22 years, ranging from 1 to 9 years. The mean serum ferritin level was 2444.76 ± 3159.25 ng/mL, with values ranging from 164 ng/mL to 18,500 ng/mL, indicating wide variability in iron overload among the patients (*Table II*).

Table II
Quantitative variables and biochemical test results of the study patients (*n* = 50).

Variables	N	Minimum	Maximum	Mean	Std. Deviation
Age of the patients (years)	50	1	12	8.16	3.395
Duration of illness (years)	50	1	12	5.44	3.085
Age at first blood transfusion (years)	50	1	9	2.81	2.215
Serum ferritin level (ng/mL)	50	164	18500	2444.76	3159.245

Regarding recent transfusion practice, 21 patients (42%) received blood at 1–2-month intervals with a mean serum ferritin level of 1637.24 ng/mL. Twenty patients (40%) received transfusions at intervals of less than 1 month and had the highest mean serum ferritin level (4192.45 ng/mL). Nine patients (18%) received transfusions at intervals greater than 2 months and showed the lowest mean ferritin level (408.70 ng/mL), indicating higher iron burden with more frequent transfusions (*Table III).*

Table III (a)
Recent blood transfusion (BT) interval during the last 1 year and mean serum ferritin level (*n* = 50).

Recent BT interval (last 1 year)	Number of patients	Percentage (%)	Mean serum ferritin (ng/mL)
<1 month	20	40.0	4192.45
1–2 months	21	42.0	1637.24
>2 months	9	18.0	408.70
Total	50	100.0	—

Previously, the majority of patients, 28 (56%), received blood transfusions at 1–2-month intervals. Seventeen patients (34%) had transfusions at intervals of more than 2 months, while only 5 patients (10%) required transfusions at intervals of less than 1 month. This indicates that most patients were maintained on a moderate transfusion schedule in the past *Table III* (b).

Table III (b)
Previous blood transfusion interval of the patients (n = 50).

Previous BT interval	Number of patients	Percentage (%)
<1 month	5	10.0
1–2 months	28	56.0
>2 months	17	34.0
Total	50	100.0

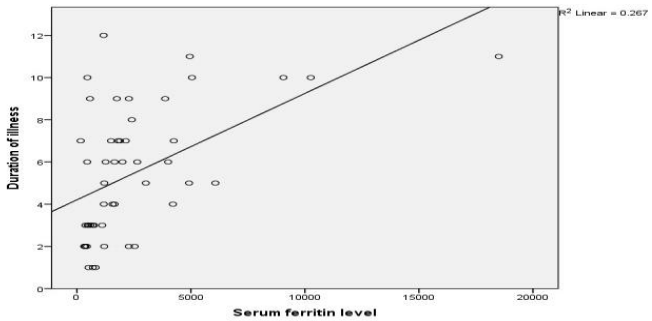

Figure 1 Correlation of serum ferritin level with duration of illness.

Figure I indicate that there is a positive correlation between ferritin levels in the blood and the duration of the illness. The higher the ferritin levels, the longer the duration of the illness, although the spread of the points indicates that there is some variation in the levels of the variables. The R^2 value of 0.267 indicates that the relationship is moderate in prediction.

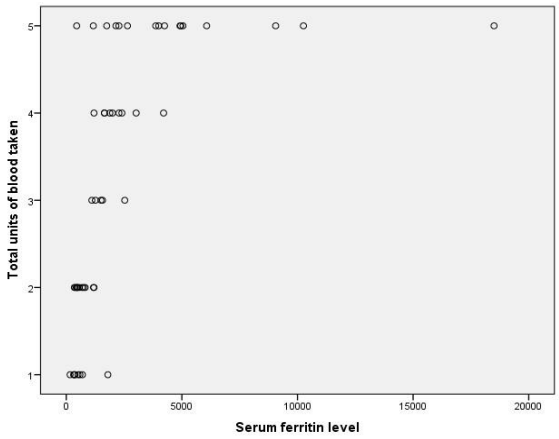

Figure 2 Correlation of serum ferritin level with total number of blood taken.

Figure 2 illustrates the positive correlation between the total units of blood drawn and the levels of serum ferritin. The graph has approximately 50 points, suggesting that the higher the blood units, the higher the iron levels in the blood, though the variation is significant in all categories.

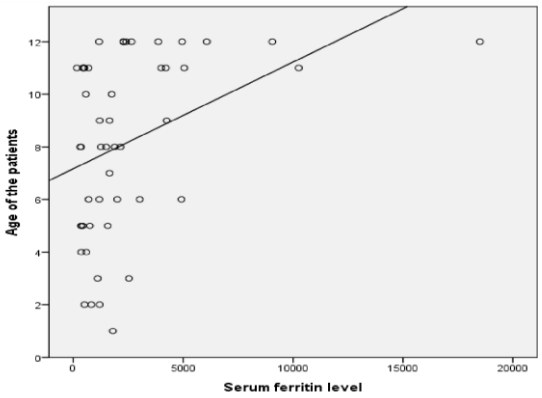

Figure 3 Correlation of age of patients with serum ferritin level.

Figure 3 depicts a positive correlation between patient age and serum ferritin levels. With increasing age, serum ferritin levels tend to rise, indicating a progressive accumulation of iron. The scatter plot indicates around 50 data points and shows considerable variability among individuals.

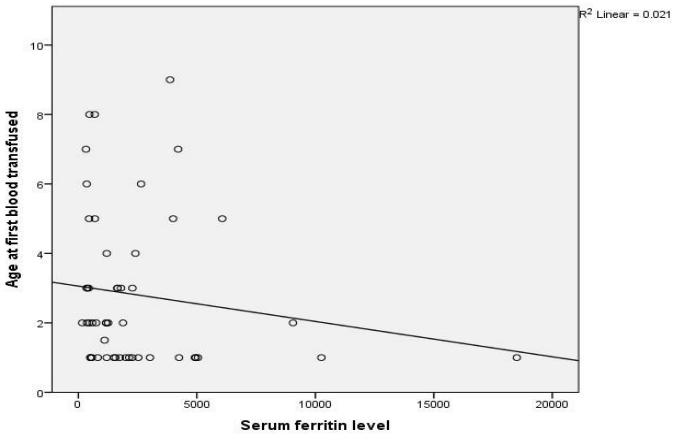

Figure 4 Correlation of Age of first BT and serum ferritin.

Figure 4 indicates a weak negative correlation where R^2=0.021. The graph has approximately 50 points, suggesting that the earlier the transfusions begin, the higher the iron levels that may accumulate in the body. However, the predictability of the levels is low.

Serum ferritin level showed a weak positive correlation with weight-for-height (r = 0.003, p = 0.981) and a weak negative correlation with height-for-age (r = -0.040, p = 0.784) and weight-for-age (r = -0.129, p = 0.374); however, none of these associations were statistically significant (p > 0.05). This suggests that higher serum ferritin levels were not significantly associated with wasting but tended to be related to stunting and chronic undernutrition. Regarding nutritional status based on height-for-age, 23 patients (46%) were severely stunted, 20 patients (40%) were moderately stunted, and only 7 patients (14%) had normal height. The mean serum ferritin level was 2542.13 ng/mL among severely stunted patients, 2689 ng/mL among moderately stunted patients, and 1087 ng/mL among those with normal height. Based on weight-for-age, 24 patients (48%) had moderate malnutrition, 12 patients (24%) had severe malnutrition, and 14 patients (28%) had normal nutritional status. In terms of weight-for-height, the majority of patients, 44 (88%), had no wasting, while only 6 patients (12%) had moderate wasting, indicating that chronic malnutrition (stunting) was more prevalent than acute malnutrition (wasting) in the study population (*Table IV*).

Table IV
Correlation of serum ferritin with growth parameters (*n* = 50).

Variables	Serum ferritin level	Height for age	Weight for height	Weight for age
Serum ferritin level	r = 1	r = -0.040	r = 0.003	r = -0.129
	—	p = 0.784	p = 0.981	p = 0.374
Height for age	r = -0.040	r = 1	r = 0.776**	r = 0.649**
	p = 0.784	—	p < 0.001	p < 0.001
Weight for height	r = 0.003	r = 0.776**	r = 1	r = 0.591**
	p = 0.981	p < 0.001	—	p < 0.001
Weight for age	r = -0.129	r = 0.649**	r = 0.591**	r = 1
	p = 0.374	p < 0.001	p < 0.001	—

Note: Correlation is significant at the 0.01 level (2-tailed)

DISCUSSION

In the present study, out of 50 patients, transfusion dependent Hb E-ß thalassemia is 35 (70%) and beta thalassemia major is 15 (30%), which is similar to other studies done in Bangladesh and 32 (64%) of patients were male and 18(36%) of the patients were female. Male to female ratio was 1.77:1 [10,11]. Patients with thalassemia major in the early transfusional period need to have some ferritin levels determined every 1-2 months in order to have a baseline value of iron load to initiate iron chelation therapy which should be started when serum ferritin levels exceed 1000 ng/ml and periodic monitoring of serum ferritin every 3 months should be done for patients on iron chelation therapy. Serum ferritin level was found higher as the duration of illness was more with repeated history of blood transfusion. Close to our results, Cario et al found that 76/102 patients (75%) younger than 10 years had serum ferritin less than 1800 ng/ml while 51/98 (52%) of thalassaemic patients who were older than 10 years had serum ferritin above 2500ng/ml [12]. In this study previously 28(56%) patients were transfused at 1-2 months interval, 17(34%) patients at >2 months interval and only 5(10%) patients at<1month interval, but recent blood transfusion interval was 1-2 month in 21 (42%) patients with mean serum ferritin level 1637ng/ml, <1 month in 20(40%) patients with mean serum ferritin level 4192.45 ng/ml and > 2 months in 9(18%) patients with mean serum ferritin level 408.7 ng/ml. It suggests that with increasing age of the patient the frequency of blood transfusion and serum ferritin level increases. Mishra A K, Tiwari A also found that serum ferritin level increases as the frequency of blood transfusion and the age of patient increases as in this study [13]. Another study by Ikram N et al also found mean serum ferritin levels 3396 ng/ml with gradually increasing frequency of blood transfusion with age [14]. In the present study results of serum ferritin were significantly correlated with both advancing age of the patients and increased number of blood transfusion to date which is comparable to those of Faris Y et al study [15]. Significant positive correlation was found between serum ferritin level with age of

patients(r=0.233, p<0.02) and total number of blood transfused(r= 0.365, p<0.001).In their study they found the patients not started using DFO had significantly lower mean serum ferritin values 1462.96 ng/ml compared to both groups on DFO therapy those with good compliance to DFO (mean serum ferritin of 1701.19 ng/ml) and those with poor compliance to desferrioxamine therapy with a mean serum ferritin of 2395.28 ng/ml. The probable cause for this lower mean serum ferritin value in the group of patients not started using desferrioxamine was the younger mean age of these patients compared to other groups on desferrioxamine therapy (3.4 years mean age of patients not use desferrioxamine versus 9.4 years in patients with compliance and 9.49 years in patients with poor compliance to desferrioxamine respectively) [15]. In the present study patients who were using DFO were excluded so we are unaware about this condition. Cario et al study also found that serum ferritin values correlate to total amount of blood transfusions [12]. Another study by Shah N R et al reported similar result to the present study. They found a linear relationship between the age of thalassemia major patients and total number of blood transfusions received so far. Their study depicted with increase in age, frequency of blood transfusions received per month also goes up [16]. In terms of pre transfusion hemoglobin level (taking 10 gm% as cut off), 53.5% of patients are under transfused. In this study 34 patients were found severely anemic with pretransfusion Hb level <7gm/dl, and 16 patients were found moderately anemic with pre transfusion hemoglobin <9gm/dl, where it should be 9.5 to 10.5 mg/ dl. This might be a reflection of less awareness of the people and general physician about the disease management. Among 50 patients 45(90%) have hemolytic facies, 5 (10%) patients have normal facies and all patients have organomegaly. Massive hepatomegalaly and splenomegaly is present in 20 and 33 patients respectively, moderate hepatomegaly and splenomegaly is present in 19 and 15 patients respectively and mild hepatomegaly and splenomegaly presents in11 and 4 patients respectively. This picture corresponds with other study where severe anemia, facial dysmorphism and hepatoslenomegaly were found in all cases [17]. In the present study significant correlation was found among different parameters of nutritional status and serum ferritin level. Serum feritin level was found positively correlated with weight for height (P<0.05) and negatively correlated with height for age and weight for age (P>0.05). In this study 23(46%) patients are found severely stunted, 20(40%) patients are moderately stunted and 7(14%) patients have normal height. Mean serum ferritin level in severe stunted patients is 2542.13 ng/ml and moderate stunting patient is 2689 ng/ml and in normal height is 1087 ng/ml which corresponds with other study [16]. Among 50 patients, 24(48%) patients have moderate malnutrition, 12(24%) patients have severe malnutrition and 14(28%) patients had normal nutritional status. Regarding W/H 44(88%) patients had no wasting only 6(12%) patients had moderate wasting. Similar result was reported by Hashemi A MD, Ghilian R MD et al on seventy patients with transfusion dependent thalassemia major patients and found mean serum ferritin level 2664+/-1446 ng/ml and 46(65.71%) of patients had height less than five percentile, and 24(34.29%) more than five percentile. Mean serum ferritin in patients with height more than five percentile was 2252+/-1040 and with height less than was 2962+/-1606 (p value=0.072) [17]. Shah N K etal study also found out of 142 patients 103(72%) were below 2standard deviations of ICMR 1990 standards of weight for age (<80% of W/A) and 76(53%) were 2SD below ICMR 1990 standards of height for age (<90% of H/A). While 63 (44%) were lagging behind in both W/A and H/A, they were both wasted and stunted [16].

LIMITATIONS

The study was conducted in a single hospital with a small sample size. So, the results may not represent the whole community.

CONCLUSION

The results of the present study revealed that increasing age of the patients, number of blood transfusions to date and increased frequency of blood transfusion are associated with increased serum ferritin level. Majority of the patients have high serum ferritin level more than 1000 ng/ml. Significant correlation was found among different parameters of nutritional status and serum ferritin level. With increased serum ferritin level more patients present with stunting and chronic malnutrition but no wasting.

RECOMMENDATION

Routine monitoring of serum ferritin at regular intervals (every 3–6 months) should be performed in transfusion-dependent thalassemic patients and ideally initiated after 10–20 transfusions to enable early detection of iron overload. Patients with serum ferritin levels exceeding 1000 ng/mL should be promptly started on appropriate iron chelation therapy to prevent organ damage. Regular screening for growth retardation, endocrine dysfunction, and cardiac complications is essential, particularly in patients with persistently elevated ferritin levels, along with proper counseling of patients and guardians regarding the risks of iron overload and the importance of adherence to treatment. In resource-limited settings where serum ferritin testing may not be feasible due to cost, chelation therapy may be judiciously initiated in patients with a long history of frequent transfusions. Furthermore, larger-scale studies are recommended to better understand the burden of iron overload and optimize management strategies.

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CONFLICT OF INTEREST

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