SAS Journal of Surgery ISSN 2454-5104
SAS J. Surg., Volume-1; Issue-3 (Sep-Oct, 2015); p-74-79
Available online at http://sassociety.com/sasjs/

Research Article

A Prospective Study Correlating Serum Ferritin, Splenic Size and Amount of Transfusion in β Thalassemia Major Patients Undergoing Splenectomy

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Abstract: In the homozygous state, β thalassemia (i.e. thalassemia major) causes severe anaemia which necessitates chronic hyper transfusion therapy which ultimately leads to transfusion iron overload and often require splenectomy. The commonly adopted criteria for splenectomy is a blood consumption greater than 50% above the mean annual transfusion requirement of the splenectomised population. Serum ferritin has been used as an easily accessible serum marker for transfusion-induced iron overload. The purpose of this study was to determine serum ferritin level and preoperative splenic size and correlating with amount of transfusion in order to establish whether iron overload or splenic size can be a criterion for early splenectomy. A total of 30 patients of β thalassemia major have been evaluated. In the study it was found that neither amount of transfusion nor serum ferritin correlate significantly with splenic size (p-value being 0.323 and 0.883 respectively). But Pearson correlation coefficient of Total number of units Transfused with Serum Ferritin was calculated to be 0.858 (p-value <0.01) emphasizing statistically significant correlation between Total number of units Transfused and Serum Ferritin. So, from this study, it can be said that serum ferritin can be a good indicator for transfusional iron overload and can be used as a criterion for assessing need for splenectomy.
Keywords: Serum ferritin, Splenic size, Blood transfusion, β Thalassemia, Iron overload, Splenectomy

INTRODUCTION

β thalassemia syndromes are a group of hereditary disorders characterized by a genetic deficiency in the synthesis of beta-globin chains. In the homozygous state, Beta thalassemia (i.e.thalassemia major) causes severe transfusion-dependent anaemia. The disease is found most commonly in the Mediterranean region, Tropical Africa, the Indian subcontinent, and Southeast Asia, and in aggregate are among the most common inherited disorders of humans. The incidence may be as high as 10% in these areas [1].

Many patients require chronic hyper transfusion therapy designed to maintain a hematocrit of at least 27–30% so that erythropoiesis is suppressed [2]. The commonly adopted criteria for splenectomy is a blood consumption greater than 50% above the mean annual transfusion requirement (volume of RBCs per kilogram of body weight per year) of the splenectomised population i.e. more than 200-250 ml/kg/year of pure red cell, to maintain a pre-transfusion Hemoglobin of 9 gm/dl [3].

Serum ferritin determination is widely accepted as a simple method for following iron load in patients with primary hemochromatosis and still remains an essential monitoring tool in this regard though there are confounding factors such as inflammation, chelation treatment changes and specific disease. However, several reports on thalassemia patients emphasize that ferritinemia is not accurate [4, 5]. There is a difference between the standard values of Serum ferritin concentration in males and females [normal range 10–220 µg/L (ng/ml) in males; 10–85 µg/L (ng/ml) in females [6]. It has been suggested that, in transfused patients, iron is preferentially distributed to the reticulo-endothelial system and that ferritin synthesis and release is responsible for higher serum ferritin levels [7]. Serum ferritin has been extensively used as an easily accessible serum marker for transfusion-induced iron overload. The major drawbacks of ferritin are a lack of specificity and inter-patient variability [8].

The size and weight of the spleen vary with age and sex. It can also vary slightly in the same individual under different conditions. In the adult it is usually 12 cm long, 7 cm broad, and 3–4 cm wide. Splenomegaly (enlarged spleen) is common in thalassemia major and intermedia due to the high rate of hemolysis (red blood cell destruction). This takes place because the spleen sees the defective red cells of the thalassemic as deficient and the transfused red cells as invaders (much the same as with host versus graft disease) and removes them from circulation. Poulin et al. defined splenomegaly as moderate if the largest

dimension is 11-20 cm, and severe if the largest dimension is greater than 20 cm [9].

The purpose of this study was to determine serum ferritin level and preoperative splenic size and correlating with amount of transfusion in order to establish whether iron overload or splenic size can be a criterion for early splenectomy.

MATERIAL AND METHODS

This was an institution-based, prospective study conducted in Department of Surgery, Medical College, Kolkata, India from January 2013 to June 2014 (16 months). Informed consent was taken from all the patients. The study got clearance from Institutional Ethical Committee.

30 β Thalassemia patients were selected, having splenomegaly and is being planned for splenectomy.

Inclusion Criteria

The following patients will be included in the study population

- Patients who are β-Thalassemia major requiring repeated blood transfusions (at least 2 per month).
- Patients who have not undergone chelation therapy.
- Patients who are > 12 years of age.

Exclusion Criteria

The following patients will be excluded from the study population:-

- Patients having any congenital or acquired liver disease.
- Patients with chronic Hepatitis B or Hepatitis C infection or any other disease complicated by splenomegaly.
- Patients suffering from any malignancy.
- Patients who refuses to be part of study.

All operable cases of β-thalassemia patients requiring repeated blood transfusions and who have not taken iron chelation therapy were subjected to a detailed history using a structured questionnaire and examined clinically.

Ultrasonography (Whole abdomen) was performed and size of spleen (Cranio-caudal) was noted. Baseline investigations of the patients were done. Serum Ferritin was measured before preparing for surgery.After the patients was found fit for surgery from anaesthetic point of view, splenectomy with or without cholecystectomy was done.

All statistical analyses were performed with SPSS® software version 21.0 for Windows 8.1 (SPSS, Chicago, IL, USA). The Pearson correlation test was used to examine association between all continuous variables. Pearson Correlation Coefficient was calculated. All bivariate analysis was appropriately done and p value < 0.01 were considered significant.

RESULTS

In this study, 30 β Thalassemia major patients were studied.Out of 30 patients, 7 were males (23%) and 23 females (77%).

Descriptive Statistics of Age:

Out of 30 patients, minimum age of presentation was 12 years and maximum age of presentation was 18 years with a standard deviation of 1.431.

Table-1: Descriptive Statistics of Age

	N	Range	Minimum	Maximum	Mean		Std. Deviation
	Statistic	Statistic	Statistic	Statistic	Statistic	Std. Error	Statistic
Age	30	6	12	18	15.23	.261	1.431
Valid N (listwise)	30						

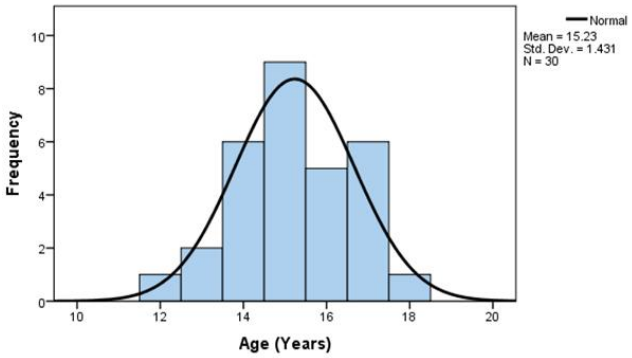

Chart-1: Histogram and Distribution curve depicting descriptive statistics of Age

Descriptive Statistics of Amount of Blood Transfusion

Total duration of transfusion varied widely among the 30 patients. So amount of blood transfused is taken into consideration. Mean amount of transfusion was 41 units ± 10.22 (S.D). The range was from 21 units to 68 units.

Table-2: Descriptive Statistics of Amount of Blood Transfusion

	N	Range	Minimum	Maximum	Mean		Std. Deviation
	Statistic	Statistic	Statistic	Statistic	Statistic	Std. Error	Statistic
Total Number of unitsTransfused	30	47	21	68	41.00	1.866	10.222
Valid N (listwise)	30						

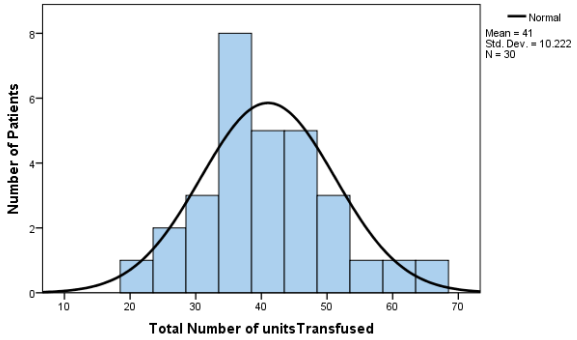

Chart-2: Histogram and Distribution curve depicting descriptive statistics of Amount of Blood Transfusion

Descriptive Statistics of Serum Ferritin

Out of 30 patients, Serum ferritin ranged from 1008 ng/ml to 4075 ng/ml with a mean of 1756 ng/ml. Standard Deviation was 595.452.

Table-3: Descriptive Statistics of Serum Ferritin.

	N	Range	Minimum	Maximum	Mean		Std. Deviation
	Statistic	Statistic	Statistic	Statistic	Statistic	Std. Error	Statistic
Ferritin (ng/ml)	30	3067	1008	4075	1755.93	108.714	595.452
Valid N (list wise)	30						

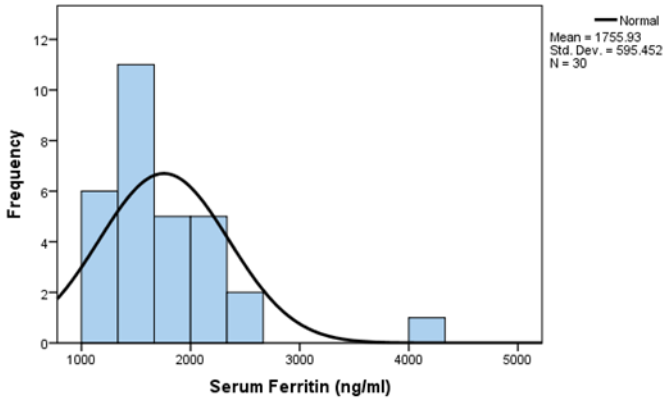

Chart-3: Histogram and Distribution curve depicting descriptive statistics of Serum Ferritin.

Descriptive Statistics of Splenic Size

Splenic size varied among the 30 patients. Mean Splenic Size 17.657 cm ± 1.8417(S.D). The range was from 15 cm to 22 cm.

Table-4: Descriptive Statistics of Splenic Size.

	N	Range	Minimum	Maximum	Mean		Std. Deviation
	Statistic	Statistic	Statistic	Statistic	Statistic	Std. Error	Statistic
SplenicSize in cm	30	7.0	15.0	22.0	17.767	.3363	1.8417
Valid N (list wise)	30						

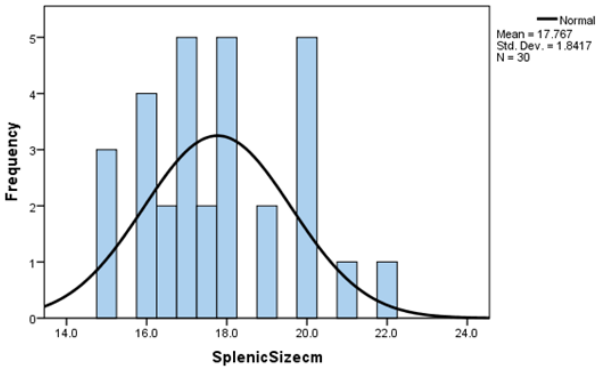

Chart-4: Histogram and Distribution curve depicting descriptive statistics of Splenic Size.

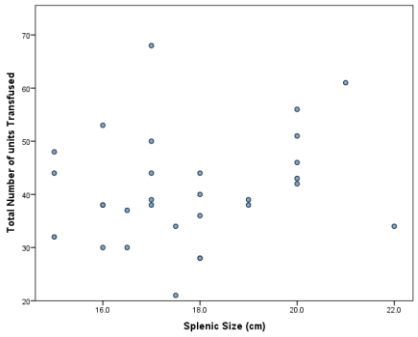

Chart-5: Scatter Dot Graph showing Correlation of Total units of Blood Transfused with splenic size.

Correlation of total number of units of blood transfused with splenic size

Correlations between total number of transfusions and splenic size are calculated using Pearson's Correlation coefficient as both are parametric variables. P-value was calculated. Since p-value is 0.323 (>0.01) and Pearson's Correlation coefficient is 0.187, it can be concluded that the correlation is not statistically significant.

Table-5: Correlation of Correlation of Total units of Blood Transfused with splenic size

Pearson Correlation Coefficient	p-value
0.187	0.323

Correlation of total number of units of blood transfused with serum ferritin

Table 6: Correlation of Total number of units Transfused with Serum Ferritin

Pearson Correlation Coefficient	p-value
0.858	**< 0.01**

Since Pearson Correlation coefficient value is 0.858 and p-value is < 0.01, it can be concluded that the correlation between serum ferritin and total number of units transfused is statistically significant.

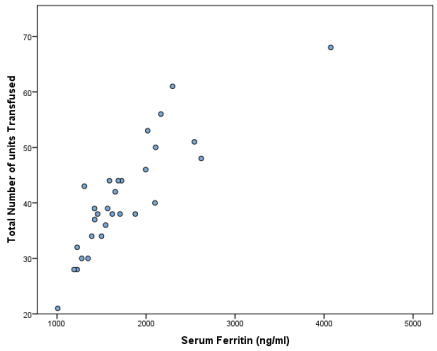

Chart-6: Scatter Dot Graph showing Correlation of Total number of units Transfused with Serum Ferritin.

Correlation of serum ferritin with splenic size

Table-7: Correlation of Splenic Size with Serum Ferritin

Pearson Correlation Coefficient	p-value
0.028	0.883

Since p-value is 0.883 (>0.01) and Pearson's Correlation coefficient is 0.187, it can be concluded that the correlation is not statistically significant.

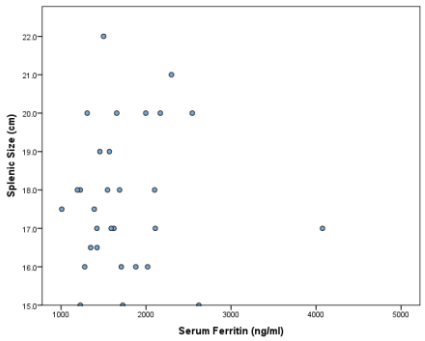

Chart-7: Scatter Dot Graph showing Correlation of Splenic Size with Serum Ferritin.

DISCUSSION

In this study, 30 β-thalassemia major patients, fulfilling the selection criteria of this study, were examined. The mean age of the study population was 15.23 years ± 1.431 (S.D.). The range was from 12 years to 18 years. Most of the patients have started transfusion at the age of 5-7 years and so there is not much difference in the duration of transfusion among the groups.

Out of 30 patients, 7 were males (23%) and 23 females (77%). Since β-thalassemia is a form of inherited autosomal recessive blood disorder, not much inference should be drawn from this observation.

Transfusion history was taken and amount of transfusion is emphasized upon. Out of 30 patients, Mean amount of transfusion was 41 units ± 10.22 (S.D). The range was from 21 units to 68 units.

Out of 30 patients, Serum ferritin ranged from 1008 ng/ml to 4075 ng/ml with a mean of 1756 ng/ml ± 595.452 (S.D). The standard error of mean was 108.714 and the variance was 354563.01.In the study by Takatoku et al, 90% of patients with either cardiac or hepatic complications had high Serum Ferritin levels of more than 1,000 µg/L (ng/ml). Since all of the values here are above 1000 ng/ml, the amount of transfusion needed to reach there was not definitely determined but could be inferred. This emphasizes regular and early measurement of serum ferritin is necessary for proper evaluation [10].

Correlation test was applied to the parametric variables.

Pearson correlation coefficient of Total units of Blood Transfused (amount of blood transfused) with splenic size was calculated to be 0.187 with p-value 0.323. Thus, there was no statistically significant correlation between Total units of Blood Transfused and splenic size.

Correlation test between Splenic Size and Serum Ferritin revealed the Pearson correlation coefficient to be 0.028 with p-value 0.883. Thus, there exists no statistically significant correlation between Serum Albumin and Serum Ferritin.

Pearson correlation coefficient of Total number of units Transfused with Serum Ferritin was calculated to be 0.858 with p-value <0.01. Thus, there was statistically significant correlation between Total number of units Transfused and Serum Ferritin. The clinical studies concerning the relationship between blood transfusion and Serum Ferritin have been conducted mainly in the Europe and US, showing that there is a clear cut positive correlation between the amount of chronic blood transfusion and the elevation of Serum Ferritin in patients with β-thalassemia [11, 12]. So, the findings is consistent with these studies.

From these correlation tests, it is obvious that amount of blood transfusion vary significantly with serum ferritin but does not vary significantly with splenic size.

CONCLUSION

Total units of Blood Transfused (amount of transfusion) does not correlate significantly with splenic size. This emphasizes that the size of spleen does not vary significantly with the amount of transfusion. So Splenic size cannot be made a criterion for considering splenectomy in β-thalassemia patients.

Serum Ferritin also does not correlate significantly with splenic size emphasizing once again

that Splenic Size is an unreliable indicator for iron overload.

There was statistically significant correlation between Total number of units Transfused and Serum Ferritin. The more the amount of transfusion, the more is the serum ferritin level in the patients of β-thalassemia major who has come for and undergone splenectomy in Medical College, Kolkata. So serum ferritin can be a good indicator for transfusional iron overload and can be used as a criterion for assessing need for splenectomy.

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