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Iron Toxicity Measurement by Serum Ferritin Levels Due to Blood Transfusion in Patients of Thalassemia Major

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Abstract

Introduction: Thalassemia is genetic blood disorders inherited from a person's parents that can result in the abnormal formation of hemoglobin. In beta thalassemia major ineffective erythropoiesis, frequent blood transfusions lead to iron overload. Excessive iron can cause irreversible organ damage. Iron overload can be measured by serum ferritin levels. *Aims and objectives:* To study iron toxicity due to blood transfusion in patients of thalassemia major. To study the correlation between iron toxicity and serum ferritin levels. Correlation between iron toxicity and number of blood transfusions. To study growth parameters in thalassemia penitents pertaining to iron toxicity. *Methods:* Fifty cases of thalassemia major were enrolled. Detailed history and clinical examination was done and blood samples collected to test for serum ferritin levels. Ferritin levels were performed by using indirect enzyme-linked immunosorbent assay (ELISA) kit along with normal and abnormal controls. Data were analyzed to determine the association between variables. *Results:* Majority of the patients were in ≤5 years of age (40%) followed by 6–10 years (32%). Sixty-four percent subjects were male and 36% were female. At baseline majority of the children (44%) were having serum ferritin level between 1000 and 2500 ng/ml followed by 2501 and 4000 ng/ml (32%) and 4001 and above (14%). At the last follow-up serum ferritin level was observed to be increased with majority having serum ferritin level between 1000–4000 ng/ml (68%). At the last follow-up it was observed that the total dose of iron chelator was increased as compared to baseline and was statistically significant. *Conclusion:* Thus we conclude that majority of the children suffering from thalassemia major were having iron toxicity due to blood transfusion at the baseline and at the last follow-up also. Increasing age and number of transfusions were significantly associated with serum ferritin levels statistically. Positive correlation between Sr. Ferritin level and chelation was observed at the baseline and at the time of last follow-up also.

Keywords: Thalassemia; Enzyme-linked immunosorbent assay (ELISA); Serum; Hemoglobin.

Introduction

Thalassemia is genetic blood disorders inherited from a person's parents that can result in the abnormal formation of hemoglobin.[1] There are two major types, alpha and beta thalassemia. The severity depends on how many of the four genes for alpha or two genes for beta globin are missing.[1]

Thalassemia occurs when there is decreased or absent production of one of the types of globin

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chains (most commonly either α or β), that cause insufficient amount of normal structure of globin chains.

Children affected with thalassemia have pallor, poor development, and abdominal enlargement. Anemia is due to a combination of ineffective erythropoiesis, excessive peripheral red blood cell hemolysis, and progressive splenomegaly.[2] The red cells are microcytic (mean corpuscular volume <70 fL) with marked anisochromasia. The bone marrow shows marked erythroid hyperplasia, and the serum ferritin level is elevated. Because of chronic anemia and iron overload, endocrinopathies such as hypopituitarism, hypothyroidism, hypoparathyroidism, diabetes mellitus, cardiomyopathy, and testicular or ovarian failure become common as the child with thalassemia grows older.[3,4]

The current management of β-thalassemia major patient is based on regular transfusion of packed red cells and effective chelating therapy.[5–8] The aim of the transfusion therapy is to correct anemia and to maintain sufficient circulating level of hemoglobin (Hb) to suppress endogenous erythropoiesis.[9] Major complication in chronically transfused patients is iron overload.[10] Iron stores in the body exist primarily in the form of ferritin. In the body, small amounts of ferritin are secreted into the plasma. The concentration of this plasma (or serum) ferritin is positively correlated with the size of the total body iron stores in the absence of inflammation. Excess iron is extremely toxic to all cells of the body and can cause serious and irreversible organic damage, such as cirrhosis, diabetes, heart disease, and hypogonadism.[11]

A target ferritin of approximately 1000 mg/L is generally recommended standard practice in thalassaemia major (TIF Guidelines, 2000) and other forms of iron overload resulting from blood transfusion. When the serum ferritin level reaches 1000 ng/L (usually after 10^{th} to 12^{th} transfusion), it is generally taken as the point to initiate iron chelation therapy.

Aims and Objectives

Aim

To study iron toxicity due to blood transfusion in patients of thalassemia major.

Objectives

1. To study the correlation between iron toxicity and serum ferritin levels.
2. Correlation between iron toxicity and number of blood transfusions.
3. To study growth parameters in thalassemia penitents pertaining to iron toxicity.

Materials and Methods

Fifty cases of thalassemia major were enrolled from a teritiary hospital in Pune. Detailed history and clinical examination was done and blood samples collected to test for serum ferritin levels. Ferritin levels were performed by using indirect enzyme linked immunosorbent assay (ELISA) kit Orgentec, Germany along with normal and abnormal controls. Data were analyzed to determine the association between variables.

Results

Majority of the patients were in ≤5 years of age (40%) followed by 6–10 years (32%). 64% subjects were male and 36% were female. At the baseline 34% children had received 41–80 transfusions while 24% had received 1–40 transfusions. At the last follow-up 36% had received 41–80 transfusions while 14% had received 1–40 transfusions. At baseline majority of the children (44%) were having serum ferritin level between 1000 and 2500 ng/ml followed by 2501 and 4000 ng/ml (32%) and 4001 and above (14%). At the last follow-up serum ferritin level was observed to be increased and majority of the children were having serum ferritin level between 1000–4000 ng/ml (68%). At baseline maximum mean serum ferritin level was observed among 6–10 years children (3400.76 ± 1564.89) followed by >10 years children (2986 ± 1403.816) and the difference was statistically significant. At the last follow-up also maximum mean serum ferritin level (4036.63 ± 1907.302) was observed among 6–10 years children followed by >10 years children were observed (3656.81 ± 1533.986). Mean dose of chelation drug at baseline was 625 ± 235.135 in >10 years age children while it was 546.88 ± 187.50 in 6–10 years age children with statistically significant difference. At the last follow-up it was observed that the total dose of iron chelator was increased as compared to baseline. The mean serum ferritin level at baseline among 81–120 transfusion was 3190.71 ± 667.032 while 121–160 transfusions was 3107.24 ± 1170.836 and the difference observed was statistically significant. Serum ferritin level was significantly increased after last follow-up, i.e. 13.59%. The mean serum ferritin level among the children with 81–120

transfusion was 4371.88 ± 2487.551 ng/ml while among 121–160 transfusion was 3861.18 ± 1540.155 ng/ml. At baseline maximum requirement of iron chelator dose (750 ± 250.00) was among the patients who had 81–120 transfusions followed by 161–200 transfusions (678.57 ± 237.797) and the difference was statistically significant (Figs 1–3).

At last follow-up the requirement of iron chelators was increasing with number transfusions. And the difference observed was statistically significant. At the baseline there was positive correlation between the number of transfusions and serum ferritin and chelation (0.4 and 0.56 respectively) with significant *p* value. Weak negative correlation between number of transfusion and BMI was observed with non significant *p*-value (p = 0.97). At the follow-up there was positive correlation between number of transfusion and serum ferritin level and chelation (0.36 and 0.57 respectively) with significant *p*-value. Negative correlation between number of transfusion and BMI (–0.33) with significant *p*-value. In the baseline group positive correlation between Sr. Ferritin level and chelation was observed (r = 0.402) while weak negative correlation between Sr. Ferritin level and BMI was observed (r = –0.06). In the follow-up group association between Sr. Ferritin level and chelation and BMI was not significant. At the baseline weak negative correlation between serum ferritin and height, weight and MAC was observed (r = –0.07, –0.02, –0.14 respectively) but the correlation was not significant. At the last follow-up positive correlation between serum ferritin level and height, weight and MAC was observed (r = 0.26, 0.53, 0.28 respectively) but the correlation was not statistically significant (Tables 1 and 2).

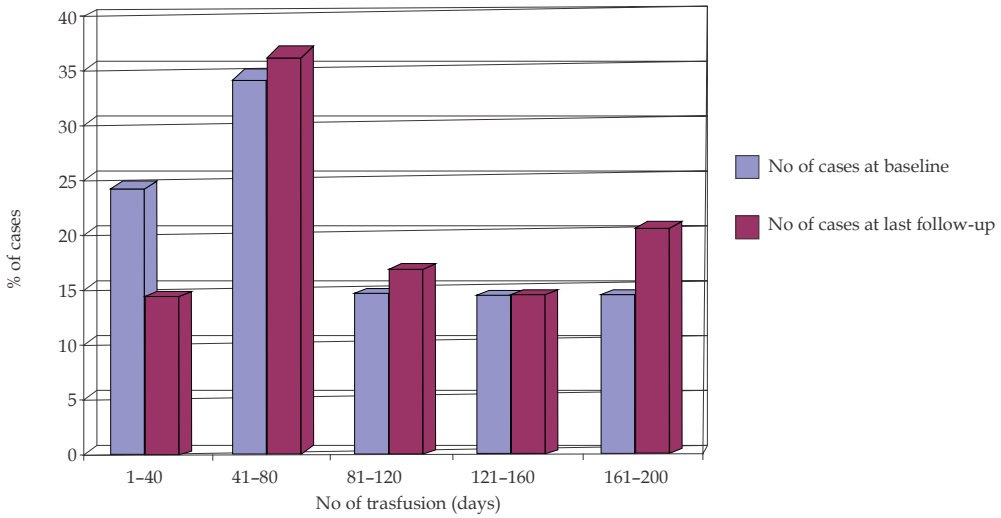

Fig. 1: Bar diagram showing No of blood transfusion wise distribution of cases in study group.

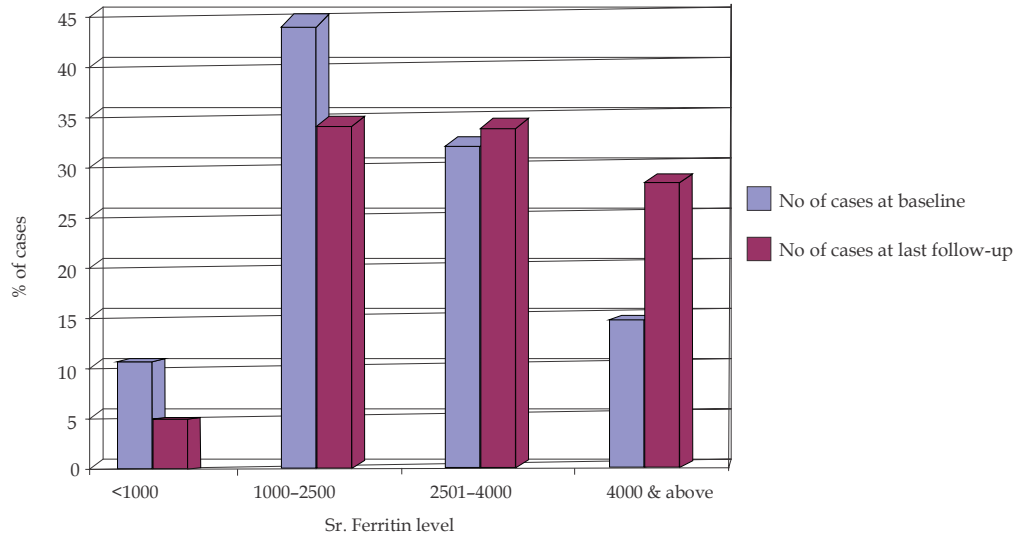

Fig. 2: Bar diagram showing comparison of Sr. Ferritin level at baseline, last follow-up according to number of transfusion in study group.

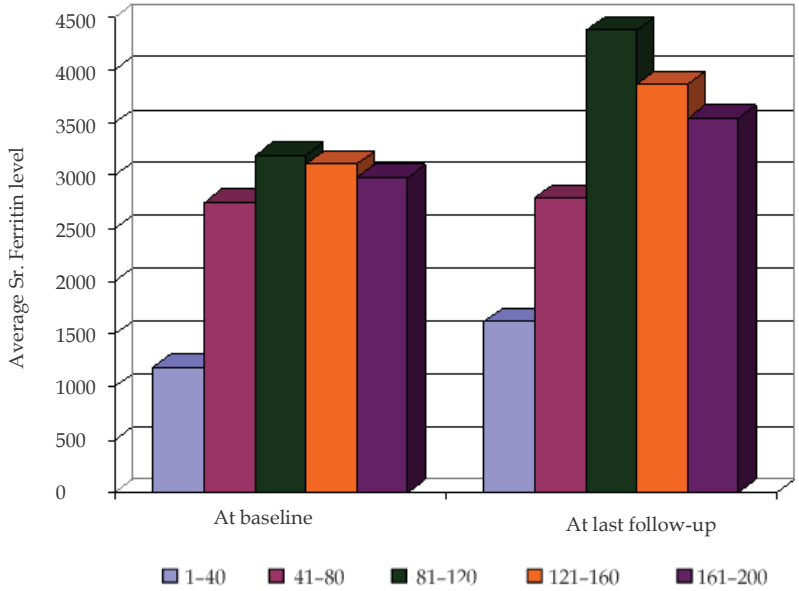

Fig. 3: Bar diagram showing comparison of Sr. Ferritin level at baseline, last follow-up according to no of transfusion in study group.

Table 1: Correlation between number of transfusion and Sr. Ferritin level, chelation, BMI at baseline in study group

Correlation between no of transfusion and	*r*-value	*p*-value
Sr. Ferritin level (*n* = 50)	0.40	0.004
Chelation (*n* = 47*)	0.56	<0.0001
BMI (*n* = 39**)	–0.01	0.97

*3 cases had age <2 years **11 cases had age <5 years

Table 2: Correlation between number of transfusion and Sr. Ferritin level, chelation, BMI at last follow-up in study group

Correlation between no of transfusion and	*r*-value	*p*-value
Sr. Ferritin level (*n* = 50)	0.36	0.011
Chelation (*n* = 47*)	0.57	<0.0001
BMI (*n* = 39**)	–0.33	0.044

*3 cases had age <2 years **11 cases had age <5 years

Conclusion

Thus we conclude that majority of the children suffering from thalassemia major were having iron toxicity due to blood transfusion at the baseline and at the last follow-up also. Increasing age and number of transfusions were significantly associated with serum ferritin levels statistically. Positive correlation between Sr. Ferritin level and chelation was observed at the baseline and at the time of last follow-up also.

Negative correlation of Sr. Ferritin level with height, weight, BMI and MAC in study group was observed. Thus there was growth retardation along with iron overload but the difference was not statistically significant.

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