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ASSOCIATION OF LIVER ENZYMES WITH SERUM FERRITIN LEVELS IN β - THALASSEMIA MAJOR

Pediatrics

Dr. Raman Kishore Senior Resident, Department of Pediatrics, All India Institute of Medical Sciences Patna, Bihar

Dr. (Prof.) Radha Krishna Sinha* Professor, Department of Pediatrics, Jawaharlal Nehru Medical College and Hospital, Bhagalpur, Bihar.*Corresponding Author

ABSTRACT

INTRODUCTION: Liver is the earliest site of iron deposition in transfusion dependent β -thalassemia major and iron induced liver injury is the common cause of morbidity. Liver enzymes are raised and indicative of liver injury in transfusion dependant β-thalassemia major patients. The current study aimed to determine the correlation of serum ferritin with liver enzymes. **METHODS:** The study was carried out in pediatric department, Jawaharlal Nehru Medical College and Hospital, Bhagalpur during a period from June 2013 to May 2014. Fifty five (55) β-thalassemia major children of 4-20 years who were on regular chelation therapy with Deferasirox since at least 1 year were taken for study. Serum ferritin levels and serum SGOT and SGPT levels were estimated and results were correlated. **RESULTS:** Out of total fifty five (55) children, most were in the age group of 4 to 8 years. Mean rate of blood transfusion in subjects was 157.01ml/kg/year and mean duration of chelation therapy was 2.34 years. Serum ferritin levels were increased in β-thalassemic children with average of 2130.33±859.85ng/ml. The SGOT and SGPT were also raised significantly (p value <0.05) with mean of 71.37±24.16 IU/L and 62.3 5±25.75 IU/L respectively. The values of SGOT & SGPT becomes highly significant (p value <0.001) when serum ferritin becomes more than 2000 ng/ml. Onset of liver enzyme derangement starts at serum ferritin level of more than 1000 ng/ml We found positive correlation between serum ferritin and deranged liver enzymes (Pearson's bivariate correlation coefficient r = 0.84±84). **CONCLUSIONS:** There was a significant correlation between serum ferritin level and liver enzymes.

KEYWORDS

β-Thalassemia, Hemolytic Anemia, Liver Enzymes, Serum Ferritin

INTRODUCTION

Beta-Thalassemia major is the most common congenital hemolytic anemia characterized by reduction or absence of beta globin chains synthesis resulting in reduction of hemoglobin (Hb) in Red Blood Cells (RBC) and decreased RBC production and anemia [1, 2]. The regular blood transfusion is known as a basic therapeutic regimen in patients with Thalassemia Major (TM). However, frequent blood transfusion causes progressive iron overload which is major complication of treatment. Blood transfusion is the primary way of treating thalassemia; it allows the normal growth of the child as well as restrains abnormal erythropoiesis [3]. Iron-chelating agents should be used properly; otherwise, multiple blood transfusions can lead to iron overload. Yet, with no blood transfusion, the increase rate of erythropoiesis intensifies dietary iron absorption from the gut, leading to a severe form of iron overload [4]. Iron overload can result in serious damage to various organs such as endocrines, liver and heart. Liver is the earliest site of iron overload in regularly transfused children and common cause of morbidity. Iron overload occurs both in hepatocytes and reticuloendothelial cells. The iron induced liver injury is characterized by development of fibrosis and even Liver enzymes such as SGOT, SGPT are raised in transfusion dependent β-thalassemia major patients. Liver injury is assessed by estimation of liver enzymes which are raised due to oxidative injury and direct toxic effect of iron on liver cells [5]. This study was planned to study the correlation of liver enzymes (SGOT and SGPT) with serum ferritin levels in children with transfusion dependent β-thalassemia major.

METHODS

The study was carried out in pediatric department, Jawaharlal Nehru Medical College and Hospital, Bhagalpur during a period from June 2013 to May 2014. Fifty five (55) β-thalassemia major children of 4-20 years who were on regular chelation therapy with Deferasirox since at least 1 year were taken for study. Written consent was taken from parents of children before entering into the study .All children were transfusion dependent at the rate of once or twice a month. These children were seronegative for HIV, HCV and HbsAg and were not having any other significant medical or surgical condition. Other than routine Complete Blood Count (CBC), venous blood was taken for serum ferritin and serum SGOT, SGPT estimation after blood transfusion. Serum ferritin level was measured with Elecys 210. Ferritin specific antibody sandwich principle is used by this test which takes 18 minutes. The sample passes through two faces in which two different ferritin specific antibody coats the ferritin. Serum SGOT and SGPT estimation was done by semi auto analyser. Serum level of SGOT >50 IU/L and SGPT >40 IU/L were considered abnormal. Results were correlated and statistical analysis was done using Pearson's bivariate coefficient test.

RESULTS

Out of fifty five (55) children, majority of children 33 (60%) were in the age group of 4-8 years. Only 11 (20%) children were more than 12 years old. Female preponderance in subjects 31 (56.4%) was seen. Mean Hemoglobin Concentration after Blood transfusion was 9.7gm/dl. Various basic variables of β-thalassemia patients were shown in Table 1.

Table 1: general variables in β-thalassemic children

Variable	Mean	Standard deviation
Age (year)	8.80	3.88
Age at Diagnosis(in Months)	29.91	31.04
No. of blood transfusions	84.65	85.71
Rate of Blood transfusion(in ml/Kg/yr)	157.02	21.33
Dose of Deferasirox (in mg/kg/day)	34.40	26.86
Duration of chelation therapy in years	2.35	1.87

Mean serum ferritin was 2130±859.85 ng/ml. 23 (41.81%) patients revealed serum ferritin levels between 1000 and 2000 ng/ml while 20 (36.36%) children had even higher serum ferritin levels between 2000 and 3000 ng/ml inspite of chelation. Only 3 (5%) patients maintained serum ferritin levels <1000 ng/ml. Mean SGOT was 71.37±24.16 IU/L and mean SGPT was 62.35±23.75IU/L which were higher than normal value (p <0.05) Serum liver enzymes at various levels of serum ferritin levels were as shown in Table 2. The statistically highly significant difference in SGOT and SGPT was observed once the serum ferritin crossed level of 2000 ng/ml (p Value <0.001).

Table 2: Liver enzymes at different serum ferritin levels

S. Ferritin(ng/ml) (No.)	SGOT	SD	p Value	SGPT	SD	p Value
<1000 (3)	45.34	25.37	>0.05	35.15	24.2	>0.05
1000 - <2000 (23)	53.45	24.17	>0.05	45.92	23.8	>0.05
2000 - <3000 (20)	79.94	24.57	<0.001	71.78	23.7	<0.001
>3000 (9)	106.75	24.71	<0.001	92.47	23.7	<0.001
Mean 2130±859.85	71.37	24.16	<0.05	62.35	23.7	<0.05

When liver enzymes were analysed at different serum ferritin levels, they were continuously rising as the serum ferritin was increasing and after the level of 2000 ng/ml, there was steep rise in liver enzyme levels. When serum ferritin levels were correlated with no. of blood transfusions, we found that after 30 blood transfusions the serum ferritin increases to large extent and it continues to rise as no. of transfusion further increases. The pearson bivariate coefficient

correlation was positive (r = +0.33). When we correlated serum ferritin levels with liver enzymes we found a positive correlation. As the serum ferritin level increases more than 1000 ng/ml, the levels of SGOT and SGPT rise significantly.

DISCUSSION

As liver is the earliest organ affected by iron overload in thalassemia children and serum SGOT and SGPT are raised due to peroxidative injury and direct toxic effect of iron on liver cells. So this study was conducted to know the effect of iron toxicity on liver enzymes and their correlation with serum ferritin levels.In present study the serum ferritin concentration was very high in β-thalassemic children inspite of chelation therapy. A positive correlation was noted between number of transfusions and serum ferritin level with correlation coefficient (r=+.33). As Iron deposition in liver takes place, its functions are affected which are predicted by raised SGOT and SGPT. SGOT and SGPT were raised significantly (p Value <0.05) and continue to rise as ferritin crosses 1000 ng/ml. There was a positive correlation between serum ferritin and liver enzymes (Pearson's bivariate correlation coefficient r=+0.87±84).Patients with iron overload have increased levels of thiobarbituric acid reactant and increased hepatic level of aldehyde protein adduct indicating lipid peroxidation. Collagen formation and portal fibrosis starts as early as 2 years of onset of transfusion. In absence of chelation, cirrhosis may develop in first decade of life [6].

Chekir KA et al conducted a study on 56 thalassemic children and determined various metabolic parameters. The study suggested that in beta thalassemia first organ impaired was liver. Plasma thiobarbituric acid reactive substances (TBARS) were significantly raised leading to deranged liver functions[7] Similar finding were seen by Ameli M et al by study conducted in Iran (2006). In their study they found that mean serum ALT (Alanine aminotransferase) was significantly high in thalassemic children with high serum ferritin and high transfusion index[8].Sedigheh shams et al noted the similar findings from study in Iran with significantly raised liver enzymes (ALT, AST) in homozygous thalassemia major patients than in controls[9]. Asharaf soliman et al observed during a study that some disturbances occur in liver functions in hepatitis negative thalassemia patients with iron overload. Use of Desferroxamine is associated with decrease in liver enzymes [10]. Barton JC et al noted similar results as serum ferritin increases liver enzymes also increases [11].

CONCLUSION

Iron overload is a principle reason for raised liver enzyme and there was a positive correlation with serum ferritin.

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