ORIGINAL RESEARCH PAPER

Physiology

KEY WORDS: BTM,SGOT, SGPT, ALP

A COMPREHENSIVE STUDY TO ASSESS STATUS OF LIVER FUNCTION TESTS IN BETA THALASSEMIC MAJOR PATIENTS IN JHALAWAR MEDICAL COLLEGE JHALAWAR

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ABSTRACT

Introduction – Beta thalassemia major patients develop iron overload due to multiple blood transfusionscausing injury to liver indicated by altered liver enzymes.

Objective -To study correlation between s. ferritin level and liver enzymes (SGOT, SGPT & ALP) in BTM patients.

Material and Methods – Eighty patients of Beta thalassemia major, from Paediatrics ward JMC Jhalawar, were studied for their serum ferritin level and liver enzymes , and statistical analysis was done.

Result – Mean values of s. Ferritin, SGOT, SGPT & ALP were 2336.29 +/- 1422.11 ng/ml, 101.26 +/- 49.76 U/L , 95.34 +/- 50.76 U/L , and 193.49 +/- 50.98 U/L . We found positive correlation between s.ferritin and SGOT, SGPT, & ALP. Correlation with SGOT & SGPT was statistically significant.

Conclusion – SGOT & SGPT showed positive correlation with serum ferritin (r=0.740 & 0.735 respectively), while ALP was not significantly correlated.

INTRODUCTION

Thalassemia is a heterogeneous group of disorder, with a genetically determined reduction in the rate of synthesis of one or more types of normal hemoglobin polypeptide chain. β-thalassemia major is the homozygous form of the disease, characterized by total suppression of β chain synthesis which results in moderate to severe anemia.Prevalence of thalassemiagene in different region of India varies between 1-17% with mean prevalence of about 3.39 %.[ą]

Blood transform is the mainstay of treatment in beta thalassemic major patients who require it frequently, usually at least once in a month. This has significantly improved their long term survival, leading them to survive till adulthood or more, as compared to early childhood deaths. On one hand, it reduced death rate in thalassaemic patients due to anaemia, but on the other hand it increased complications due to iron overload and resulting deaths[¸-ł]. Iron overload may be attributable to hypertransfusion, inadequate chelation, erythrocyte catabolism and excessive iron absorption from the gut as a consequence of ineffective erythropoiesis[(4)].

Excessive iron causes direct injury to various tissues and organ by depositing in them. Furthermore, it potentially catalyzes free radicals formation in the body causing impairment in cellular functioning. Thus it causes injury to various organ-systems like-liver, heart, pancreas, and endocrine system.

During the last few years, liver disease has emerged as a major cause ofmortality in patients with β-thalassemia major. Liver disease in these patients can manifest as hepatomegaly, increased aspartate and alanine transaminase activities, hepatitis B and C.

So aim of our study is to assess the status of liver functions in beta thalassemia major patients and to correlate them with the serum ferritin level.

MATERIAL AND METHOD

Our study is a cross sectional study, conducted at tertiary center of JMC, Jhalawar. Eighty patients of beta thalassemia major, receiving regular blood transfusion, were chosen from Pediatric Ward. Out of these, 28 were female and 52 were male. Age of these patients ranged from 2 to 15 years. All of these patients were on chelation therapy with tablet Asunra (Deferasirox) for at least 6 months. The study was conducted between April, 2018 to November, 2018.

Diagnostic Criteria- 1).Clinical diagnosis made by treating pediatrician. 2).Haemoglobin ElElectrophores.

Inclusion CCriteria1) - Patients receiving regular blood transfusion.2) Patient on chelation therapy from at least 6 months.

Exclusion Criteria - 1).Viral hepatitis. 2). Any infectious disease 3).Any acute or chronic gastro-intestinal disease. 4).Family history of liver disease. 5) .History of consumption of any hepatotoxic drug. 6).Any oncological disease 7). Any autoimmune disease 8).History of any type of vaccination or surgery in the last 1 month. Permission of institutional ethical committees was received before conducting the study. Informed consent in writing was taken from guardians of the patients before entering into the study.

All cases underwent - I. Complete history taking: II. Complete physical examination: Ill. Laboratory investigations to asses- a) hemoglobin concentration b) serum ferritin level . C) Liver functions as indicated by serum level of total bilirubin, Alanine transaminase (ALT), Aspartate transaminase (AST), Alkaline phosphatase (ALP), and total protein.

For measurement of serum ferritin, Immuno-assay analyzer maglumi 1000 was used. Hemoglobin estimation was done by sahli's method. For measurement of serum bilirubin, SGOT, SGPT, ALP and serum total protein Beckman AU680 fully automated analyzerbased on wet chemistry (Random assay analyzer) was used.

Normal reference range –

S. Ferritin = 5-275 ng/m
Total bilirubin = 0.2 -1.0 mg%
SGOT = 5-40 U/L
SGPT = 5-36 U/L
ALP =105-350 U/L(in children)
Total protein = 6 - 8.5 mg%

Statistical analysis:

was done by the help of SPSS 20.0Software (trail Version). Unpaired-T test, Correlation and One Way ANOVA tests were used in data analysis. P value <0.05 was considered as significant.

RESULTS & DISCUSSION

Table 1 : Mean distribution of Parameters

	N	Minimum	Maximum	Mean	Std. Deviation
Age (in years)	80	2.00	15.00	7.1375	3.12399
Weight (in kg)	80	9.50	34.40	17.6587	5.46681
Height (in cm)	80	80.00	138.00	106.7625	16.41105
Liver (incm)	80	.00	8.00	2.4375	1.92152
Frequency of BT(in one Year)	80	9.00	25.00	15.1250	3.28932
Tota BT	80	14.00	238.00	90.3500	44.35190
Hb (in gm/dl)	80	5.00	9.00	7.4613	.98745
S.Ferritin (in ng/dl)	80	269.00	7530.00	2336.2875	1422.10930

S.Bilirubin (in mg%)	80	.30	5.80	1.5288	1.06262
SGOT (U/L)	80	24.00	254.00	101.2625	49.76572
SGPT(U/L)	80	18.00	268.00	95.3375	50.75953
ALP (U/L)	80	25.00	354.00	193.4875	50.98225
T. Protein (gm%)	80	4.80	8.00	6.8875	.60261
Valid N (listwise)	80				

In this study, 80 patients with beta thalassemia major were selected, their age ranged from 2 to 15 years with a mean age of 7.14 ± 3.12 years. They were 52 males (65%) and 28 (35%) females. Out of these eighty patients, 15 patients (18.75%) had positivefamily history of other members affected. All patients were on regular blood transfusion. Average size of palpable liver on physical examination was 2.4375 +/- 1.9217 cm. Average hemoglobin concentration of the patients was 7.4613 +/- 0.9874.

Mean & SD for s.total bilirubin, SGOT, SGPT, ALP & s.total proteins were 1.5288 +/- 1.0626 mg%, 101.2625 +/- 49.7657 U/L, 95.3375 +/- 50.7595 U/L, 193.4875 +/- 50.9822 U/L, 6.8875 +/0.6026 mg%.

Beta thalassemia major is characterized by total suppression ofsynthesis of beta chain of the hemoglobin. This leads to moderate to severe degree of anemia. Regular blood transfusion is the mainstay of treatment in these patients. These patients develops iron overload, probably due to - multiple blood transfusion, increased dietary iron absorption and inadequate chelating therapy[4].

Iron overload causes injury to various organ-systems includingliver, heart, kidney, endocrine system etc. Liver injury can be measured by assessing liver enzymes, bilirubin and protein levels in serum.

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[5].

Present study tries to assess the effect of iron toxicity on liver function tests and their correlation with serum ferritin levels.

Average frequency of blood transfusion was – 15.1250 +/- 3.2893, while average number of total blood transfusions was – 90.3500 +/44.3519. It indicates that patients of beta thalassemia major require regular blood transfusion once or twice a month, on an average. Similar findings were received in study by **Suman RL et al (2016)**[6].

Patients in this study havemean s.ferritin level of 2336.2876 +/- 1422.1093 ng/ml. The human body has many mechanisms to absorb and store dietary iron, but not to excrete excess amounts. It is therefore inevitable that patients who undergo regular transfusion therapy to treat chronic anemia, such as those with - thalassemia, will develop iron overload, since every unit of blood contains approximately 200 mg of iron[7]. Iron overload from transfusions may be exacerbated in some patients due to increased absorption of iron from the diet in response to ineffective erythropoiesis[8].

Mean & SD for s. total bilirubin, SGOT, SGPT, ALP & s. totalproteins were – 1.5288 +/- 1.0626 mg%, 101.2625 +/- 49.7657 U/L, 95.3375 +/- 50.7595 U/L, 193.4875 +/- 50.9822 U/L, 6.8875 +/0.6026 mg%.

Thus, LFTs including t. bilirubin, SGOT, & SGPT werefound significantly elevated from the normal range. **Sedigheh shams et al** found significantly raised liverenzymes (ALT, AST) in homozygous thalassemia major patients than in controls[9].**Chekir KA et al** conducted a study on 56 thalassemic children andtheir 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[10].

Table 2 : Correlation of LFTs with serum ferritin levels

	Mean	Std. Deviation	N	r value	P value
Ferritin	2336.2875	1422.10930	80		
T.Bilirubin	1.5288	1.06262	80	0.469	<0.0001*
Ferritin	2336.2875	1422.10930	80		
SGOT	101.2625	49.76572	80	0.740	<0.0001*
Ferritin	2336.2875	1422.10930	80		
SGPT	95.3375	50.75953	80	0.735	<0.0001*
Ferritin	2336.2875	1422.10930	80		
ALP	193.4875	50.98225	80	0.138	0.223
Ferritin	2336.2875	1422.10930	80		
T. Protein	6.8875	.60261	80	-0.519	<0.0001*

Chart 1

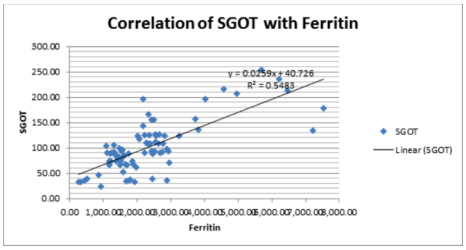


Chart 2

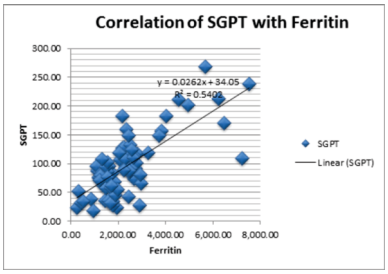
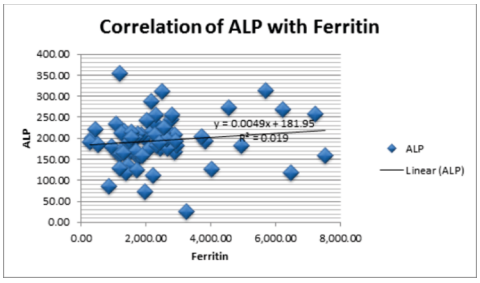


Chart 3



We found statistically significant positive correlationof s. ferritin with SGOT and SGPT(r=0.740 &0,735 respectively, with p= <0.0001) . While correlation of ALP was not significant(r=0,138, p > 0.05).

Worwood et alalso showed a strong correlation betweenserum ferritin concentration and ALT activity[ąą]. Similarly, **Ameli M et al (2006**), found that mean serum ALT(Alanine aminotransferase) was significantly high in thalassemic children with high serum ferritin and high transfusion index[ą]. Similarly, **Barton JC et al** noted similar results as serum ferritinincreases liver enzymes also increases[ął]. **Mohammed II et al (2012**) found a significant positivecorrelation of ferritin with ALT in thalassaemic patients[ą]. Similarly, **AAL et al (2015)** found a positive correlation betweenserum ferritin and age of the patient and elevated liver enzymes[ą]**.**

Liver disease associated with chronic blood transfusions inthalassemic patients is caused either by hepatotropic infections or hepatic siderosis. Both factors may act either synergistically or independently in promoting chronic liver disease, inducing cellular damage through similar oxidative pathways[ąº]. Injury to the liver cells causes leakage of the enzymes into thecirculation. ALT and bilirubin levels are used largely to determine if the liver has been damaged and its function is impaired[ą].

At multivariate analysis, **Parti et al** showed that necroinflam mation was related to the increased serum aminotransferases and higher iron stores including serum ferritin (p<0.05)[7].

In contrast with the above mentioned studies, **Saral N et al (2015)**found no significant correlation between serum iron and LFT[8]. Similarly, **Asif M et al** (2014) observed a weak insignificantpositive correlations between serum ALT (Pearson Correlation 0.097; P = 0.181), serum AST (Pearson Correlation 0.045; P = 0.335) and serum ALP (Pearson Correlation 0.036; P = 0.364) with serum ferritin levels[9].Similarly, **Salma KM et al (2015**) found that serum ferritin levelcorrelated significantly positively with GGT level (r = 0.23 and p = 0.006), but not significantly with ALT or AST levels[10].

In our study, we found no significant correlation of s. ferritin withALP levels. In contrast, **Fathi FH et** al found that ALP activity wassignificantly higher in cases (receiving regular blood transfusion & chelation therapy) in comparison to controls[11].

These results could be accounted to the fact that serum ALPactivity may originate from the bone, intestine and placenta, in addition to hepatobiliary causes of elevated serum ALP activity[12].Chronic request for blood cell production can cause overstimulation of the hematopoietic system which lead to an increase in the number of osteoclasts and osteoblasts, thus resulting in accelerated bone turnover and increase serum ALP activity[13].

CONCLUSION

SGOT & SGPT showed statistically significant positive correlation with serum ferritin levels. SGOT showed the strongest correlation among all LFTs with ferritin levels.

Serum ferritin level measuringfacility is not available in many of government hospitals. It is anexpensive investigation in commercial laboratories. Furthermore, it is inaccessible in many rural and semi urban areas of the country. In contrast, LFTs are readily available & relatively cheaper investigations.

As SGOT showed the strongest correlation with s ferritin levels, it can be used as an alternative investigation to s.ferritin levels to estimate the iron status of the patients, subjected to further research with more number of patients across various geographical areas.It can serve to guide the chelation therapy in the absence of s. ferritin measuring facility. This can improve the long term survival of the beta thalassemia major patients.

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