EVALUATION OF LIVER PARAMETERS IN BETA THALASSEMIA MAJOR PATIENTS

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Abstract

Introduction: The study was performed in beta thalassemia major patients to evaluate liver parameters. Beta-thalassemia is most common hereditary hematologic disorder characterized by severely impaired beta-globulin synthesis. Repeated blood transfusion in beta thalassemia major patient is highly challenging for many developing countries where the disease is prevalent, representing a major and unsustainable health burden.
Aim: This study aims to investigate liver parameters in patients diagnosed with beta-thalassemia major.
Materials and Methods: The study comprises a total of 80 subjects between age group of 4 to 14 years including patients with beta-thalassemia major (n=40) and healthy volunteer (n=40). Blood samples were collected and serum was separated to be tested for aspartate aminotransferase, alanine aminotransferase and total bilirubin were done by Erba XL-640 fully automated analyser.
Results: The levels of aspartate aminotransferase, alanine aminotransferase and total bilirubin in serum were found to be extremely statistically significant ($p<0.05$) in beta-thalassemia major patients than in healthy volunteer.
Conclusion: Repeated blood transfusions in beta thalassemia major patients causing significant liver damage that results in elevated levels of serum aspartate aminotransferase, alanine aminotransferase. Serum total bilirubin can be a good marker for monitoring bile duct obstruction resulted from hemolysis and blood transfusion.

Keywords: Beta-thalassemia major, aspartate aminotransferase, alanine aminotransferase, total bilirubin.

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1. Introduction

Thalassemia is derived from the Greek word (Thalas-which means sea and emia- means blood) signifying that it is more common in the Mediterranean region.[1] Thalassemia caused by defect in the synthesis of one or more of the hemoglobin chains. Imbalance of globin chains causes hemolysis and impair erythropoiesis. It is a group of inherited autosomal recessive disorder.[2] Beta-thalassemia major patients undergo repeated blood transfusion which may lead to increase iron absorption from the gastrointestinal tract and increases risk of an iron overloading in various organs.[3] Iron overload cause injury to the liver. Iron-induced liver injury is often characterized by the development of fibrosis and cirrhosis.[4] The progressive iron overload observed in beta-thalassemia major patient is the side effect of ineffective erythropoiesis, increased gastrointestinal absorption of iron, lack of physiological mechanism for excreting excess iron and multiple blood transfusions which results in hemochromatosis.[5] Liver disease in these patients can be manifested as hepatomegaly, increased aspartate and alanine transaminase activities and increase serum total bilirubin.[6] The high rate of hemolysis in beta-thalassemia patient causes an over production of bilirubin, which is a precursor for gallstone formation especially among the older ones.[7]

2. Methods

This study was conducted in Department of Biochemistry, Dr. Shankarrao Chavan Govt. Medical College and Hospital, Vishnupuri, Nanded. A total of 40 clinically diagnosed beta-thalassemia major patients (4-14 Years) which were on regular blood transfusion therapy and 40 healthy controls were taken for study. Written consent was taken from parents/guardians. This work was approved by ethical committee of Dr. Shankarrao Chavan Govt. Medical College and Hospital, Vishnupuri, Nanded. The evaluation of biochemical parameters such as aspartate aminotransferase, alanine aminotransferase and total bilirubin in serum were done by Erba XL 640 fully automated analyser. Statistical Analysis: All the results were expressed as mean ± SD and student's unpaired t-test were used to compare the two groups. $p<0.05$ was considered statistically significant. GraphPad software was used for data analysis.

3. Results

Table 1: Comparison of measured parameters between cases (beta thalassemia major patients) and control

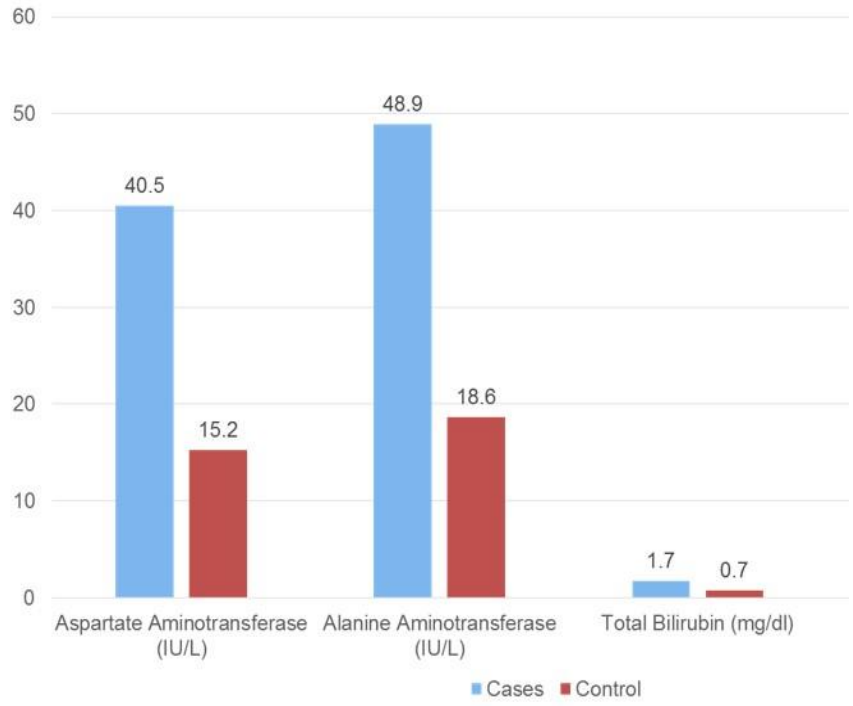
Parameters	Cases(n=40) mean ± S.D	Control(n=40) mean ± S.D	p-values	
AST (IU/L)	40.5 ± 17.5	15.2 ± 5.0	0.0001	
ALT (IU/L)	48.9 ± 19.1	18.6 ± 5.8	0.0001	
TB (mg/dl)	1.7 ± 0.7	0.7 ± 0.1	0.0001	

AST- Aspartate Aminotransferase, ALT - Alanine Aminotransferase, TB - Total Bilirubin

The result obtained after estimating liver parameters in cases and controls are extremely statistically significant (0.0001) as p value <0.05 as tabulated in table no.1

Figure:

Figure 1: Bar diagram showing comparison of parameters between cases (beta-thalassemia major patients) and controls



Above figure shows that serum aspartate aminotransferase, alanine aminotransferase and serum total bilirubin in cases (beta-thalassemia major patients) are higher as compared to controls.

4. Discussion

Our result revealed a significant increase in serum AST and ALT levels in beta-thalassemia major patients compared to controls (Table 1). A significant elevation in aspartate and alanine aminotransferases were observed in beta thalassemia major patients, the reason behind above findings could be, repetitive blood transfusions resulted in iron overload, 70% of iron stored in liver causes hepatocellular damage, that leads to leakage of liver enzymes in circulation as a result of hepatic necro-inflammation.[8,9] The iron deposition is associated with increased oxidative stress, liver cell damage and lipid peroxidation in transfusion-dependent beta-thalassemia major patients. Jensen et al. also observed that serum aspartate and alanine aminotransferases increases as liver iron concentration increases.[10] Seng Suk et al. found that liver functions to be increased three- to four-folds in beta-thalassemia major patients than normal individuals.[11] The liver is the earliest site of iron deposition in regularly transfused beta- thalassemia patients and a common cause of morbidity. Iron overload occur in hepatocytes of liver and free radical production is increased through the Fenton reaction in beta-thalassemia major patients. These free radicals accumulate in the liver and causes extensive tissue damage and play havoc.[12] As hepatic iron overload cannot be avoided, it is crucial to measure serum aspartate and alanine aminotransferase enzymes periodically to assess the scale of hepatic damage[13]. Hemolysis of red blood cell forms bilirubin which is metabolized in the liver and stored in the gallbladder. Most of beta-thalassemia major patient shows a high

level of serum bilirubin.[14] Increased level of bilirubin clarify high risk of bile duct narrowing and gallstone formation. Increased bilirubin level that cannot be excreted by the body, will accumulate in the gallbladder as calcium bilirubinate that leading to gallstones, obstructing the bile duct.[15] The observed increase in bilirubin due to ineffective erythropoiesis and repetitive blood transfusion and due to deposition of iron in liver.[16] Bilirubin is an antioxidant, its level is increased in serum due to oxidative stress seen in beta-thalassemia major patient.[17] Beta-thalassemia major patient could potentially induce bilirubin level and hepatic toxicity, that arises from decrease in activity of cytochrome c oxidase disrupting the mitochondrial respiration.[18]

5. Conclusions

This study concluded that repeated blood transfusion is a principle reason for increased serum aspartate aminotransferase, alanine aminotransferase and total bilirubin. Serum bilirubin proved to be a good marker for prognosis of gallstones as long as their elevation depends on the rate of hemolysis and blood transfusion in beta thalassemia major patients. From this study we can improve the liver damage caused by repeated blood transfusion by monitoring serum AST, ALT and total bilirubin and provide appropriate treatment for that.

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Author's contribution:
Author Dr Swati Choudhary has given substantial contribution to the conception or the design of the manuscript, author Dr Kavita Rathod and author Dr Santosh Pawar to acquisition, analysis and interpretation of the data. All authors have participated to drafting the manuscript, author Dr Swati Choudhary and author Dr. Sachin Bhavthankar revised it critically for important intellectual content. All author's contributed equally to read and approved the final version of the manuscript.

Declarations:

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