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Effect of Iron over Load on Circulating Liver Enzymes and Blood Glucose in Beta Thalassemia Major Patients

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Abstract

Thalassemias are a heterogeneous group of disorders with a genetically determined decrease in the rate of production of one or more forms of normal hemoglobin chains. Thalassemia patients need regular blood transfusions for their existence. As a result of frequent blood transfusions majority of the patients develop iron overload. The present work was planned to study liver dysfunctions and blood glucose estimation in patients with β-thalassemia major due to iron overload. Fifty-three individuals (12 to 23 years) were selected from which 43 were beta thalassemia major patients and 10 normal individuals were taken as a control. Serum ALT, AST, ALP, glucose, Hb, and Ferritin were measured. A significant increase ($p<0.05$) was recorded in levels of ALT, AST, ALP, glucose, and ferritin in β-thalassemia major patients with comparison to control subjects. A significant decrease ($p<0.05$) was observed in hemoglobin of β-thalassemia patients as compared to control group. The outcomes of the study revealed a rise in ALT, AST, ALP, Glucose and Ferritin levels and a significant decrease in Hb level in β-thalassemia Major patients as compared to control subjects.

Introduction

Thalassemias are a heterogeneous group of disorders with a genetically determined decrease in the amount of production of single or more sorts of normal hemoglobin polypeptide chains [1]. Affected individuals need regular red cells transfusions for their survival. Frequent blood transfusions develop Iron over load in patients. Signs & symptoms develop from the 6th month of age to 2 years. Affected babies unable to thrive with delayed growth and gradually developing anemia, loose stools, irritability, fever attacks, Jaundice, Pallor, leg ulcers enlarged liver and spleen Growth of masses due to extramedullary RBC production and bony changes arise from marrow tissue expansion [2]. In poor countries, the limited facilities result in the improper management of patients. The world health organization WHO declared thalassemia as the highly prevalent inherited disorder globally, that existing in more than sixty countries with a carrier rate upto 150 million. Approximately 250 million persons in the world are heterozygotes for β-thalassemia, and at least 20 thousand homozygotes are born every year [3].

There is the highest frequency of transfusion-dependent children in Pakistan due to increased occurrence of the gene, cousin marriages, frequent births and increased population. A survey revealed that about 7000 cases of β-thalassemia major are born in Pakistan annually, and the carrier frequency is reported 5.3% and in various regions, it differs from 1.4 to 8 % with an average of 5 %. β-thalassemia is most common in the province Punjab, Sindh and Baluchistan besides the Arabian sea and the Khyber Pakhtunkhwa (KPK) where migrants-from various regions of the world have been staying throughout in the history [2,4]. Affected children need regular blood transfusions as part of treatment. Excessive red cells transfusion leads to iron overload and increased iron level deposited in various body parts like heart, Pancreas, hepatic tissue and renal tissue. To remove excess iron from the body, chelation therapy is used. Chelating agents bind with iron and remove from the body [5,6].

Affected children need regular blood transfusions as part of treatment. Excessive red cells transfusion leads to iron overload [7]. Hence iron overload is a condition secondary to thalassemia major caused by the repeated blood transfusions as well as an increased intestinal absorption of iron. This excessive iron has a direct or indirect effect on the normal functioning of almost all the body systems including the endocrine, cardiovascular and hepatobiliary systems. The earliest site for iron deposition is within the hepatocytes and reticuloendothelial cells, causing irreversible damage to liver resulting in fibrosis and consequently liver cirrhosis [8, 9]. To remove excess iron from the body, chelation therapy is used. Chelating agents bind with iron and remove from the body [6, 8].

Materials and methods

This study was conducted in Institute of Molecular Biology and Biotechnology, The University of Lahore. Blood samples were collected from Sundas foundation of thalassemia 880 Shadman Lahore, Pakistan, after taking informed consent from the patients and their guardians. Out of these 53 samples, forty-three were confirmed cases of β-Thalassemia major and ten normal individuals were selected as a control. All the individuals and their parents enrolled in this study were explained the purpose of the study and written consent was obtained from them. Age, blood pressure and previous clinical history were also recorded from patients. Venous blood was collected in vacuum BD tubes containing sodium fluoride (BD, USA) and serum was separated (3000 rpm/15 min). Laboratory parameters were measured to complete the analysis in the biochemistry lab (University College of medicine The University of Lahore).

Glucose was measured by the Glucose Oxidase method (*P. Trinder* GOD method), ALT was measured by the IFCC Reference method, AST was also measured by the IFCC Reference method, alkaline phosphatase was determined by Deutshe Gesellschaft fur Klinishe Chemie method, Hemoglobin was measured by cyanmethemoglobin (Van Kampen, E.J. and Zijlstra hemoglobin-cyanide method Randox Kit UK) and ferritin was measured by Elisa by Beckman Coulter method.

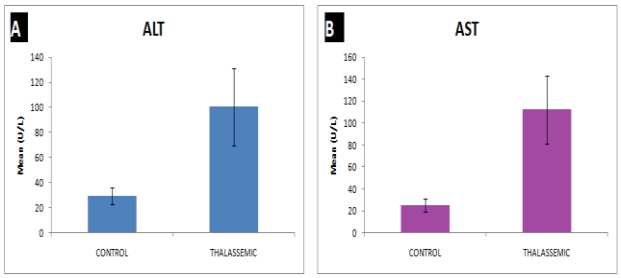

Figure 1: A: Estimation of ALT in control and thalassemic individuals. B: Estimation of AST levels in control and thalassemic individuals.

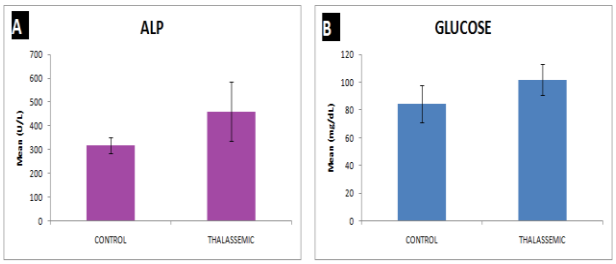

Figure 2: A: Estimation of ALP in control and thalassemic individuals. B: Estimation of glucose levels in control and thalassemic individuals.

Results

The obtained blood samples from patients suffering from β-thalassemia major were obtained to evaluate the biochemical variations by estimation of ALT, AST, ALP, glucose, hemoglobin, and ferritin.

In this study the mean value of ALT was 100.54±30.85 in β-thalassemia major patients as compared to control group 29.4±6.79 showing a significant (p =0.0004) increase in serum ALT levels in β-thalassemia major patients. The mean value of AST was 112.32±31.16 in β-thalassemia major patients as compared to control group 24.9±5.87 showing a significant (p =0.00001) increase in serum AST levels in β-thalassemia major patients (**Fig 1**). The mean ALP level in β-thalassemia major patients was 460.15±124.42 as compared to control group 317.5±34.12 showing a significant (p =0.003) increase in serum ALP levels in β-thalassemia major patients (**Table 1**). The mean value of blood glucose was significantly (p =0.003) increased in beta thalassemia major patients 101.76±11.26mg/dL as compared to control group 84.17±13.31 (**Fig 2**). The mean value of hemoglobin levels was 7.11±1.06 g/dL in β-thalassemia major patients as compared to control group 12.69±0.91g/dL which shows a significant decrease (p =0.0002) in hemoglobin levels in β-thalassemia major patients. The mean value of serum ferritin was 2836.71±1519.62ng/mL in patients of β-thalassemia major as compared to control group 105±16.2ng/mL showing a significant (p =0.000) increase in serum ferritin levels in β-thalassemia major patients (**Fig 3**).

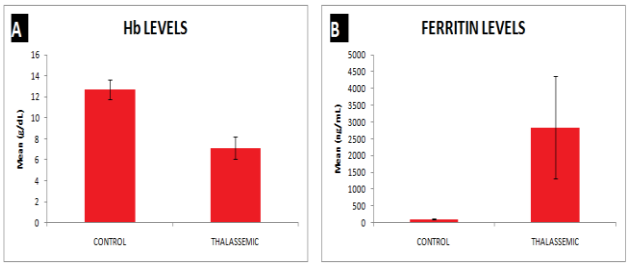

Figure 3: A: Estimation of Hb levels in control and thalassemic individuals. B: Estimation of Ferritin levels in control and thalassemic individuals.

Table 1: Mean values of Serum ALT, AST, ALP, Glucose, Hemoglobin and Ferritin in β-thalassemia major individuals and normal controls.

Parameters	Normal range	Sample	Control	*P* value
ALT (U/L)	Upto 40U/L	100.54±30.85	29.4±6.79	0.0004*
AST(U/L)	Upto 40U/L	112.32±31.16	24.9±5.87	0.00001*
ALP(U/L)	250 - 420IU/L	460.15±124.42	317.5±34.12	0.003*
Glucose(mg/dl)	110-180 mg/dL	101.76±11.26	84.17±13.31	0.003*
Hemoglobin(G/dL)	11-16 G/dL	7.11±1.06	12.69±0.91	0.0002*
Ferritin(ng/mL)	12-200 ng/mL	2836.71±1519.62	105±16.2	0.000*

Discussion

Ferritin estimation is economical, easy to perform and indirect test to access iron load in the body, but a single test may not provide confirmation of iron load [10]. The latest non-invasive technique for estimation of iron quantity in the body, like The latest non-invasive technique for estimation of iron quantity in the body, like SQUID or MRI, have better sensitivity, however, these have partial use in developing world due to limited budgets and complex technology, have better sensitivity, however, these have partial use in developing world due to limited budgets and complex technology [6, 7, 10, 11, 13].

The present study showed high levels of ALT, AST and ALP in beta-thalassemia patients as compared to control group these findings are in line with the work of [9, 12, 14] as they found increase level of ALT, AST, and ALP in β-thalassemia major patients during the investigation of hepatocellular injury. Study of [15, 16] also supports our findings.

When the level of glucose and ferritin was measured in patients of β-thalassemia major, significantly ($p<0.05$) high concentrations were observed, and these outcomes are in accordance with the studies of

[17, 18]. As they observed glucose intolerance and high ferritin level in patients of β-Thalassemia major due to frequent blood transfusions, ineffective erythropoiesis and increased gastrointestinal iron.
In contrast to glucose and ferritin, significantly ($p<0.05$) low hemoglobin levels were calculated in these patients. Our results are in conformity with the work of [19] they observed decreased levels of hemoglobin in β-thalassemia major patients.41 out of the 43 subjects in our study had serum ferritin levels above 2000 ng/mL that was approximately ten folds higher than the upper normal limit. Our study is linear with [22] they also stated a low serum ferritin concentrations predicted higher survival rate, and low possibility of several complications. [15, 20, 21].

Conclusions

It is concluded from the outcomes of our study that significant rise in serum levels of ALT, AST, ALP, Glucose and serum Ferritin occurs in patients of beta thalassemia major. Hemoglobin level showed a significant decrease in β-thalassemia major patients even after repeated transfusions. An elevated level of Ferritin in β-thalassemia major patients that is responsible for great alterations in liver enzymes. Monitoring the levels of serum ferritin and hemoglobin along with liver enzymes and blood glucose of patients with β-thalassemia major on repeated blood transfusion may help in maintaining the quality of life.

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