DOI Number: 10.37506/v20/i1/2020/mlu/194462

Comparison Study of Major Thalassemia, Thalassemia Intermedia of Iraqi Patients and Control Groups for Effectiveness of Liver Enzymes

Shatha H. Jwaid[1], Abbas Mehsen Gata[1]

[1]*Lecturer, Collage of Medical and Health Technique, Middle Technique University/ Baghdad, Iraq*

Abstract

Beta-thalassemia is an autosomal recessive disease caused by absence or reduction in the synthesis of the β-globin chain, which is one of three special scientific types, thalassemia grand, secondary and medium. In Iraq, the β-thalassemia is a real problem due to the lack of medicines and equipment during the exclusive periods of wars and insecurity. The aim of this study is to evaluate some liver enzymes among Iraqi thalassemia and β-thalassemia patients and the volunteer group. The study included 100 patients (57 females and 43 males) who were divided into two groups (53 with major thalassemia and 47 with moderate thalassemia), with an average age ± SD (14.28). The study also included 30 healthy individuals (16 males and 14 females) with average age of 15.25 years as a control group. The groups were matched by gender and age and had the same geographical and socio-economic status. The colorimetric methods were used to estimate the values of serum transaminases (GOT, GPT), bilirubin and alkaline phosphatase (ALP). There were no statistically significant differences between primary thalassemia and the control group regarding, mean age, sex, WBC count and serum serotonin, while there was statistically significant differences between thalassemia (grand) and thalassemia (mean) compared to control groups (P=0.001) in regard to (GPT), (GOT), bilirubin and (ALP) values**.**

Keywords: *ß-thalassemia major, ß-thalassemia intermedia, Serum ferritin, GOT,GPT, Alkaline phosphatase, Serum bilirubin.*

Introduction

Thalassemia is a genetic disease that takes place in blood cells, is a major health problem all over the world where the value of hemoglobin (the main component of the red blood cells and oxygen transporter) is below normal [1]. Thalassemia results from a genetic defect affecting the hemoglobin production process, and this genetic defect is transmitted from parents to their children. Thalassemia depends upon the severity and type of the disease, as some children exhibit symptoms since birth, while others develop symptoms during the first two years of life. Symptoms may not be shown in people with the disorder i.e (those who have a single gene disorder) [2]. More than 200 different mutations (defects) can be caused to the *ß*-globin gene, which is present on chromosome 11. The majority of the mutations that cause *ß*-thalassemia are bitmap mutations i.e changing one letter of the genetic code. Various ß-chain dysfunction mutations can happen in different ways [3]. Molecular DNA tests to detect mutations in patients allow prediction of disease severity. With the aid of those molecular methods, the disease can be identified in the fetus during the earlier periods of pregnancy (Prenatal diagnosis) [4].

Beta thalassemia happens as a result of a deficiency or defect in two beta type series [5], which consists of hemoglobin and divided into a) thalassemia minor, results from a defect in a single chain and the patient is asymptomatic, but shows a simple anemia during routine blood tests [6], and intermediate thalassemia, which is an intermediate condition between minor and major types, where patients may live a normal life, but need occasional blood transfusion in times of illness and pregnancy [7]. In thalassemia major type, patients suffer from severe anemia, bone marrow and hypertrophic swelling and need regular blood transfusions to live normally, and the symptoms do not occur at child's birth, but appear during the first two years of the child's life [8].

The liver performs a focal task in iron homeostasis. However, iron discharged from transfused red cells, an upgraded rate of gastrointestinal iron assimilation has been proposed. This overabundant iron is initially limited to the hepatic Kupffer cells, and when transfusion necessities produce iron over-burden, overflow to hepatic parenchyma cells quickly occurs, with the risk of recent cirrhosis and fibrosis. In β-thalassemia patients, without co-factors, the limit of hepatic iron for the development of fibrosis is about 16 mg/g of dry weight liver [9]. During clinical investigations, it is recommended to find a link between appearance of iron-incited hepatotoxicity and hepatic iron fixation [10].

Materials and Method

Blood samples were collected from 100 thalassemia patients (57 females and 43 males) who attended the thalassemia center in Al–Karama hospital/Baghdad city during the period from January to December 2018. The patients were divided into two groups (53 with major thalassemia and 47 with moderate thalassemia), with an average age ± SD (14.28). The study also included 30 healthy volunteer individuals (16 males and 14 females) with average age of 15.25 years as a control group.

Sample collection

Venous blood samples (5 ml) were taken from all the study groups by means of disposable syringes. Two ml of this blood was transferred to EDTA tube for estimation of hematological parameters, while the rest of blood was transferred to poly ethylene plane tube, to obtain serum after allowing blood to clot, then centrifuged at 3000 RPM for 5 minutes and frozen at(-6 ºC) in anew disposable tubes until analysis of other parameters.

Serum ferritin was determined using the ELFA technique (enzyme linked fluorescent assay) .Vida's ferritin (FER) is an automated quantitative test for use on Vidas technique. Transaminases (GOT and GPT), serum bilirubin and Alkaline Phosphatase (ALP) were estimated by using colorimetric methods.

Statistical analysis

Data were analyzed using statistical package for social science (SPSS). Percentage prevalence rates were calculated with their respective 95% confidence intervals. Differences between proportions were evaluated using T- tests, and significance were achieved at $p < 0.05$.

Results and Discussion

The study was performed on 53 patients having thalassemia major and 47 Thalassemia intermediate in Al–Karama hospital in Baghdad city.

Table (1) shows the demographic and laboratory characteristics of thalassemia major and thalassemia intermedia patients. There were no significant differences between BTM and BTI patients regarding age, sex, W.B.C and PCV. The mean value of ferritin was (3215, 27) mg / dl in BTM and BTI which also showed non-significant difference ($p > 0.05$).

Table (1): Demographic and laboratory characteristics of thalassemia patients (thalassemia major & thalassemia intermedia) (values other than sex are reported as mean ± SD)

	BTM (n =53)	**BTI (n = 47)**	**P - value**
Age (year)	12.32 ± 7.42	16.58 ± 13.75	NS *
Sex (M / F)	28 / 25	29 / 18	NS *
W.B.C count (cell/c.mm)	7.93 ± 3.55	7.21 ± 2.83	NS *
P.C.V (%)	29.39 ± 4.59	28.82 ± 3.81	NS*
Ferritin (mg/dl)	3215 ± 1693	2720 ± 1425	NS*

NS*: Not significant

Table (2) shows a very high GOT and GPT level increases in both BTM and BTI in comparison with the control group (P> 0.001). While there was no significant difference between patients in both BTM and BTI levels regarding ALP and total serum bilirubin, although there was a significant increase in their levels in thalassemia patients compared to the control group (P> 0.001)

Table (2) : Mean ± SD values of different parameters in BTM, BTI patients and the control group (GOT, GPT, ALP, bilirubin and ferritin)

	BTM n = 53	**BTI n = 47**	**Controls n=30**	**P-value ANOVA**	**I vs II**	**I vs III**	**II vs III**
GOT	44.707±24.09	41.53±16.68	20.70±8.80	P<0.00	0.00*	0.001*	0.01
GPT	54.83±20.12	50.31±11.21	15.08±3.34	P<0.05	0.000*	0.00*	0.001
ALP	157.53±90.31	146.37±88.21	75.09±25.3	P<0.00	0.93	0.00*	0.00*
Bilirubin	24.31±11.31	29.61±15.31	9.11±3.12	P<0.00	0.09	0.00*	0.001*
Ferritin	3215±1693	2720±1425	113.54±93.23	P<0.05	0.086	0.001*	0.001*

There was no significant difference in relation to age, gender, WBC count, PCV value and serum ferritin between BTM and BTI patients as shown in Table (1), although the level of stock iron amount was significantly higher (P> 0.001) in both BTM and BTI compared to the control group. The test of ferritin is useful for monitoring treatment in patients who have not yet experienced marked increase in the amount of stored iron. increased iron observed in β-thalassemia patients may be due to chronic blood transfusion and hypercalcemia. Similar results were seen in some studies [11]. Iron overload in β-thalassemia can lead to iron intestinal uptake and an increase in the abnormal molecular form of iron. elevated iron may play a main role in the oxidation of cell membranes and the formation of epithelial cell antigens, which can play one of the major pathways in removing the red blood cells.

There was a significant increase in GOT, GPT, ALP, Bilirubin and ferritin levels in both BTM and BTI compared to the control group, and these results were consistent with other studies [12,13]. The results also showed a significant increase in ALP and bilirubin levels among patients with BTM and BTI and the control group. The level of ALP in obstructive jaundice is expected to increase more than hepatic jaundice resulting from hepatitis C infection. There was no significant variation between BTM and BTI [16].

Iron-induced liver diseases are usually aggravated by viral infections. Despite ilon chelation treatment, the hepatic siderosis, portal cirrhosis and even fibrosis may develop [13-15]. The high serum ALT levels must alert the clinician about the possibility of hepatitis resulting from multiple blood transfusions. Liver diseases caused by hepatitis, cirrhosis, biliary stenosis, gall bladder inflammation, biliary duct infection and hepatic liver tumors can result in liver enzyme and alkaline phosphatase elevations [14].

Thalassemia patients suffer from a high bilirubin amount in the blood because of the increased destruction of the red blood cells. This is the major cause of hyperbilirubinemia resulting in the damage of other hepatic cells due to the side effects of iron overload [15].

Conclusion

Prevention of thalassemia lies in prenuptial screening through a medical examination. However, out-of-court marriage and the marriage of minors were the reasons why these tests were ignored and therefore the rate of infection in Iraq has increased in recent years. Liver disease is a notable cause of death in patients with beta-thalassemia (major and moderate). Liver disease in thalassemia patients can be observed as hepatotoxicity, hepatitis B and C. Hepatic cirrhosis due to iron overload, which is the result of excessive blood transfusions, rupture of red blood cells and excessive

iron retention of the gastrointestinal tract due to non-intractable erythropoietin.

Financial Disclosure: There is no financial disclosure.

Conflict of Interest: None to declare.

Ethical Clearance: All experimental protocols were approved under the Collage of Medical and Health Technique, Middle Technique University/ Baghdad, Iraq and all experiments were carried out in accordance with approved guidelines.

References

1. Patel S, Siddiqui A, Kareem I. A Correlative Study of Serum Bilirubin and Liver Enzymes with Serum Ferritin in Beta Thalassaemia Major". 2018; 17: 62-67**.**
2. Taher A, Musallam K, Cappellini M. Thalassemia intermedia: an update, "Mediterranean Journal of Hematology and Infectious Diseases.2009; 1.
3. Vincenzo D, Christos K. β-Thalassemia Distribution in the Old World: an Ancient Disease Seen from a Historical Standpoint" (2017); 9(1): e2017018
4. NA Al-Allawi, K Hassan. βthalassemia mutations among transfusion dependent thalassemia major patients in Northern Iraq," Molecular Biology International. 2010; 4.
5. Akhavan H, Derakhshandeh P, Banihashemi A, Mostafazadeh A, Asghari B, Ahmadifard MR, Azizi M, Youssefi A, Elmi MM. A comprehensive molecular characterization of beta thalassemia in a highly heterogeneous population. Blood Cells Mol Dis.2011; 15;47(1):29-32.
6. Martin A, Thompson AA. Thalassemias. Pediatr Clin North Am.2013; 60:1383.
7. May C. Vikramjit S Kanwa ", Thalassemia Intermedia". 2018; 24.
8. Martin, A., & Thompson, A.A., "Thalassemias *Pediatric Clinics.*2013;*60*: 1383–1391.
9. Angelucci E, Muretto P, Nicolucci A, et al. Effects of iron overload and HCV positivity in determining progression of liver fibrosis in thalassaemia following bone marrow transplantation. Blood. 2002;100:17–21
10. Andreani M, Nesci S, Lucarelli G, Tonucci P, Rapa S. Long-term survival of ex-thalassemic patients with persistent mixed chimerism after bone marrow transplantation. Bone Marrow Transplant.2000; 25:401–404.
11. Asma K, Sandrine L, Selima F, Amel H. Oxidant, antioxidant status and metabolic data in patients with beta-thalassemia.2003; (338):1-2,.
12. Wanachi W, Ueengrojanakul P, Sirangkapracha P, Leo W. prevalence and clinical significance of hepatitis C virus infection in these patients with thalassemia In"t.2003; (4)78:374-8,.
13. Israa M, Fadhila S. Assessment of Liver Functions in Thalassaemia", Department of Medical Physiology, College of Medicine, University of Mosul.2012: (1) 8:
14. Okuda M, Sasaki S, Kunitsugu I. Iron load and liver enzymes in 10,and-13-year-olds"PediatrGastroenterol. Nutr(2011): (3)52.
15. Huang YY, Huang MJ, Wang HL, Chan CC, Huang CS. Bilirubin Concentration in thalassemia heterozygotes in university students " EurJHaematol. 2011; (4)86: 317-23
16. Liver M, pintail A. Oxatative stress and antioxidant states in B-thalassemia major or over Load and depletion of Lipid-solubl BlooD, 1996;(9)88: 3608-3614.