Pak. J. Biotechnol. Vol. 15 (1) 181-184 (2018) ISSN Print: 1812-1837
www.pjbt.org ISSN Online: 2312-7791

STUDY OF SOME LIVER FUNCTIONS PARAMETERS IN THALASSAEMIC PATIENTS IN AL-NAJAF PROVINCE

Karrar Saleem Zayed

University of Kufa, Faculty of Science, Department of Laboratory Investigations
E-mail: karrars.alshebly@uokufa.edu.iq

Article received 15.1.2018, Revised 10.3.2018, Accepted 15.3.2018

ABSTRUCT

The current study was carried out in Al-Zahra Hospital in Al-Najaf province during the period from 2017/1/3 till 2017/9/15. The study was undertaken to evaluate the effect of major thalassemia disease on liver function criteria (ALT, AST, ALP and bilirubin) in a number of patients. Forty-eight major thalassaemic patients in both gender (24 males and 24 females) participated in the study, their ages ranged from (2-19) years divided into three groups (8/group) according to the ages (2-7, 8-13, 14-19) years. Also contribute thirty health individuals divided into 15 males and 15 females as a control subjects, their age ranged from (2-20) years.

Results of this study revealed that the thalassaemia disease in patients with both gender and ages causes a significant elevation of ALT, AST, ALP and bilirubin levels. On the other hand, the results showed no apparent difference in these parameters when compared between males and females. So, the study was suggested that thalassaemia may be causes lesions in liver tissues indicated by elevation of serum liver function criteria levels.

Keywords: Thalassemia, ALT, AST, ALP and bilirubin

INTRODUCTION

Thalassemia is a genetic disease caused by a gene mutation in hemoglobin protein (Hb) in red blood corpuscle (RBC) that decrease the production of globin chains (one or more) e.g. β-chains or α-chain (Shah et al., 2010). Thalassemia is inherited congenital disorder in which a quantitative or qualitative (structural) abnormality caused by exchanges in the genetic code of DNA that contain coded one or more globin chains in Hb. The structural changes involve a deletion, addition or replacement of amino acids (one or more) of the globin chains (Waseem et al., 2011). Quantitative anomalies include a complete or partial repressed production of normal polypeptide chains (one or more) which causes all thalassemia syndromes (splenomegaly and anemia) (Dongiovanni et al., 2011).

The hemolysis of RBC in thalassemia causes accumulation of residue of the heme component breakdown in Hb like bilirubin & heme. Increased erythroid damage causes elevated of indirect bilirubin levels. Thalassemia patients have a large amount of iron in their bodies result from the repeated blood transfusions or the disease itself. The overload iron causes damage to the endocrine system, liver, and heart. All patients Beta-thalassemia will accumulate lethal iron levels in their bodies, So, it is necessary to get an adequate iron chelation therapy (Wirawan et al., 2003).

SUBJECTS & METHODS:

Subjects: Forty eight major thalassemic patients in both gender (24 males and 24 females) participated in the study and diagnosed by a physician, their ages ranged from (2-19) years divided into three groups (8/group/gender) according to (A1, A2,A3) ages that represent (2-7, 8-13, 14-19) years. Patients with a heart attack, gallstones disease, heart failure, and pancreatitis diseases were excluded from this study, these diseases may alter the liver functions.

Control group: Thirty apparently healthy individuals divided into 15 males and 15 females as control group, their age ranged from (2-20) years.

Methods:

Collection of samples: Five ml of venous blood were obtained from controls and patients. The blood was centrifuged to get a serum used for evaluation of ALP, AST, ALT, and bilirubin.

Determination of liver enzymes and bilirubin activity in Serum: Serum ALT, AST, ALP & bilirubin measured by a colorimetric method by using a spectrophotometer at 546 nm (Randox, kit). To determine the activity of these parameters in (U/L), A standard calibration curve was used.

Statistical analysis: Statistical analysis was performed with SPSS, version 18. All results were expressed as the mean ±SD. One-way analysis of variance (ANOVA) was done to determine the influence of thalassemia according to the gender and ages on liver functions parameters. The P. value < 0.05 was regarded as statistically significant.

The present study was performed to assess the serum liver parameters that include Alkaline transaminase (ALP), Alanine aminotransferase (ALT), Bilirubin and aspartate aminotransferase (AST) in a number of thalassaemic patients in

both genders and different ages and compared to control group.

RESULTS:

Effect of Thalassemia on liver functions parameters in male thalassaemic patients:

ALT levels were increased significantly ($p < 0.05$) (14.52±3.24), (12.11±2.91) and (11.98 ± 3.02) in patients at different ages A1, A2 and A3 when compared with controls (7.71±0.82), (8.11 ± 1.21) and (8.98±1.03) respectively. Table 1 also indicates that AST levels increased significantly ($p<0.05$) (18.75±5.01), (18.03±5.88) and (16.88 ± 3.44) in patients at different ages A1, A2 and A3 when compared with controls (9.01 ±1.85), (9.84±1.09) and (9.22±1.77) respectively as illustrated in table 1.

On the other hand, ALP levels elicited a significantly increase ($p<0.05$) (23.11±2.27), (20.78 ±3.12) and (24.10±2.94) in patients at different ages A1, A2 and A3 when compared with controls (18.85±1.21), (17.46±2.23) and (19.06 ±2.09) respectively. Similar significant showed in bilirubin concentration (22.10±4.42), (19.71 ±5.05) and (21.70±3.92) in patients at different ages A1, A2 and A3 When compared with controls (9.11 ± 0.88), (8.55±0.67) and (9.39±1.23) respectively.

Table 1: Effect of Thalassaemia on liver functions parameters in male thalassaemic patients.

Gender	Parameters			
	ALT (U/L) Mean±SD	AST (U/L) Mean±SD	ALP (U/L) Mean±SD	Bilirubin (µmol/L) Mean±SD
Male	12.88±3.05	17.55±4.90	22.66±2.77	20.67±4.17
Female	12.18±2.09	15.12±4.99	22.99±2.91	20.07±4.11

C: control, P: Patients, number of patient males: 8/age
number of healthy males: 5 / age
*: means, there are a significantly increased ($p < 0.05$)

Effect of thalassemia on liver functions parameters in female thalassaemic patients: ALT levels was increased significantly ($p< 0.05$) 13.42±2.79, 11.19±3.03 and 11.69±3.26 in patients at different ages A1, A2 and A3 when compared with controls 6.11±1.06, 6.97±0.92 and 7.60 ±1.14 respectively. Also, AST increased significantly ($p< 0.05$) 16.94±6.22, 14.55 ±4.78 and 13.88 ±3.98 in patients at different ages A1, A2 and A3 when compared with controls 8.45±1.12, 9.01 ± 1.50 and 8.70±2.56 respectively as shown in table 2. On the other hand, ALP levels increased significantly ($p < 0.05$) 22.65±3.10, 23.71±3.62 and (21.72 ±2.91) in patients at different ages A1, A2 and A3 when compared with controls 17.70±0.93, 18.08± 1.23 and 17.10±1.85 respectively. Bilirubin concentration also increased significantly ($p< 0.05$) 20.92±4.88, 20.11±3.3) and 19.20 ±4.14 in patients at different ages A1, A2 and A3 When compared with controls 7.83 ±0.71, 7.94±1.03 and 8.45±1.29 respectively.

Table 2: Effect of thalassaemia on liver functions parameters in female thalassaemic patients.

Ages (Years)	**Groups**	**Parameters**			
		ALT (U/L) Mean±SD	**AST (U/L) Mean±SD**	**ALP (U/L) Mean±SD**	**Bilirubin (µmol/L) Mean±SD**
2-7 (A1)	**C**	**7.71±0.82**	**9.01±1.85**	**18.85±1.21**	**9.11±0.88**
	P	**14.52±3.24 ***	**18.75±5.01 ***	**23.11±2.27 ***	**22.10±4.42 ***
8-13 (A2)	**C**	**8.11±1.21**	**9.84±1.09**	**17.46± 1.03**	**8.55±0.67**
	P	**12.11±2.91 ***	**18.03±5.88 ***	**20.78±3.12 ***	**19.71±5.05 ***
14-19(A3)	**C**	**8.98±1.03**	**9.22±1.77**	**19.06±2.09**	**9.39±1.23**
	P	**11.98±3.02 ***	**16.88±4.44 ***	**24.10±2.94 ***	**21.70±3.92 ***

C: Control, P0000: Patients, number of patient females : 8/age
number of healthy females: 5/age,
*: means, there are a significantly increased ($p < 0.05$)

Effect of thalassaemic patient's gender on liver functions parameters: The results demonstrated no significant increase in all liver functions parameters in thalassaemic patients when compared theses parameters in male and female as illustrated in table 3.

Table 3: Effect of thalassaemic patient's gender on liver functions parameters.

Ages (Years)	Groups	Parameters			
		ALT (U/L) Mean±SD	AST (U/L) Mean±SD	ALP (U/L) Mean±SD	Bilirubin (µmol/L) Mean±SD
2-7 (A1)	C	6.11±1.06	8.45±1.12	17.70±0.93	7.83±0.71
	P	13.42±2.79 *	17.94±5.22 *	24.65±3.10 *	20.92±4.88 *
8-13 (A2)	C	6.97±0.92	9.01±1.50	16.88± 1.23	7.94±1.03
	P	11.19±3.03 *	14.55±3.78 *	23.71±3.62 *	20.11±3.31 *
14-19(A3)	C	7.60±1.14	8.70±2.56	17.10±1.85	8.45±1.29
	P	12.69±2.26 *	15.88±4.98 *	21.72±2.91 *	19.20±4.14 *

Effect of thalassaemic patients at different ages on liver functions parameters: Patients ages classified into A1, A2 and A3 that mean 2-7, 8-13 and 14-19 years respectively. There was no significant increase in liver functions para-meters (ALT, AST, ALP and Bilirubin) in thalassaemic patients when compared different ages of thalassemia patients as illustrated in table 4.

Table 4: Effect of different ages of thalassaemic patients on liver functions parameters.

Ages (Years)	Parameters			
	ALT (U/L) Mean±SD	AST (U/L) Mean±SD	ALP (U/L) Mean±SD	Bilirubin (µmol/L) Mean±SD
2-7 (A1)	13.97±3.01	17.84±5.61	22.88±2.68	21.51±4.65
8-13 (A2)	11.65±2.97	16.29±5.52	22.24± 2.92	19.91±4.18
14-19(A3)	11.83±3.14	14.86±3.71	22.91±2.93	20.45±4.03

DISCUSSION

The estimation of liver enzymes activities regarded as a valuable tool to evaluate the efficiency of liver functions, thus it is a useful marker to determine the degree of liver disorders (Abd-Allh and Rahiem, 2016, Zayed, 2017a). Liver cells damage as a result of necrosis induces severe release of intracellular components into the bloodstream. Sensitive parameters of liver damage can be assessed by measurement of the plasma levels of the enzymes alanine (ALT; GPT), transaminases ALP, aspartate (AST; GOT) and bilirubin (Warnes, 2016, Zayed ,2017b).

Concerning the effect of thalassemia on liver parameters in male and female patients, this study showed increased in ALT, AST, ALP and bilirubin levels in patients compared to healthy control group. This study showed no effect of patient's age on these parameters. The current result can confirm with results obtained from studies which cleared that thalassaemia causes elevation in liver parameters and this effect does not depend on patients ages (Larson et al., 2003, Borgna-Pignatti, 2008, Zamboni et al., 2008, Ragab, 2010, Fargion et al., 2011, Ibraheem and AL-Ardhi, 2017, Zayed, 2018). Elevations of liver parameters in this study were seen. The iron deposition may cause damage of hepatocyte (ALT & AST elevation) and cholestasis (bilirubin & ALP elevation), liver Injury may be as necrosis of heaptocellular, cholestatic disease or mixed between these two diseases like granulomatous hepatitis (Fargion et al., 2011, Zayed, 2017c). Dabrowska et al., (2001) showed that liver damage is the main cause of elevated liver function parameters in thalassemia patients. Rahim (2017) revealed that the increased serum liver parameters may be caused by iron storage in the liver which is regarded as a notable victim of iron deposition.

Major thalassemia is correlated with liver damage at varying degree leads to a raised activity of plasma transaminases in those patients (Lucarelli et al., 2000). Iron overload in these patients causes of congestive cardiomyopathy in heart, restrictive cardiomyopathy, angina, and pericarditis which causes an increased level of aminotransferase (Liu and Olivieri, 2004). Furthermore, thalassemia stimulates free radical construction through cytochrome P450, these radicals bind to

proteins or unsaturated lipids causing lipid peroxidation, the overall result of lipid peroxidation is to alter the chemical and physical properties of membranes (damage membranes) and liberate of serum liver transaminase, ALP and bilirubin (Poonknzhali et al., 1999). While, Williams et al (2012) stated that the serum liver enzymes increased but don't reach the signifcant level these patients.

REFERENCES:

Abd-Allh S.O. and S.A. Rahiem, Anabolic anabolic androgenic steroids and liver dysfunction in male adult mice. Pak. J. Biotechnol. 13(4): 245 – 251 (2016).

Ibraheem N. J. and AL-Ardhi G. H. Evaluation of serotonin hormone levels association with obesity in some adult men. Pak. J. Biotechnol. 14(2): 215- 220 (2017).

Rahim S.A., Effect of injection of human menopausal gonadotrophin and human chorionic gonadotrophin hormone on spermatogenesis of adult male mice. Pak. J. Biotechnol. 14(1): 1 – 8 (2017).

Borgna-Pignatti, C; Rugolotto, S and P. De Stefano, Survival and disease complications in thalassaemia major. Ann. Acad. Sci. 850: 227–31 (2008).

Dabrowska E., Jablonska-Kaszewska I., Bielawski K. and B. Falkiewicz, Aminotransferae in thalassaemic patients. Med. Sci. Monit. 1: 190-196 (2001).

Dongiovanni, P., Fracanzani, AL, Fargion, S. and L. Valenti, Iron in fatty liver and in the metabolic syndrome: a promising therapeutic target. J. Hepatol. 55: 920–32 (2011).

Fargion, S., Valenti, L. and A.L. Fracanzani, Beyond hereditary hemochromatosis: new insights into the relationship between iron overload and chronic liver diseases. Dig. Liver Dis. 43: 89–95 (2011).

Larson, A.M., Taylor, S.L. Bauermeister, D., Rosoff, L. and K.V. Kowdley, Pilot Study of the Relationship Between Histologic Progression and Hepatic Iron Concentration in Chronic Hepatitis C. J. Clin. Gastroenterol. 37: 406–411 (2003).

Liu, P. and N. Olivieri, Iron state and hepatic dise -ase in patients with thalassaemia major, treated with longterm subcutaneous desferrioxamine. Cardiovas. Drugs Therap. J. 8: 101-110 (2004).

Lucarelli, G., Galimberti, M., Polchi, P., Angelucci, E., Baronciani, D., Giardini, C., Politi, P., Durazzi, S., Muretto, P. and F. Albertini, Hepatic iron concentration and total body iron stores in 44. thalassemia major. Engl. J. Med. 332: 417-421(2000).

Poonknzhali, B., Srivastava, A., Querni, M.; Dennison, D., Aigrain, E. Krishnamoorthy, R. and Chandy, M. Complications of beta-thalassemia major in North 18. America. Blood. Bone Marrow Transp. J. 24: 5-11 (1999).

Ragab, L., Helal, S., Zaghloul, N., El-Raziky, M., Afifi, R., Musallam, K.M. and A.T.Taher, Clinical virologic analysis of hepatitis C infec-tion in transfusion-dependent β thalassemia major children. Int. J. Lab. Hem. 32:184–190 (2010).

Shah, N., Mishra, A., Chauhan, D., Vora, C. and N.R. Shah, Study on effectiveness of transfusion program in thalassemia major patients receiving multiple blood transfusions at a transfusion center in western India. Asian J. Transfus. Sci. 4(2): 94–98 (2010).

Zamboni, G., Marradi, P., Tagliaro, F., Darizzi, R. and L. Tota, Parathyroid hormone, calcitonin and vitamin D metabolites in beta-thalassaem ia major. Eur. J. Pediatr. 145: 133-136 (2008).

Zayed, K.S., Effect of Simvastatin drug on liver function parameters in men patients with hyperlipidemia in Al-Najaf province. Int. J. Chem. Tech. R. 10(1): 429-436 (2017a).

Zayed K.S., Association of T45G genetic polymerphism in the ADIPOQ gene with polycystic ovary syndrome patients in Al-Najaf Province. Med. J. of Babylon. 14(3): 50-63 (2017b).

Zayed K.S., Determination of I/D genetic variation of the Angiotensin Converting Enzyme (ACE) gene in Iraqi patients with Renal Failure. Al-Kufa University J. for Biol. 9(3): 1-8 (2017c).

Zayed K.S., Detection of mutation in codon 12 of KRAS gene in Iraqi patients with colorectal adenocarcinoma. Res. J. of Pharm. Techn. 11 (3): 110-124 (2018).

Warnes T., Iron-chelating therapy and the treatment of thalassemia. Brit. J. Hosp. Med. 28: 385-391 (2016).

Waseem, F., Khemomal, K.A. and R. Sajid, Antioxidant status in beta- thalassemia major: a single-center study. Indian J. Pathol. Microbol. 54(4): 761-63 (2011).

Williams, B., Morris, L., Toogood, I., Penfold, T. and B. Foster, Limb deformity and metaphysical abnormalities in thalassaemia major. Am. J. Pediatr. Hematol. Oncol. 14: 197-201 (2012).

Wirawan, R., Setiawan, S., Kusnandar, S. and B.G. Munthe, Diabetes mellitus in ß-thalasse- mia major patients. Med. J. Indonesia 12(2): 87-93 (2003).