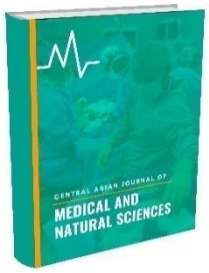
CENTRAL ASIAN JOURNAL OF MEDICAL AND NATURAL SCIENCES



Volume: 04 Issue: 01 | Jan-Feb 2023 ISSN: 2660-4159

http://cajmns.centralasianstudies.org

Evaluation of the Effectiveness of Liver Enzymes for Patients with Beta Thalassemia in Baghdad City Taking Iron Chelation Drugs Deferoxamine and Deferosirox

1. **Hussein Ali Kamel**
2. **Asma Hassan Juma Al-Samarrai**

Received 2nd Nov 2022,
Accepted 3rd Dec 2022,
Online 13th Jan 2023

[1] Assistant professor, University of Samarra/College of Education/Department of Biology

[2] University of Samarra/College of Education/Department of Biology

Huseein974@gmail.com
asmahasan@uosamarra.edu.iq

Abstract: The study was conducted for the period from September 2022 to January 2023, and samples were collected in the city of Baghdad at the Genetic Blood Diseases Center of Ibn Al-Baladi Hospital for Children on the Rusafa side, the Hereditary Blood Diseases Center of Al-Karama Teaching Hospital on the Karkh side, and private clinics for hematologists in Baghdad. And blood samples were drawn from 70 patients with thalassemia major who were treated with regular blood transfusions and iron-chelating treatments Deferoxamine (DFO) and Deferasirox (DFX), where they were divided into two groups, each group 35 patients according to the type of treatment, and the control group (healthy) numbered 30 and in each group Three age groups, the first age group G1 / 5-10 years, the second age group G2 / 11-20 years, and the third age group G3 / 21-30 years All biochemical tests were performed, including liver enzymes [Alanine aminotransferase (ALT), Aspartate aminotransferase (AST)] and the concentration of iron and ferritin. The results of the current study are explained. There was a significant increase ($P \leq 0.05$) for liver enzymes in ALT and AST for the two groups of beta thalassemia patients, and the deferoxamine group was higher, which was taken subcutaneously. AST enzyme was elevated for all age groups in the DFO group, while ALT enzyme was elevated in the first age group compared to the same group

Key words: Deferoxamine, deferosirox, liver enzymes, beta thalassemia .

For those taking oral deferoserx treatment, AST increased over the control group for all age groups, and ALT decreased in the second and third age groups compared to the control group. There was a significant increase ($P \leq 0.05$) in the concentration of iron in the two groups of patients with beta thalassemia who take deferoxamine treatment subcutaneously and deferoserx orally. There was a

significant increase (P≤0.05) for ferritin in the two groups of beta thalassemia patients who were taking deferoxamine subcutaneously and deferoserx orally for all age groups compared to the healthy group, and the deferoxamine group was higher.

Introduction:

Thalassemia is the most common form of chronic hemolytic anemia due to impaired synthesis of one of the globin chains. Since they are caused by qualitative and quantitative disturbances in the synthesis of the globin chain, so they can be classified according to the globin chains that are produced in reduced quantities. Those with decreased β-globin chains are termed β-thalassemia, while those with decreased β-chain production are termed β-thalassemia (2018, Farashi and Harteveld). And that beta thalassemia is the most dangerous and most clinical symptom, and it is considered one of the genetic diseases distinguished by abnormal hemoglobin (hemoglobin). It is usually accompanied by symptoms of hemolytic anemia and is associated with a global mortality rate of 15% (Crippa *et al.*, 2019). According to incomplete statistics, there are 4 million children born with beta-thalassemia syndrome every year, highly concentrated in the Mediterranean and Southeast Asia. It should be noted that in areas with scarce medical resources, children with β-thalassemia may die before diagnosis (Taher and Musallam, 2021). There are three subtypes of beta thalassemia: beta thalassemia major, thalassemia intermedia, and thalassemia intermedia. and beta thalassemia minor (Thalassemia intermedia (Asadov *et al*., 2019). The clinical severity of anemia in these three types depends on the number of copies of mutation genes inherited from the parents of the affected individual, where beta thalassemia minor patients are carriers of the disease usually asymptomatic, although it may They have mild anemia. Patients with thalassemia intermedia have different degrees of clinical anemia associated with the inheritance of secondary β-globin mutations (Angastiniotis,2019). For this reason, patients with beta thalassemia need a special treatment strategy and receive blood transfusions from time to time, as blood transfusion is a major reason for continuing their lives. But this particular treatment is not without disadvantages and risks. Where frequent blood transfusions lead to the accumulation of iron, which is stored in the form of ferritin, and in turn, its accumulation leads to serious complications, including deformation of the jaw and facial bones, growth retardation, and a direct effect on the physiology and functions of organs, including the liver, spleen, kidneys, and heart failure (Cullis *et al.*, 2018) and to prevent these effects Side effects and symptoms Doctors resorted to the use of iron-chelating drugs that have the ability to bind to iron by forming groups with iron that is not bound to transferrin in plasma, and there are several types of them. Deferoxamine, which is currently used in the Thalassemia treatment program in Iraq, is the first iron chelate to be taken in the form of subcutaneous injections.

and a chelator (Deferasirox), which is taken in the form of solid tablets (tablets) that are taken orally and metabolized in the liver and excreted through the stool (Garcia *et al*,.2021). The use of these drugs for long periods of time and in large doses is also not without risk. As it leads to phenotypic changes in the skin, as well as an imbalance in the physiological and biochemical functions of the body, liver and kidney functions, heart failure, vision, and deformities of the jaw, teeth and gums (Ghazzanfari *et al.*, 2019).

Materials and Methods:

Experiment Designs:

This study was conducted on 70 patients with thalassemia major who were treated with regular blood transfusions and iron-chelating therapies, where they were divided into two groups according to the type of treatment and the control group (healthy) numbered 30, and in each group there were three age

groups. Each of them consisted of 35 people with thalassemia major, and they were divided into three age groups as follows

The first age group is G1 / 5-10 years old

The second age group is G2/ 11-20 years

The third age group is G3 / 21-30 years old

The control group also consisted of 30 healthy subjects distributed as follows

The first age group is G1 / 5-10 years old

The second age group is G2/ 11-20 years

The third age group is G3 / 21-30 years old

All laboratory tests were performed on the samples

Sample Collection:

Blood samples were collected from the samples, and they were placed in tubes that did not contain an anticoagulant substance and contained only gel, in which the remaining 4 ml of blood samples were placed.

It was left for half an hour (30) minutes for the coagulation process to take place at room temperature, after which it was placed on a centrifuge (3000) rpm/min to obtain serum.

The amount of serum was transferred using a precise pipette to the Abpendorf tubes, and the sample number was noted on it, and it was kept in a refrigerated box until it was preserved in the freezer and awaiting the completion of the rest of the forms to start the process of conducting the required tests.

Biochemical and Physiological parameters:

I used the ready-made kit (Kit) of the American-made Beckman Coulter AU480 (for the purpose of estimating the effectiveness of liver enzymes), (Iron and ferritin)which is a self-analysis device that can measure several variables at the same time, with high speed and accurate results.

Statistical Analysis

The results obtained from the current study were analysed by using SAS 2001. The ANOVA test was used. The significant differences between the arithmetic averages were tested by using the Duncan multiple range test to compare between the groups, and the significance level of 0.05.

The Results and Discussion:

Evaluation of liver enzyme activity in serum

Table (1) shows that there is a significant increase in the results at ($P \geq 0.05$) in the effectiveness of (ALT, AST) for the three age groups of patients receiving deferox (DFX) treatment for the ALT enzyme for the age groups G1 (29.24 ± 19.10) G2 (24.75 ± 14.28) G3 (24.81 ± 18.78) and G1 enzyme AST (39.08 ± 18.05) G2 (36.38 ± 12.61) G3 (34.42 ± 20.83) and deferoxamine treatment for ALT enzyme for the three age groups, respectively (53.30 ± 48.4) (40.47 ± 31.390.3) (40.47 ± 31.392.3)) and AST enzyme (53.64 ± 28.83) (51.61 ± 30.31) (52.38 ± 16.12) compared to the control group (healthy) for the enzyme (ALT) for the three age groups, respectively (21.38 ± 5.28), (28.04 ± 9.74) (28.15 ± 7.94), and AST (26.68 ± 5.24) (29.21 ± 10.07) (23.82 ± 8.16), respectively.

Table (1): Evaluation of liver enzyme activity in serum.

Mean ± StDev			Groups Liver Enzymes	
Control Group (Healthy Subjects)	Group Patients Taking DFO	Group Patients Taking DfX		
30	35	35		
21.38 ± 5.28 b	53.30 ±48.4 a	29.24 ± 19.10 b	G1	ALT
28.04 ± 9.74 b	40.47 ± 31.32 a	24.75 ± 14.28 b	G2	
28.15 ± 7.94 b	48.90 ± 14.33 a	24.81 ± 18.78 b	G3	
26.68 ± 5.24 b	53.64 ±28.83 a	39.08 ±18.05 ab	G1	AST
29.21 ±10. 07 b	51.61 ±30.31 a	36.38 ±12.61 b	G2	
23.82 ± 8.16 b	52.38 ± 16.12 a	34.42 ± 20.83 b	G3	

These results agreed with Al-Salhi (2018) and its conclusions. In our current study, serum ferritin concentration was elevated in beta thalassemia patients of all age groups more than 1000 ng/ml, despite the use of iron chelation drugs. A positive correlation was observed between the number of blood transfusions and serum ferritin levels. When iron deposition occurs in the liver, its function is affected, which can be predicted by the elevation of ALT and AST, and thus the level of liver enzymes was significantly elevated (Suman *et al*., 2016); (Jafar, 2018).

The activity of the AST enzyme increases in the case of liver diseases, which lead to hepatitis and acute pancreatitis, as it rises in patients with beta thalassemia, and thus leaks from the liver into the plasma and then causes many diseases that may eventually lead to death. The liver function is disturbed with the rise. The relative concentration of this enzyme also affects the secretion of bile significantly (Waseem and Sajid, 2011).

As for the increase in the ALT enzyme due to the blockage that occurs in the liver cells, and causes fibrosis and enlargement in the liver cells, ALT is secreted and found mainly in the liver and in small proportions in the heart and skeletal muscles. Viral hepatitis, all of which are associated with patients with beta thalassemia (Jafar, 2018).

More detailed studies should be conducted to explore the exact cause of this age-group variability in the future and to find out the associations.

Serum Iron Concentration

The results of measuring iron concentration for the three age groups showed that there was no significant difference between the two groups of patients at (0.05 ≥ P) between them, while there was a significant difference compared to healthy subjects as in Table (2), where the group of users of Deferoserox treatment had G1 (37.02 ± 7.85) and G2 (42.98). ± 11.85 (G3) (35.62 ± 10.36) As for deferoxamine users, the first age group had G1 (42.18 ± 12.72) G2 (40.08 ± 10.80) G3 (43.46 ± 11.05) compared to the control group G1 (19.11 ± 6.25) G2 (20.075 ± 7.075) G3(17.95 ±3.26).

Table (2): Iron concentration in serum (micromol/L)

Mean ± StDev			Groups	
Control Group (Healthy Subjects)	Group Patients Taking DFO	Group Patients Taking DfX		
30	35	35		
19.11 ± 6.25 b	42.18 ± 12.72 a	37.02 ± 7.85 a	G1	IRON
20.09 ± 7.75 b	40.08 ± 10.80 a	42.98 ± 11.85 a	G2	
17.95 ± 3.26 b	43.46 ± 11.05 a	35.62 ± 10.36 a	G3	

In this study, very significant differences in serum iron levels were found between patients taking DFO and DFX for all age groups compared to controls. It agrees with (Rujito 2020) and others, where they indicated that there is a significant difference between DFO and DFX chelator users, compared to healthy subjects.Also, the results of our study agreed with the study of Mohammed and his group (2018), where they confirmed that serum iron increases in patients with beta thalassemia as a result of a decrease in hepcidin, which works to increase iron absorption. Excess iron is toxic to many tissues, including the liver, endocrine glands, and heart. , which causes a series of complications that cause disease and then death for patients. Also, an increase in the concentration of iron may occur in thalassemia patients as a result of an excessive increase in the production of a protein called GDF15 (Growth Differentiation Factor 15), and this protein works to prevent the production of the liver protein hepcidin, which has a role in increasing the absorption of dietary iron inside the intestine. This increase in the concentration of iron In the blood, it is a risk factor, as many studies indicate, including the Bonfils (2015) study.

Serum ferritin concentration:

The results of measuring ferritin concentration for the three age groups showed a significant difference at ($0.05 \geq P$) as in Table (3), where the group of DFX treatment users had G1 (1271.0 ± 766) G2 (1442.0 ± 838) G3 (1405.0 ± 1019) and the group of thalassemia patients The DFO users were G1 (3920.0 ± 570), G2 (4526.0 ± 1587), G3 (4384.0 ± 526), as compared to the control group, G1 (132.7 ± 92.8), G2 (109.7 ± 63.8), and G3 (111.2 ± 56.2).

Table (3): Serum Ferritin Concentration (ng/L)

Mean ± StDev			Groups	
Control Group (Healthy Subjects)	**Group Patients Taking DFO**	**Group Patients Taking DfX**		
30	**35**	**35**		
132.7 ± 92.8 c	3920.0 ± 570 a	1271.0 ± 766 b	**G1**	**Ferretin**
109.7 ± 63.8 c	4526.0 ± 1587 a	1442.0 ± 838 b	**G2**	
111.2 ±56.2 c	4384.0 ± 526 a	1405.0 ± 1019 b	**G3**	

The current study agreed with previous studies obtained by Hashmi (2008) *et al*., as well as Mahmoud *et al.* (2017), where the results showed an increase in serum ferritin in all age groups. Ferritin. Ferritin is essential for iron balance and estimation of ferritin levels in the blood is the most common test for estimating iron overload and serves as a benchmark for starting iron chelation therapy in patients with beta thalassemia, when the level of ferritin in the blood reaches 1000 ng / ml, and this is usually after a blood transfusion from the tenth to Twelfth, treatment begins with chelation drugs (Dreuzy *et al*., 2016).

References

1. **Al-Salhi, Haider Fadel Akab. (2018).** Evaluation of the immune status and viral infections of thalassemia patients dependent on blood transfusions in Thi-Qar Governorate. Master Thesis. College of Science. Dhi Qar University.
2. **Angastiniotis, S. Lobitz, (2019)** Thalassemias: an overview, Int. J. Neonatal Screen. 5 (1) 16.
3. **Asadov, Z. Alimirzoeva, T. Mammadova, G. Aliyeva, S. Gafarova, J. Mammadov,** (2019) beta-Thalassemia intermedia: a comprehensive overview and novel approaches, Int. J. Hematol. 108 (1) 5–21.

4. **Bonfils, L.; Ellervik, C.; Friedrich, N.; Linneberg, A. and Sandholt, (2015)**.C. H. Fasting serum levels of ferritin are associated with impaired beta cell function and decresed insulin sensitivity ; A population based study . Diabetologian,;58: 523 – 533
5. **Crippa, Annamaria Aprile, Laura Silvestri, Silvia Rivis, Samantha Scaramuzza, Stefania Pirroni, Maria Antonietta Avanzini, Luca Basso-Ricci, Raisa Jofra Hernandez, Marco Zecca, Sarah Marktel, Fabio Ciceri, Alessandro Aiuti, Giuliana Ferrari, Maria Ester Bernardo, (2019)** Bone marrow stromal cells from b-thalassemia patients have impaired hematopoietic supportive capacity, JCI 129 1566–1580.
6. **Cullis, J. O., Fitzsimons, E. J., Griffiths, W. J., Tsochatzis, E., Thomas, D. W., and British Society for Haematology. (2018).** Investigation and management of a raised serum ferritin. British journal of haematology, 181(3): 331-340.
7. **Dreuzy, E.; Bhukhai, K.; Leboulch, P.; & Payen, E. (2016).** Current and Future Alternative Therapies for Beta-thalassemia Major. *Biomedical Journal*, *39*(1), 24–38.
8. **Farashi, S.; & Harteveld, C. L. (2018).** Blood Cells , Molecules and Diseases Molecular basis of α -thalassemia. *Blood Cells, Molecules and Diseases*, *70*(10), 43–53.
9. **Garcia, A. J., Okeagu, C. N., Kaye, A. D., and Abd-Elsayed, A. (2021).** Metabolism, Pathophysiology, and Clinical Considerations of Iron Overload, a Comprehensive Review. Essentials of Blood Product Management in Anesthesia Practice, 289-299.
10. **Ghazanfari, A., Jafarzadehpour, E., Heydarian, S., Dailami, K. N., and Karami, H. (2019).** Comp rison of contr st sensitivity in β-thalassemia patients treated by deferoxamine or deferasirox. Journal of optometry, 12(3):168-173.
11. **Hashmi, H.; Muslahi, M.; Muslahi, H.; & Lamki, M. Al. (2008).** Prevalence of Endocrinopathies in Patients with Beta-Thalassaemia Major - A Cross-Sectional Study in Oman. *Iranian Academic Journal*, *23*(4), 257–262.
12. **Jafar, N. A. (2018).** The use of Interleukin -10 as a Biomarker for Diagnosis of Viral Hepatitis type C Infections and Related Liver Function in Beta- thalassemic Major Patients. *Journal of Medent Alelem College*, *10*(1), 8–13.
13. **Mohammadi, S.; & Khodabandehloo, M. (2017).** Prevalence of Hepatitis C Virus Antibodies among Beta-Thalassemia Major Patients in Kurdistan Province , Iran. *Iranian Academic Journal*, *12*(3), 23–31.
14. **Mohammed, Z.; & Jeddoa, A. (2018).** Molecular Characterization of Beta- thalassemia Mutations in Holy Karbala. Journal of Science College University of Kerbala, 88(August), 12–19 Contemporary Medical Sciences, 2(5), pp. 15–19.
15. **Rujito, L., Widodo, Y. R., Sakina, G., Santosa, Q., & Hapsari, A. T. (2020).** Glutathione S transferase and catalase gene polymorphisms did not tend to influence the severity of hemoglobin E/β-thalassemia. Universa Medicina, 39(1): 19-26.
16. **Suman, R. L.; Sanadhya, A.; Meena, P.; & Goyal, S. (2016).** Correlation of liver enzymes with serum ferritin levels in β -thalassemia major. *International Journal of Research in Medical Sciences*, *4*(8), 3271– 3274.
17. **Taher, K.M. Musallam, M.D**. **(2021)** Cappellini, beta-Thalassemias, N. Engl. J. Med. 384 (8) 727–743.
18. **Waseem, F.; Khemomal K. A. and Sajid.(2011).**R. Antioxidant status in beta – thalassemia major: A Single – center study. Indian Journal of pathology and Microbiology.;54 (4): 761 – 763.