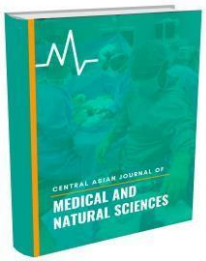

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Article

Effect of Iron Overload on the Liver Enzymes of Thalassemia Patients in Dhi Qar province

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Abstract: Hereditary hematologic diseases arise from hereditary factors that lead to disturbances in the balance of blood. The aim of this study was to assess the physiological characteristics of liver enzymes and investigate the impact of iron on these enzymes. For this investigation, a total of 150 blood samples were gathered. At the Thi-Qar Centre for Incendiary Disease in Nasiriyah City/Thi-Qar Province, fifty samples were taken from patients suffering from thalassemia, while twenty-five samples were taken from healthy individuals. Both the severity of the disease (thalassemia major and intermediate) and the gender of the patient are being taken into consideration while categorizing the patients into two groups. After receiving consent from the patients, samples were obtained between the months of January 2024 and February 2024. In this study, patients with thalassemia had substantially greater levels of ferritin, alanine transaminase, aspartate transaminase, and alkaline phosphatase compared to the control group. Liver enzyme levels did not differ significantly between thalassemia major and thalassemia intermediate, according to the study. In contrast, ferritin levels were much greater in thalassemia major than in thalassemia intermediate or minor. However, there was no statistically significant difference between the sexes when it came to ferritin and liver enzymes. Considering the study's conclusions , it was determined that the ferritin level brought about several difficulties and had a negative impact on the enzymes in the liver.

Keywords: Thalassemia, Iron, Liver Enzymes, ALT, AST, ALP.

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1. Introduction

The typical α- or β-globin components of hemoglobin (Hb) A proteins are either not made or do not mature normally in thalassemia. According to [1], the genes responsible for producing β-globin are located on chromosome 11, while the genes responsible for producing α-globin are on chromosome 16. Red blood cells, which contain the protein hemoglobin (Hb), transport oxygen from the air sacs called alveoli to the cells and tissues that require it [2]. In adults, you can find three different kinds of hemoglobin: hemoglobin A, hemoglobin A2, and hemoglobin F. Based on references 3, 4, Figure 1 reveals that these variants include $\alpha 2$; $\beta 2$, $\alpha 2$; $\delta 2$, and $\alpha 2$; $\gamma 2$ subunits, in that order. The exact globin chain that is affected determines the type of thalassemia, which can be β, α, $\delta\gamma$, $\delta\gamma$, and $\gamma\delta\beta$. Two primary forms of thalassemia, α-thalassemia and β-thalassemia are recognised. In contrast to β-thalassemia, which is defined by two genes, α-thalassemia is dictated by four genes [5, 6]. The uninterrupted DNA strand undergoes multiple changes to make it. A lack of linkage between globin chains makes them very unstable. They shorten the half-life of adult red blood cells (RBCs) in circulation and hasten the demise of RBC precursors

[7]. Iron and heme are produced during the breakdown of hemoglobin (Hb). When combined with other compounds, they serve as catalysts for reactions that generate reactive oxygen species (ROS) or free radicals. Radicals and reactive oxygen species (ROS) disrupt hepatocyte function and the islets of Langerhans' ability to do their job properly [8]. Several medical illnesses can be classified as iron overload disorders, all of which include an abnormal accumulation of iron in the body that can cause harm to various organs. Hereditary hemochromatosis (HH) is the most prevalent cause of primary iron overload (IO), although iatrogenic iron administration, hematologic problems leading to inadequate IE, frequent packed red blood cell (PRBC) transfusions, or liver pathology can induce secondary IO [9]. Duodenal cytochrome B is a brush border protein that helps convert ferric iron (Fe3+) from food to ferrous iron (Fe2+) inside enterocytes. Then, a divalent metal iron transporter (DMT1) carries the ferrous iron over the apical brush barrier [10]. The transporter responsible for exporting iron and facilitating the movement of ferrous iron across the basolateral membrane of enterocytes is ferroprotein. Being bound to transferring, the iron is then transported into the bloodstream [11, 12]. Iron linked to transferrin is taken up by cells through a process called transferrin receptor 1-mediated endocytosis. In the absence of iron removal, the enterocyte will retain the iron, which will be released by villi shedding a few days later [13].

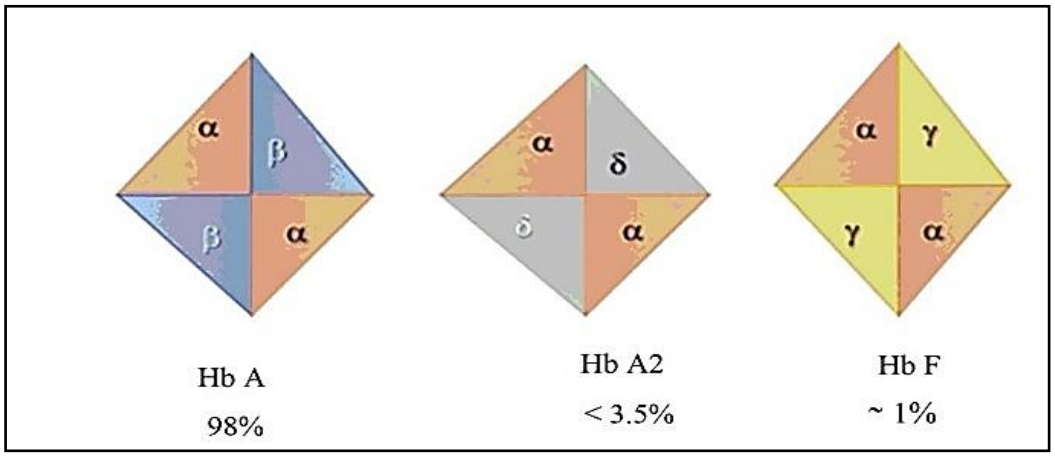

Figure 1: Types of Hemoglobin in human

2. Materials and Methods

Study Design

This study analyzed 150 blood samples collected from 100 thalassemia patients at the Thi-Qar Centre for Incendiary Disease in Nasiriyah City, located in Thi-Qar Province. Patients are categorised into two groups based on the severity of their condition (thalassemia major and intermediate) and their gender. Specimens were obtained in January 2024 with the patients' consent.

Sample Collection

A total of 150 blood samples were gathered from patients, with three milliliters of blood extracted from each pre-selected group. These samples were then separated into two groups: 50 samples from thalassemia patients and 25 samples from healthy individuals.

Serum Preparation

It begins the coagulation process, which separates the serum from the blood, as soon as the blood is taken into the gel tube. The first step in extracting the serum is to spin the gel tube in a centrifuge at 4000 rpm for five minutes. We next place the Eppendorf tube containing the serum into storage at -20 degrees Celsius. Our last step is to examine the ferritin and liver enzyme levels. The Cobas method was used to evaluate the liver enzymes, whereas the VIDAS method was used to investigate the ferritin levels.

Statistical Analysis

Statistical Package for the Social Sciences (SPSS) version 26 was used to analyses the data from the present study. The analysis was based on the independent sample t test and the person coefficient for correlation, with a p-value less than 0.05.

3. Results

Comparison of Thalassemia Patients and a Control Group on LFT Parameters

Table 1 shows that compared to the control group, thalassemia patients had substantially higher levels of all liver enzymes (ALT, AST, and ALP). More specifically, a p-value of less than 0.05 indicated that ferritin levels were significantly higher in the thalassemia group compared to the control group.

Table 1: Evaluation of LFT parameters in thalassemia patients and control group

LFT Parameters	Patients No. 100	Control No. 50	p. value
	Mean ± S. D		
ALT	30.65 ± 9.56	16.2 ± 3.63	0.001
AST	42.43 ± 10.9	36.7 ± 9.74	0.001
ALP	174.5 ± 38.7	151.5 ± 39.3	0.001
Ferritin	2060.0 ± 557.5	39.86 ± 11.38	0.001

Classification of Thalassemia Patients for LFT Parameter Evaluation

All liver function marker values were unaltered by illness type, according to a comprehensive review of the present results. Patients with thalassemia major had significantly greater ferritin levels than those with thalassemia intermediate, as seen in Table 2 (p-value less than 0.05).

Table 2: Analysing LFT parameters in thalassemia patients categorized of disease

Parameters	Intermediate No. 28	Major No. 72	p. value
	Mean ± S. D		
ALT	33.8 ± 9.34	32.6 ± 9.01	0.907
AST	43.6 ± 10.0	41.5 ± 8.04	0.685
ALP	125.9 ± 22.7	142.6 ± 35.4	0.211
Ferritin	1608 ± 504.8	2168.8 ± 599.6	0.003

Evaluating Ferritin and LFT Parameters in Sexually Oriented Thalassemia Patients

There was no correlation between the patients' gender and any of the liver function parameters (Table 3), including ferritin levels. This result was achieved by using a p-value that was lower than 0.05.

Table 3: Analyzing LFT characteristics in thalassemia patients based on sex

LFT Parameters	Female No. 42	Male No. 58	p. value
	Mean ± S. D		
ALT	30.4 ± 7.70	32.8 ± 8.77	0.357
AST	38.9 ± 7.16	44.1 ± 12.8	0.083
ALP	145.8 ± 42.0	135.6 ± 35.5	0.745
Ferritin	2141 ± 615.8	2178.7 ± 612.3	0.395

Person Correlation between Ferritin and Liver Enzymes

The current investigation found a statistically significant association between ferritin and liver enzymes, as well as between liver enzymes themselves, as evidenced by the data presented in table 4.

Table 4: Person correlation between physiological parameters and ferritin

		AST	ALP	Ferritin
ALT	r. value	0.766	0.433	0.588
	p. value	0.001	0.001	0.001
AST	r. value		0.699	0.499
	p. value		0.001	0.001
ALP	r. value			0.789
	p. value			0.001

4. Discussion

Liver Enzymes

The elevated serum ferritin level in thalassemia patients is directly linked to the excessive accumulation of iron resulting from frequent blood transfusions. There is a correlation between the increased levels of blood liver enzymes (ALT, AST, and ALP) and the enhanced serum ferritin level. Based on our research, the correlation between these variables is weak. Thus, it may be inferred that the increased levels of liver enzymes are likely caused by liver damage, which is a consequence of excessive iron accumulation in thalassemia patients who have undergone many blood transfusions. Both the research conducted by Al-Moshary et al. [14] and the study conducted by Yan et al. [15] share the same viewpoint regarding the increased levels of liver enzymes in thalassemia patients. Multiple studies have presented a description of the proposed mechanism of action; yet the exact mechanism is still unknown.

Therefore, it is necessary to perform additional comprehensive investigations in the future to determine the precise cause of this phenomenon and to identify the potential associations in thalassemia patients who undergo many blood transfusions.

Our findings indicate a direct correlation between elevated serum ferritin levels and the extent of hepatocellular injury, as well as an increase in liver enzyme levels. When the serum ferritin level exceeds 1000 ng/ml, there is a notable increase in

the levels of ALT, AST, and ALP [16]. The current study observed that an increase in serum ferritin levels leads to liver cell injury, which in turn affects the liver enzymes. The serum ferritin levels in β-thalassemia patients were significantly elevated despite undergoing chelation therapy.

A relationship between the number of blood transfusions and serum ferritin levels was notice. When iron accumulates in the liver, it impairs its activities, which can be indicated by elevated levels of ALT, AST, and ALP. Elevated liver enzymes were observed in conjunction with rising levels of serum ferritin, with a positive correlation between the two. The findings were consistent with a prior investigation conducted by Suman et al. [17] and Hindawi et al. [18].

Serum Ferritin

All βTM patients had a higher blood ferritin level compared to the control group, according to the results of the current analysis. Inadequate erythropoiesis, the lack of a natural mechanism to remove excess iron, and the accumulation of iron from repeated blood transfusions lead to progressive iron overload, which is manifested by high serum ferritin levels in BTM. Beverina et al. [19] found that the human body can only excrete 1 mg of iron each day, even though each transfused RBC contains over 250 mg of iron. The plasma contains non-transferrin bound iron, which is an excess of iron beyond what transferrin can bind to [20]. The most common way to determine if a patient with beta-thalassemia major (BTM) has iron overload is to measure their blood ferritin levels, since ferritin is essential for iron balance. Iron chelation therapy is usually initiated when the serum ferritin level reaches 1000 ng/ml, which usually occurs after the tenth or twelfth transfusion [21]. Iron overload stimulates the production of additional ferritin proteins. When these excess proteins encounter surplus iron, they undergo destruction and transform into hazardous hemosiderin [22]. The elevated serum ferritin levels observed in the present investigation are consistent with the findings reported by Heris et al. [23]. Lymphocytes can store excess iron in ferritin, which could potentially clarify the immune system irregularities observed in individuals with iron overload [24].

5. Conclusion

The researchers found that ferritin and liver enzyme levels were significantly greater in thalassemia patients than in the control group. Moreover, it was discovered that the kind of disease affected ferritin levels but had no effect on liver enzyme levels. Additionally, we found that ferritin levels are significantly correlated with liver enzyme levels.

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