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Evaluation Of Hepcidin And Iron Concentrations With Liver And Kidney Functions In Beta-Thalassemia Patients

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ABSTRACT

The goal of this research was to estimate the concentrations of iron and hepcidin with liver and kidney functions in beta-thalassemia patients, the study involved the collection of 80 blood samples from both sexes, and the samples were distributed into 45 samples for beta thalassemia patients, their ages ranged between 15-25 years, the samples were collected from the Thalassemia Specialization Center in Baquba General Hospital, and 35 blood samples for healthy people as a control group, their ages extended from 15 to 25. years, during the period from the beginning of March 2023 until the end of May 2023. The study's findings revealed a considerable increase in the concentrations of hepcidin and iron in patients group compared with the healthy ones. It also displayed a significant reduce in the patients' albumin and creatinine concentrations as compared with healthy group, while the results here were no significant variations in total protein, urea and uric acid levels.

Keywords: Beta-thalassemia, Hepcidin, Iron, Liver, Kidney.

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Introduction

Thalassemia refers to a range of genetic blood disorders that impact the inability of a person to make hemoglobin, which causes anemia, leading to anemia [1], or it is a genetic disorder resulting from a defect in the composition of a globin chain or several globin chains, meaning that the alpha and beta chains in hemoglobin are made equally in normal cases, but in the case of thalassemia, the speed of making one of these two chains is slower than the other, and as a result the chain increases the other compared to the first, and an abnormality of hemoglobin occurs in an abnormal form that leads to a decrease [2].

In the nations that surround it—the Middle East, India, the Mediterranean, and the Far East—thalassemia is a major problem. The Maldives has the highest percentage of thalassemia carriers 18%, Cyprus has 14 percent, Sardinia has 10.3%, and Southeast Asia has 3-5 percent [3]. Due to population mobility and interethnic marriages, thalassemia has spread around the world as a result of the selection pressure of sickle Plasmodium malaria in these areas [4].

The pathogenesis of thalassemia is mainly related to incompetent erythropoiesis and hemolysis, which hemoglobinopathies are a diverse set of hereditary illnesses characterized by impaired production of the alpha or beta chains of hemoglobin, which function as oxygen-carrying components of red blood cells. α/β-globin chain ratio leading to chronic hemolytic anemia, compensatory hematopoietic expansion [5]. If there is insufficient production of these two chains by the body, red blood cells do not form properly and are unable to carry enough oxygen, leading in anemia that begins in early childhood and lasts throughout one's life. Thalassemia is a hereditary condition that requires at least one of the parents to be a carrier. It is caused by a genetic mutation or deletion of specific essential natural components [6].

Thalassemia comes in two forms: alpha [α-] and beta (β-). Whereas beta thalassemia occurs when all four -globin genes are damaged or altered, alpha thalassemia is caused by changes or deletions in one or more of the four -globin genes [6,7]. Unique of the greatest frequent danger elements for thalassemia is consanguineous marriage. [7]. The legacy of faulty and altered genes intricate in the manufacture of hemoglobin from the parents is one of the causes of thalassemia. Another explanation is that if one of the parents has thalassemia, even if the child has no symptoms the child might grow up to carry the illness. The youngster may possibly have thalassemia minor, in which case his symptoms may be minimal [8].

Hepcidin is a peptide hormone that was first identified in 2000. It is mostly produced by hepatocytes and consists of 25 amino acids as well as four disulfide bridges [9]. By enabling iron from daily meals to cross the oral-enteric membrane by means of a divalent metallic transporter,

where it is either delivered to the plasma by hepcidin or stored as ferritin. Hepcidin is involved in the regulation of the iron balance in the human body, hepcidin is an acute-phase reactant, one of many molecules whose plasma concentration changes in response to inflammation. During acute or chronic inflammation, hepcidin and other acute-phase reactant levels rise, which causes serum iron levels to decrease as hepcidin levels rise. Elevated hepcidin is associated with the pathophysiology of chronic disease anemia; elevated inflammation lowers serum iron levels because hepcidin decreases iron transport out of cells; on the other hand, a lack of hepcidin production can lead to iron overload, as in hereditary hemochromatosis [10,11].

This study aimed to determine the concentrations of hepcidin and iron with liver and kidney functions in beta-thalassemia patients.

Materials and Methods

Samples Collection

A total of 45 Patients diagnosed with beta-thalassemia at the Thalassemia Center at Baquba General Teaching Hospital in Diyala Governorate provided blood samples. The age range of the patients was 15 to 25 years old, and 35 blood samples were taken from healthy individuals in the same age range. The patients' information was recorded using a customized questionnaire form that was created specifically for each patient.

Blood Collection

Blood samples were taken using disposable plastic syringes to draw (4-6) ml of venous blood. The blood was then placed in test tubes and allowed to coagulate for 30 minutes at room temperature. The separated sera were then centrifuged for 15 minutes at 5000 x g and stored at -20 ° C for further biochemical analysis.

Biochemical Parameters

By means of the hepcidin kit manufactured by Shanghai Biological Technologies, identified by the numeral YHB1535Hu, the concentration of hepcidin was measured make use of the enzyme-linked immunosorbent assay (ELISA) method, while iron, total protein, albumin, urea, creatinine and uric acid determined by using the analyzer Autonomous Cobas integra 400 puls system supplied by the German company Roche.

Statistical analysis

The mean and standard deviation (SD) for each measurement were used in the SPSS statistical software to examine the results that were obtained. To compare biochemical variables between two groups, the T-test was run at the probability level (P≤ 0.05).

Results

Table 1 displays the findings of study, Mean ± SD of hepcidin and iron concentrations in the two groups of patients and healthy people.

Table 1: The mean ± SD of hepcidin and iron in the two groups.

Parameters	Control (n=35)	Patients (n=45)	P-value
Hepcidin (ng/ml)	531.048±211.343	1539.846±601.945	0.001*
Iron (µmol/L)	21.587±3.3152	40.673±7.352	0.001*

* This sign means different significant at P ≤0.05.

Table 1 shows that the concentrations of hepcidin and iron in thalassemia patients were 1539.846 ± 601.945 ng/ml and 40.673 ± 7.352 µmol/L respectively, while it was 531.048 ± 211.343 ng/ml and 21.587 ± 3.3152 µmol/L respectively in the healthy people. Results showed that the concentrations of hepcidin and iron increased significantly (p ≤ 0.05) in the thalassemia patients compared to healthy people, as evidenced by figures 1 and 2.

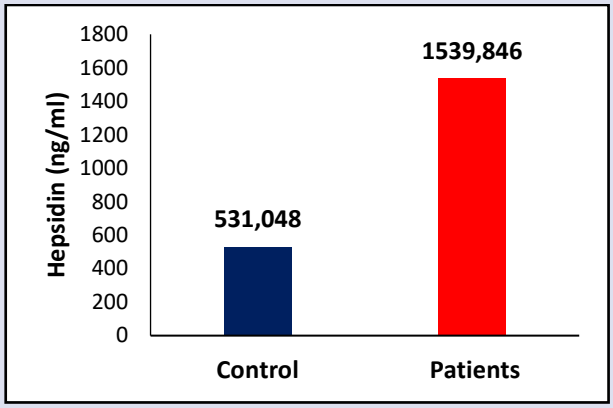

Figure 1: The mean of hepcidin concentration in two groups.

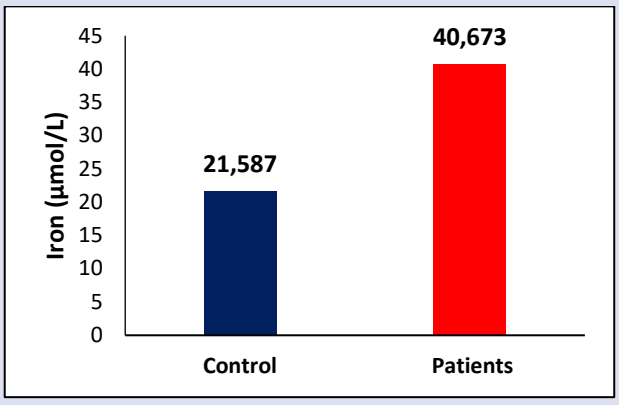

Figure 2: The mean of iron concentration in two groups

Liver and kidney functions were also evaluated in both groups of patients and healthy by measuring the concentrations of total protein, albumin, urea, uric acid and creatinine, as shown in Table 2.

Table 2: Mean ± SD levels of liver and kidney functions in the two groups.

Parameters	Control (n=35)	Patients (n=45)	P-value
Total protein (g/dl)	68.930±11.818	66.392±7.918	0.224
Albumin (g/dl)	51.092±5.505	46.404±5.978	0.001*
Urea (mg/dl)	27.627±8.398	25.965±8.922	0.35
Uric acid (mg/dl)	4.976±1.046	5.032±1.731	0.849
Creatinine (mg/dl)	0.785±0.182	0.388±0.088	0.001*

* This sign means different significant at P ≤0.05.

Table 2 shows that the mean ± SD of total protein and albumin levels in thalassemia patients were (66.392 ± 7.918) g/dl and (46.404 ± 5.978) g/dl respectively, while were (68.930 ± 11.818) g/dl and (51.092±5.505) g/dl respectively in the healthy group.

There were no significant variations in total protein level, according to the findings, but there was a significant reduce in the level of albumin at a probability level of p ≤ 0.05 in the patients group matched to the healthy group, as showen in figures 3 and 4.

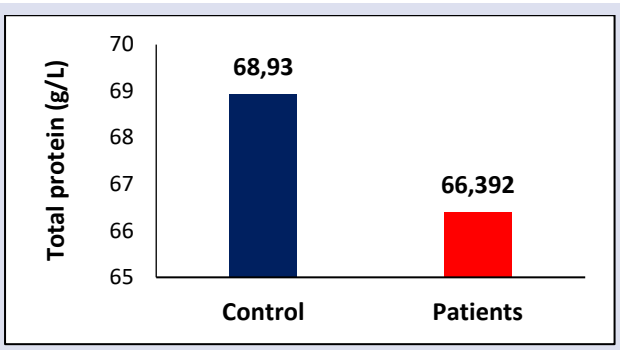

Figure 3: Total protein concentration in two groups.

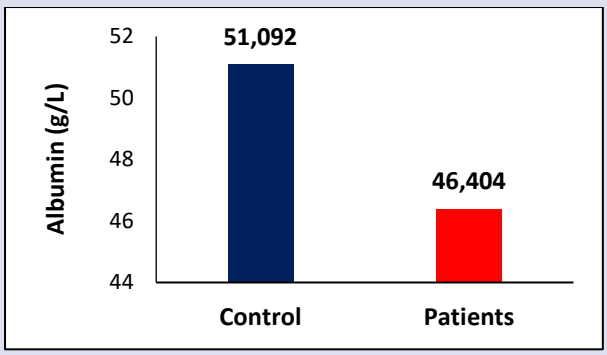

Figure 4: Albumin concentration in two groups.

Table 2 showed that the mean ± SD of urea levels of (25.965 ± 8.922) mg/dl, uric acid (5.032 ± 1.731) mg/dl, and creatinine (0.388 ± 0.088) mg/dl, respectively in thalassemia patients, while it was (27.627 ± 8.398) mg/dl and (4.976±1.046) mg/dl and (0.785±0.182) mg/dl respectively in the healthy group.

Results displayed that there were no significant differences at the probability levels of ≤ 0.05 in each of urea and uric acid in patients group compared to the healthy group, while creatinine level decreased significantly at the probability of ≤ 0.05 in the patients compared to the healthy group as in figures (5-7).

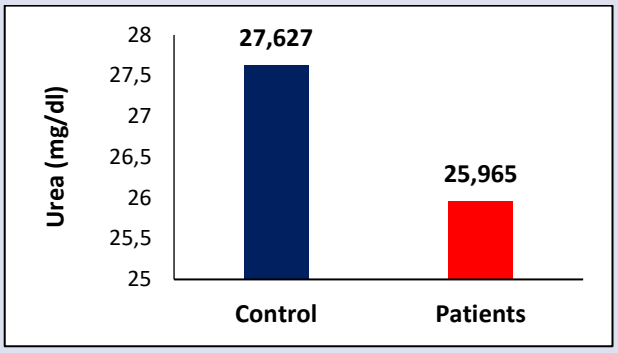

Figure 5: Urea concentration in two groups

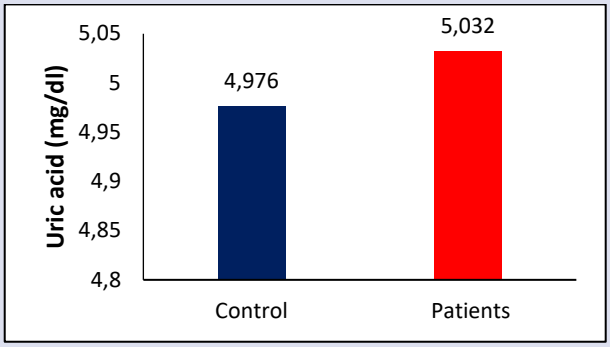

Figure 6: Uric acid concentration in two groups.

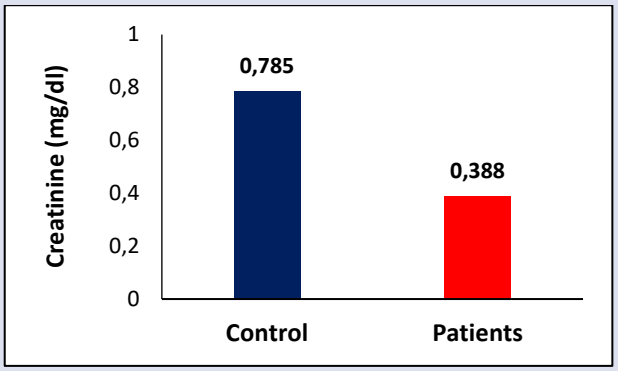

Figure 7: Creatinine concentration in two groups.

Discussion

The findings of this study are consistent with the study of Abd and Al Samarrai [12], as they suggest that the reason of high hepcidin was due to regular blood transfusions, and blood transfusions inhibit the red blood cell move, so that both lead to an increase in hepcidin in thalassemia patients.

Hepcidin is secreted primarily by hepatocytes into the circulation, it is an important controller of iron homeostasis in the body, and it plays a job in a variety of iron metabolism metabolic pathways. It acts by directly inhibiting ferroportin, a protein that transports iron out of its storage cells, and this protein is present in intestinal absorption cells and macrophages, hepcidin blocks intestinal absorption cells from secreting iron in the hepatic portal system by blocking ferroportin, limiting iron absorption and preventing iron from exiting macrophages., liver, spleen, endothelial cells and

duodenum, preventing its export to the plasma, and thus leads to iron balance in the body. Hepcidin gene expression is down-regulated by low tissue oxygen tension and by increased erythropoietic demand and up-regulated by increased body iron stores and infection or inflammation [13].

The recent study discovered that iron levels in beta-thalassemia patients had increased, and are in agreement with Hasoon's et al findings [12,14], the excessive iron levels in beta-thalassemia patients were caused by both the frequent red blood cell transfusions and high iron absorption, these results indicate insufficient chelation.

Excess iron is harmful to many tissues, including the liver, endocrine glands, and heart, according to a research [15], resulting in a variety of consequences that cause sickness, and death in Mention the name of the disease studied by Neufeld et al [15]. Iron can work a major job and is essential for oxidation of membrane cell, aging, and the production of cell antigen, which is one of the key erythrocyte clearance pathways. Additionally, patients' significantly elevated blood iron levels are caused by defects in the control of iron absorption, including the genetics of hemochromatosis. Recurrent blood transport also raises blood iron levels because recipients lack the biological mechanisms of iron excretion, which results in higher than normal levels of iron stores in the body [16].

The present study's findings agreed with the results of Hosen et al [17], who noticed that there were no significant differences for total protein level in patients compared to healthy controls, and also agreed with the results of Abd et al. [18], who discovered that thalassemia patients' albumin levels were much lower than healthy controls.

Total protein is the most abundant compound in the blood serum and includes enzymes, hormones, and antibodies, as well as regulators of osmotic pressure balance. The decrease in total protein in the serum of thalassemia patients is related to the liver's inability to synthesize secondary protein [19].

Albumin is the main component of serum protein (usually more than 50%) and is synthesized in the liver and aids in osmotic pressure, nutrient transport, and waste removal [20]. Albumin is the major fatty acid-binding protein in plasma and has seven fatty acid-binding sites with medium and high affinity [21], and it regulates osmotic pressure, transports fatty acids, bilirubin, and cholesterol. Also, it has been proven to play a key function in blood plasma's antioxidant capability against *reactive oxygen species* [22]. Albumin is produced mainly by hepatocytes and hepatic dysfunction, malnutrition, or systemic inflammation can lead to low serum albumin levels [23].

Our study results agreed with the results of Althanoon and Alkazzaz [24], who they noted that there were no significant differences in the concentration of urea and uric acid with a significant decrease in creatinine in serum of thalassemia patients compared to healthy controls. The result also agrees with the study of Ghazala et al., [25], who they noted that there were no significant differences in urea concentration between thalassemia patients and healthy controls. Outcomes of study also agreed with Shanaki et al [26], as they observed a significant reduce in the concentration of creatinine in thalassemia patients compared to healthy controls.

Increased transfusion frequency and hypercalcemia are linked to impaired renal function in thalassemia patients, highlighting the significance of monitoring calcium levels in thalassemia patients on a regular basis, as it is considered a risk factor for renal function [27,28]. And that the reason for the low concentration of creatinine in the blood is related to a decrease in body mass index due to a delay in growth or a decrease in body muscle mass in thalassemia patients, the creatinine is the most widely used measure in knowing the functions of the kidneys, and this in turn leads to the disruption of the filtration process carried out by the kidneys [29,30]. The low concentration of creatinine in the blood is due to a deficiency in the functions of the kidneys that reduce the glomerular filtration process, and that the glomerular filtration rate is clinically important because it is a measure of kidney function [30].

Conclusion

According to the current study, there has been Hepcidin and iron concentrations in beta-thalassemia patients were significantly higher than in healthy controls. Also showed a significant difference in some liver and kidney functions in beta-thalassemia patients compared to healthy controls.

Conflict of interest

There are no conflicts of interest in this work.

Acknowledgments

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