

Estimation of Hepcidin Role and some Biochemical Parameters in Patients with Beta- thalassemia in Thi-Qar Governorate/ Iraq

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Received: 2024-02-02, Revised: 2024-03-09, Accepted: 2024-03-12, Published: 2024-06-01

Abstract—The β -thalassemias are a group of recessively inherited genetic disorders that cause varying amounts of hemoglobin production. The study's aim was to look at hepcidin, ferritin, iron, PCV, Hb, ALT, AST, and albumin levels. Serum hepcidin, ferritin, iron, PCV, Hb, ALT, AST, and albumin levels were determined in 55 patients with beta-thalassemia and 55 healthy individuals. The results demonstrated a substantial rise in serum concentrations of ferritin, iron, ALT and AST in the beta-thalassemia group as compared to the control group ($p < 0.001$). There was also a significant decrease in the concentrations in the serum of hepcidin, packed cell volume, hemoglobin and albumin ($p < 0.001$).

Keywords—Hepcidin, Ferritin, β -thalassemia, Hemoglobin

I. INTRODUCTION

The β -thalassemias are a group of recessively inherited genetic disorders with varying levels of hemoglobin synthesis [1]. Patients with β -thalassemia are distinguished by the uneven production of globin chains, which is caused by an increase in the alpha chain due to a lack of β -chain manufacture countered by a normal rate of chain synthesis. Thalassemia is a genetic disorder that affects hemoglobin production and is common worldwide, with particular prevalence in the Mediterranean, tropical and subtropical regions, the Caucasus, Central Asia, and Southeast Asia [2]. The more prevalent of the two forms of beta- and alpha-thalassemia, which causes severe anemia, is B-thalassemia. This leads to varied degrees of blood anemia due to a lack of equilibrium in the production of globin chains, the synthesis of inactive RBCs, and hemolysis [3]. The most well-known form of β -thalassemia, which results in impaired beta globin chain synthesis, is β thalassemia major. It is classified into three broad groups based on clinical features: β thalassemia major, β thalassemia intermedia, and β thalassemia minor [4]. Clinically, thalassemia minor syndrome is defined by moderate anemia and ongoing microcytosis. Thalassemia characterized by a moderate, variable compensated hemolytic anemia, it intermedia may or may not require a

routine blood transfusion. Clinical signs may arise during physiological stress, such as an infection, pregnancy, or surgery [5].

Clinically, beta-thalassemia is classified into three groups according to the severity condition: The three kinds of thalassemia are minor, intermediate, and major. Minore thalassemia is assumed to be symptomatic, Intermediate thalassemia causes anemia but is less effect than the major thalassemia, which requires monthly blood transfusions for the rest of the patient's life [6]. Four protein molecules make up hemoglobin. Two of the molecules are chains, while the other two are β -chains. Unlike the gene for α -globin, which is located on chromosome 11, the gene for β -globin is located on chromosome 16 [7]. Different beta-thalassemias have different molecular compositions. Over 200 mutations that cause disease have been identified so far. Most mutations are caused by frameshifting insertions, oligonucleotide deletions, and single nucleotide changes. Beta-thalassemias are relatively seldom caused by gross gene loss [8]. β -thalassemia results in a decrease in the amount of β -globin chains generated, leading to an increase in the creation of α -chains. The production of hemoglobin without beta chains increases, and as a result, unbound α chains continue to exist as α -type (α_4) tetramers. This leads to their accumulation in red blood cells (RBCs) and an early disintegration of RBCs [9]. Patients with thalassemia may experience iron overload, a dangerous side effect that can be caused by the illness or by receiving frequent blood transfusions [10].

It has been demonstrated that people with beta-thalassemia had higher levels of certain liver enzyme markers, indicating a potential issue with liver function. The liver is the first organ affected by an excess of iron in thalassemia patients [11]. Hepcidin is a hepatic peptide hormone that regulates the process of iron homeostasis. Hepcidin controls the amount of iron in plasma, the distribution of iron in tissues, and the absorption of iron from food. Hepcidin deficiency is the main cause of iron excess in iron-loading anemias such as thalassemia. Patients with β -thalassemia have elevated erythropoietic activity, which results in a hepcidin deficiency [12].



Examining the levels of hepcidin, ferritin, iron, hemoglobin, packed cell volume (PCV), and liver functions in a sample of β -thalassemia patients in the Thi-Qar governorate of Iraq is the aim of this study..

II. MATERIALS AND METHODS

A. Design of study

This investigation was carried out at the Central Private Laboratory, the Hereditary Blood Diseases and Thalassemia Center in the Iraqi Thi-Qar Governorate. The study had 110 participants: 30 female and 25 male controls and 26 female and 29 male patients with β -thalassemia major (BTM) ranging in age from 5 to 35. It should be noted that only individuals with β -thalassemia major (BTM) were sampled because the Thalassemia and Genetic Blood Disease Center did not have any intermediate or beta-thalassemia minor samples available.

B. Collection of a blood sample

Five milliliters of blood were drawn from the veins of both controls group participants and thalassemia patients using needles. The blood was then separated into the following categories:

To compute Hb and PCV using hematology analyzer (CBC) by Abbott CEEL-DYN Ruby, USA . Two milliliters of the blood sample were placed in EDTA-containing tubes. . The material is extracted into three milliliters, which are then put in a centrifuge tube and allowed to coagulate for ten minutes at room temperature before being spun at 3000 (Xg). Serum samples were removed and stored at -20 °C for future use. Hepcidin serum was measured with an ELISA spectrophotometer. Serum ALT and AST were obtained from Abbott C4000 (USA). Human (Germany) supplied serum albumin and iron; Abbott i1000 (USA) supplied serum ferritin.

C. Statistical Analysis

The statistical analysis was conducted utilizing SPSS version 20.0 software. The findings were presented as

mean $\pm$ SD, or mean plus standard deviations. The one-way ANOVA test was run to compare parameters across research groups. A p-value of less than 0.001 was employed to ascertain statistical significance.

III. RESULTS AND DISCUSSION

Serum hepcidin and hemoglobin concentrations in the patient group were significantly lower than in the control group ($p < 0.001$), as shown in Table 1. The overload of Iron primarily was by this hormone deficiency, or iron-loading anemias like beta-thalassemia influenced by it. Hepcidin expression significantly impacted by the increased erythropoietic activity, which might have a negative effect on the hormone's levels in the body. Low hepcidin and the resulting hyperabsorption of dietary iron are the primary causes of systemic (Fe) overload in semi-thalassemia patients. Even though iron contributes less to the iron burden in patients with hemoglobinopathies major than transfusions do. This is because excessive iron absorption from food is ZAQ by low hepcidin [13]. Patients with β -thalassemia have genetic abnormalities that restrict the manufacturing of hemoglobin, resulting in lower hemoglobin levels in their bloods and then having blood anemia [14, 15]. Additionally, from the same table, it was noticed that the serum ferritin, iron, and PCV value concentrations in the patient were significantly higher than that in the controls samples ($p \leq 0.001$). These outcomes agreed with the previous work in [16]. This is an indication that external gastrointestinal absorption, as the opposed to transient iron supplementation, was the cause of elevated serum ferritin levels. The buildup of extra iron in the body is due frequent blood transfusions or thalassemia, which raises iron levels [17]. Red blood cell (RBC) counts are stabilized by monthly blood carting, hemolysis, and increased iron absorption from the duodenum and proximal jejunum, which results in an iron increase [18]. The hemoglobin levels in the patient bloods were linked to these decreases in the PCV values, which explains why individuals with β -thalassemia had lower PCV values. The results showed a positive, and strong connection ($p \leq 0.001$) between PCV levels and β -thalassemia the standard deviation for the patients group and the controls group are 3.98 and 0.98, respectively

TableI. Serum hepcidin, ferritin, Iron, PCV and Hb concentrations of controls and patients groups

Groups	Hepcidin Concentration(pg/mL) Mean $\pm$ SD	Ferritin Concentration(ng/nL) Mean $\pm$ SD	Iron Concentration (g/dL) Mean $\pm$ SD	PCV Mean $\pm$ SD	Hb% Mean $\pm$ SD
Patients	47.8122 $\pm$ 8.69520	4313.3273 $\pm$ 743.80732	203.13 $\pm$ 38.589	23.242 $\pm$ 3.9861	7.885 $\pm$ 1.3636
Controls	152.8896 $\pm$ 30.04205	59.5851 $\pm$ 13.73219	86.29 $\pm$ 21.289	40.187 $\pm$ 4.0577	13.425 $\pm$ 1.0242
p-value	<0.001**				

Table 2 demonstrates a statistically significant rise ($p < 0.001$) in the serum ALT and AST concentrations in

the patient group compared to the control group. The results here agree with the findings of (Salama *et al.* 2015)

[19]. Researchers found that an iron excess in β -thalassemia patients is the primary cause of elevated liver enzymes. They also found that β -thalassemia patients raised in the ALT and AST levels and significantly higher serum ferritin levels than the control group [20]. They also found a significant relationship between ALT and AST and a high correlation between ferritin level and HCV status. Liver is one of the organs most susceptible to harm, and it is a common target for damage in people with beta-thalassemia. A high AST level in human bodies indicates the existence of an infection or inflammation in the liver [21]. With a carrier incidence of 9–10.2%, beta-

thalassemia is the most common form of chronic hemolytic anemia in Egypt, accounting for 85,1% of cases. Whether liver injury is acute or chronic, the serum values of ALT and AST rise progressively (AST) [19]. Additionally a significant drop in the serum albumin concentration was shown in the patient group compared to the control group ($p \leq 0.001$), according to the same data. The results were consistent with those of [21]. When comparing the control group in this study to the thalassemia patient group, the albumin levels in the former group were significantly lower.

TABLE II. Serum ALT, AST and Albumin concentrations of controls and patients groups

Groups	ALT Concentration(U/L) Mean $\pm$ SD	AST Concentration(U/L) Mean $\pm$ SD	Albumin Concentration(g/dL) Mean $\pm$ SD
Patients	41.1725 $\pm$ 5.90261	44.14535 $\pm$ 7.707559	39.98 $\pm$ 9.148
Controls	14.5091 $\pm$ 3.57912	23.67273 $\pm$ 6.333493	45.49 $\pm$ 3.179
p-value	<0.001**		

IV. CONCLUSIONS

- 1- Hepcidin levels in the patient group were considerably lower than in the control group, demonstrating a direct correlation between hepcidin levels and beta-thalassemia.
- 2- The patient group had a higher blood iron level than the controls group. The statistics of our results revealed that the patient group had significantly higher serum iron levels than the control group.
- 3- Our results demonstrated that there is no correlation between hepcidin levels and ferritin levels. Moreover, the hepcidin insufficiency may be a factor 'in elevating the ferritin levels in the patients and that ferritin might be used as a tool to assess Fe in the patients.
- 4- Our results showed that the hepcidin levels in the patients have no effect on ALT and AST levels.
- 5- Hemoglobin and PCV in the patients are strongly correlated with hepcidin levels.

CONFLICT OF INTEREST

Authors declare that they have no conflict of interest

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