Research Article

# Integrating Molecular and Biochemical Findings in β-Thalassemia Major for Improved Pharmacotherapy , Iraq

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**ABSTRACT**:

Beta thalassemia is one of the most prevalent genetic disorders worldwide and a common inherited condition affecting newborns when parents are carriers or affected. It represents a severe form of anemia associated with multiple clinical complications. This study aimed to evaluate hematological and biochemical markers in patients with beta thalassemia major in Thi Qar province, Iraq, with a focus on monitoring treatment outcomes and improving pharmacological management, including the effectiveness of iron chelation therapy.A total of 100 transfusion-dependent beta thalassemia patients and 100 healthy controls were included. Most patients received regular blood transfusions along with iron chelation therapy, mainly deferoxamine. However, many patients still exhibited elevated serum ferritin levels, suggesting inadequate chelation or poor compliance. Hematological analysis revealed significantly lower values in patients compared to controls, including hemoglobin (Hb), hematocrit (PCV), mean corpuscular volume (MCV), and mean hemoglobin ($p<0.05$–$0.01$), while mean corpuscular hemoglobin concentration (MCHC) showed no significant difference ($p>0.05$). Biochemical findings indicated increased levels of blood glucose, triglycerides, alkaline phosphatase (ALP), alanine transaminase (ALT), aspartate transaminase (AST), and kidney function markers in patients. Lipid profile analysis showed lower LDL and HDL levels in controls. No significant differences were observed in serum albumin, calcium, sodium, and potassium levels ($p>0.05$). Additionally, primary hypothyroidism was identified in 5.31% of patients, characterized by elevated thyroid-stimulating hormone (TSH >4.5 mIU/L) and reduced T4 levels (<5.6 mIU/dL). This study highlights the importance of continuous monitoring and comprehensive evaluation of beta thalassemia patients to optimize treatment strategies and improve clinical outcomes.

**KEYWORDS**: β-thalassemia; biochemical evaluations; thyroid iron chelation treatment; medication effectiveness

## 1. INTRODUCTION

Beta-thalassemia (β-TM), a hereditary anemia brought on by a lack of the beta-globin chain, is inherited from carriers or afflicted parents. Thalassemia is one of the most common hereditary diseases in the world. Patients with beta-thalassemia major are at risk for iron overload in multiple organs as a result of frequent blood transfusions and increased iron absorption by the gastrointestinal tract. This can cause harm, especially to the heart, liver, and endocrine glands [1-2]. Patients with β-TI and β-T M are affected differently by iron accumulation and oxidative stress, which causes lipid peroxidation and eventually liver damage [3]. The clinical features of thalassemia, including altered endocrine function, heightened vulnerability to infections, and vascular consequences including thrombosis, may be influenced by lipids and lipoproteins. Abnormal lipid levels are associated with carotid artery intima-media its thickness and early atherosclerosis in these patients [5]. Iron-metabolizing agents, such as deferiprone (DFP) and deferasirox (DFX), are therapies that regulate lipid production and metabolism in β-TM patients with hepatitis C virus infection or IOL.Increased bone marrow activity, which needs extra cholesterol to produce red cell membranes, and lipid peroxidation brought on by iron excess are other causes of lipid abnormalities in thalassemia [6]. Furthermore, prior research has shown that patients with severe thalassemia have a significant prevalence of endocrine abnormalities. A trace mineral deficit may be the cause of endocrinopathies. In these patients, it is especially important to examine for trace minerals such calcium, sodium, and potassium [7]. Thalassemia is the most common monogenic genetic condition worldwide. The expansion of malaria in the Mediterranean, Middle East, and Southeast Asia corresponded with its historical occurrence (carriers of the thal genes are assumed to be resistant to the malaria parasite). Thal sufferers are now found worldwide3 as a result of extensive migration, and their frequency is

steadily increasing [8]. Beta thalassemia is caused by a quantitative reduction in β globin chains, which are frequently structurally normal. 2. They result from a wide range of mutations, nearly all of which harm the β globin gene. It has been discovered that beta thalassemia has almost every possible issue affecting transcriptional or post-transcriptional gene expression, including translation. 3. These genetic defects limit the production of β globin in a number of ways, ranging from a modest deficit to [9]. Patients with thalassemia are more likely to get infected with a virus. For example, pathological hepatitis may be caused by long-term exposure to blood and blood transfusion products. While the lack of a vaccination makes it very difficult for thalassemia patients and donors to have hepatitis C, the availability of immunizations can greatly reduce the prevalence of hepatitis B among these individuals [10]. All people have defective hemoglobin (Hb) beta-chain production, but the phenotypes that follow vary widely, from severe anemia to no clinical signs at all. The main criteria for categorization and severity grading are spontaneous Hb levels and clinical tolerance, regardless of the underlying genotype. Because the hemoglobin levels in the blood of people with beta-thalassemia intermedia range between 7 and 10 g/dL, they do not require regular transfusions. Numerous genetic and environmental variables, together with the degree of alpha to non-alpha globin chain imbalance, might cause them to display a wide range of clinical symptoms. Among the numerous problems they may encounter are pulmonary hypertension, thrombotic episodes, infection, endocrine dysfunction, and leg ulcers [11]. For individuals with beta-thalassemia major to survive, red blood cell transfusions are required. However, iron excess from repeated transfusions can lead to endocrine dysfunction, liver disease, cardiomyopathy, and early death, among other potentially deadly adverse effects. Patients with betathalassemia major die within the first five years of their life if they do not get transfusions, and only 50–65% of people in high-income countries live past the age of 35.Numerous studies are now underway [12]. Because β-thalassemia is a common disorder with little research, this study aims to improve management and treatment procedures by analyzing the hematological and biochemical features of individuals with the condition in Dhi Qar Governorate.

## 2. MATERIALS AND METHODS

Patients who were sent to the Dhi Qar Governorate's Thalassemia Center participated in this study. 100 β-thalassemia major patients, ages 10–42 (44 males and 56 females), were included in the statistical population. On the other hand, 100 healthy individuals in the same age range made up the control group. Blood samples were collected from all patients in ethylene diamine tetraacetic acid tubes as an anticoagulant. DNA was extracted from blood samples. The patients' medical and laboratory records were used to gather demographic information about them, such as age, gender, and medical history. Hemoglobin electrophoresis and peripheral blood smears have been used to diagnose β-thalassemia major in early childhood. The study excluded patients with acute sickness and those with thalassemia mild and intermedia

### 2.1 Study Design

A cross-sectional study was designed at the molecular and physiological levels, to investigate the different genetic mutations of β-thalassemia (β-thal) major patients in Thi-Qar Province, southern Iraq. This study was performed on a total of 100 patients with β-thal major disease who were transfusion dependent, and were attending Thalassemia Care Unit/Thi-Qar province. The total sample size collected in the current study is 100 samples. Blood samples were taken and the demographic data of the patients were collected before blood samples taking. Ethylene diamine tetra-acetic acid (EDTA) as anticoagulants was used and transferred to tube with 2-3 mm EDTA within 24-48 h to liquid nitrogen, −20 °C. Genomic DNA extraction from blood samples was performed using DNA extraction kit. Extraction was performed based on the manufacturer instructions. Ethanol precipitation method was also used to increase the concentration of DNA. The working concentration of DNA was 100 ng/µl. The working concentration of extracted DNA was confirmed at agarose gel (1%). PCR was done to amplify the selected exons of the target gene. Amplified products were sequenced after being purified. The detection of mutations with amplification refractory mutation system technique was also done. This study has been conducted by reviewing the Thalassemia Care Unit/ Thi-Qar/ Iraq records from November 2024 till May 2025, Patients who were sent to the Dhi Qar Governorate's Thalassemia Center participated in this study. 100 β-thalassemia major patients, ages 10–42 (44 males and 56 females), were included in the statistical population. On the other hand, 100 healthy individuals in the same age range made up the control group. identified for the purpose of the study. From those patients, the demographic data including age, sex, consanguinity, and parent's age and ethnic group were collected and stored in a computerized database. Additional data collection included clinical and hematological data which was done by an electronic-based medical record system using a designed

comprehensive questionnaire that included the name, age, sex, phone number, complications, and past history of blood transfusions, chelation therapy, and hydroxyurea medication with indication. Complications assessed by reviewing past medical records included cholelithiasis, hypothyroidism, osteoporosis, hypoparathyroidism, skin infection, and hypogonadism. The hematological data included hemoglobin concentration (Hb), and serum ferritin (SF).

**2.2 Sample Collection**

Blood samples were collected from 100 transfusion-dependent β-thalassemia patients whose ages ranged between 10-42 years residing in Thi-Qar Province, Southern Iraq. The patients were screened at Thalassemia Center for Blood Transfusion in Thi-Qar Province based on transfusion requirement. The patients were diagnosed as having thalassemia from CBC data, peripheral blood, and hemoglobin electrophoresis results by a clinical hematologist. Individuals who were currently pregnant and patients with major thalassemia syndromes other than β-thalassemia or with other major blood disorders were excluded from participation. Control blood samples were collected from healthy individuals of the same age and gender attending Thi-Qar Health Directorate; the samples were confirmed free from molecular and hereditary disease history. The blood samples were collected in 5 mL EDTA tubes by venipuncture. Prior to analysis, the samples were stored at -20°C. All patients provided written informed consent, and the study was approved by the Medical Research Ethics Committee of Thi-Qar University.

**3. RESULTS & DISCUSSION**

In this study, patients with β-thalassemia major in the Iraqi province of Dhi Qar were analyzed for hematological and biochemical traits. The control group was 30.2 years old, whereas the average age of β-thalassemia major cases was 28.6 years. Most patients received iron chelation in addition to deferoxamine. The majority of patients received regular blood transfusions in addition to iron chelation therapy, which included deferoxamine. Many patients continued to have high blood ferritin levels in spite of this treatment, which may indicate insufficient chelation therapy or poor treatment compliance.This section compares patients with β-thalassemia major to the control group in terms of age and gender (Table 1).

The study found no significant variations in either gender or age with the control group and the patients ($p > 0.05$). The majority of patients were between the ages of 18 and 29. The mean height was 156 ± 10.80 cm, and the mean weight was 48.32 ± 10.12 kg. Pre-transfusion hemoglobin levels were 8.5 ± 0.5 (g/dL) for males and 7.94 ± 0.96 (g/dL) for females.

Table 2 shows that the patients' hematological parameters (Hb, HCT, MCV, and MCH) were, except for MCHC, which was not important ($p > 0.05$), significantly lower than those of the control group. Table 3 shows that patients had significantly higher serum FBS levels compared to the control group ($p < 0.05$). In addition, 35 patients (38.5%) had FBS levels that exceeded 110 mg/dL. The patients' lipid profiles differed significantly from those of the control group ($p<0.05$). 18 patients (18.9%) had serum TG levels above 210 mg/dL. 70 patients (70.9%) had serum HDL levels less than 32 mg/dL. Moreover, 56 patients (52%), and all patients, had cholesterol levels below 105 mg/dL and below 200 mg/dL, respectively.

Biochemical markers in β-thalassemia major patients and controls are compared in Table 3. Blood urea nitrogen and serum creatinine levels did not change substantially from the control group ($p > 0.05$). Although blood levels of K, Na, and Ca did not change substantially from the control group ($p > 0.05$), 83.1% of the patients had elevated serum PH. According to Table 3, the patients' levels of ALT, AST, ALP, direct, and total bilirubin were substantially higher than those of the control group ($p < 0.05$). Of the patients, 59.8% had increased blood total bilirubin and 78.4% had elevated direct bilirubin levels. Ninety-two percent of the patients had normal albumin levels, and the study and control groups did not vary significantly ($p > 0.05$).The results of the study and control group showed no discernible difference ($p > 0.05$), and 94% of patients had normal albumin levels. This could lead to improper iron metabolism and persistent anemia [10].

Frequent blood transfusions are essential to avoid complications such as bone abnormalities and prolonged anemia.

Patients in this study exhibited significantly lower levels of all hematological indices, including HCT, Hb, MCH, and MCV, than controls. In comparison to the control group, MCHC did not change much. Al-Sulaiti AM et al. found significant reductions in hematological indices, including Ň, NPT, MCV, and MCH, with the exception of

MCHC[10]. At 3624 µg/L, the mean ferritin level was substantially greater ($p < 0.01$) in the study participants than in the control group. The consistently high ferritin levels found in this study could be a sign of inadequate iron chelation treatment efficacy or low patient compliance. Therefore, improving chelation regimens is crucial to lowering iron excess and the problems that come with it.The findings concur with those of other relevant studies[13] .The detrimental effects of high iron and peroxidative damage on liver cells, which elevate liver enzyme levels, have been the subject of several research [14, 15]. Regular monitoring of liver function during therapy is crucial because, in addition to iron overload, the raised liver enzymes may also be partially caused by long-term use or inadequate dose of iron chelating drugs.Due to the abnormalities in liver function, the subjects' mean AST, ALT, and ALP values were 46.2 U/L, 44.5 U/L, and 325.8 U/L, as well. These results were much higher than the average values of 52 U/L, 60.1 U/L, and 140.7 U/L reported in a Qatari study by Hashemieh et al. [16]. The study group had significantly greater levels of total and direct serum bilirubin compared to the control group due to increased red blood cell mortality ($P<0.05$) obtained similar results [17]. Those with κ-thalassemia major had reduced levels of total cholesterol, LDL-C, and HDL-C compared to the control group. Nonetheless, a high amount of triglycerides has been noted. Iron excess, liver damage, hormone imbalances, or aging may be the source of these alterations [15]. Despite continuous chelation therapy, certain metabolic disorders, such as hyperglycemia and dyslipidemia, may be connected to chronic iron accumulation in endocrine organs, indicating the need for improved therapeutic control and early pharmacological intervention. Our findings are consistent with those of [17, 18, 19], there was no discernible difference between the triglyceride level and the control group. FBS levels exceeding 128 mg/dl were seen in 15% of patients in this study, which is in line with previous research of this type. Investigations conducted in Pakistan revealed that 29.4% of 1246 individuals with κ-thalassemia major had FBS levels ≥ 128 mg/dl [20]. Our study's mean blood urea netrogen and serum creatinine levels fell below normal limits and showed no discernible differences from the control group. Our results are in agreement with those of [21, 22]. In those with κ-thalassemia major, renal injury can result from iron overload, deferoxamine overdose, and chronic anemia [23]. Renal problems may emerge over time due to cumulative drug toxicity or prolonged disease duration, hence ongoing monitoring is advised even though renal measures were within normal ranges.Additionally, the patients' K and Na levels differed somewhat from the control group's. Similar results were obtained in earlier investigations [20, 24]Similar findings have been found in other studies [25]. Furthermore, the patients' average blood calcium levels were not substantially different from those of the control sample. Our findings correspond with those of. [26].

Table 3 shows that the average T4 and TSH levels were within the normal range. There was no significant difference between β-thalassemia major patients and controls on any thyroid function test ($p >0.05$).

**Table 1.** Patients with β-thalassemia main and the control group (n = 100) by gender and age

| **Parameters** | **Gender** | **β-thalassemia** | **Controls** |
|---|---|---|---|
| **gender** | Female | 56 | 56 |
| | Male | 44 | 44 |
| **Age** | **Female** | **10-42** | **10-42** |
| | **Male** | **11-42** | **12-42** |

**Table 2.** Hematological traits of people with β-thalassemia main and controls (n=100)

| **Parameters (Unit)** | **Mean for Patients ± SD** | | **Mean for Controls ± SD** | | **P- value** |
|---|---|---|---|---|---|
| | **Female** | **Male** | **Female** | **Male** | |
| **Hb (g/dl)** | 7.94 ± 0.96 | 8.5 ± 0.5 | 12.2 ± 1.4 | 13 ± 1.0 | P<0.01 |
| **PCV %** | 28.0 ± 1.4 | 27.90 ± 1.4 | 40.19 ± 80 | 45.1± 90 | P<0.01 |
| **MCV ($um^3$)** | 75.0 ± 5.0 | 77.90 ± 7.0 | 86.0 ± 10.5 | 88.0± 11.6 | P<0.05 |
| **MCHC (g/dL)** | 33.92 ± 1.6 | 34.10± 1.8 | 35.6 ± 1.5 | 37.20 ± 1.2 | P<0.05 |
| **MCH (pg)** | 27.0 ± 1.8 | 26.90 ± 2.4 | 31.4 ± 2.0 | 33.20± 2.5 | P<0.05 |
| **P-value < 0.05: Significant** | | | | | |

**Table 3.** Tests of thyroid, liver, kidney, and sugar levels in male and female patients with β-thalassemia major in comparison to control.

| Parameters (Unit) | Mean for Patients ± SD | | Mean for Controls ± SD | | P<0.05 |
|---|---|---|---|---|---|
| | Female | Male | Female | Male | |
| FBS (mg/dl) | 118± 78 | 122 ± 70 | 98± 80 | 100 ± 55 | P<0.05 |
| TG (mg/dl) | 145 ± 90 | 145± 65 | 95 ± 85 | 98± 20 | P<0.05 |
| T C (mg/dl) | 129 ± 25 | 114 ± 29 | 192 ± 28 | 185 ± 34 | P<0.05 |
| HDL (mg/dl) | 28.7 ± 12.1 | 29.6 ± 11.3 | 61.9 ± 14.2 | 63.8 ± 12.9 | P<0.05 |
| LDL(mg/dl) | 58.6 ± 22.8 | 56.5 ± 18.4 | 73.6 ± 24.6 | 78.6 ± 14.8 | P<0.05 |
| B.Urea (mg/dl) | 17.3 ± 5.5 | 19.2 ± 7.1 | 16.1 ± 3.5 | 17.5 ± 5.1 | P<0.05 |
| S. Cr (mg/dl) | 0.45 ± 0.31 | 0.67± 0.41 | 0.42 ± 0.28 | 0.48± 0.41 | P<0.05 |
| Sodium (mEq/L) | 129.9 ± 2.8 | 133.6 ± 3.5 | 133.8 ± 2.5 | 135.3 ± 3.8 | P<0.05 |
| $K^+$ (mol/L) | 4.6 ± 0.33 | 4.5 ± 0.5 | 4.3 ± 0.29 | 4.3 ± 0.8 | P<0.05 |
| Calcium (mg/dL) | 8.9± 1.8 | 9.6 ± 0.9 | 9.0± 1.5 | 9.8 ± 1.0 | P<0.05 |
| Ferritin | 3657± 1987 | 3843± 2543 | 43.1± 17.0 | 48.1± 20.0 | P<0.05 |
| ALT(U/L) | 43.1± 17.0 | 48.2± 23.1 | 19.9± 7.9 | 20.8± 6.8 | P<0.05 |
| AST (U/L) | 46.2± 20.5 | 48.1± 24.2 | 18.9± 7.2 | 20.8± 6.0 | P<0.05 |
| ALP(U/L) | 310± 169 | 341± 118 | 188± 118 | 208± 112 | P<0.05 |
| Total bilirubin(mg/dL) | 1.7± 0.9 | 2.9± 1.1 | 0.49± 0.19 | 0.6± 0.5 | P<0.05 |
| Direct bilirubin(mg/d) | 0.63± 0.19 | 0.55± 0.23 | 0.21± 0.2 | 0.2± 0.09 | P<0.05 |
| Albumin(g/dL) | 3.7± 0.5 | 4.5± 0.3 | 3.9± 0.25 | 3.9± 0.4 | P<0.05 |
| T4 (ug/dl) | 8.2 ± 1.6 | 7.6 ± 2.4 | 10.22± 1.5 | 9.87 ± 1.0 | P<0.05 |
| TSH (mIU/l) | 2.7 ± 1.8 | 3.2 ± 2.8 | 2.5 ± 1.8 | 3.1.1± 2.2 | P <0.05 |

**P-value < 0.05: Significant**

## 4. CONCLUSION

This study, which involved 100 individuals with thalassemia and 100 individuals without the condition, was carried out by following up with thalassemia patients in the Dhi Qar Governorate, Iraq, who had frequent trips to the Thalassemia Center connected to the Dhi Qar Health Department over extended periods of time.We found that individuals with β-thalassemia and controls had different hematological and biochemical markers. Most of the patients in our study had high serum ferritin levels because the body stores iron due to repeated blood transfusions and red blood cell breakdown, and elevated ferritin levels have been associated with higher blood levels of liver enzymes. The most recent study found that hypothyroidism affected 15.8% of patients, while low cholesterol levels and hypertriglyceridemia affected 55% and 21%, respectively. Patients with serious β-thalassemia should undergo regular checks and an iron toxicity evaluation to prevent long-term tissue damage from excessive iron. Our results could affect a guideline for the early diagnosis and treatment of patients with β-thalassemia major.

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## 6. Conflict of Interest

The authors declare that there is no conflict of interest regarding the publication of this study.

## 7. Ethical Approval

This study was conducted in accordance with the ethical standards of the Medical Research Ethics Committee of Al-Ayen Iraqi University, Iraq. Written informed consent was obtained from all participants or their legal guardians before sample collection and participation in the study.

**8. Authors' Contributions**

- **Muntadher Mohammed JABER**: Conceptualization, study design, laboratory investigation, data analysis, manuscript drafting, and supervision.
- **Hussein Ali Nayyef**: Methodology, clinical data collection, statistical analysis, and manuscript review.
- **Sarab Abbas Mohaisen**: Sample collection, laboratory procedures, and data interpretation.
- **Adyan Nafea ABBAS**: Data organization, literature review, manuscript editing, and final approval of the manuscript.

All authors read and approved the final version of the manuscript.

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