ORIGINAL ARTICLE

AL-ANBAR MEDICAL JOURNAL
Anb. Med. J. 21(3): 191–197, 2025

A Comparative Study of Liver and Kidney Function Indicators in Patients with Beta-thalassemia Major and Beta-thalassemia Trait

Enaam Ahmed Hamza AL-Dagestani,[1] Mohammad Ahmad Hamza,[2,*] and Nabaa Yahyaa Yusif[3]

[1] *Department of Medical Physics, College of Science, University of Mosul, Mosul, Iraq.*
[2] *Department of Chemistry, College of Science, University of Zakho, Duhok, Iraq.*
[3] *Department of Biophysics, College of Science, University of Mosul, Mosul, Iraq.*

(Received : 6 March 2025; Accepted : 25 May 2025; First published online: 1 July 2025)

ABSTRACT

Background: Comparative analysis of liver and kidney function in patients with beta-thalassemia major (BTM) and beta-thalassemia trait (BTT) is relatively underexplored in the existing literature.
Objectives: This study compares liver and kidney function in children with BTM, BTT, and healthy controls, and investigates the potential protective role of ferritin in reducing iron-related tissue damage in BTT patients.
Materials and methods: A case-control study was conducted on 93 male children (ages 2–12) from Ibn Al-Atheer and Ibn Sina Hospitals in Mosul, Iraq, divided into three groups: BTM (31), BTT (31), and healthy controls (31). Serum levels of liver and kidney biomarkers (ALT, AST, ALP, DBIL, TBIL, urea, creatinine, uric acid, and ferritin) were measured. Statistical analysis was performed using SPSS (version 26.0) with a significance level of P-value < 0.05.
Results: In the BTM group, levels of ALP, AST, urea, and uric acid were significantly higher compared to the control group, while no significant differences were observed between the BTT and control groups for these parameters. ALT, TBIL, DBIL, creatinine, and ferritin levels were elevated in both BTM and BTT groups relative to controls. Notably, all parameters except TBIL were significantly higher in the BTM group than in the BTT group. Additionally, a significant positive correlation was observed between ferritin and ALP in the BTM group, whereas a significant negative correlation was found between ferritin and creatinine in the BTT group.
Conclusion: BTM significantly impaired liver and kidney function, while BTT showed mild increases in ALT, TBIL, DBIL, creatinine, and ferritin. In BTM, ferritin correlated with ALP, indicating potential iron toxicity, whereas in BTT, the negative correlation with creatinine may suggest a protective mechanism. Further research is needed to clarify ferritin thresholds for toxicity versus protection.
Keywords: liver; kidney; Beta thalassemia trait; Beta-thalassemia Major.

DOI: 10.33091/amj.2025.158019.2143

INTRODUCTION

Thalassemia is an inherited disorder that diminishes haemoglobin production, leading to varying degrees of anaemia and increased mortality risk. It was first recognized by Dr. Thomas Cooley in 1925 as 'erythroblastic anaemia,' later renamed thalassemia by Whipple and Brad Ford [1, 2]. The disorder is more prevalent in regions like Southeast Asia, the Middle East, and the Mediterranean, but migration has contributed to its rising rates in North America and Northern Europe [3].

According to the gene involved, two main classes of thalassemia are recognized: Beta-thalassemia and Alpha-thalassemia. Further classification of beta-thalassemia describes three subtypes: Major, intermediate, and minor (thalassemia trait). Beta-thalassemia major (BTM) is the most severe form, leading to severe anaemia [4].

Although iron plays vital cellular and physiological roles, it

* Corresponding author: E-mail: mohammad.hamza@uoz.edu.krd

could induce organ toxicity and death, particularly in people undergoing chronic red blood cell transfusions, as in BTM. Ferritin acts as the primary iron storage protein, and this, to some extent, could reduce the iron toxicity effect in the tissues [5]. In patients with beta-thalassemia, the lowest level of iron in the liver that can cause fibrosis is about 16 milligrams per gram of dry-weight liver without any additional factors [6].

A clinical study, revealed that there is significant connection between iron-induced liver damage and iron deposition in the liver [7]. However, iron chelating therapy and antioxidants have a potentially helpful effect in lowering the risk of metabolic disorders and reducing iron overload that results from lifelong transfusions in BTM patients [2, 8]. Systemic effects extend beyond the liver; moreover, a study demonstrated that systemic iron overload in BTM patients can result in iron deposition within the parathyroid glands over time, potentially leading to hypoparathyroidism, particularly in individuals over the age of 10 years [9].

Beta thalassemia trait (BTT) is traditionally known as a benign carrier state. Its effect on the liver and kidneys is still unclear, and the subclinical iron-induced toxicity raises questions. A study noticed a reduction in hemoglobin levels in pregnant women with BTT, raising concerns about potential subclinical hemolysis and non-transferrin-bound iron release [10]. Such events could lead to hepatic and renal stress or toxicity, indicating a need for further investigation. Interestingly, research on other chronic conditions like celiac disease has shown that kidney function and trace element levels can alter even when no clear symptoms are present [11]. This highlights the importance of investigating subtle renal and hepatic biochemical changes in patients with BTT.

Progressive kidney failure is the main problem in people with beta-thalassemia. It is worth finding out early if patients are likely to develop kidney failure because they can take steps to slow down the damage to their kidneys. Thers actions can help reduce the number of people who reach the point of needing a kidney transplant or dying from kidney failure [12].

Previously conducted studies have been concerned mainly with BTM and beta-thalassemia intermedia (BTI) as serious health issues. In BTM, the association between high ferritin levels and liver dysfunction is well established in the literature [13–15]. While there is insufficient literature and information about the impact of BTT disorder on liver and kidney functions. A study revealed that subtle tubular abnormalities existed even without transfusion-related iron overload, indicating that iron metabolism changes in BTT could affect renal function [16]. Elevated ferritin levels signify a greater capacity for iron sequestration, which may provide indirect protection against iron toxicity and potential kidney injury [4]. This perspective is often overlooked in discussions about BTT. In addition, the comparison between the effects on liver and kidney functions in BTM patients versus carriers of BTT patients is not mentioned in the previous works. Detecting any alteration in the specific parameters of liver and kidney tests, particularly in BTT patients, will increase our current understanding of thalassemia and positively influence future research.

This study aims to provide insights into the comparative analysis of liver and kidney functions among children with BTM, BTT, and healthy controls, contributing to understanding the systemic implications of these disorders and demonstrating the extent to which liver and kidney functions are affected in individuals with BTT. It also aims to highlight the sequestration role of ferritin against iron-mediated damage to the kidneys.

MATERIALS AND METHODS

Design and subjects

A case-control study was designed for the comparisons of liver and kidney function parameters among the three groups: 31 patients with BTM, 31 patients with BTT, and 31 healthy controls. A prior-power analysis was performed by G*power software to estimate the proper sample size, the values were set to be: power $(1 - \beta$ err prob) of 0.80, an err prob of 0.05, and effect size (f) of 0.33, three groups, and a one-way ANOVA test. After the calculation, the total sample size was 93. Over three months of monitoring in Ibn Al-Atheer Hospital and Ibn Sina Hospital in Mosul, Iraq, male children (aged range 2–12 years) were enrolled as two groups of patients (BTM and BTT) and healthy group according to the inclusion and exclusion criteria. A questionnaire form was included age, family history of thalassemia, treatment protocol, medications, and the existence or not the following conditions: Hematological and chronic illnesses, autoimmune disorders, chronic infections, heart failure, diabetes, severe kidney and liver diseases, and pre-transfusion time.

The Scientific Affair Committee of the Medical Physics Department, College of Science, University of Mosul approved the study proposal (Reference number 4/74 on 14-6-2023) which was in compliance with the Declaration of Helsinki. Informed consent was also obtained from parents or legal guardians of all participants before enrolment in the study.

Inclusion criteria of patients with BTM

The inclusion criteria for the BTM group consisted of boys aged 2 to 12 years who had been diagnosed with BTM by a specialized physician based on a complete blood count (CBC) and haemoglobin electrophoresis, supported by family history of their respective conditions. Eligible patients had pre-transfusion haemoglobin levels within the range of about 9-10.5 g/dL, adhered to the standard treatment protocol, and agreed to participate.

Inclusion criteria of patients with BTT

The inclusion criteria for the BTT group comprised boys aged 2 to 12 years who were diagnosed with mild to moderate anaemia, indicated by a routine complete blood count (CBC) showing haemoglobin levels slightly above 10 g/dL along with microcytosis. These patients had an asymptomatic condition and had no history of regular blood transfusions or chelation therapy and agreed to participate.

Exclusion Criteria of BTM and BTT

Beta thalassemia patients with sickle cell disease, autoimmune disorders, chronic infections, heart failure, uncontrolled diabetes, and severe liver disease. were excluded. Patients with BTT who received blood transfusions within the last 6 months were also excluded.

Inclusion and exclusion criteria of healthy control group

The inclusion criteria for the healthy control group consist of boys who were matched in age with the patient groups and had no known history of thalassemia, anaemia, or other haematological or chronic illnesses. Additionally, they had no family history of thalassemia. Participants who were taking

http://doi.org/10.33091/amj.2025.158019.2143

other medications, such as iron supplements, multivitamins, or corticosteroids, were excluded from the study. Those who had received a blood transfusion within the past year were also excluded.

Sample collection

Using disposable syringes, venous blood samples (5 ml) were drawn from each research group. After allowing the blood to clot, two millilitres of it were transferred to an ethylenediaminetetraacetic acid tube for the evaluating haematological parameters, and the remaining blood was transferred to a gel tube for separation and serum extraction. The blood was then centrifuged at 2000 RPM for ten minutes, serum was fresh frozen into several Eppendorf tubes, where the biochemical parameters were analysed later.

Biochemical assays

The CBC examination was performed using the French Horiba device (Horiba Yumizen H550 6-part CBC, French company). Biochemical tests were performed, including alanine aminotransferase (ALT) (reference range: 3–36 U/L), aspartate aminotransferase (AST) (reference range: 15–50U/L), alkaline phosphatase (ALP) (reference range: 65–300), direct bilirubin (DBIL) (reference range: 1.7–5.1 µmol/L), total bilirubin (TBIL) (reference range: 5.1–17 µmol/L), and kidney function indicators such as urea (reference range: 1.8–6.4 mmol/L), creatinine (reference range: 26.5–61.9 µmol/L), and uric acid (reference range: 120–320 µmol/L) were estimated by using the Thermo-Fasher device (Thermo scientific Indiko, American Company, fully automated, benchtop clinical chemistry analyser). Ferritin (reference range: 7–142 ng/mL) was estimated by Vidas (bioMérieux SA, France).

Statistical analysis

A statistical package for the social sciences (SPSS) software for Windows, version 26.0 (IBM Corp., Armonk, NY, USA) was used to analyse the data. Normally distributed data were expressed as mean and standard deviation (Mean ± SD), while abnormally distributed data were stated as median and interquartile range (IQR). The Shapiro-Wilk test was used to estimate data normality. The Kruskal-Wallis and analysis of variance (ANOVA) tests were performed for multiple comparisons. Post-hoc comparisons were applied using the Bonferroni method. Spearman's rank correlation analysis was also used to detect potential relationships between ferritin and other studied parameters. Throughout our analysis, a P-value below 0.05 was considered a statistically significant difference.

RESULTS

The ANOVA test showed no significant differences in age between the BTT and BTM groups and the control group (Mean ± SD: 6.74 ± 1.56, 7.29 ± 1.46, and 7.34 ± 1.80, respectively; P-value = 0.247), as shown in Figure 1.

The Kruskal-Wallis and ANOVA tests found significant differences in ALP, AST, ALT, TBIL, and DBIL among the three groups. Thereafter, the significant P-values of the Bonferroni correction were used for multiple tests to adjust the pairwise comparisons and determine the significant differences. The results showed that the levels of ALP, AST, ALT, TBIL, and DBIL were significantly higher in the BTM group than in the healthy control group (P-value < 0.05). Additionally, a significant increase was observed in ALT, TIBL, and DBIL in the BTT group in comparison with the healthy control group (p < 0.05). No significant differences were identified in the levels of ALP and AST between the BTT and control. The comparisons between the BTM and BTT groups revealed a significant increase in ALP, AST, ALT, and DBIL in the BTM group (P-value < 0.05). In contrast, no significant variations were observed in the levels of TBIL between the BTM and BTT groups (Table 1).

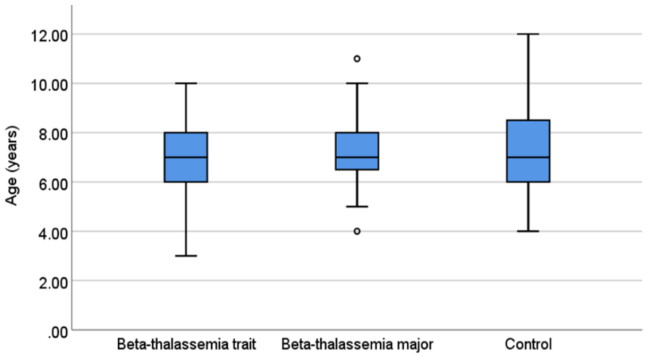

Figure 1. The age distribution for beta-thalassemia patient groups and their age-matched controls. The P-value = 0.247 and ANOVA test was used.

The results showed a significant increase in the levels of urea, uric acid, creatinine, and ferritin in the BTM group compared to the healthy control group (P-value < 0.05). Creatinine and ferritin levels were significantly higher in the BTT group compared to the control (P-value < 0.05). In contrast, there was no significant difference in urea and uric acid levels between the BTT and healthy control groups. Furthermore, the levels of urea, uric acid, creatinine, and ferritin were significantly higher in the BTM group compared to the BTT (P-value < 0.05) as seen in Table 2.

The Spearman correlation was conducted to identify significant correlations between ferritin and liver and kidney parameters in both the BTM and BTT groups. The results showed a significant positive correlation between ferritin and ALP levels in the BTM group (correlation coefficient = 0.397, P-value = 0.036), as seen in Table 3 and Figure 2. Additionally, a significant negative correlation was found between ferritin and creatinine in the BTT group (correlation coefficient = − 0.490, P-value = 0.005), as seen in Table 4 and Figure 3. No significant differences were detected between ferritin and other parameters in both groups.

DISCUSSION

The hereditary haemolytic disorder beta-thalassemia is the most prevalent disorder among children, in which haemolysis has a direct impact on the parameters of the liver and then the kidneys. To the best of the authors' knowledge, this is the first study that compares liver and kidney function parameters between BTM and BTT. Our results showed elevated ALT, AST, ALP, TIBL, and DBIL in the BTM group compared with the control groups. Similarly, studies showed significant increases in liver enzymes and TBIL in BTM patients compared to healthy controls [17, 18]. BTM leads to severe disruption in the normal synthesis of haemoglobin, re-

Table 1. Comparison of liver function parameters between major, trait, and control[†].

Parameters	BTM No.=31	BTT No.=31	Control No.=31	P-value
	[Mean ± SD] or [Median (IQR)]			
ALP (U/ L)	215(115)^{A**,B**}	95(24)^{A**}	79(30)^{B**}	0.0001^{**K}
AST (U/ L)	175(22)^{A**,B**}	33(15)^{A**}	22(9)^{B**}	0.0001^{**K}
ALT (U/ L)	190(50)^{A**,B**}	42.3 ± 10.4^{A**,C*}	27.3 ± 5.9^{B**,C*}	0.0001^{**K}
TBIL (µ m/L)	25(12)^{B**}	18.5 ± 2.7^{C**}	8.1 ± 2.3^{B**,C**}	0.0001^{**K}
DBIL (µ m/l)	9.5 ± 2.4^{A**,B**}	5.6 ± 1.8^{A**,C**}	2.5 ± 0.7^{B**,C**}	0.0001^{**N}

[†] SD: Standard deviation, IQR: Interquartile range, BTM: Beta thalassemia major, BTT: Beta thalassemia trait, ALP: Alkaline Phosphatase, ALT: Alanine Aminotransferase, AST: Aspartate Aminotransferase, DBIL: Direct bilirubin, TBIL: Total bilirubin, No.: Number, A: Significant between BTM *vs.* BTT, B: Significant between BTM *vs.* Control, C: Significant between BTT vs. Control, *; significant p-value < 0.05, **; highly significant P-value = 0.0001, K: Kruskal-Wallis Test, N: ANOVA test. P-value < 0.05 was considered significant.

Table 2. Comparison of kidney function parameters and ferritin between major, trait, and control[†].

Parameters	BTM No.=31	BTT No.=31	Control No.=31	P-value
	[Mean ± SD] or [Median (IQR)]			
Uria (mmol/L)	8(1.7)^{A**,B**}	4.7 ± 0.69^{A**}	4.0 ± 0.8^{B**}	0.0001^{**K}
Uric acid (mmol/L)	371.6 ± 73 ^{A**,B**}	226.9 ± 37.7 ^{A**}	233(60)^{B**}	0.0001^{**K}
Creatinine (µmol/L)	190(50)^{A**,B**}	42.3 ± 10.4^{A**,C**}	27.3 ± 5.9 ^{B**,C**}	0.0001^{**K}
Ferritin (ng/mL)	25(12)^{A**,B**}	18.5 ± 2.7^{A**,C**}	8.1 ± 2.3^{B**,C**}	0.0001^{**K}

[†] SD: Standard deviation, IQR: Interquartile range, BTM: Beta thalassemia major, BTT: Beta thalassemia trait, No.: Number, A: Significant difference between BTM *vs.* BTT, B: significant difference between BTM *vs.* control, C: Significant difference between BTT *vs.* control, *: Significant P-value < 0.05, **: Highly significant P-value < 0.0001, K: Kruskal-Wallis Test

Table 3. Ferritin correlation with liver and kidney parameter in beta thalassemia major group[†].

Parameter	Correlation coefficient	P-value
ALP U/L	0.379*	0.036
AST U/L	-0.07	0.702
ALT U/L	0.031	0.867
TBIL µm/l	0.302	0.098
DBIL µm/l	0.262	0.155
Uria mmol/l	-0.271	0.140
Uric acid mmol/l	-0.014	0.94
Creatinine µmol/l	0.02	0.909

[†] ALP: Alkaline Phosphatase, AST: Aspartate Aminotransferase, ALT: Alanine Aminotransferase, TBIL: Total bilirubin, DBIL: Direct Bilirubin, P-value less than 0.05 was significant.

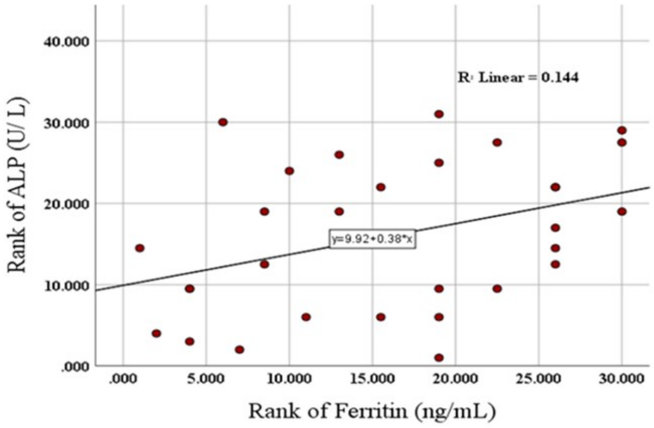

Figure 2. Correlation of ferritin levels with alkaline phosphatase (ALP) levels in beta thalassemia major group.

quiring patients with this genetic disorder to undergo periodic blood transfusions. These transfusions can result in iron accumulation in the body, causing complications that primarily affect the liver and other vital organs [19].

In addition, the storage of excess iron and the synthesis of ferritin and transferrin occur in the liver as a central site. Normal liver function involves protein-bound iron, and free ferrous has extreme toxicity. Iron, when in its unbound state, catalyses the generation of free radicals, a process linked to both hepatotoxicity and lipid peroxidation [20]. Oxidative stress caused by iron overload leads to lipid peroxidation in the liver cell membrane, which changes its permeability. Consequently, liver cell destruction occurs, leading to elevated levels of ALP, AST, and ALT in the blood [21].

The present study indicated that ferritin had significant correlations with ALP in individuals diagnosed with BTM. Usually, liver enzymes and bilirubin elevations can be a sign of liver diseases resulting from cirrhosis, hepatitis, narrowing of the bile ducts, inflammation of the gallbladder, infection of the biliary ducts, and liver tumours [22]. In this study, patients with BTM exhibited significantly higher bilirubin levels

http://doi.org/10.33091/amj.2025.158019.2143

Table 4. Ferritin correlation to liver and kidney parameter in beta thalassemia trait[†].

Parameter	Correlation coefficient	P-value
ALP U/L	0.330	0.069
AST U/L	0.062	0.742
ALT U/L	0.349	0.054
TBIL µm/l	-0.226	0.221
DBIL µm/l	0.017	0.926
Uria mmol/l	-0.041	0.826
Uric acid mmol/l	0.088	0.638
Creatinine µmol/l	-0.490*	0.005

[†] ALP: Alkaline Phosphatase, AST: Aspartate Aminotransferase, ALT: Alanine Aminotransferase, TBIL: Total bilirubin, DBIL: Direct bilirubin, P-value less than 0.05 was significant.

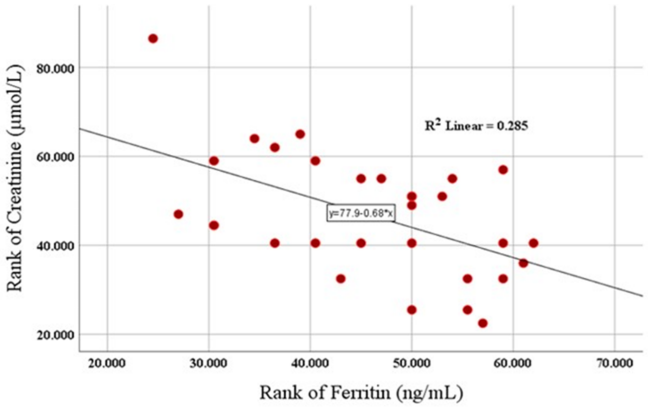

Figure 3. Correlation of ferritin levels with creatinine levels in beta thalassemia trait group.

compared to those with BTT and healthy controls. The elevated level may be due to increased erythrocyte lysis. This is the primary cause of hyperbilirubinemia, which has the adverse effect of causing damage to other hepatic cells as a result of iron overload [23]. While the levels of AST, ALT, and ALP were elevated in the beta thalassemia groups compared to controls, their elevations were significantly higher in BTM than in BTT. Additionally, in patients with BTT, only ALT was significantly elevated compared to the control group. BTM is characterized by a more severe deficiency in beta-globin synthesis, leading to severe anaemia and iron overload, which often results in extensive organ damage and dysfunction. In contrast, BTT typically presents with mild anaemia, iron overload, and elevated ferritin levels, but does not usually require transfusion therapy. Ferritin levels in the BTT group were significantly elevated compared with the control group, similar to the BTM group. In the same context, Bhowad et.al. showed a significant elevation in ferritin levels and creatinine of BTM patients compared to controls [24]. Repeated transfusions in BTM cause significant elevation in the levels of ferritin and free iron, which contribute to additional liver, renal, and endocrine abnormalities [25].

In a previous study, a decline in renal function was observed in severe beta thalassemia patients undergoing transfusion therapy and treated with deferasirox as an iron-chelating agent. The authors reported findings of proteinuria and elevated levels of urine uric acid, consistent with the results of the current study [26]. Our study revealed significant elevations in urea, creatinine, and uric acid levels in BTM patients compared to both BTT and control groups. Urea, uric acid, and creatinine are waste products that are filtered out of the blood by the kidneys. In patients with BTM, elevated levels of urea, creatinine, and uric acid may result from various factors, including increased red blood cell turnover, renal dysfunction secondary to iron overload, or adverse effects of iron chelation therapy. However, the absence of a significant correlation between serum ferritin and these renal markers may be attributed to the fact that iron metabolism and renal waste filtration are governed by distinct physiological pathways. Consequently, although both systems may be independently affected in BTM, their biochemical markers do not necessarily exhibit a direct correlation.

The association between renal dysfunction and BTT has been highlighted in two recent studies. The first study showed that common tests for kidney function, like serum creatinine, urea, and uric acid, did not differ much between BTT patients and healthy people, but other signs of kidney tubule problems were present. These included higher levels of uric acid and potassium being lost in urine, along with increased amounts of neutrophil gelatinase-associated lipocalin (NGAL), which is a sensitive marker for early kidney damage [16]. The second study further revealed that renal dysfunction can develop in both BTM and, to a lesser degree, in BTT, suggesting that even milder forms of the disease may carry a risk of subclinical renal impairment [2]. The current study demonstrated a significant elevation in creatinine levels among patients with BTT, while urea and uric acid levels did not differ significantly compared to controls. Ferritin levels were significantly higher in BTT patients than in controls but remained lower than those observed in BTM patients. Notably, a negative correlation was identified between ferritin and creatinine levels in BTT patients, despite both being elevated compared to controls. Ferritin, a key indicator of iron storage, reflects iron overload and is commonly linked to kidney dysfunction, especially in transfusion-dependent BTM cases. The potential role of ferritin in sequestering excess iron may offer a degree of protection to renal and other tissues from iron-induced toxicity. This protective mechanism may partially explain the observed inverse correlation between ferritin and creatinine levels. However, the dual role of ferritin, as both a marker of iron burden and a possible protective agent, requires further investigation to clarify its implications in renal function within the context of thalassemia.

Similarly, Bhowad et al. reported a significant negative correlation between ferritin and creatinine levels in patients with BTM and thalassemia intermedia, suggesting that higher ferritin levels may not directly reflect renal impairment in these cases [24]. This inconsistent correlation challenges the conventional view of ferritin as a straightforward indicator of kidney dysfunction. The relationship between ferritin and renal function in beta-thalassemia appears to be more nuanced than a simple linear association. Moderately elevated ferritin levels may exert a protective effect by safely storing excess iron, potentially contributing to lower creatinine levels and mitigating renal damage. However, once ferritin exceeds a certain threshold, it may instead reflect significant iron overload, leading to oxidative stress and subsequent kidney injury, as evidenced by elevated creatinine levels. These findings suggest a threshold-dependent dual role of ferritin in renal pathophysiology among beta-thalassemia patients, war-

ranting further investigation.

The complicated relationship here highlights the need for a more careful understanding of iron markers in beta-thalassaemia, especially in research with more participants. Identifying a potential inflection point in the correlation between ferritin and creatinine could yield valuable insights for clinical management.

As with any study, we must acknowledge several limitations. While creatinine clearance provides a more accurate assessment of renal function than serum creatinine alone, the practical challenge of obtaining timed urine samples from children restricted this study to serum-based measurements. Additional limitations include the narrow age range (2–12 years) and the inclusion of only male participants.

CONCLUSION

Pediatric male patients with BTM showed significant elevations in ALP, AST, ALT, TBIL, DBIL, urea, uric acid, creatinine, and ferritin levels, indicating multi-organ involvement. In contrast, patients with BTT exhibited subclinical increases in ALT, total and direct bilirubin, creatinine, and ferritin. The positive correlation between ferritin and ALP in BTM patients suggests potential hepatic iron toxicity. Conversely, the inverse correlation between ferritin and creatinine in BTT patients may reflect a protective compensatory mechanism, wherein excess iron is sequestered in ferritin to reduce free iron toxicity. However, this remains a hypothesis requiring further investigation. These findings highlight the need for regular hepatic and renal function monitoring in BTT cases. Future longitudinal studies should also establish ferritin thresholds to differentiate between protective and toxic effects.

ETHICAL DECLARATIONS

Acknowledgments

We acknowledge the staff of Ibn Al-Atheer Hospital and Ibn Sina Hospital in Mosul, Iraq, for their valuable assistance and support throughout the course of this study.

Ethics Approval and Consent to Participate

The study proposal was approved by the Scientific Affairs Committee of the Medical Physics Department, College of Science, University of Mosul (Reference number: 4/74, dated 14/06/2023), in accordance with the Declaration of Helsinki. Informed consent was obtained from the parents or legal guardians of all participants prior to their enrolment in the study.

Consent for Publication

Not applicable. This manuscript does not contain any person's data in any form (including individual details, images, or videos).

Availability of Data and Material

The data that support the findings of this study are available from the corresponding author upon reasonable request.

Competing Interests

The authors declare that there is no conflict of interest.

Funding

No external funding was received for this study.

Authors' Contributions

All listed authors made significant, direct, and intellectual contributions to the work. They have read and approved the final version of the manuscript.

REFERENCES

[1] S. Patel, A. Siddiqui, and I. Kareem. Correlative study of serum bilirubin and liver enzymes with serum ferritin in beta thalassaemia major. *IOSR Journal of Dentaland Medical Sciences*, 17(2):62–67, 2018.

[2] G. De Simone, A. Quattrocchi, B. Mancini, A. di Masi, C. Nervi, and P. Ascenzi. Thalassemias: from gene to therapy. *Molecular Aspects of Medicine*, 84:101028, 2022.

[3] A. Kattamis, G. L. Forni, Y. Aydinok, and V. Viprakasit. Changing patterns in the epidemiology of β-thalassemia. *European journal of haematology*, 105(6):692–703, 2020.

[4] A. T. Taher, K. M. Musallam, and M. D. Cappellini. β-thalassemias. *N. Engl. J. Med.*, 384(8):727–743, 2021.

[5] G. J. Kontoghiorghes. Iron load toxicity in medicine: from molecular and cellular aspects to clinical implications. *International journal of molecular sciences*, 24(16):12928, 2023.

[6] E. Angelucci *et al.* Effects of iron overload and hepatitis c virus positivity in determining progression of liver fibrosis in thalassemia following bone marrow transplantation. *Blood, The Journal of the American Society of Hematology*, 100(1):17–21, 2002.

[7] M. Andreani *et al.* Long-term survival of ex-thalassemic patients with persistent mixed chimerism after bone marrow transplantation. *Bone marrow transplantation*, 25(4):401–404, 2000.

[8] S. Setoodeh, M. Khorsand, and M. A. Takhshid. The effects of iron overload, insulin resistance and oxidative stress on metabolic disorders in patients with β-thalassemia major. *Journal of Diabetes & Metabolic Disorders*, 19(2):767–774, 2020.

[9] A. I. Ansaf *et al.* Hypoparathyroidism in patients older than 10 years of age with beta-thalassemia. *Journal of Applied Hematology*, 15(2):116–120, 2024.

[10] E. A. Mohammed and N. A. Muhammed. Effect of maternal beta-thalassemia minor on obstetrical and neonatal outcomes in kirkuk province, iraq. *Al-Anbar Medical Journal*, 19(2):135–140, 2023.

[11] N. M. A. Atarbashi and E. A. H. Al-Dagestani. A study of some biochemical indicators of kidney function and estimation of some elements concentration in the blood serum of patients with celiac disease. *International Journal of Applied Sciences and Technology*, 4(22):157–167, 2022.

[12] E. Voskaridou *et al.* Early markers of renal dysfunction in patients with sickle cell/β-thalassemia. *Kidney international*, 69(11):2037–2042, 2006.

http://doi.org/10.33091/amj.2025.158019.2143

[13] S. M. Rabadiya, M. Yogesh, J. Nagda, R. Gandhi, and N. Makwana. Association of serum ferritin trends with liver enzyme patterns in β-thalassemia major: A longitudinal correlational study. *Journal of Family Medicine and Primary Care*, 13(7):2698–2702, 2024.

[14] A. Faruqi, T. Zafar, S. Subuctageen, and I. A. Mughal. Iron overload and liver function in patients with beta thalassemia major: A cross sectional study. *Pakistan Journal of Medical Sciences*, 40(9):2000, 2024.

[15] K. M. Musallam *et al.* Elevated liver iron concentration is a marker of increased morbidity in patients with β thalassemia intermedia. *Haematologica*, 96(11):1605, 2011.

[16] M. V. Sadeghi, M. Mirghorbani, and R. Akbari. β-thalassemia minor & renal tubular dysfunction: is there any association? *BMC nephrology*, 22(1):1–7, 2021.

[17] H. K. Jabbar, M. K. Hassan, and L. M. Al-Naama. Lipids profile in children and adolescents with β-thalassemia major. *Hematology, Transfusion and Cell Therapy*, 45(4):467–472, 2023.

[18] V. De Sanctis, A. Eleftheriou, and C. Malaventura. Prevalence of endocrine complications and short stature in patients with thalassaemia major: a multicenter study by the thalassaemia international federation (tif). *Pediatric endocrinology reviews: PER*, 2(suppl. 2):249–255, 2004.

[19] A. Y. D. Bashi and F. H. Fathi. Evaluation of hepatic enzymes in major β-thalassemic patients using deferasirox. *Iraqi Journal of Pharmaceutical Sciences*, 31(2):237–243, 2022.

[20] S. Sobhani, F. Rahmani, M. Rahmani, M. Askari, and F. Kompani. Serum ferritin levels and irregular use of iron chelators predict liver iron load in patients with major beta thalassemia: a cross-sectional study. *Croatian medical journal*, 60(5):405–413, 2019.

[21] I. S. Young and J. V. Woodside. Antioxidants in health and disease. *Journal of clinical pathology*, 54(3):176–186, 2001.

[22] M. Okuda, S. Sasaki, I. Kunitsugu, R. Sakurai, N. Yoshitake, and T. Hobara. Iron load and liver enzymes in 10- and 13-year-olds. *Journal of pediatric gastroenterology and nutrition*, 52(3):333–338, 2011.

[23] Y.-Y. Huang, M.-J. Huang, H.-L. Wang, C.-C. Chan, and C.-S. Huang. Bilirubin concentrations in thalassemia heterozygotes in university students. *European journal of haematology*, 86(4):317–323, 2011.

[24] S. Bhowad, P. Samant, and B. Seth. Biochemical assessment of renal function and its correlation with iron overloading in different variants of thalassemia. *Journal of Applied and Natural Science*, 14(3):1016, 2022.

[25] M. F. Karim, M. Ismail, A. K. M. M. Hasan, and H. U. Shekhar. Hematological and biochemical status of beta-thalassemia major patients in bangladesh: A comparative analysis. *International journal of hematology-oncology and stem cell research*, 10(1):7, 2016.

[26] O. Tanous *et al.* Renal function in β-thalassemia major patients treated with two different iron-chelation regimes. *BMC nephrology*, 22(1):418, 2021.