Alkindy *et al.,* Babcock Univ. Med. J.2026 9(1):236-241
https://doi.org/10.38029/babcockuniv.med.j..v9i1.1232
eISSN: 2756-4657

RESEARCH ARTICLE OPEN ACCESS

Hepatic steatosis and fibrosis in patients with thalassemia major: A cross-sectional study using transient elastography

Alkindy MA[1, 2ID], Alareedh MD[1], Gataa ZK[3ID]

[1]Faculty of Medicine, University of Kufa, Iraq
[2]Najaf GIT Hospital, Iraq
[3]Al Hakeem Hospital

Submitted: 30th October 2025
Accepted: 1st November 2025
Published: 31st March 2026
ID: Orcid ID

Abstract
Objective: This study aimed to assess the prevalence and severity of hepatic steatosis and fibrosis in patients with transfusion-dependent thalassemia major (TM) using transient elastography (TE) and to investigate their correlations with serum ferritin, liver enzymes, and body mass index (BMI).
Methods: A cross-sectional study was conducted at the Thalassemia Centre in Najaf, Iraq, from January to June 2024. Eighty TM patients aged ≥12 years were enrolled. Liver stiffness and controlled attenuation parameter (CAP) were measured via TE to stage fibrosis (F0-F4) and grade steatosis (S0-S3). Serum levels of alanine transaminase (ALT), aspartate transaminase (AST), and ferritin were analysed. Statistical analyses included Spearman's correlation and binary logistic regression.
Results: The mean age of participants was 22±6.3 years, with a mean BMI of 20.5±3.0 kg/m². Significant fibrosis (F3-F4) was present in 32.5% of patients, while 67.5% had no or mild fibrosis (F0-F2). Severe steatosis (S3) was found in 8.6% of patients. ALT and AST levels showed a significant positive correlation with fibrosis stage ($p<0.001$ for both). Serum ferritin was significantly higher in patients with significant fibrosis ($p=0.012$). No significant correlations were found between steatosis and ALT ($p=0.275$), AST ($p=0.375$), BMI ($p=0.835$), or ferritin ($p=0.323$). BMI was not correlated with fibrosis ($p=0.193$).
Conclusions: Elevated liver enzymes and serum ferritin are significantly associated with liver fibrosis in TM patients, while steatosis appears less prevalent and is not correlated with traditional metabolic risk factors like BMI. Transient elastography is a crucial non-invasive tool for the simultaneous assessment of fibrosis and steatosis in high-risk population.

Keywords: Thalassemia Major, Liver Fibrosis, Hepatic Steatosis, Transient Elastography, Ferritin, Alanine Transaminase

Plain English Summary

Patients with thalassemia major, a serious inherited blood disorder, require regular blood transfusions to survive. A side effect of these transfusions is iron overload, where too much iron builds up in the body, particularly in the liver. This can cause liver scarring (fibrosis) and fatty liver (steatosis). Our study used a quick, painless, and non-invasive test called transient elastography (FibroScan) to measure liver scarring and fat in 80 thalassemia patients. We found that nearly one-third of patients had significant liver scarring. Higher levels of liver enzymes and ferritin (a blood marker of iron stores) were strongly linked to more severe scarring. In contrast, fatty liver was less common and was not linked to the patient's body weight or iron levels. This suggests that in thalassemia patients, liver damage is primarily driven by iron overload. We recommend using FibroScan regularly alongside blood tests to monitor liver health in these patients, allowing for earlier intervention.

Correspondence:
Alkindy, Mahmoud A
Faculty of Medicine
University of Kufa
Iraq
mahmouda.alkindy@uokufa.edu.iq

Introduction

Thalassemia major (TM) is a hereditary hemoglobinopathy characterised by defective synthesis of the beta-globin chain, necessitating lifelong regular blood transfusions for survival (1). A paramount consequence of this therapy is chronic iron overload, as the human body lacks an active mechanism to excrete excess iron. The liver, a primary site for iron storage, is particularly vulnerable, leading to oxidative stress, hepatocyte injury, and inflammation, which can progress to fibrosis and ultimately cirrhosis (2).

The early detection of liver injury is critical for preventing irreversible damage. Serum alanine transaminase (ALT) and aspartate transaminase (AST) are established biochemical markers of hepatocellular injury, often elevating before clinical signs of liver dysfunction become apparent (3). Furthermore, hepatic steatosis, the accumulation of fat in the liver, has been reported in TM patients at a young age, potentially independent of iron overload and linked to metabolic alterations and body composition changes resulting from chronic anaemia and sedentary lifestyle (4).

Historically, liver biopsy was the gold standard for assessing fibrosis and steatosis, but its invasive nature, sampling error, and procedural risks limit its utility for routine monitoring. The advent of transient elastography (TE) has revolutionised the non-invasive assessment of liver disease. TE simultaneously measures liver stiffness, a surrogate for fibrosis, and the controlled attenuation parameter (CAP), a quantitative measure of steatosis, with high reproducibility (5).

While data on liver complications in TM patients from Western and some Asian countries exist, such studies are scarce from the Iraqi population. This study, therefore, aimed to evaluate the prevalence and severity of hepatic steatosis and fibrosis in Iraqi patients with TM using TE and to investigate their correlations with serum ferritin, liver enzymes (ALT, AST), and body mass index (BMI).

Materials and Methods

Study Design and Population

A cross-sectional study was conducted over six months (January to June 2024) at the Thalassemia Centre of Al-Zahraa Teaching Hospital in Najaf, Iraq. A total of 80 patients with a confirmed diagnosis of beta-thalassemia major, established via high-performance liquid chromatography (HPLC), and aged 12 years or older, were enrolled. Participants were recruited consecutively during their routine follow-up visits. The exclusion criteria were designed to minimise confounding factors and included: a history of chronic viral hepatitis (B or C), autoimmune liver diseases, other haematological disorders (e.g., sickle cell disease), diabetes mellitus, active systemic infections, febrile illness at the time of assessment, and pregnancy.

Data and Sample Collection

Demographic and clinical data, including age, sex, and type of iron chelation therapy, were recorded. The height and weight of each participant were measured to calculate the body mass index (BMI) as weight in kilograms divided by height in meters squared (kg/m²). A 5 mL venous blood sample was drawn from each participant. Serum was separated and analysed for ALT, AST (using an enzymatic colourimetric method on a Monarch 240 analyser, Biorex Diagnostics, UK), and ferritin (measured by chemiluminescent immunoassay on a Mindray CL900i analyser, China).

Transient Elastography Assessment

All participants underwent transient elastography (TE) using the FT100 Mini560/800 Shear Wave Quantification Ultrasound Diagnostic System. The procedure was performed by a certified gastroenterology and hepatology specialist. With the patient in a supine position and the right arm in maximal abduction, the probe was placed on the skin over the right lobe of the liver. Ten valid measurements were obtained for each patient, and the median value was recorded.

Liver stiffness measurement (LSM) was reported in kilopascals (kPa) and interpreted for fibrosis staging as follows (6):

F0-F1: No or minimal fibrosis (2 – 7.0 kPa)
F2: Moderate fibrosis (7.1 – 9.4 kPa)
F3: Significant fibrosis (9.5 – 14.4 kPa)
F4: Cirrhosis (≥14.5 kPa)

For analysis, patients were categorized into two groups: no/mild fibrosis (F0-F2) and significant fibrosis (F3-F4).

Steatosis was graded using the controlled attenuation parameter (CAP) measured in dB/m, as follows (7):

S0: No steatosis (<248 dB/m)
S1: Mild steatosis (248 – 267 dB/m)
S2: Moderate steatosis (268 – 279 dB/m)
S3: Severe steatosis (≥280 dB/m)

Statistical Analysis

Data were analysed using SPSS Statistics version 30 (IBM Corp., USA). Continuous variables were expressed as mean ± standard deviation (SD), and categorical variables as frequencies and percentages. The association between continuous variables (e.g., liver enzymes, ferritin, BMI) and ordinal outcomes (fibrosis stage, steatosis grade) was assessed

using Spearman's rank correlation coefficient (ρ). Binary logistic regression was used to evaluate the predictive value of liver enzymes for significant fibrosis (F3-F4). A p-value of less than 0.05 was considered statistically significant.

Results

Baseline Characteristics of the Study Population

A total of 80 TM patients were studied, with a mean age of 22 ± 6.3 years and a near-equal gender distribution (51.2% male, 48.8% female). The cohort had a low mean BMI of 20.5 ± 3.0 kg/m², indicative of a generally thin population. Most patients (60%) were on oral iron chelation therapy. Mean serum ALT and AST levels were elevated at 35.7 ± 29.4 U/L and 45.4 ± 30.8 U/L, respectively. Serum ferritin was markedly elevated in all participants, with a mean of 3292 ± 2515 ng/mL (Table 1).

Table 1: Baseline Characteristics of the Study Participants (n=80)

Variable	Value
Age (Years)	22 ± 6.3
BMI (kg/m²)	20.5 ± 3.0
Sex	**n (%)**
Male	41 (51.2%)
Female	39 (48.8%)
Iron Chelation	**n (%)**
Oral	48 (60.0%)
Intravenous	27 (33.8%)
Combined	5 (6.3%)
Ferritin (ng/mL)	3292 ± 2515
ALT (U/L)	35.7 ± 29.4
AST (U/L)	45.4 ± 30.8

Prevalence of Hepatic Fibrosis and Steatosis

Assessment by TE revealed that 67.5% of participants had no or mild fibrosis (F0-F2), while 32.5% had significant fibrosis (F3-F4), as detailed in Table 2 and illustrated in Figure 1. The distribution of fibrosis stages was: F0-F1: 46.3%, F2: 21.3%, F3: 26.3%, and F4: 6.3%.

Table 2: Distribution of Hepatic Fibrosis Stages (n=80)

Fibrosis Stage (TE)	Frequency	Percentage
F0-F1	37	46.30%
F2	17	21.30%
F3	21	26.30%
F4	5	6.30%
No/Mild Fibrosis (F0-F2)	54	67.50%
Significant Fibrosis (F3-F4)	26	32.50%

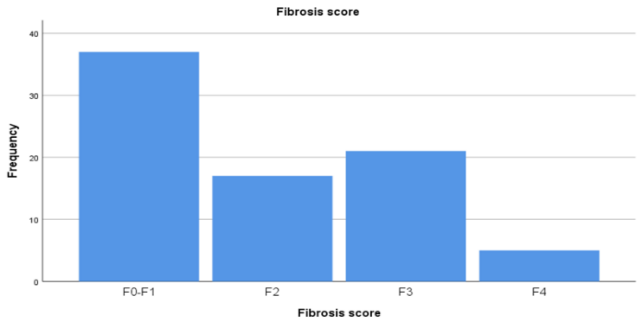

Figure 1: Bar chart showing the distribution of hepatic fibrosis stages among the study participants

Regarding hepatic steatosis, most patients (56.7%) had no or mild steatosis (S0-S1). Moderate steatosis (S2) was present in 34.6% of patients, and severe steatosis (S3) was found in 8.6% (Table 3, Figure 2).

Table 3: Distribution of Hepatic Steatosis Grades (n=80)

Steatosis Grade (CAP)	Frequency	Percentage
S0 (None)	7	8.60%
S1 (Mild)	38	48.10%
S2 (Moderate)	28	34.60%
S3 (Severe)	7	8.60%

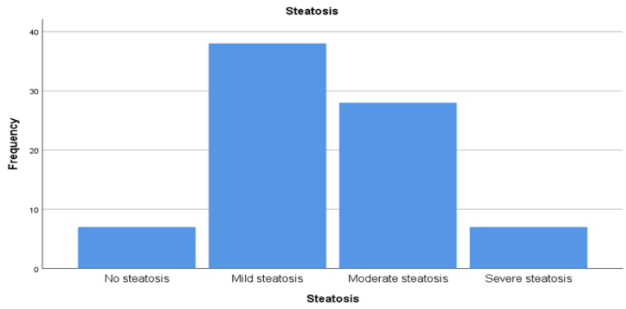

Figure 2: Bar chart showing the distribution of hepatic steatosis grades among the study participants

Correlations with Liver Enzymes, Ferritin, and BMI

A key finding was the strong positive correlation between liver enzyme levels and the severity of hepatic fibrosis. Both ALT and AST demonstrated statistically significant correlations with fibrosis stage ($p<0.001$ for both), as shown in Figure 3.

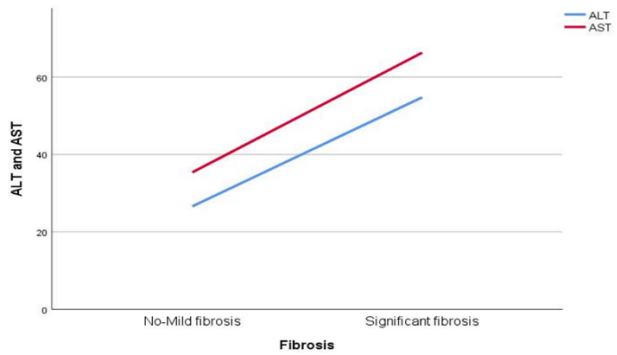

Figure 3: Scatter plots illustrating the positive correlation between (A) ALT levels and liver fibrosis stage, and (B) AST levels and liver fibrosis stage

In contrast, no significant correlation was found between either ALT ($p=0.275$) or AST ($p=0.375$) and hepatic steatosis grade.

Serum ferritin levels showed a significant positive correlation with the degree of liver fibrosis ($p=0.012$). Patients with significant fibrosis (F3-F4) had markedly higher ferritin levels compared to those with no/mild fibrosis. However, ferritin was not significantly associated with hepatic steatosis ($p=0.323$).

Body mass index (BMI) demonstrated no significant correlation with either hepatic steatosis ($p=0.835$) or fibrosis ($p=0.193$). Furthermore, no significant association was found between hepatic steatosis and liver fibrosis stage ($p=0.151$).

Discussion

This cross-sectional study provides a comprehensive assessment of liver health in Iraqi patients with TM, using the non-invasive transient elastography. Our findings indicate that significant liver fibrosis is prevalent in a substantial proportion (32.5%) of patients, underscoring the persistent burden of iron-overload-related hepatotoxicity despite chelation therapy. Conversely, severe steatosis was less common, affecting only 8.6% of the cohort.

The prevalence of significant fibrosis in our study aligns closely with reports from Italian cohorts by Ferraioli et al. (33.6%) and Fraquelli et al. (35%) (8, 9). This consistency across different populations highlights the universal challenge of managing iron-induced liver damage in TM. The lower prevalence of significant fibrosis (32.5%) compared to the 60% reported by Al-Khabori et

al. (10) could be attributed to differences in chelation regimens, genetic factors, or the exclusion of diabetic patients in our study, which removed a key driver of progressive liver disease.

The strong, statistically significant correlations between ALT, AST, and fibrosis severity are a central finding of our research. This aligns with previous studies by Khan et al. and Ferraioli et al., reinforcing the role of these enzymes as accessible, non-invasive biomarkers for predicting fibrotic progression in TM patients (8, 11). Similarly, the significant association between elevated serum ferritin and advanced fibrosis is consistent with the pathophysiological understanding of iron-mediated hepatotoxicity and is supported by the work of Ali et al. and Khan et al. (3, 12). This confirms that ferritin remains a crucial indirect marker for monitoring the risk of iron-overload-related organ damage.

Interestingly, our study found no significant association between BMI and either hepatic steatosis or fibrosis. This contrasts with studies in the general population, where BMI is a key risk factor for metabolic dysfunction-associated steatotic liver disease (MASLD). This discrepancy can be explained by the unique body composition of TM patients, who often have low muscle mass and altered fat distribution due to chronic anaemia and endocrinopathies, meaning a normal BMI may mask underlying metabolic imbalances (4). The lack of correlation between steatosis and fibrosis further suggests that in TM, the primary driver of liver fibrosis is iron overload rather than steatosis-related inflammatory pathways.

Study Limitations and Future Directions

This study has several limitations. Its cross-sectional design allows for the identification of associations but not causal relationships. The sample size, while adequate for initial assessment, limits the power for more complex multivariate analyses. The absence of histological confirmation, while ethically and practically justified for a monitoring study, means the TE findings are not validated against the traditional gold standard. Furthermore, we did not assess other potential contributors to liver disease, such as hepatitis status via PCR or genetic factors.

Future prospective, longitudinal studies with larger cohorts are warranted to validate the predictive value of ALT/AST and ferritin for fibrosis progression. Incorporating additional biomarkers and advanced imaging techniques could provide a more holistic view of liver health in TM patients.

Conclusion

In patients with thalassemia major, elevated liver enzyme levels and serum ferritin are significantly associated with the severity of liver fibrosis, as assessed by transient elastography. Hepatic steatosis is present but less severe and not correlated with BMI or iron overload in this cohort. These findings underscore that the primary hepatotoxic driver in TM is iron overload. The integration of transient elastography into routine clinical practice, complemented by vigilant monitoring of liver enzymes and ferritin, provides a powerful, non-invasive strategy for the early detection and management of hepatic complications, ultimately aiming to improve long-term outcomes for these patients.

List of Abbreviations

ALT: Alanine Transaminase
AST: Aspartate Transaminase
BMI: Body Mass Index
CAP: Controlled Attenuation Parameter
HPLC: High-Performance Liquid Chromatography
LSM: Liver Stiffness Measurement
MASLD: Metabolic Dysfunction-Associated Steatotic Liver Disease
SD: Standard Deviation
TE: Transient Elastography
TM: Thalassemia Major

Declarations

Ethics Approval and Consent to Participate

The study protocol received ethical approval from the Medical Ethics Committee of Kufa University (Ref: MEC-206/2024). Before enrolment, all participants (or their legal guardians for minors) received a comprehensive verbal explanation of the study's objectives and procedures. Written informed consent was obtained from all participants or their legal guardians.

Consent for Publication

Availability of Data and Materials

The datasets used and analysed during the current study are available from the corresponding author on reasonable request.

Competing Interests

The authors declare that they have no competing interests.

Funding

This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

Authors' Contributions

AMA conceived the study, collected data, and drafted the manuscript. AMD performed statistical analysis and interpreted data. GZK supervised the project and critically revised the manuscript. All authors read and approved the final manuscript.

Acknowledgements

The authors thank the staff and patients at the Thalassemia Centre of Al-Zahraa Teaching Hospital for their participation and support.

References

1. Fragkou N, Vlachaki E, Goulis I, Sinakos E. Liver disease in patients with transfusion-dependent β-thalassemia: The emerging role of metabolism dysfunction-associated steatotic liver disease. World Journal of Hepatology. 2024 May 27;16(5):671. https://doi.org/10.4254/wjh.v16.i5.671
2. Mehta KJ, Farnaud SJ, Sharp PA. Iron and liver fibrosis: Mechanistic and clinical aspects. World Journal of Gastroenterology. 2019 Feb 7;25(5):521. https://doi.org/10.3748/wjg.v25.i5.521
3. Khan H, Panjwani V, Al Rahbi S, Eltigani A, Qureshi RN, Unissa K, Sehar N, Mittal A, Pathare AV. Correlation of transient elastography with liver iron concentration and serum ferritin levels in patients with transfusion-dependent thalassemia major from Oman. Mediterranean Journal of Hematology and Infectious Diseases. 2023 Sep 1;15(1):e2023048. https://doi.org/10.4084/MJHID.2023.048
4. Ricchi P, Pistoia L, Positano V, Spasiano A, Casini T, Putti MC, Borsellino Z, Cossu A, Messina G, Keilberg P, Fatigati C. Liver steatosis in patients with transfusion-dependent thalassaemia. British Journal of Haematology. 2024 Jun;204(6):2458-67. https://doi.org/10.1111/bjh.19496
5. Fraquelli M, Cassinerio E, Roghi A, Rigamonti C, Casazza G, Colombo M, Massironi S, Conte D, Cappellini MD. Transient elastography in the assessment of liver fibrosis in adult thalassemia patients. American journal of Haematology. 2010 Aug;85(8):564-8. https://doi.org/10.1002/ajh.21752
6. Ferraioli G, Lissandrin R, Tinelli C, Scudeller L, Bonetti F, Zicchetti M, Longo F, Murgia M, Bernuzzi S, Zecca M, Casula P. Liver stiffness assessed by transient elastography in patients with β thalassaemia major. Annals of Hepatology. 2016 Jul 8;15(3):410-7. https://doi.org/10.5604/16652681.1198817
7. De Ledinghen V, Vergniol J. Transient elastography (fibroscan). Gastroenterologie Clinique et Biologique. 2008 Sep 1;32(6):58-67. https://doi.org/10.1016/S0399-8320(08)73994-0
8. Ferraioli G, Lissandrin R, Tinelli C, Scudeller L, Bonetti F, Zicchetti M, Longo F, Murgia M, Bernuzzi S, Zecca M, Casula P. Liver stiffness assessed by transient elastography in patients with β thalassaemia major. Annals of Hepatology. 2016 Jul 8;15(3):410-7. https://doi.org/10.5604/16652681.1198817
9. Fraquelli M, Cassinerio E, Roghi A, Rigamonti C, Casazza G, Colombo M, Massironi S, Conte D, Cappellini MD. Transient elastography in the assessment of liver fibrosis in adult thalassemia patients. American Journal of Hematology. 2010 Aug;85(8):564-8. https://doi.org/10.1002/ajh.21752
10. Al-Khabori M, Daar S, Al-Busafi SA, Al-Dhuhli H, Alumairi AA, Hassan M, Al-Rahbi S, Al-Ajmi U. Noninvasive assessment and risk factors of liver fibrosis in patients with thalassemia major using shear wave elastography. Hematology. 2019 Jan 1;24(1):183-8. https://doi.org/10.1080/10245332.2018.1540518
11. Khan SU, Baxla S, Jha S, Verma A, Akhtar S. Correlation of the liver function test with physical status of liver in the patients with hemoglobinopathy; cross-sectional study. European Journal of Molecular & Clinical Medicine.;11(2):2024.
12. Ali MS, Borhany M, Butt AJ, Ali RM, Kashif S, Wahaj M, Shamsi T. Correlation Between Serum Ferritin and Degree of Hepatic Fibrosis on Fibroscan in Thalassemic Patients. Cureus. 2023 Jul 18;15(7). https://doi.org/10.7759/cureus.42069