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Research Article

MRI Quantification of Liver and Cardiac Iron and its Correlation with Serum Ferritin Levels in Patients with Beta-Thalassemia

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Abstract: ***Introduction:*** Beta-thalassemia major requires lifelong blood transfusions, leading to progressive iron overload in the liver and heart, with cardiac siderosis remaining the leading cause of mortality in transfusion-dependent patients. Serum ferritin is an unreliable surrogate for tissue iron burden, while liver biopsy is invasive and prone to sampling error, creating a need for non-invasive organ-specific quantification. T2/R2 MRI relaxometry enables accurate, reproducible measurement of hepatic and cardiac iron deposition, guiding chelation therapy. This study evaluates T2 MRI for quantifying liver and cardiac iron burden in thalassemia major patients and correlates findings with serum ferritin levels.**Objective:** To evaluate magnetic resonance imaging (MRI) T2 relaxometry for quantifying hepatic and myocardial iron burden in transfusion-dependent beta-thalassemia major and to determine its correlation with serum ferritin levels.**Methods:** This cross-sectional study enrolled 38 transfusion-dependent beta-thalassemia major patients. All underwent serum ferritin measurement and 1.5 Tesla MRI using a multi-echo gradient-echo Fat Analysis and Calculation Technology (FACT) protocol, from which liver T2 , liver iron concentration (LIC), and cardiac T2 were derived and graded as normal, mild, moderate, or severe. Pearson correlation, chi-square/Fisher tests, one-way ANOVA, and multiple linear regression were applied; $p < 0.05$ was significant.**Results:** Mean age was 18.76 ± 7.30 years and mean transfusion duration 10.91 ± 4.46 years. Mean serum ferritin was 828.75 ± 324.96 ng/mL, mean liver T2 8.76 ± 3.55 ms, mean LIC 5.69 ± 4.16 mg/g, and mean cardiac T2 21.27 ± 4.39 ms. Hepatic iron overload was near-universal (86.8% mild, 7.9% moderate, 5.3% severe by LIC), whereas cardiac T2 was abnormal in 13.2%. Serum ferritin correlated significantly with liver T2 ($r = -0.649$), LIC ($r = 0.659$), and cardiac T2 ($r = -0.690$) (all $p < 0.001$). LIC correlated strongly with cardiac T2 ($r = -0.730$, $p < 0.001$). Ferritin categories were significantly associated with LIC ($p = 0.001$), liver T2 ($p = 0.002$), and cardiac T2 ($p = 0.001$) severity. On regression, LIC ($B = -0.516$, $p = 0.001$) and serum ferritin ($B = -0.005$, $p = 0.011$) were independent predictors of cardiac T2 ($R^2 = 0.648$). **Conclusion:** MRI provides sensitive, organ-specific quantification of hepatic and cardiac iron that correlates with serum ferritin but detects clinically important siderosis even at moderate ferritin values. Serum ferritin remains a useful screening marker, yet MRI is superior for grading severity and guiding chelation. Combined use of both is recommended in beta-thalassemia major.

Keywords: Beta-thalassemia major; Iron overload; Magnetic resonance imaging; T2 relaxometry; Serum ferritin.

INTRODUCTION

Beta-thalassemia is an inherited hemoglobin disorder in which the synthesis of beta-globin chains is reduced or absent, most often owing to point mutations in the beta-globin gene. The resulting imbalance in globin-chain production leads to ineffective erythropoiesis and chronic hemolytic anemia, and the condition is classified according to severity into thalassemia major, intermedia, and minor [1]. India carries a substantial burden of the disorder, with the beta-thalassemia trait reported in up to 5% of central India, rising to approximately 35–40% in some southern regions and 28–30% among certain eastern tribal populations, making it an important public health concern [2,3].

Patients with thalassemia major depend on lifelong regular blood transfusions to maintain adequate hemoglobin. Although life-saving, repeated transfusions cause progressive iron overload because the body has no physiological mechanism to excrete excess iron, which is deposited in the liver, heart, pancreas, and endocrine glands. Cardiac siderosis is among the most serious complications and remains the leading cause of death in transfusion-dependent patients worldwide, while hepatic iron accumulation contributes to fibrosis, cirrhosis, and portal hypertension if untreated [4].

Serum ferritin has traditionally been used as an indirect indicator of total body iron stores. Although it broadly correlates with liver iron, its reliability is limited because ferritin is an acute-phase reactant whose levels rise in infection, inflammation, liver disease, and malignancy, and it may therefore either overestimate or underestimate the true iron burden [5]. Liver biopsy, long regarded as the reference standard for hepatic iron measurement, is invasive, painful, and prone to sampling error from heterogeneous iron distribution; furthermore, liver iron does not reliably reflect cardiac iron, and severe cardiac siderosis can occur despite apparently low liver iron.

Cardiac biopsy is rarely performed, and echocardiography is insensitive to early myocardial iron deposition, creating a clear need for a reliable, non-invasive, and reproducible method of organ-specific iron quantification [6].

MRI using T2 and T2 relaxometry has become the preferred technique for assessing iron deposition in the liver and heart. Because iron is paramagnetic, it produces local magnetic-field inhomogeneity that accelerates signal decay and shortens the T2 relaxation time; as iron content rises, T2 falls predictably while its inverse, R2 , increases proportionally, permitting quantitative estimation of iron without biopsy [7]. This approach has improved the monitoring of iron overload by delivering accurate, organ-specific measurements that guide chelation therapy and help prevent serious complications [8]. Modern advances, including multi-echo gradient-echo sequences, fat–water separation, and automated T2/R2 mapping such as Fat Analysis and Calculation Technology (FACT), have further improved the accuracy and reproducibility of iron quantification and allow classification of iron overload into mild, moderate, and severe grades to individualize treatment [9].

Several studies support these principles. Öncel et al. reported significant associations between myocardial iron deposition, hepatic iron accumulation, and serum ferritin, demonstrating the value of MRI in evaluating organ-specific overload in thalassemia major [10]. Shehata et al. observed a strong correlation between liver iron concentration and T2 values in pediatric patients, supporting MRI as a non-invasive tool for monitoring chelation [11]. Heris et al. found significant correlations between serum ferritin and both cardiac and hepatic T2 , emphasizing the importance of comprehensive imaging rather than reliance on ferritin alone [12]. The paramagnetic behaviour of iron underlies these relationships, as excess non-transferrin-bound iron and labile plasma iron are readily taken up by tissues and drive oxidative injury [13].

Because cardiac complications remain the principal cause of mortality, early detection of myocardial iron is critical, and MRI can identify iron-related myocardial change before systolic dysfunction develops, allowing timely intensification of chelation [14]. Given the limitations of conventional biochemical markers and invasive sampling, MRI-based quantification offers a safe, accurate, reproducible, and non-invasive alternative, and examining its relationship with serum ferritin also clarifies how reliably ferritin reflects tissue iron in local populations. The present study was therefore undertaken to evaluate the role of T2 MRI in quantifying liver and cardiac iron burden in transfusion-dependent beta-thalassemia major patients, to assess the correlation between myocardial iron deposition, hepatic iron accumulation, and serum ferritin, and to grade the degree and severity of iron deposition radiologically.

MATERIALS AND METHODS

Study design and setting

This was a hospital-based cross-sectional study conducted in the Department of Radiodiagnosis, Bangalore Medical College and Research Institute (BMCRI), Bengaluru, over an 18-month period from March 2024 to August 2025. A cross-sectional design was chosen because the objective was to quantify iron overload at a single point in time and to correlate MRI-derived iron indices with serum ferritin rather than to assess longitudinal change. The study was approved by the Institutional Ethics Committee and conducted in accordance with the Declaration of Helsinki. Written informed consent was obtained from all participants, and assent was obtained from children aged 12–18 years. Patient confidentiality was maintained by anonymizing all records.

Participants

Eligible patients attending the radiology, pediatrics, and hematology units for routine evaluation or transfusion follow-up were screened and enrolled consecutively. Inclusion criteria were: age greater than 8 years; a diagnosis of beta-thalassemia major on repeated blood transfusions (three or more); and willingness to provide informed consent. Exclusion criteria were: other hemoglobinopathies; other cardiac or liver diseases; and contraindications to MRI examination such as metallic implants or pacemakers. A purposive, consecutive sampling method was used so that the sample was representative of transfusion-dependent beta-thalassemia patients attending the tertiary-care centre while minimizing sampling bias.

Sample size

The sample size was calculated from the findings of Shehata et al., who reported a mean liver iron concentration of 13.3 ± 9.4 mg/g in pediatric thalassemia patients evaluated by MRI [11]. Using the formula $n = Z^2\sigma^2/d^2$ with $Z = 1.96$, $\sigma = 9.4$, and an absolute precision $d = 3$ at a 95% confidence level, the required sample size was 37.7, rounded to 38. The final sample therefore comprised 38 beta-thalassemia major patients meeting the eligibility criteria.

Imaging technique / protocol

All patients underwent serum ferritin estimation followed by MRI. Examinations were performed on a United Imaging uMR 570LH 1.5 Tesla scanner equipped with FACT software. A quick 3D multi-echo gradient-echo sequence (six echoes) with a small flip angle (5°) was used to minimize T1 bias and to generate R2 maps. FACT processing automatically produced water maps, fat maps, in-phase and out-of-phase images, fat fraction, and R2 values. R2 values were converted to T2 using the relationship T2 = 1000/R2 . Liver measurements used multiple regions of interest (approximately four to five), preferentially placed in the right lobe (segments

VI/VII) to reduce cardiac-motion and gastric-susceptibility artefacts, and cardiac T2 was assessed in the interventricular septum. T2 values were interpreted using validated normograms and relaxometry calculators, and iron deposition in the liver and heart was graded as mild, moderate, or severe according to established reference charts. R2 values of the kidney and pancreas, organs typically spared in thalassemia major, were obtained as internal controls. All imaging and laboratory data were recorded in a structured proforma, and MRI datasets were archived in the picture archiving and communication system for review and verification.

Statistical analysis

Data were analyzed using Microsoft Excel and appropriate statistical software. Continuous variables were expressed as mean ± standard deviation and categorical variables as frequencies and percentages. Pearson correlation analysis was used to examine the relationship between serum ferritin and MRI T2 /iron concentration, and inter-organ relationships between hepatic and cardiac parameters. Chi-square or Fisher's exact test was used to evaluate categorical associations, one-way analysis of variance (ANOVA) was used to compare means across severity categories, and multiple linear regression was used to identify independent predictors of cardiac T2 . A p-value of less than 0.05 was considered statistically significant. All 38 enrolled patients completed both serum ferritin estimation and MRI, and complete data were available for every participant; there were no exclusions after enrolment and no missing data.

RESULTS

A total of 38 transfusion-dependent beta-thalassemia major patients were studied. The baseline demographic and clinical characteristics are presented in Table 1. The mean age was 18.76 ± 7.30 years (range 8–30 years), and the cohort was dominated by older adolescents and young adults, the largest proportion being aged 22 years or more (36.8%). The sex distribution was exactly equal, with 19 males (50.0%) and 19 females (50.0%). The mean duration of transfusion therapy was 10.91 ± 4.46 years (range 4.0–19.8 years), and most patients had been transfused for 5–9 years (31.6%) or 10–14 years (28.9%), indicating substantial cumulative exposure to transfusional iron.

Table 1. Baseline demographic and clinical characteristics of the study participants (n = 38).

Characteristic	Category	Percentage (%)
Age group (years)	8–11	18.4
	12–15	21.1
	16–18	18.4
	19–21	5.3
	≥22	36.8
Sex	Male (n = 19)	50.0
	Female (n = 19)	50.0
Duration of transfusion (years)	<5	13.2
	5–9	31.6
	10–14	28.9
	≥15	26.3

Mean age 18.76 ± 7.30 years; mean duration of transfusion 10.91 ± 4.46 years.

Table 2. Descriptive statistics of baseline continuous variables (n = 38).

Variable	n	Minimum	Maximum	Mean	Std. deviation
Age (years)	38	8.00	30.00	18.76	7.30
Duration of transfusion (years)	38	4.00	19.80	10.91	4.46
Serum ferritin (ng/mL)	38	500.80	1906.40	828.75	324.96
Liver T2* (ms)	38	0.99	13.41	8.76	3.55
Liver iron concentration (mg/g)	38	2.06	22.93	5.69	4.16
Cardiac T2* (ms)	38	7.63	25.92	21.27	4.39

Table 3. Distribution of participants according to iron-burden severity categories (n = 38).

Parameter	Category	Frequency (n)	Percentage (%)
Serum ferritin (ng/mL)	<1000	30	78.9
	1000–1500	6	15.8
	>1500	2	5.3
Liver T2*	Normal	31	81.6
	Mild	2	5.3

	Moderate	3	7.9
	Severe	2	5.3
Liver iron concentration (LIC)	Mild	33	86.8
	Moderate	3	7.9
	Severe	2	5.3
Cardiac T2*	Normal	33	86.8
	Mild	1	2.6
	Moderate	2	5.3
	Severe	2	5.3

Descriptive statistics for the continuous variables are shown in Table 2. Mean serum ferritin was 828.75 ± 324.96 ng/mL (range 500.80–1906.40 ng/mL). Mean liver T2 was 8.76 ± 3.55 ms (range 0.99–13.41 ms), mean liver iron concentration (LIC) was 5.69 ± 4.16 mg/g (range 2.06–22.93 mg/g), and mean cardiac T2 was 21.27 ± 4.39 ms (range 7.63–25.92 ms), reflecting overall mild hepatic iron overload with preserved mean cardiac T2 but a subset of patients with markedly abnormal values.

The distribution of iron-burden severity categories is summarized in Table 3 and Figure 1. Most patients (78.9%) had serum ferritin below 1000 ng/mL, while 15.8% had 1000–1500 ng/mL and 5.3% exceeded 1500 ng/mL. Liver T2 was normal in 31 patients (81.6%), with 5.3% mild, 7.9% moderate, and 5.3% severe reduction. By LIC, hepatic iron overload was almost universal but predominantly mild: 33 patients (86.8%) had mild, 3 (7.9%) moderate, and 2 (5.3%) severe overload. Cardiac T2 was normal in 33 patients (86.8%), while 1 patient (2.6%) had mild, 2 (5.3%) moderate, and 2 (5.3%) severe reduction, so 10.6% had moderate-to-severe myocardial iron deposition.

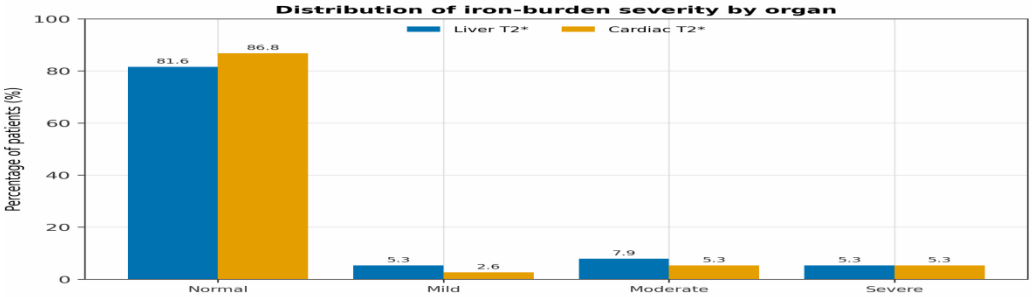

Figure 1. Distribution of iron-burden severity categories for liver T2 and cardiac T2 , expressed as the percentage of the 38 patients in each grade. Normal grades predominated for both organs (liver T2 81.6%, cardiac T2 86.8%), with only a small minority reaching the moderate or severe categories (data from Table 3).

Table 4. Correlations among serum ferritin and hepatic/cardiac MRI parameters (n = 38).

Variable pair	Pearson's r	p-value
Serum ferritin (ng/mL) vs liver T2* (ms)	−0.649	< 0.001
Serum ferritin (ng/mL) vs LIC (mg/g)	0.659	< 0.001
Serum ferritin (ng/mL) vs cardiac T2* (ms)	−0.690	< 0.001
Liver T2* (ms) vs LIC (mg/g)	−0.697	< 0.001
Liver T2* (ms) vs cardiac T2* (ms)	0.594	< 0.001
LIC (mg/g) vs cardiac T2* (ms)	−0.730	< 0.001

Table 5. Association between serum ferritin category and LIC category (n = 38).

Serum ferritin category (ng/mL)	Mild LIC n (%)	Moderate LIC n (%)	Severe LIC n (%)	Row total (n)
<1000	29 (96.7)	1 (3.3)	0 (0.0)	30
1000–1500	4 (66.7)	1 (16.7)	1 (16.7)	6
>1500	0 (0.0)	1 (50.0)	1 (50.0)	2
Total	33	3	2	38

Chi-square test: $\chi^2 = 18.885$, df = 4, p = 0.001.

Table 6. Association between serum ferritin category and liver T2* category (n = 38).

Serum ferritin category (ng/mL)	Normal n (%)	Mild n (%)	Moderate n (%)	Severe n (%)	Row total (n)
<1000	28 (93.3)	1 (3.3)	1 (3.3)	0 (0.0)	30
1000–1500	3 (50.0)	1 (16.7)	1 (16.7)	1 (16.7)	6
>1500	0 (0.0)	0 (0.0)	1 (50.0)	1 (50.0)	2

Total	31	2	3	2	38

Chi-square test: $\chi^2 = 21.206$, df = 6, p = 0.002.

The correlations among serum ferritin and the MRI-derived hepatic and cardiac parameters are presented in Table 4 and Figures 2–4. Serum ferritin showed a significant negative correlation with liver T2 (r = −0.649, p < 0.001) and cardiac T2 (r = −0.690, p < 0.001) and a significant positive correlation with LIC (r = 0.659, p < 0.001). Liver T2 correlated inversely with LIC (r = −0.697, p < 0.001) and positively with cardiac T2 (r = 0.594, p < 0.001), while LIC correlated strongly and negatively with cardiac T2 (r = −0.730, p < 0.001), indicating that higher hepatic iron burden was closely linked with greater myocardial iron deposition.

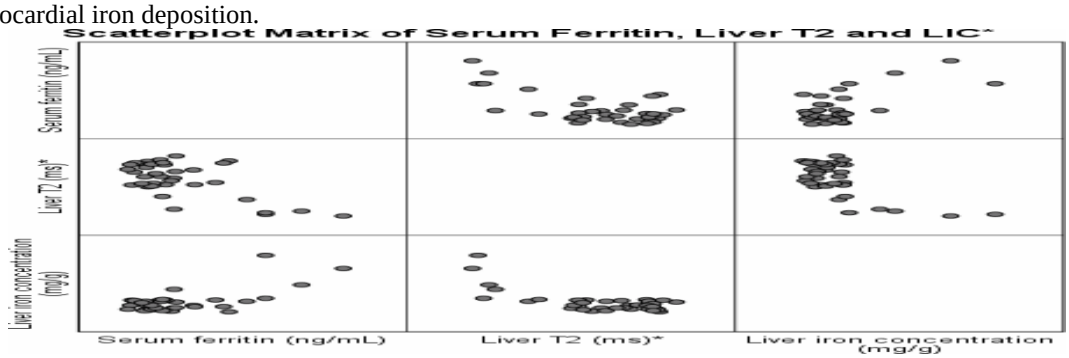

Figure 2. Scatterplot matrix of serum ferritin, liver T2 , and liver iron concentration (LIC) derived from the study's own data, illustrating the significant negative ferritin–liver T2 relationship, the positive ferritin–LIC relationship, and the strong inverse liver T2 –LIC relationship (the study's own correlation analysis; corresponding coefficients in Table 4).

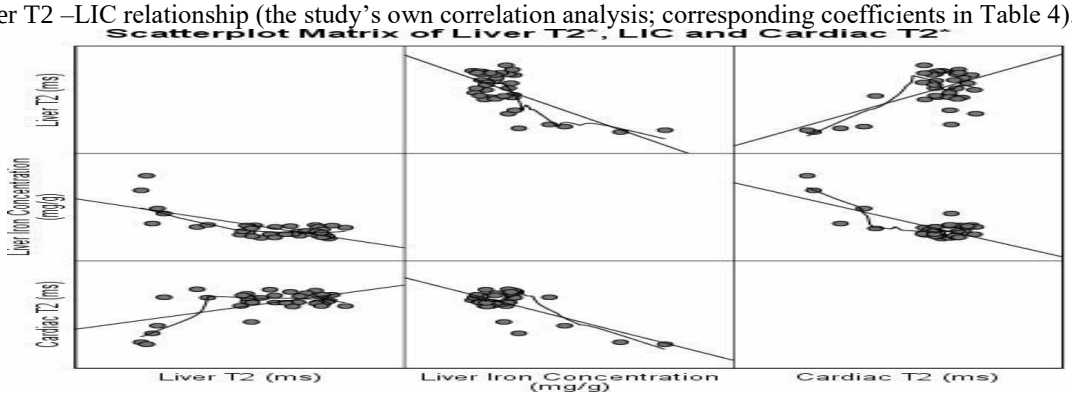

Figure 3. Scatterplot matrix of liver T2 , liver iron concentration (LIC), and cardiac T2 derived from the study's own data, illustrating the strong negative LIC–cardiac T2 correlation and the positive liver T2 –cardiac T2 relationship, indicating parallel progression of hepatic and myocardial iron loading (the study's own correlation analysis; corresponding coefficients in Table 4).

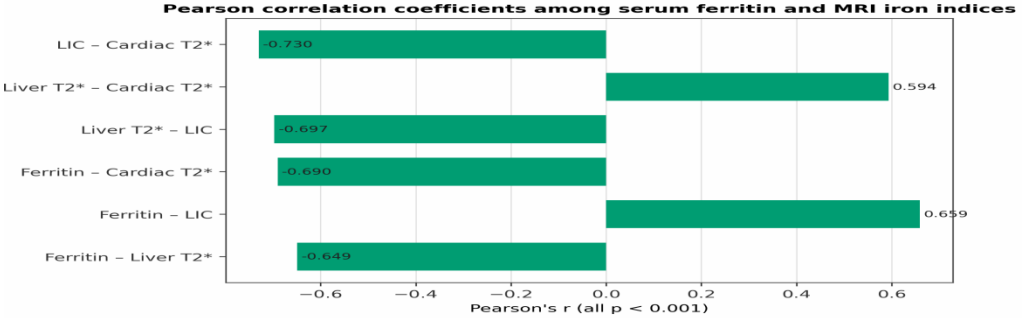

Figure 4. Pearson correlation coefficients (r) among serum ferritin and the MRI-derived hepatic and cardiac iron indices. Bars to the left of zero denote inverse relationships and bars to the right positive relationships; all six correlations were significant at p < 0.001 (data from Table 4).

Table 7. Association between serum ferritin category and cardiac T2* category (n = 38).

Serum ferritin category (ng/mL)	Normal n (%)	Mild n (%)	Moderate n (%)	Severe n (%)	Row total (n)
<1000	29 (96.7)	1 (3.3)	0 (0.0)	0 (0.0)	30
1000–1500	4 (66.7)	0 (0.0)	1 (16.7)	1 (16.7)	6
>1500	0 (0.0)	0 (0.0)	1 (50.0)	1 (50.0)	2
Total	33	1	2	2	38

Chi-square test: $\chi^2 = 23.952$, df = 6, p = 0.001.

Table 8. Comparison of serum ferritin across LIC categories (n = 38).

LIC category	n	Mean ferritin (ng/mL)	SD (ng/mL)
Mild	33	737.97	191.69
Moderate	3	1278.00	428.69
Severe	2	1652.65	358.86
Total	38	828.75	324.96

One-way ANOVA: F(2,35) = 23.391, p < 0.001.

Table 9. Comparison of serum ferritin across cardiac T2* categories (n = 38).

Cardiac T2* category	n	Mean ferritin (ng/mL)	SD (ng/mL)
Normal	33	744.33	190.17
Mild	1	592.00	—
Moderate	2	1516.05	165.96
Severe	2	1652.65	358.86
Total	38	828.75	324.96

One-way ANOVA: F(3,34) = 22.377, p < 0.001.

Table 10. Comparison of cardiac T2* across LIC categories (n = 38).

LIC category	n	Mean cardiac T2* (ms)	SD (ms)
Mild	33	22.55	2.13
Moderate	3	16.10	6.33
Severe	2	7.98	0.49
Total	38	21.27	4.39

One-way ANOVA: F(2,35) = 37.855, p < 0.001.

Serum ferritin category was significantly associated with the severity of organ iron overload on all three cross-tabulations. Ferritin category was associated with LIC category ($\chi^2 = 18.885$, df = 4, p = 0.001; Table 5): 96.7% of patients with ferritin below 1000 ng/mL had mild LIC and none had severe LIC, whereas patients above 1500 ng/mL had only moderate (50%) or severe (50%) LIC. Ferritin category was likewise associated with liver T2 category ($\chi^2 = 21.206$, df = 6, p = 0.002; Table 6), with 93.3% of the low-ferritin group showing normal liver T2 , and with cardiac T2 category ($\chi^2 = 23.952$, df = 6, p = 0.001; Table 7), where 96.7% of the low-ferritin group had normal cardiac T2 while all patients above 1500 ng/mL had moderate or severe myocardial involvement.

Table 11. Pattern of organ involvement based on MRI (n = 38).

Pattern of involvement	Frequency (n)	Percentage (%)
Isolated hepatic	33	86.8
Combined hepatic & cardiac	5	13.2
Total	38	100.0

Table 12. Multiple linear regression — predictors of cardiac T2* (n = 38).

Predictor	B	SE(B)	β	t	p-value
Constant	27.905	1.983	—	14.074	< 0.001
LIC (mg/g)	−0.516	0.147	−0.489	−3.518	0.001
Serum ferritin (ng/mL)	−0.005	0.002	−0.374	−2.686	0.011
Age (years)	0.111	0.066	0.184	1.678	0.103
Duration of transfusion (years)	−0.145	0.109	−0.148	−1.337	0.190

Model summary: R = 0.805, $R^2 = 0.648$, adjusted $R^2 = 0.605$, standard error of estimate = 2.76 ms; ANOVA F(4,33) = 15.181, p < 0.001.

Mean-comparison analyses confirmed a graded relationship between biochemical and imaging severity (Figure 5). Mean serum ferritin rose progressively across LIC categories from 737.97 ± 191.69 ng/mL (mild) to 1278.00 ± 428.69 ng/mL (moderate) and 1652.65 ± 358.86 ng/mL (severe) (F(2,35) = 23.391, p < 0.001; Table 8). A similar gradient was seen across cardiac T2 categories, mean ferritin increasing from 744.33 ± 190.17 ng/mL in normal patients to 1516.05 ± 165.96 ng/mL and 1652.65 ± 358.86 ng/mL in moderate and severe cardiac involvement respectively (F(3,34) = 22.377, p < 0.001; Table 9). Conversely, mean cardiac T2 fell sharply across LIC categories, from 22.55 ± 2.13 ms (mild) to 16.10 ± 6.33 ms (moderate) and 7.98 ± 0.49 ms (severe) (F(2,35) = 37.855, p < 0.001; Table 10).

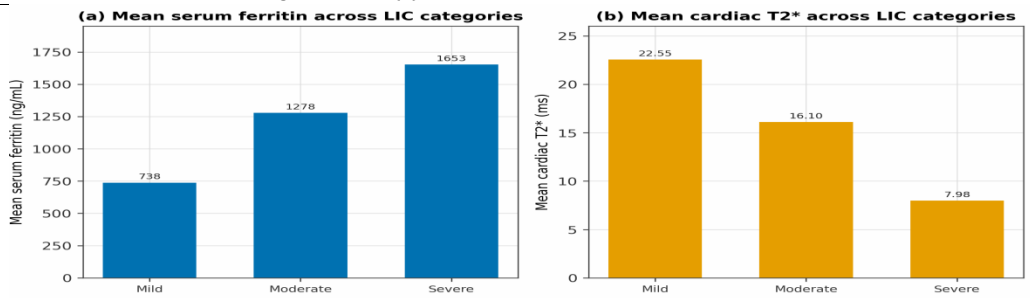

Figure 5. Graded relationship between hepatic iron severity and systemic/cardiac indices across liver iron concentration (LIC) categories: (a) mean serum ferritin rose progressively from mild to severe hepatic overload, while (b) mean cardiac T2 fell progressively over the same categories (data from Tables 8 and 10).

The pattern of organ involvement is shown in Table 11 and Figure 6. Most patients (33; 86.8%) had isolated hepatic iron overload, whereas 5 (13.2%) had combined hepatic and cardiac overload; no patient had isolated cardiac involvement. Finally, multiple linear regression with cardiac T2 as the dependent variable and LIC, serum ferritin, age, and transfusion duration as predictors explained 64.8% of the variance ($R = 0.805$, $R^2 = 0.648$, adjusted $R^2 = 0.605$; $F(4,33) = 15.181$, $p < 0.001$; Table 12). LIC ($B = -0.516$, $p = 0.001$) and serum ferritin ($B = -0.005$, $p = 0.011$) were independent predictors of cardiac T2 , whereas age ($p = 0.103$) and transfusion duration ($p = 0.190$) were not significant after adjustment.

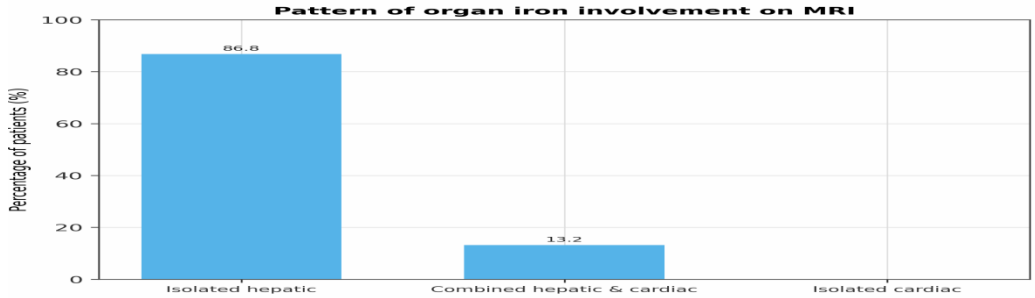

Figure 6. Pattern of organ iron involvement on MRI. Most patients had isolated hepatic overload (86.8%) and a minority had combined hepatic and cardiac overload (13.2%); no patient had isolated cardiac involvement (data from Table 11).

DISCUSSION

This cross-sectional study evaluated MRI-based quantification of hepatic and cardiac iron in 38 transfusion-dependent beta-thalassemia major patients and its correlation with serum ferritin. The principal findings were that hepatic iron overload was near-universal while clinically important cardiac siderosis was confined to a smaller high-risk subgroup, that serum ferritin correlated significantly with both hepatic and cardiac MRI indices, and that LIC and ferritin independently predicted cardiac T2 . Together these results reinforce the complementary roles of biochemical and imaging assessment in monitoring iron overload.

The cohort was dominated by older adolescents and young adults (mean age 18.76 ± 7.30 years), reflecting improved survival of transfusion-dependent patients into adulthood. This age profile is broadly comparable with Majd et al. (mean 22.7 ± 7 years) and Yuksel et al. (mean 25 ± 7 years), both of whom studied similarly mature transfusion-dependent cohorts [21,22]. In contrast, Shehata et al. (mean 10.9 ± 2.9 years) and Chuansumrit et al. (mean 14.8 ± 3.2 years) evaluated younger populations at an earlier stage of organ iron deposition [11,23]. The wider age range extending to 30 years in the present series supports the need for long-term MRI-based iron surveillance beyond childhood, as cumulative transfusional exposure increases with age. The exactly equal sex distribution (50% male, 50% female) indicates no sex predilection and mirrors the near-balanced distributions reported by Shehata et al. (47.7% male, 52.3% female) and Öncel et al., supporting uniform screening strategies for both sexes [10,11].

The mean transfusion duration of 10.91 ± 4.46 years confirmed prolonged transfusional exposure, consistent with the pathophysiology of beta-thalassemia major, in which lifelong transfusion support produces progressive iron accumulation unless adequately chelated. Comparable chronically transfused populations were described by Chuansumrit et al., whose patients had been transfusion-dependent from a mean age of 3.8 years and had begun chelation at a mean age of 8.4 years, and by Majd et al. [21,23]. Although transfusion duration was not an independent predictor of cardiac T2 in the regression model, its descriptive relevance as a marker of lifelong exposure and cumulative iron toxicity is clear. A notable observation was that the mean serum ferritin of 828.75 ± 324.96 ng/mL, with 78.9% of patients below 1000 ng/mL, was lower than in several previous series. Majd et al. reported a median ferritin of 1434 ng/mL, Chuansumrit et al. a mean of 1673 µg/L, Karakus et al. a median of 1693 ng/mL, and Mandal et al. a mean of 2150 ng/mL, all reflecting heavier biochemical burden [21,23,24,25]. This comparatively lower ferritin may indicate better chelation control or earlier detection in the

present cohort. Critically, however, apparently moderate ferritin did not exclude organ iron deposition, echoing Mandal et al., who found that among patients with ferritin below 1000 ng/mL, several nonetheless had abnormal LIC and myocardial iron concentration [25]. This finding underlines the mechanism by which excess iron, once transferrin is saturated, circulates as non-transferrin-bound and labile plasma iron and is deposited in parenchymal organs independent of the ferritin value [13].

Hepatic assessment showed that although liver T2 was categorically normal in 81.6% of patients, LIC revealed measurable hepatic iron in essentially the entire cohort (86.8% mild, 7.9% moderate, 5.3% severe), consistent with the liver being the earliest and principal storage organ for transfusional iron. The strong internal consistency of hepatic MRI quantification, with liver T2 and LIC inversely correlated ($r = -0.697$, $p < 0.001$), matches the significant LIC–T2 relationship reported by Shehata et al. [11]. Serum ferritin correlated significantly with both liver T2 ($r = -0.649$) and LIC ($r = 0.659$), comparable to the strong relationships described by Majd et al. ($r = -0.698$ for liver T2 and 0.718 for LIC) and stronger than the weaker association reported by Eghbali et al. ($r = -0.297$) [20,21]. Chuansumrit et al. similarly linked liver T2 to ferritin through a logarithmic regression equation, and reported that ferritin above 1000–2500 µg/L conferred a 6.8- to 13.3-fold risk of moderate-to-severe hepatic overload [23]. Nonetheless, because the correlation was imperfect, ferritin cannot replace MRI for tissue-level hepatic assessment.

Cardiac T2 was normal in 86.8% of patients, but 13.2% had myocardial iron deposition, including 10.6% with moderate-to-severe involvement. This is clinically significant because cardiac siderosis is the principal determinant of thalassemia-related mortality [4]. The present cardiac burden lay between the extremes reported in the literature: Majd et al. found abnormal myocardial iron in 58% and severe involvement in 36%, and Heris et al. reported severe cardiac overload in 22%, whereas Chuansumrit et al. observed no myocardial overload in their younger cohort [12,21,23]. A major finding was the significant negative correlation between serum ferritin and cardiac T2 ($r = -0.690$, $p < 0.001$), stronger than the moderate correlations reported by Majd et al. ($r = -0.329$), Yuksel et al. ($r = -0.34$), and Heris et al. ($r = -0.34$), and in clear contrast to Eghbali et al., who found no significant association ($r = -0.120$, $p = 0.361$) [12,20,21,22]. Öncel et al. likewise linked myocardial iron deposition to serum ferritin with respect to both presence and severity [10]. These differences likely reflect variation in age, transfusion duration, chelation practice, and severity distribution. Because ferritin is influenced by inflammatory and hepatic factors, cardiac T2 remains indispensable for direct myocardial assessment and monitoring, particularly as myocardial iron can be reversed with timely intensive chelation [18].

The relationship between hepatic and cardiac iron indices was particularly informative. Liver T2 correlated positively with cardiac T2 ($r = 0.594$), and LIC correlated strongly and negatively with cardiac T2 ($r = -0.730$, $p < 0.001$), suggesting that iron deposition in the liver and heart tended to progress in parallel in this cohort. Mean cardiac T2 fell dramatically from 22.55 ms in mild LIC to 7.98 ms in severe LIC, marking the transition from an acceptable myocardial range to severe siderosis. This contrasts with Öncel et al., who found no significant association between hepatic and cardiac iron accumulation, but aligns with Mandal et al., who reported significant correlations of ferritin with both LIC and myocardial iron concentration [10,25]. The present data therefore support a stronger hepatic–cardiac linkage, implying that markedly elevated LIC should act as a warning sign prompting dedicated cardiac T2 assessment. Because organ-specific discordance can still occur, however, direct cardiac MRI remains necessary even when hepatic status is known.

The categorical and regression analyses integrated these observations. Ferritin categories were significantly associated with worsening LIC, liver T2 , and cardiac T2 severity ($p = 0.001$, 0.002, and 0.001 respectively), producing clear stepwise gradients consistent with the risk relationships described by Chuansumrit et al. and Majd et al. [21,23]. The regression model explained 64.8% of the variance in cardiac T2 , identifying LIC and serum ferritin as independent predictors while age and transfusion duration were not significant after adjustment; the lack of an age effect accords with Shehata et al., who found no correlation between cardiac T2 and age [11]. This indicates that current hepatic and systemic iron load are more informative predictors of myocardial siderosis than demographic duration markers alone, reinforcing MRI and ferritin as complementary tools for risk stratification.

Mechanistically, iron toxicity in these organs is driven by the generation of reactive oxygen species and consequent oxidative injury, to which the myocardium is especially vulnerable because of its limited capacity to store excess iron [19]. The demonstrated ability of cardiac T2 to detect subclinical myocardial iron underlies its established prognostic value: T2 -guided surveillance predicts cardiac complications and has been associated with markedly improved survival in transfusion-dependent thalassemia [15,16]. These considerations are reflected in international recommendations, and the present findings support the incorporation of routine MRI-based liver and cardiac iron quantification into thalassemia care alongside serum ferritin [17].

The study has several strengths. It provided a focused, organ-specific evaluation of both hepatic and cardiac iron in transfusion-dependent beta-thalassemia major patients using MRI rather than relying on indirect biochemical markers alone, and it simultaneously

assessed serum ferritin, liver T2 , LIC, and cardiac T2 , allowing direct comparison between conventional laboratory assessment and advanced imaging. The analysis extended beyond descriptive frequencies to include correlation analysis, categorical association testing, ANOVA, and multiple linear regression, adding analytical depth, and it reported the distribution of severity categories rather than mean values alone, improving clinical applicability. The equal sex distribution and broad age range (8–30 years) enhanced representativeness across pediatric, adolescent, and young-adult patients.

Certain limitations should be considered. The sample size of 38 patients restricts statistical power and generalizability, and the cross-sectional design captured only a single time point, precluding assessment of longitudinal progression or chelation response. Several subgroups, particularly moderate and severe LIC and cardiac T2 categories, contained very few patients, which may have affected the stability of category-wise estimates. The study relied on serum ferritin, which is influenced by inflammation and liver dysfunction, and did not incorporate detailed treatment variables such as specific chelation regimen, adherence, transfusion frequency, splenectomy status, or cardiac functional indices. As a single-institution cohort without histopathological comparison, the findings should be interpreted as institution-based evidence requiring broader multicentric validation.

CONCLUSION

MRI-based quantification of hepatic and cardiac iron provided clinically relevant, organ-specific information in transfusion-dependent beta-thalassemia major and correlated significantly with serum ferritin. Although the mean serum ferritin was 828.75 ± 324.96 ng/mL and most patients had ferritin below 1000 ng/mL, MRI revealed near-universal hepatic iron overload and cardiac iron overload in a clinically important minority. Serum ferritin correlated significantly with liver T2 , LIC, and cardiac T2 , and LIC and ferritin were independent predictors of cardiac T2 , whereas age and transfusion duration were not. These findings indicate that serum ferritin remains a useful and accessible screening marker of systemic iron burden but cannot replace MRI for detecting subclinical organ siderosis, grading severity, and guiding individualized chelation. Combined use of serum ferritin and MRI is recommended for early detection, risk stratification, and prevention of long-term hepatic and cardiac complications in beta-thalassemia major.

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