Research Article

Received: 28 September 2026
Accepted: 12 November 2026
Published: 19 November 2026

Correlation Between Serum Ferritin Levels and Cardiac Ejection Fraction in Children With Thalassemia Major

Hafiza Tarum Naveed
Department of Pediatrics, Holy Family Hospital, Rawalpindi Medical University, Rawalpindi, Pakistan; htarum.naveed@gmail.com

Naghmana Iftikhar
Department of Pediatrics, Holy Family Hospital, Rawalpindi Medical University, Rawalpindi, Pakistan

Israr Liaquat
Assistant Professor, Department of Pediatrics, Holy Family Hospital, Rawalpindi Medical University, Rawalpindi, Pakistan

Huma Ahmed
Department of Pediatrics, Holy Family Hospital, Rawalpindi Medical University, Rawalpindi, Pakistan

Cite this article:

H. T. Naveed et al. (2026). Correlation Between Serum Ferritin Levels and Cardiac Ejection Fraction in Children With Thalassemia Major. Revista Cultura Científica, (24), pp. 2722–2732. https://doi.org/10.70517/revcc2624218

2026 © The Author(s). Published by Revista Cultura Científica. This article is published as open access under the Creative Commons Attribution 4.0 International (CC BY 4.0) license (http://creativecommons.org/licenses/by/4.0/).

Abstract

Beta-thalassemia major is a hereditary, transfusion-dependent blood disorder in which repeated red blood cell transfusions cause progressive systemic iron accumulation, potentially affecting cardiac function. The objective of this study was to assess the correlation between serum ferritin levels and left ventricular ejection fraction (LVEF) in children with thalassemia major. This cross-sectional study was conducted in the Department of Pediatrics, Holy Family Hospital, Rawalpindi, and included 120 children aged 5–18 years who had undergone more than 10 blood transfusions and were receiving iron chelation therapy. Serum ferritin concentrations were measured using a standardized automated immunoassay, and LVEF was evaluated by transthoracic echocardiography. The mean age was 11.3 $\pm$ 3.6 years, and 67 participants (55.8%) were male. The median serum ferritin concentration was 3185 ng/mL (interquartile range: 2240–4410 ng/mL), whereas the mean LVEF was 58.1 $\pm$ 6.4%. A statistically significant, weak inverse correlation was observed between serum ferritin and LVEF ($r = -0.211$, $p = 0.021$). Mean LVEF declined across increasing ferritin categories, from 60.6 $\pm$ 5.3% in children with ferritin <2000 ng/mL to 56.0 $\pm$ 6.8% in children with ferritin $\geq$4000 ng/mL ($p = 0.010$). These findings indicate an association between higher serum ferritin concentrations and lower LVEF in this pediatric clinical population; they do not establish a causal relationship or directly demonstrate cardiac iron deposition. Regular monitoring of iron burden alongside clinical and cardiac assessment may support the identification of children requiring further evaluation and appropriate review of chelation therapy.

Keywords: Thalassemia major; Serum ferritin; Iron overload; Ejection fraction; Cardiac dysfunction; Children

1. INTRODUCTION

Beta-thalassemia major is a severe inherited disorder of hemoglobin synthesis, generally resulting from pathogenic variants that reduce or eliminate beta-globin production. The resulting imbalance in globin-chain synthesis produces ineffective erythropoiesis, chronic anemia, and, in affected children, a need for regular red blood cell transfusions. Although transfusion therapy improves oxygen delivery and supports growth and survival, repeated transfusions contribute substantial quantities of iron to the body. Humans have no regulated mechanism for eliminating excessive iron, and iron may accumulate in the liver, endocrine tissues, and myocardium. Cardiac complications associated with iron overload remain important causes of morbidity in transfusion-dependent beta-thalassemia, making careful surveillance of cardiac health a central aspect of ongoing treatment [1, 2].

Echocardiography provides a noninvasive assessment of cardiac structure and function, and left ventricular ejection fraction (LVEF) is a widely reported indicator of systolic performance. LVEF represents the proportion of end-diastolic left ventricular blood volume ejected during ventricular contraction. A reduction in LVEF may indicate established systolic impairment, although relatively normal values do not necessarily exclude early myocardial injury. Previous comparisons of children with beta-thalassemia major and age-matched controls have demonstrated differences in multiple echocardiographic parameters. In one comparative study of 50 affected children and 50 controls, mean ejection fraction was lower in the thalassemia group ($63.42 \pm 5.17\%$ versus $68.12 \pm 2.5\%$), supporting the importance of systematic cardiac evaluation [3].

Serum ferritin is an accessible laboratory indicator used in the assessment and monitoring of systemic iron burden. Ferritin generally increases with iron accumulation, but it is also an acute-phase reactant affected by inflammation, liver injury, and other clinical conditions. Consequently, a single ferritin value does not reliably quantify cardiac iron deposition, and its relationship with echocardiographic function is not uniform across patients or clinical settings [4]. This distinction matters when assessing cardiac risk in children who have undergone repeated transfusions and who may have differing durations or levels of adherence to iron chelation therapy. Both serial ferritin measurements and objective cardiac assessment are valuable, but their results should be interpreted together rather than treated as interchangeable measurements.

Published findings concerning serum ferritin and cardiac function have been inconsistent. A 2023 cross-sectional study from Kolkata, India, involving 85 children with beta-thalassemia major found a negative relationship between serum ferritin and ejection fraction and reported associations with several additional echocardiographic measurements [1]. In a pediatric cohort from Surabaya, Indonesia, a separate investigation of 45 children with transfusion-dependent thalassemia reported an inverse relationship between ferritin concentration and ejection fraction, as well as associations with other cardiac measurements, including tricuspid annular plane systolic excursion and the E/A ratio [4]. These investigations support consideration of serum ferritin as part of a broader cardiac assessment, although their populations, analytic approaches, and measured outcomes differ.

Other clinical studies have reported less consistent associations. A retrospective investigation involving 131 patients with transfusion-dependent thalassemia in Slemani, Iraq, examined relationships between serum ferritin and echocardiographic findings, illustrating the importance of considering individual clinical characteristics and the methods used to assess ventricular function [5]. A separate pediatric investigation at Dr. Soetomo Hospital in Indonesia likewise evaluated ferritin levels alongside cardiac measurements, adding to the evidence for possible variation between clinical populations [6]. Advanced echocardiographic techniques, including myocardial deformation imaging, may identify functional changes not readily apparent from conventional LVEF measurements alone [7]. Together, these findings justify further evaluation of the association between ferritin concentrations and conventional measures of cardiac function in children receiving transfusion and chelation therapy.

In Pakistan, the accessibility of routine ferritin testing and echocardiography makes their combined clinical interpretation particularly relevant. Establishing the magnitude and direction of their association may help clinicians recognize patients who warrant more detailed cardiac investigation while acknowledging the diagnostic limitations of serum ferritin. The objective of this cross-sectional study was therefore to determine the correlation between serum ferritin levels and left ventricular ejection fraction in children with beta-thalassemia major at a tertiary-care hospital in Rawalpindi. The study additionally examined the distribution of ferritin concentrations, the frequency of reduced LVEF, and relationships with relevant clinical and transfusion characteristics.

2. METHODOLOGY

This descriptive analytical cross-sectional study was conducted in the Department of Pediatrics, Holy Family Hospital, Rawalpindi, Pakistan, between June 2026 and September 2026. A sample of 120 participants was enrolled. The original sample-size planning was documented as having been undertaken with the MedCalc sample-size calculator, using an anticipated correlation coefficient of $r = -0.211$, a two-sided significance level of 5% (α=0.05), and 80% statistical power ($1-\beta$=0.80). Recruitment was based on non-probability consecutive sampling, and eligible children attending during the

study period were approached sequentially until the intended number of participants had been enrolled. The observational nature of the study allowed the relationship between serum ferritin and cardiac performance to be evaluated at a defined clinical assessment rather than through prospective follow-up.

Children aged 5–18 years of either sex with a diagnosis of transfusion-dependent beta-thalassemia major were eligible. The clinical eligibility criteria included a history of more than 10 blood transfusions, documented iron chelation treatment, and an available serum ferritin measurement or a measurement performed during the study assessment. Exclusion criteria included congenital heart disease or other clinically significant pre-existing cardiovascular disorders, active infections or inflammatory diseases that might affect serum ferritin concentrations, and known non-transfusion-related iron-overload disorders, including hereditary hemochromatosis. Children who had undergone liver transplantation were also excluded. All enrolled children were receiving prescribed chelation treatment; adherence was assessed separately and classified as regular or suboptimal for comparison between participants. These classifications describe the reported treatment history and were not used to remove participants from the analysis.

Following institutional ethical approval, eligible children attending the pediatric hematology clinic were screened using the predefined inclusion and exclusion criteria. Written informed consent was obtained from parents or legal guardians, and age-appropriate assent was sought where applicable under institutional requirements. Demographic and clinical information was recorded on a structured data collection proforma, including age, sex, body weight, duration of thalassemia, age at commencement of transfusion therapy, transfusion duration, transfusion frequency, total transfusion history, type and duration of iron chelation treatment, and reported adherence to chelation. These characteristics were collected to describe the enrolled patients and to explore possible associations with ferritin concentration and LVEF. Recording the treatment history also assisted in interpreting differences among children with varying cumulative transfusion exposure.

Serum ferritin and cardiac function were assessed at the study encounter or within a predefined short interval. Approximately 3–5 mL of venous blood was obtained using aseptic technique and processed in the hospital laboratory. Serum ferritin concentration was measured using the laboratory's standardized automated immunoassay and reported in ng/mL. Transthoracic echocardiography was undertaken by a consultant cardiologist or an experienced echocardiographer using the clinical examination protocol. Two-dimensional and M-mode echocardiographic assessments were conducted while the child was at rest. Left ventricular ejection fraction, expressed as a percentage, was the principal indicator of systolic cardiac function. The laboratory and cardiac measurements were linked for each participant to facilitate correlation analysis. Blinding of the echocardiographic assessors to serum ferritin results was not documented in the available study description.

Data were entered and analyzed using IBM SPSS Statistics, version 28.0. Data completeness and internal consistency were assessed before analysis. The distribution of continuous variables was examined using the Shapiro–Wilk test and graphical methods, including histograms and quantile–quantile plots. Normally distributed variables were summarized as means and standard deviations, whereas variables with non-normal distributions were summarized as medians and interquartile ranges. Categorical characteristics were presented as frequencies and percentages. Pearson's correlation coefficient was specified for approximately normally distributed variables with a linear relationship, with Spearman's rank correlation considered when these assumptions were not met. Differences between ferritin categories and LVEF groups were evaluated using the statistical tests reported with the results. Multiple linear regression was used to examine the association of serum ferritin with LVEF alongside selected clinical covariates. Statistical significance was defined as a two-sided p-value <0.05. Correlation coefficients, regression estimates, corresponding confidence intervals when available, and p-values were reported to describe the direction, magnitude, and precision of the associations.

3. RESULTS

The demographic and clinical characteristics of the 120 enrolled children are presented in Table 1. The mean age of the children with thalassemia major was 11.3 ± 3.6 years, with a slight male predominance as 67 (55.8%) were male and 53 (44.2%) were female. The mean body weight was 31.8 ± 10.7 kg. The average duration of thalassemia was 9.4 ± 3.8 years, while the mean duration of transfusion therapy was 8.9 ± 3.7 years. Participants received an average of 15.1 ± 3.4 transfusions per year, and the mean age at first transfusion was 10.7 ± 5.8 months.

As summarized in Table 2, the median serum ferritin level was 3185 ng/mL, with an interquartile range of 2240–4410 ng/mL. The corresponding mean LVEF was $58.1 \pm 6.4\%$, and the detailed distribution of ejection fraction categories is shown in the same table. Ferritin levels below 2000 ng/mL were observed in 25 (20.8%) children, while 54 (45.0%) had levels between 2000 and 3999 ng/mL and 41 (34.2%) had levels of 4000 ng/mL or higher.

Table 3 presents the comparison of mean LVEF across the three serum ferritin categories. Children with ferritin levels below 2000 ng/mL had the highest mean LVEF at $60.6 \pm 5.3\%$, followed by $58.5 \pm 6.0\%$ among those with ferritin levels of 2000–3999 ng/mL and $56.0 \pm 6.8\%$ among those with ferritin levels of 4000 ng/mL or higher. The difference across the three groups was statistically significant ($F = 4.79$, $p = 0.010$).

Table 1. *Baseline Demographic and Clinical Characteristics of Children With Thalassemia Major (n = 120)*

Variable	n (%) / Mean ± SD
Age, years	11.3 ± 3.6
Male	67 (55.8%)
Female	53 (44.2%)
Weight, kg	31.8 ± 10.7
Duration of thalassemia, years	9.4 ± 3.8
Duration of transfusion therapy, years	8.9 ± 3.7
Transfusions per year	15.1 ± 3.4
Age at first transfusion, months	10.7 ± 5.8
Duration of chelation therapy, years	7.1 ± 3.5
Regular chelation adherence	79 (65.8%)
Suboptimal chelation adherence	41 (34.2%)

Table 2. *Serum Ferritin Levels and Cardiac Ejection Fraction Among Study Participants (n = 120)*

Variable	n (%) / Mean ± SD / Median (IQR)
Serum ferritin, ng/mL	3185 (2240–4410)
Ferritin <2000 ng/mL	25 (20.8%)
Ferritin 2000–3999 ng/mL	54 (45.0%)
Ferritin ≥4000 ng/mL	41 (34.2%)
Left ventricular ejection fraction, %	58.1 ± 6.4
LVEF ≥55%	88 (73.3%)
LVEF 50–54%	21 (17.5%)
LVEF <50%	11 (9.2%)

Table 3. *Comparison of Left Ventricular Ejection Fraction Across Serum Ferritin Categories*

Serum ferritin category	n	LVEF, mean ± SD (%)	Test statistic	p-value
<2000 ng/mL	25	60.6 ± 5.3	F = 4.79	0.010
2000–3999 ng/mL	54	58.5 ± 6.0		
≥4000 ng/mL	41	56.0 ± 6.8		

The distribution of serum ferritin concentrations is illustrated in Figure 1, complementing the categorical results provided in Table 2.

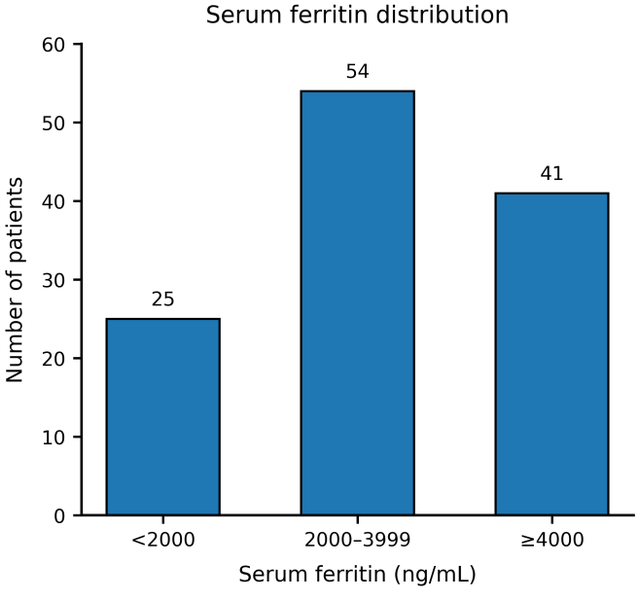


Figure 1. *Distribution of Serum Ferritin Levels Among Children With Thalassemia Major*

The relationships between serum ferritin and the cardiac and clinical variables are detailed in Table 4. Serum ferritin showed a statistically significant, weak inverse correlation with left ventricular ejection fraction (r = −0.211, p = 0.021), indicating that higher ferritin levels were associated with lower cardiac ejection fraction. Serum ferritin also showed significant positive correlations with age (r = 0.284, p = 0.002), duration of transfusion therapy (r = 0.326, p < 0.001), and number of transfusions per year (r = 0.193, p = 0.035). The correlation between serum ferritin and duration of chelation therapy was weak and did not reach statistical significance (r = 0.174, p = 0.058).

Table 4. *Correlations of Serum Ferritin With Cardiac and Clinical Variables*

Variable pair	Correlation coefficient (r)	p-value
Serum ferritin vs LVEF	−0.211	0.021
Serum ferritin vs age	0.284	0.002
Serum ferritin vs duration of transfusion	0.326	<0.001
Serum ferritin vs transfusions per year	0.193	0.035
Serum ferritin vs duration of chelation	0.174	0.058

A comparison of children with preserved and reduced left ventricular ejection fraction is provided in Table 5. The mean age was significantly higher among children with LVEF <50% than among those with LVEF ≥50% (14.0 ± 2.7 vs 11.0 ± 3.5 years; t = 2.78, p = 0.006). Median serum ferritin was also significantly higher in the reduced-LVEF group (4720 [3510–5840] ng/mL vs 3010 [2180–4140] ng/mL; U = 326, p = 0.012). Similarly, the mean duration of transfusion therapy was longer among children with LVEF <50% (12.0 ± 2.9 vs 8.6 ± 3.6 years; t = 2.99, p = 0.003). Suboptimal chelation adherence was more frequent in children with reduced ejection fraction, occurring in 7 (63.6%) compared with 34 (31.2%) children with LVEF ≥50% (χ^2 = 4.79, p = 0.029).

Table 5. *Comparison of Children According to Cardiac Ejection Fraction Status*

Variable	LVEF ≥50% (n = 109)	LVEF <50% (n = 11)	Test statistic	p-value
Age, years	11.0 ± 3.5	14.0 ± 2.7	t = 2.78	0.006
Serum ferritin, ng/mL, median (IQR)	3010 (2180–4140)	4720 (3510–5840)	U = 326	0.012
Duration of transfusion, years	8.6 ± 3.6	12.0 ± 2.9	t = 2.99	0.003
Suboptimal chelation adherence	34 (31.2%)	7 (63.6%)	χ^2 = 4.79	0.029

Figure 2 illustrates the distribution of left ventricular ejection fraction, providing a visual summary of the cardiac outcome categories described in Table 2.

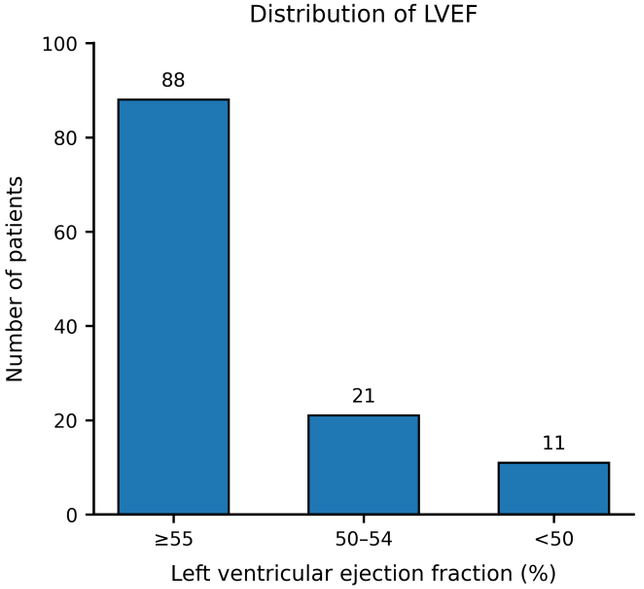


Figure 2. *Distribution of Left Ventricular Ejection Fraction Among Study Participants*

The adjusted regression coefficients for LVEF are presented in Table 6. Each 1000 ng/mL increase in serum ferritin was associated with a 0.72 percentage-point decrease in LVEF (β = −0.72, 95% CI: −1.34 to −0.10; p = 0.023). Longer duration of transfusion therapy was also independently associated with lower LVEF (β = −0.31, 95% CI: −0.62 to −0.01;

p = 0.044). In contrast, regular chelation adherence was positively associated with cardiac ejection fraction (β = 2.18, 95% CI: 0.42–3.94; p = 0.016). Age was not independently associated with LVEF after adjustment for the other variables (β = −0.21, 95% CI: −0.49 to 0.07; p = 0.138).

Table 6. *Multiple Linear Regression Analysis of Predictors of Left Ventricular Ejection Fraction*

Predictor	Regression coefficient (β)	95% CI	p-value
Serum ferritin, per 1000 ng/mL increase	−0.72	−1.34 to −0.10	0.023
Age, years	−0.21	−0.49 to 0.07	0.138
Duration of transfusion, years	−0.31	−0.62 to −0.01	0.044
Regular chelation adherence	2.18	0.42 to 3.94	0.016

The scatter plots in Figure 3 show the relationships between ferritin and selected cardiac and clinical variables. They should be interpreted together with the numerical correlation coefficients in Table 4, recognizing that the underlying patient-level measurements are necessary to verify the plotted point distributions.

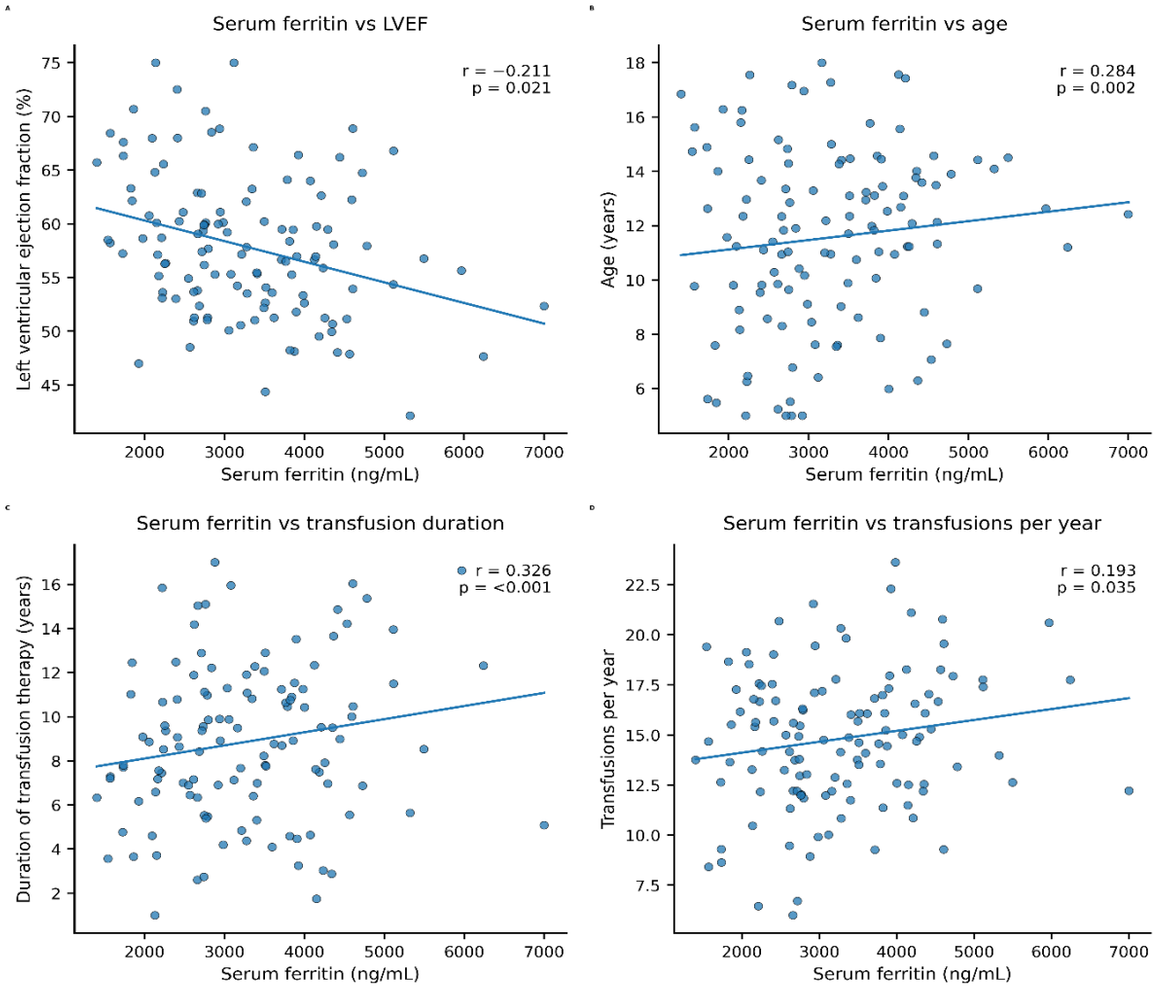


Figure 3. *Scatter Plots Showing the Relationship Between Serum Ferritin Levels and Selected Cardiac and Clinical Variables in Children With Thalassemia Major*

4. DISCUSSION

The principal finding of this cross-sectional study was a statistically significant but weak inverse association between serum ferritin concentration and left ventricular ejection fraction among 120 children with beta-thalassemia major. The observed correlation coefficient was r = −0.211 (p = 0.021), indicating that higher ferritin values tended to be accompanied by lower LVEF. This finding is relevant in the context of repeated transfusions, progressive iron accumulation, and the possibility of cardiac consequences in patients receiving long-term supportive care. Nevertheless, the magnitude of this relationship was modest, and the data do not establish that the observed LVEF differences were caused by myocardial

iron deposition. Previous research involving children treated with iron-chelating medicines has similarly demonstrated the clinical importance of assessing both serum ferritin and cardiac performance, although chelation exposure and treatment response may differ considerably across individuals [8].

The median ferritin concentration in the present sample was 3185 ng/mL, and 95 of the 120 participants (79.2%) had ferritin levels of at least 2000 ng/mL. Such concentrations suggest a considerable systemic iron burden in this treatment population but should not be viewed as direct measurements of myocardial iron. Tissue Doppler echocardiographic studies in patients with thalassemia have shown that myocardial functional changes can occur in association with altered indices of cardiac iron burden, including changes that may not be captured adequately by conventional ejection fraction alone [9]. The relationship among ferritin, myocardial iron, and cardiac function is therefore complex. Cardiac T2* magnetic resonance imaging can provide additional information about myocardial iron when this modality is clinically indicated and available [10]. These considerations support careful interpretation of high ferritin values alongside symptoms, chelation history, and cardiac imaging results.

Mean LVEF decreased across the three ferritin categories. The mean values were $60.6 \pm 5.3\%$ in children with ferritin <2000 ng/mL, $58.5 \pm 6.0\%$ among those with ferritin of 2000–3999 ng/mL, and $56.0 \pm 6.8\%$ among those with ferritin $\geq$4000 ng/mL. This gradient is consistent with the overall negative correlation and suggests that the observed relationship was present across clinically relevant ranges of ferritin concentration. However, measurements derived from different ferritin categories can be influenced by age, cumulative transfusion exposure, chelation adherence, and inflammatory status. Published comparisons of patients with beta-thalassemia major and intermedia have also demonstrated differences in cardiac function and arrhythmia patterns, highlighting the importance of considering disease phenotype and treatment history when interpreting echocardiographic findings [11]. Accordingly, the ferritin categories in this study should be understood as descriptive groups rather than validated thresholds for diagnosing cardiac iron overload.

Most participants had preserved measured systolic function: 88 children (73.3%) had an LVEF of at least 55%, 21 (17.5%) had an LVEF of 50–54%, and 11 (9.2%) had an LVEF below 50%. Children in the reduced-LVEF group had a higher median ferritin concentration (4720 versus 3010 ng/mL), were older, and had a longer duration of transfusion therapy than those with an LVEF of 50% or greater. The mean duration of transfusion therapy was 12.0 ± 2.9 years among those with reduced LVEF compared with 8.6 ± 3.6 years among the remaining children. Previous pediatric cardiac investigations have stressed the importance of serially monitoring cardiac parameters in transfusion-dependent thalassemia, particularly when transfusion exposure has been prolonged [12]. More recent pediatric studies have also examined the association between serum ferritin and electrocardiographic or echocardiographic indicators of cardiac dysfunction [13]. These findings are consistent with the view that cardiac assessment should be considered alongside a longitudinal review of transfusion history rather than determined by one laboratory result.

The association with chelation adherence deserves particular attention. Suboptimal adherence was recorded in 41 participants (34.2%) overall, including 7 of 11 children (63.6%) with LVEF <50% and 34 of 109 children (31.2%) with LVEF $\geq$50%. Although an association was reported in the manuscript, the smaller group contained only 11 participants, and the statistical result may be sensitive to the method used to analyze the contingency table. Furthermore, adherence was a descriptive clinical classification, and the data do not establish whether differences in adherence preceded the observed cardiac findings. Research assessing serum ferritin and the effects of transfusion and chelation treatment likewise supports continued monitoring of iron burden, while recognizing that the relationship between systemic and cardiac iron accumulation is not perfectly uniform [14].

In the reported multiple linear regression model, an increase of 1000 ng/mL in serum ferritin was associated with a 0.72 percentage-point decrease in LVEF after adjustment for the listed variables (β=-0.72; 95% CI: -1.34 to -0.10; p = 0.023). Longer transfusion duration was also associated with lower LVEF (β=-0.31; 95% CI: -0.62 to -0.01; p = 0.044), whereas regular chelation adherence was associated with higher LVEF (β=2.18; 95% CI: 0.42–3.94; p = 0.016). These adjusted findings suggest that ferritin concentration was related to LVEF beyond the other measured covariates, but interpretation depends on the completeness and specification of the original regression model. In particular, the cross-sectional design does not establish that reducing ferritin would necessarily produce a corresponding improvement in ejection fraction.

Where resources permit, cardiac magnetic resonance imaging, including validated methods for myocardial iron assessment, offers information that is not provided by routine serum ferritin testing. Prospective magnetic resonance studies have examined iron deposition, cardiac morphology, and functional changes across thalassemia populations with different transfusion requirements [15]. Broader clinical recommendations for transfusion-dependent beta-thalassemia also emphasize comprehensive management and appropriate iron chelation to reduce complications of long-term transfusion therapy [16]. A systematic review and meta-analysis of the relationship between serum ferritin and cardiac T2* imaging identified an overall association but also demonstrated the importance of population differences and the imperfect correspondence of these measurements [17]. Additional work using multiparametric cardiac magnetic resonance has highlighted the prognostic relevance of imaging-based assessment [18]. Technical consensus recommendations further support standardized

acquisition and interpretation of T2* and related cardiovascular magnetic resonance measurements [19].

In the local clinical setting, repeated ferritin measurements and routine echocardiography may provide complementary and more accessible information for reviewing the health of children with transfusion-dependent thalassemia. Their combined use can contribute to the recognition of patients requiring additional specialist evaluation, but neither a high ferritin concentration nor a modestly reduced LVEF alone provides a definitive diagnosis of cardiac siderosis. A comprehensive assessment should incorporate the child's clinical condition, transfusion history, iron chelation regimen, laboratory trends, and appropriate imaging findings. The present results support further investigation of this relationship in larger prospective cohorts with standardized echocardiographic protocols and direct measures of myocardial iron whenever feasible.

5. LIMITATIONS

Several methodological limitations should be considered when interpreting the results. First, the cross-sectional design does not establish the temporal sequence between ferritin elevation, chelation adherence, transfusion exposure, and changes in cardiac performance. A single-center sample of 120 children also limits generalizability to other pediatric thalassemia populations, particularly those treated in centers with different transfusion and monitoring practices. Second, serum ferritin is influenced by inflammatory status, hepatic disease, and other conditions; therefore, it cannot directly quantify myocardial iron deposition or replace cardiac T2* magnetic resonance imaging. Third, conventional LVEF was the principal echocardiographic outcome, while potentially more sensitive measures, including myocardial strain and tissue Doppler indices, were not reported. The use of LVEF alone may overlook early functional changes in patients whose systolic performance remains within conventional reference ranges.

The details of the original sample-size calculation, the type of correlation test used, and the assumptions underlying the adjusted regression were not fully documented in the available summary results. The method used to assess chelation adherence, as well as whether the echocardiographer was blinded to ferritin results, should be documented explicitly where original study records permit. Finally, the small number of children with markedly reduced LVEF means that subgroup comparisons may be imprecise. Larger prospective studies incorporating serial ferritin measurements, standardized echocardiographic evaluations, and myocardial T2* imaging would be useful to clarify the relationship between systemic iron burden and cardiac function over time.

6. CONCLUSION

This study identified a statistically significant, weak inverse correlation between serum ferritin concentration and left ventricular ejection fraction among children with transfusion-dependent beta-thalassemia major. Children in higher serum ferritin categories had lower mean LVEF values, and the observed association persisted in the reported adjusted regression analysis. A longer duration of transfusion therapy and suboptimal adherence to iron chelation were also associated with less favorable indicators of systolic cardiac performance. Although most participants had preserved LVEF, a clinically relevant minority had values below 50%, emphasizing the importance of identifying children who may benefit from closer cardiac assessment.

These findings support the use of serum ferritin monitoring alongside clinical review and periodic echocardiography as complementary components of care. The results should not be interpreted as demonstrating a causal relationship or as establishing ferritin as a substitute for direct assessment of myocardial iron. Prospective follow-up and additional investigations, including cardiac T2* magnetic resonance imaging where available, would help determine whether combined monitoring improves the early identification and management of cardiac complications in this pediatric population.

Author Contributions

All authors contributed to the conception and design of the study, the preparation of the manuscript, and its critical revision for important intellectual content. All authors reviewed and approved the final manuscript and agree to be accountable for the integrity of their respective contributions.

Conflicts of Interest

The authors declare that they have no financial or nonfinancial competing interests relevant to the conduct, analysis, or reporting of this study.

Funding

No specific financial support was received from public, commercial, or not-for-profit funding agencies for this study.

Ethics Approval and Informed Consent

The study was conducted following approval by the relevant institutional ethics committee. Written informed consent was obtained from the parents or legal guardians of participating children, and age-appropriate assent was obtained where required.

Data Availability

The availability of de-identified study data is subject to applicable institutional policies, ethical permissions, and safeguards for the confidentiality of pediatric participants. Requests concerning access should be directed to the corresponding author.

REFERENCES

[1] Das, Eshita, et al. "Correlation Between Serum Ferritin Levels and Echocardiographic Changes in Children with Beta-thalassaemia Major—A Cross-sectional Analytical Study." *Journal of Clinical and Diagnostic Research*, vol. 17, no. 5, 2023, pp. SC01–SC05. https://doi.org/10.7860/JCDR/2023/62334.17781.

[2] Khanum, Shahana, and A. N. Thobbi. "Study of Significance of Echocardiography and Estimation of Serum Ferritin Levels in Beta-thalassemia Major Patients." *Al Ameen Journal of Medical Sciences*, vol. 16, no. 4, 2023, pp. 334–42. https://ajms.alameenmedical.org/ArticlePDFs/10%20AJMS%20V16.N4.2023%20p%20334-342.pdf.

[3] Rao, Jayashree Satish, and Nagendra K. "A Study Conducted in a Tertiary Care Hospital to Assess the Cardiac Function in Paediatric Beta Thalassemia Major Patients and Correlation with Serum Ferritin Levels Which Are Indicative of Chelation Status of the Patients." *Indian Journal of Child Health*, vol. 10, no. 6, 2023, pp. 73–76. https://doi.org/10.32677/ijch.v10i6.4040.

[4] Dewanti, Carrina Nenggar, et al. "The Correlation between Serum Ferritin Levels and Impaired Heart Function in Children with Transfusion Dependent Thalassemia." *GSC Biological and Pharmaceutical Sciences*, vol. 16, no. 2, 2021, pp. 190–95. https://doi.org/10.30574/gscbps.2021.16.2.0239.

[5] Karim, Saz Rasheed, et al. "The Relation between Serum Ferritin Level and Echocardiographic Findings in Transfusion Dependent Thalassemic Patients in Slemani City, Kurdistan Region of Iraq." *Advanced Medical Journal*, vol. 9, no. 2, 2024, pp. 86–94. https://doi.org/10.56056/amj.2024.260.

[6] Frans, Evisina Hanafiati, et al. "Correlation between Serum Ferritin and Heart Function in Children with Major Thalassemia at Dr. Soetomo Hospital." *Indonesian Journal of Clinical Pathology and Medical Laboratory*, vol. 26, no. 1, 2019, pp. 96–101. https://doi.org/10.24293/ijcpml.v26i1.1401.

[7] Eroğlu, Ayşe Güler, et al. "Evaluation of Left Ventricular Function and Myocardial Deformation in Children with Beta-thalassemia Major by Real-Time Three-Dimensional (Four-Dimensional) and Speckle Tracking Echocardiography." *Echocardiography*, vol. 39, no. 10, 2022, pp. 1307–15. https://doi.org/10.1111/echo.15453.

[8] Tripathy, Isita, et al. "Comparative Efficacy and Safety between Deferiprone and Deferasirox with Special Reference to Serum Ferritin Level and Cardiac Function in Bengali β-Thalassemia Major Children." *Hemoglobin*, vol. 45, no. 5, 2021, pp. 296–302. https://doi.org/10.1080/03630269.2021.1999258.

[9] Silvilairat, Suchaya, et al. "Early Detection of Ventricular Dysfunction by Tissue Doppler Echocardiography Related to Cardiac Iron Overload in Patients with Thalassemia." *The International Journal of Cardiovascular Imaging*, vol. 37, no. 1, 2021, pp. 91–98. https://doi.org/10.1007/s10554-020-01949-8.

[10] El-Shanshory, Mohammed, et al. "Cardiac Iron Overload by MRI in Children with B-Thalassemia Major and Its Correlation with Cardiac Function by Echocardiography." *Journal of Pediatric Hematology/Oncology*, vol. 42, no. 6, 2020, pp. 398–402. https://doi.org/10.1097/MPH.0000000000001786.

[11] Amoozgar, Hamid, et al. "A Comparison of Heart Function and Arrhythmia in Clinically Asymptomatic Patients with Beta Thalassemia Intermedia and Beta Thalassemia Major." *Hematology*, vol. 22, no. 1, 2017, pp. 25–29. https://doi.org/10.1080/10245332.2016.1226699.

[12] Oztarhan, Kazim, et al. "Assessment of Cardiac Parameters in Evaluation of Cardiac Functions in Patients with Thalassemia Major." *Pediatric Hematology and Oncology*, vol. 29, no. 3, 2012, pp. 220–34. https://doi.org/10.3109/08880018.2012.671449.

[13] Kasaudhan, Vipin, et al. "Correlation Between Serum Ferritin and Electrocardiographic and Echocardiographic Markers of Cardiac Dysfunction in Children with Transfusion-Dependent β-Thalassemia Major." *Cureus*, vol. 18, no. 9, 20 Sept. 2026, article e116573. https://doi.org/10.7759/cureus.116573.

[14] Bhalodiya, Vijay R., et al. "Correlation of Serum Ferritin Level in Transfusion-Dependant Thalassemia Major Patients: A Study at a Medical College Affiliated Hospital in Gujarat Region." *International Journal of Contemporary Pediatrics*, vol. 10, no. 3, 2023, pp. 330–33. https://doi.org/10.18203/2349-3291.ijcp20230429.

[15] Meloni, Antonella, et al. "Prospective Assessment of Cardiac Iron Deposition, Morphology, and Function by Magnetic Resonance Imaging in Non-Transfusion-Dependent and Neo-Transfusion-Dependent Thalassemia." *Journal of Clinical Medicine*, vol. 14, no. 12, 2025, article 4020. https://doi.org/10.3390/jcm14124020.

[16] El-Beshlawy, Amal, et al. "Management of Transfusion-Dependent β-Thalassemia (TDT): Expert Insights and Practical Overview from the Middle East." *Blood Reviews*, vol. 63, 2024, article 101138. https://doi.org/10.1016/j.blre.2023.101138.

[17] Hosseini-Bensenjan, Mahnaz, et al. "Correlation of Serum Ferritin Level with Heart T2 MRI in Transfusion Dependent Thalassemia: A Systematic Review and Meta-Analysis." *Clinical Laboratory*, vol. 69, no. 6, 2023. https://doi.org/10.7754/Clin.Lab.2022.220916.

[18] Meloni, Antonella, et al. "Prognostic Role of Multiparametric Cardiac Magnetic Resonance in Neo Transfusion-Dependent Thalassemia." *Journal of Clinical Medicine*, vol. 13, no. 5, 2024, article 1281. https://doi.org/10.3390/jcm13051281.

[19] Messroghli, Daniel R., et al. "Clinical Recommendations for Cardiovascular Magnetic Resonance Mapping of T1, T2, T2* and Extracellular Volume: A Consensus Statement by the Society for Cardiovascular Magnetic Resonance (SCMR) Endorsed by the European Association for Cardiovascular Imaging (EACVI)." *Journal of Cardiovascular Magnetic Resonance*, vol. 19, no. 1, 2017, article 75. https://doi.org/10.1186/s12968-017-0389-8.