International Journal of Medicine
pISSN 1468-3814 | eISSN 2667-7008
https://theinternationalmedicine.com/

Original Researcher Article *DOI: 10.61336/im/26-07-108*

LIPID PROFILE ABNORMALITIES IN TRANSFUSION-DEPENDENT BETA-THALASSEMIA MAJOR CHILDREN AND THEIR CORRELATION WITH SERUM FERRITIN LEVELS: A CROSS-SECTIONAL OBSERVATIONAL STUDY.

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Received: 02-06-2026
Revised: 22-06-2026
Accepted: 06-07-2026
Published: 17-07-2026

Abstract

Background: Transfusion-dependent beta-thalassemia major is associated with chronic iron overload leading to metabolic and hepatic dysfunction. Dyslipidemia is increasingly recognized, but its correlation with iron burden remains inconsistent.***Objectives:*** To evaluate lipid profile abnormalities in transfusion-dependent beta-thalassemia major children and determine their correlation with serum ferritin levels. ***Materials and Methods:*** This cross-sectional observational study included 120 children aged 6–18 years with transfusion-dependent beta-thalassemia major. Serum ferritin and lipid profile parameters (total cholesterol, triglycerides, LDL, HDL) were assessed over a duration of one year. Atherogenic indices were calculated. Pearson correlation and regression analyses were performed. ***Results:*** The mean serum ferritin level was 3145 ± 1540 ng/mL. Lipid profile showed reduced total cholesterol (96.8 ± 23.4 mg/dL), LDL (43.9 ± 18.9 mg/dL), and HDL (20.6 ± 7.9 mg/dL), with elevated triglycerides (153.9 ± 63.8 mg/dL). Hypocholesterolaemia was observed in 63.3% and hypertriglyceridemia in 55.0% of patients. No significant correlation was found between serum ferritin and lipid parameters ($p > 0.05$), although triglycerides showed a borderline positive correlation ($r = +0.175$, $p = 0.056$). Regression analysis identified age ($\beta = 148.62$, $p = 0.001$), duration of transfusion ($\beta = 132.47$, $p = 0.001$), and triglycerides ($\beta = 6.94$, $p = 0.017$) as significant predictors of ferritin. ***Conclusion:*** Dyslipidaemia is common in transfusion-dependent beta-thalassemia major, characterized by low cholesterol fractions and elevated triglycerides. However serum ferritin did not show a significant linear correlation with lipid parameters, suggesting multifactorial mechanisms.

Keywords: Beta-thalassemia major, serum ferritin, lipid profile, dyslipidaemia, iron overload.

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INTRODUCTION

Beta-thalassemia major is a severe inherited haemoglobin disorder requiring lifelong transfusion support, and repeated transfusions lead to progressive iron overload with multisystem complications.[1,3] The liver plays a central role in lipid synthesis and clearance, so iron-mediated hepatic injury may contribute to dyslipidaemia in transfusion-dependent children.[4,5]A pattern of reduced total cholesterol, LDL, and HDL with relatively elevated triglycerides has been reported in this population. However, there are limited data from India evaluating the relationship between lipid profile abnormalities and iron burden.[6,8].

MATERIALS AND METHODS

This was a cross-sectional observational study conducted over one year in the Department of Paediatrics, MYH and CNBC, MGM Medical College, Indore, after approval by the Institutional Ethics Committee.[9] Written informed consent was obtained from parents or legal guardians, assent was taken from children above 12 years, and confidentiality was maintained.

Children aged 6-18 years with transfusion-dependent beta-thalassemia major confirmed by haemoglobin electrophoresis and receiving regular blood transfusions for at least one year were included. Exclusion criteria were diabetes mellitus or other conditions affecting lipid metabolism, use of drugs that alter lipid levels such as steroids or lipid-lowering agents, and refusal or absence of guardian consent.

A total of 120 children were enrolled. Data were collected on age, sex, age at diagnosis, transfusion history, chelation history, anthropometry, and clinical findings. Laboratory investigations included complete blood count, liver function tests, serum ferritin, and fasting lipid profile comprising total cholesterol, triglycerides, LDL-cholesterol, and HDL-cholesterol.

Atherogenic indices including LDL-C/HDL-C, CRI-I, CRI-II, and the TG/HDL ratio were calculated. Statistical analysis was performed using Microsoft Excel for data entry and SPSS version 25.0 for analysis. Continuous variables were expressed as mean ± standard deviation or median with interquartile range, categorical variables as frequencies and percentages, Pearson correlation was used for ferritin-lipid associations, chi-square tests for categorical comparisons, and multiple linear regressions for predictors of ferritin. [10,11]

RESULTS

A total of 120 transfusion-dependent children with beta-thalassemia major were studied, with a mean age of 10.5 ± 2.7 years and a near-equal sex distribution of 61 females (50.8%) and 59 males (49.2%). Most participants were aged 10-14 years (55.8%), and 56.7% were underweight by BMI-for-age criteria. Mean age at diagnosis was 1.9 ± 2.6 years, and mean duration of transfusion therapy was 8.7 ± 3.2 years.

The mean pre-transfusion haemoglobin was 7.3 ± 2.2 g/dL, with moderate anaemia in 50.8% and severe anaemia in 36.7%. The mean AST and ALT levels were 63.8 ± 36.9 IU/L and 61.2 ± 38.7 IU/L, respectively, suggesting frequent hepatocellular injury in this cohort. Mean serum ferritin was 3145 ± 1540 ng/mL, and 49 children (40.8%) had severe iron overload while 25 (20.9%) had very severe iron overload.

The lipid profile showed low mean total cholesterol (96.8 ± 23.4 mg/dL), low LDL-cholesterol (43.9 ± 18.9 mg/dL), very low HDL-cholesterol (20.6 ± 7.9 mg/dL), and relatively elevated triglycerides (153.9 ± 63.8 mg/dL). Hypocholesterolaemia was present in 76 children (63.3%), hypertriglyceridemia in 66 (55.0%), low LDL-cholesterol in 101 (84.2%), and low HDL-cholesterol in nearly all ferritin strata. Mean CRI-I, CRI-II, and TG/HDL ratios were 5.24 ± 2.48, 2.33 ± 0.98, and 8.99 ± 9.15, respectively.

Serum ferritin had no statistically significant correlation with total cholesterol ($r = 0.068$, $p = 0.458$), triglycerides ($r = 0.175$, $p = 0.056$), LDL-cholesterol, HDL-cholesterol, or atherogenic index. However, across ferritin categories, mean triglycerides increased from 132.6 ± 48.7 mg/dL in the <2500 ng/mL group to 181.5 ± 71.6 mg/dL in the >5000 ng/mL group, and mean atherogenic index rose from 2.14 ± 0.83 to 2.73 ± 1.18. Multiple linear regression identified age, duration of transfusion, and triglycerides as significant predictors of ferritin, whereas total cholesterol, LDL-cholesterol, and HDL-cholesterol were not significant independent predictors.

Table 1: Baseline Characteristics of Study Population (n = 120)

Parameter	Value
Mean age (years)	10.5 ± 2.7
Age group (10–14 years)	67 (55.8%)
Sex (Male)	59 (49.2%)
Sex (Female)	61 (50.8%)
Underweight (BMI-for-age)	68 (56.7%)
Mean age at diagnosis (years)	1.9 ± 2.6
Mean duration of transfusion (years)	8.7 ± 3.2
Mean pre-transfusion Hb (g/dL)	7.3 ± 2.2
Moderate anaemia	61 (50.8%)
Severe anaemia	44 (36.7%)

Table 2: Serum Ferritin and Lipid Profile Parameters

Parameter	Mean ± SD	Median (IQR)	Range
Serum Ferritin (ng/mL)	3145 ± 1540	2894 (1606–4230)	632.9–9203
Total Cholesterol (mg/dL)	96.8 ± 23.4	94.6 (80.3–113.2)	48.0–148.2
Triglycerides (mg/dL)	153.9 ± 63.8	146.2 (110.0–205.3)	29.3–278.1
LDL-C (mg/dL)	43.9 ± 18.9	42.0 (28.0–56.0)	12.4–80.1
HDL-C (mg/dL)	20.6 ± 7.9	21.0 (14.6–26.1)	4.0–52.0

Table 3: Distribution of Lipid Abnormalities

Parameter	Category	n (%)
Total Cholesterol	<100 mg/dL	76 (63.3%)
	100–170 mg/dL	44 (36.7%)
Triglycerides	<150 mg/dL	54 (45.0%)
	≥150 mg/dL	66 (55.0%)
LDL-C	<70 mg/dL	101 (84.2%)
	70–129 mg/dL	19 (15.8%)
HDL-C	<40 mg/dL	119 (≈99%)

Table 4: Correlation of Serum Ferritin with Lipid Parameters

Parameter	Pearson r	p-value	Significance
Total Cholesterol	+0.068	0.458	Not significant
Triglycerides	+0.175	0.056	Not significant
LDL-C	+0.041	0.658	Not significant
HDL-C	−0.046	0.615	Not significant
Atherogenic Index	+0.025	0.790	Not significant

Table 5: Ferritin vs Triglyceride Trend

Ferritin (ng/mL)	TG <150 mg/dL	TG ≥150 mg/dL	Mean TG ± SD
<2500 (n=48)	34 (70.8%)	14 (29.2%)	132.6 ± 48.7
2500–5000 (n=47)	24 (51.1%)	23 (48.9%)	159.8 ± 63.4
>5000 (n=25)	9 (36.0%)	16 (64.0%)	181.5 ± 71.6

DISCUSSION

The present study demonstrates that transfusion-dependent beta-thalassemia major children have a distinct dyslipidemic pattern characterized by low total cholesterol, low LDL, markedly reduced HDL, and raised triglycerides. This pattern is biologically plausible because chronic iron overload, oxidative stress, persistent anaemia, and hepatic dysfunction can disrupt lipoprotein synthesis, metabolism, and clearance [12, 13, 14, 15].

Our findings are consistent with those of Suman RL et al.[10], who reported significantly reduced total cholesterol, LDL, and HDL levels with elevated triglycerides in β-thalassemia major children. Similarly, Nandi S et al. [11] demonstrated decreased cholesterol fractions and a positive association between triglycerides and serum ferritin, supporting the dyslipidemic pattern observed in our study.

Comparable results were also reported by Jabbar HK et al.[20], who found significantly elevated triglycerides along with reduced HDL levels in transfusion-dependent thalassemia patients, suggesting an atherogenic lipid profile. Additionally, Ray S et al.[19] reported elevated atherogenic indices, reinforcing the increased cardiovascular risk associated with dyslipidaemia in these patients.

The underlying mechanism of lipid abnormalities has been attributed to iron overload and oxidative stress. Studies by Patel HV et al. [12] and Wallace DF [13] have shown that excess iron induces oxidative damage and interferes with hepatic lipid metabolism, while Ahmed U et al. [15] highlighted the role of hepatic iron deposition in altering lipid synthesis and clearance.

Although serum ferritin did not show statistically significant correlation with most lipid parameters in our study, a trend toward increasing triglyceride levels with higher ferritin was observed. These findings are partially consistent with Nandi S et al.[11] and Suman RL et al. [10] , who reported significant correlations between ferritin and lipid parameters, particularly triglycerides. However, in contrast to these studies, our study did not demonstrate strong linear correlations, which may be due to differences in sample size, chelation therapy, or population characteristics.

Similar observations of weak or inconsistent correlations have been reported by Islam T et al [17], suggesting that serum ferritin alone may not fully reflect the complexity of lipid metabolism in thalassemia. Additionally, Harwalkar VS et al.[16] emphasized the influence of factors such as duration of transfusion, nutritional status, and disease severity on ferritin levels and metabolic outcomes.

Furthermore, serum ferritin is known to be influenced by inflammatory states, as described by Kell DB et al.[18], which may limit its reliability as a sole indicator of iron overload in correlation studies. This may explain the lack of statistically significant associations in our findings.

Despite the absence of strong correlations, the progressive increase in triglycerides and atherogenic indices across ferritin categories in our study suggests a clinically relevant relationship between iron burden and cardiovascular risk. These findings align with previous reports indicating that dyslipidaemia in β-thalassemia is multifactorial and influenced by iron overload, oxidative stress, hepatic dysfunction, and chronic disease burden. [19, 20].

CONCLUSION

Children with transfusion-dependent beta-thalassemia major in this study had pronounced dyslipidaemia, especially low total cholesterol, low LDL, low HDL, and elevated triglycerides, along with substantial iron overload. Serum ferritin did not show significant linear correlation with most lipid variables, but higher ferritin categories were associated with higher triglyceride levels and greater atherogenic indices; however, these associations did not reach statistical significance. Routine lipid surveillance, optimized chelation, nutritional monitoring, and larger prospective studies are warranted to better define the metabolic and cardiovascular significance of these abnormalities.

LIMITATIONS

The present study has certain limitations. Being a single-centre study, the findings may not be generalizable to the broader population. Additionally, advanced imaging modalities such as MRI T2* were not used for direct assessment of organ-specific iron overload. Furthermore, serum ferritin levels, although widely used as a marker of iron burden, can be influenced by inflammatory states, which may affect the accuracy of correlation with lipid parameters.

SOURCE OF SUPPORT: Nil
CONFLICTS OF INTEREST: None declared.

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