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**Research Article**

# Serum Lipid Profile İn Children with Thalassemia Major: A Study On 184 Cases

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## Abstract:

**Background:** Patients with thalassemia major are at risk of developing abnormal lipid profiles.

**Aim:** In this study, the relationship between iron accumulation and blood lipid profile in TM children was evaluated.

**Methods:** In this study, blood hemoglobin, ferritin, and lipid levels of pediatric patients with TM aged 1-18 years were investigated. Those with other chronic diseases were excluded from the study.

**Results:** The median age of 184 patients included in the study was 8 (range 1-18), and 96 (52.2%) of the patients were girls. There is an inverse and statistically significant relationship between age and total cholesterol (TC) level ($p<0.05$) and age and low-density lipoprotein cholesterol (LDL-C) level ($p<0.05$). There was an inverse, and statistically significant correlation between ferritin- high-density lipoprotein cholesterol (HDL-C) levels (p:0.015).

**Conclusion:** As ferritin levels increase in children with thalassemia, HDL-C levels decrease. For cardiac iron accumulation, HDL-C level may be a guide instead of ferritin.

**Keywords: Thalassemia major, lipid profile, total cholesterol, triglyceride, high-density lipoprotein cholesterol, low-density lipoprotein cholesterol.**

## Introduction

Thalassemia major (TM) is a hereditary anemia resulting from defects in the production of β-globin chains and is one of the most common genetic disorders world (1). Patients with TM are at risk of developing iron overload in the heart, liver, and endocrine glands that results from repeated blood transfusions and increased iron absorption by the gastrointestinal tract (1,2). Blood transfusion and chelation are the mainstays of treatment which have considerably increased the life expectancy and significantly improved the quality of life of these patients (3).

It is known that thalassemia is associated with changes in plasma lipids and lipoproteins (4,5). An abnormal lipid profile in thalassaemic patients has been reported in various studies, but its pathophysiology is still not defined (6). This dyslipidemia includes high triglyceride (TG), low total cholesterol (TC), low high-density lipoprotein cholesterol (HDL-C), and high TC to HDL ratio (TC: HDL-C) in young thalassaemic patients (4,5,7,8). Causes of lipid abnormalities in thalassemia include higher bone marrow activity with an increased cholesterol requirement for red cell membrane formation, decreased production secondary to liver injury, and lipid peroxidation associated with iron overload (4,9-11). There is a relationship between dyslipidemia and early atherosclerosis (4,7). There are studies showing that children with TM are at risk of developing subclinical atherosclerosis (12). Subclinical atherosclerosis begins early in life and may develop into coronary heart disease later in life. Thalassaemic patients are subject to oxidative tissue injury due to free radicals and LDL-C (4,5,13). In our study, we investigated whether there is a relationship between iron load and lipid profiles in patients with TM.

## Materials and methods

Patients with a diagnosis of beta-thalassemia major between the ages of 0-18 who were followed up in the Pediatric Hematology Clinic of Şanlıurfa Training and Research Hospital were included in the study. Patients' age, gender, hemoglobin and ferritin levels, and lipid profiles (LDL, HDL, TC, TG) were retrospectively scanned from patient records, and the results were examined.

Those with chronic diseases such as viral and/or chronic liver disease, diabetes mellitus, hypothyroidism, hyperthyroidism, and renal failure and children having a family history of dyslipidemia were excluded from the study.

This study was approved by the hospital ethics committee of SBU Bakirkoy Sadi Konuk Training and Research Hospital Ethical Committee.

## Statistical Analysis

While evaluating the findings obtained in the study, IBM SPSS Statistics 22 program was used for statistical analysis. The suitability of the parameters to the normal distribution was evaluated with the Kolmogorov-Smirnov test and it was determined that the parameters did not show normal

distribution. Spearman's rho correlation analysis was used to examine the relationships between the parameters. Significance was evaluated at the p<0.05 level.

## Results

The median age of 184 patients included in the study was 8 (range 1-18), and 96 (52.2%) of the patients were girls. The median values of Hb, Ferritin, TG, TC, HDL-C, and LDL-C of the patients are summarized in Table1.

**Table1.Descriptive characteristics of operating parameters**

| | Mean (range) |
|---|---|
| Hemoglobin (g/dL) | 8,69±1,15 |
| Ferritin (ml/ng) | 2916,49±1844,78 |
| TG (mg/dl) | 146,82±69,34 |
| TC (mg/dl) | 103,14±19,34 |
| HDL-C (mg/dl) | 32,25±13,16 |
| LDL-C (mg/dl) | 52,41±27,63 |

**TG**:Triglyceride. **TC**:Total cholesterol, **HDL-C**: High-density lipoprotein cholesterol,

**LDL-C**:Low-density lipoprotein cholesterol.

There is an inverse, weak (22.5%), and significant relationship between age and TC level (p:0.002; p<0.05). There is an inverse, weak (26.3%), and statistically significant relationship between age and LDL-C level (p:0.002; p<0.05). There was no statistically significant correlation between age and TG and HDL-C (p>0.05) (Table 2).

**Table2.Correlation of age with TG, TC, HDL-C and LDL-C**

| | | Yaş |
|---|---|---|
| TG | r | 0,029 |
| | p | 0,699 |
| TC | r | -0,225 |
| | p | 0,002* |
| HDL-C | r | -0,023 |
| | p | 0,760 |
| LDL-C | r | -0,263 |
| | p | 0,001* |

*Spearman's rho korelasyon testi* **p<0.05*

**TG**:Triglyceride. **TC**:Total cholesterol, **HDL-C**: High-density lipoprotein cholesterol,
**LDL-C**:Low-density lipoprotein cholesterol.

An inverse, weak (17.3%) significant relationship between Hb-TG levels (p:0.020; p<0.05); A positive, weak (23.7%) and significant relationship between Hb-TC levels (p:0.001; p<0.05); A positive, weak (28.2%) and significant relationship between Hb-HDL-C levels (p:0.001; p<0.05); There is a positive, weak (21.9%) and significant relationship between Hb-LDL-C levels (p:0.003; p<0.05) (Table3).
There was an inverse, weak (17.9%), and significant correlation between ferritin-HDL-C levels (p:0.015; p<0.05). There was no significant correlation between ferritin and TG, TC, and LDL-C(p>0.05) (Table 3).

**Table3: Correlation of hemoglobin and ferritin with TG, TC, HDL-C and LDL-C**

| | | Hemoglobin | Ferritin |
|---|---|---|---|
| TG | R | -0,173 | 0,134 |
| | P | 0,020* | 0,070 |
| TC | R | 0,237 | 0,039 |
| | P | 0,001* | 0,600 |
| HDL-C | R | 0,282 | -0,179 |
| | P | 0,001* | 0,015* |
| LDL-C | R | 0,219 | 0,037 |
| | P | 0,003* | 0,618 |

*Spearman's rho korelasyon testi* **p<0.05*

**TG**:Triglyceride. **TC**:Total cholesterol, **HDL-C**: High-density lipoprotein cholesterol,

**LDL-C**:Low-density lipoprotein cholesterol.

## Discussion

Iron overload and oxidative stress are postulated mechanisms for causing dyslipidemia in patients with thalassemia (4,14,15). Low levels of serum TC, HDL-C and LDL-C, and elevated TGs in pediatric patients with thalassemia were reported in the studies of Ragab et al. (7) in Egypt and Bordbar et al.(16) in Iran. These alterations are likely due to diminished hepatic biosynthesis due to anemia and accelerated erythropoiesis, with excess uptake of cholesterol by macrophages of the reticuloendothelial system, while reduced extrahepatic lipolytic activity could account for the rise in the circulating TG (10).
In the study of Daswani et al., a positive correlation was found between Hb-TC levels (10).
This result can be explained by the presence of enhanced cholesterol consumption required for cell membrane formation and the presence of a hyperplastic and overactive reticuloendothelial system (17).
In our study, we found that the TC, HDL-C and LDL-C was positively correlated with hemoglobin levels, and the serum TG had a significant negative correlation with Hb among thalassemic children. This correlation can be attributed to anemia, placing patients at risk for decreased extrahepatic lipolytic activity, resulting in high serum TG (7).
In our study, the average serum ferritin was considerably higher than its peak value (1,000 µg/L). Excess iron oxidation can damage cellular lipids, nucleic acids, proteins, and carbohydrates (18). Sherief et al. (10) and Ragab et al. (7) reported that TG has a positive correlation with serum ferritin in TM. These results might support the hypothesis that both serum iron and TG are involved in the pathogenesis of LDL-C oxidation.23 (24). In our study, however, a relationship was found between ferritin levels and only HDL-C levels. This relationship is inverse. It is noteworthy that as ferritin level, which is an indicator of iron accumulation in the body, increases, HDL-C level decreases in thalassemia patients. Low HDL-C levels have been associated with heart diseases. The decrease in HDL-C as the blood ferritin level increases supports

this hypothesis.

The limitation of our study was a small sample size. More extensive studies will provide further insight and information regarding cardiovascular complications in children with thalassemia having deranged lipid profiles. This may also help in framing guidelines for monitoring lipid profiles in these children, in order to reduce long-term morbidity and mortality.

## Conclusion

Ferritin is associated with iron overload and places patients at an increased cardiovascular risk. As ferritin levels increase in children with thalassemia, HDL-C levels decrease. Such as low HDL-C may contribute as an important risk marker for future cardiac events in these patients.

## Ethıcs

**Ethics Committee Approval:**

The questionnaire and methodology for this study) were obtained from the Ethics Committee of University of Health Sciences Türkiye, Bakırköy Dr. Sadi Konuk Training and Research Hospital.

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**Conflict of Interest:**

No conflict of interest was declared by the authors.

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