

Evaluation of Lipid Profile among Transfusion Dependent Thalassemic Children and Assessing Its Correlation with Serum Ferritin

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Abstract

Original Research Article

Background: Thalassemias are inherited hemoglobin disorders that necessitate lifelong blood transfusions. Patients having transfusion-dependent thalassemia (TDT) experience excess iron deposition in different organs. Due to excess of iron in the liver, lipid metabolism of these patients become altered. **Objective:** This study was aimed to assess the lipid profile and its correlation with serum ferritin among transfusion dependent thalassemic children. **Methods:** This cross-sectional comparative study was conducted at the Department of Pediatric Hematology and Oncology, Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka, Bangladesh from October 2021 to September 2022. Total 35 children diagnosed as TDT, aged 2 to 18 years were enrolled as cases. Another 35 age and sex matched children were included as controls. Their fasting serum lipid profile [Total Cholesterol (TC), High Density Lipoprotein (HDL) Cholesterol, Low Density Lipoprotein (LDL) Cholesterol and Triglyceride (TG)] and serum ferritin levels were measured and correlation was performed accordingly. **Results:** The mean values of TC, HDL, LDL and TG were 107.3±22.17 mg/dl, 22.7±7 mg/dl, 58.7±18.4 mg/dl and 135.1±43 mg/dl in the TDT group. Among the controls the mean values of these variables were 149.09±20.78 mg/dl, 44.89±10.17 mg/dl, 86.51±21.47 mg/dl and 87.97±30.47 mg/dl respectively. In TDT group; TC, HDL, LDL levels were significantly lower (p<0.05) and TG level was significantly higher (p<0.05) compared with that of controls. There was a significant positive correlation observed between TC and TG with ferritin (p<0.05). **Conclusion:** Transfusion dependent thalassemic children have low TC, HDL, LDL and high TG level. Total Cholesterol (TC) and triglyceride (TG) levels of TDT children have a positive correlation with serum ferritin level.

Keywords: Evaluation, Ferritin, Healthy Controls, Lipid Profile, Transfusion Dependent Thalassemia (TDT).

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1. INTRODUCTION

Thalassemias are the most common inherited monogenic disorders worldwide, presenting a significant public health concern especially for developing countries [1,2]. Hemoglobinopathies such as thalassemias, hemoglobin E (Hb-E), hemoglobin S (Hb-S) diseases

affect about 7% of the world's population and 300,000 to 500,000 infants are born each year with a severe hemoglobin abnormality [3]. South Asia is the home of 23% world's population and is a hotspot for hemoglobinopathies (approximately 1.7 billion) [4, 5] The most frequent kind of thalassemia in many Asian

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nations is caused by the coexistence of β -thalassemia and Hb- E [5]. Based on hemoglobin electrophoresis (Hb-Electrophoresis) with clinical severity and transfusion requirement, thalassemia syndromes can be classified into two main groups; (1) Transfusion dependent thalassemias (TDSs) and (2) Non transfusion dependent thalassemias (NTDs). Transfusion dependent thalassemias consist of β -thalassemia major (homozygous β -thalassemia or Cooley's anemia), severe Hb- E/ β -thalassemia, transfusion dependent hemoglobin H (Hb- H) disease or Hb- H hydrops fetalis and those who survived Hb Bart's hydrops fetalis [6]. The initial clinical appearance usually occurs between the ages of 6 months to 2 years. Severe pallor, jaundice, irritability, feeding issues, failure to thrive, skeletal abnormalities, abdominal enlargement due to increasing splenomegaly and hepatomegaly or repeated episodes of infection can all be symptoms of these patients [7]. Subsequently, regular blood transfusions are necessary for their survival [7]. It was reported that, severe iron overload starts early in the 1st decade of life with peak incidence in the 2nd and 3rd decades among patients with TDTs [8]. Iron overload occurs due to increased absorption from the gut and frequent blood transfusions. and liver is the earliest site of iron overload in regularly transfused children [9]. Despite advances in development of numerous iron scavenging medications, iron excess remains a problem in these individuals. It has the potential to harm any organ's normal function, but the endocrine system, liver, heart and kidneys are the principal targets [10-11]. A lipid profile typically includes; low-density lipoprotein (LDL) cholesterol, high-density lipoprotein (HDL) cholesterol, triglycerides (TG), and total cholesterol (TC). Dyslipidemia in TDTs is manifested as low serum levels of TC, HDL, LDL and high serum level of TG [12-14]. Evidences in recent years suggested that, children with thalassemia major are at risk of developing subclinical atherosclerosis [15]. There are several studies giving ideas regarding derangement of lipid profile in TDT patients, but little is known about the relationship of serum ferritin level with dyslipidemia [14, 16-17]. The study of lipid profile and its correlation with serum ferritin in children with TDTs can help early detection of atherogenesis. This study will generate a new approach for children with TDTs that will help early detection of cardiovascular risk.

2. METHODOLOGY

This cross-sectional comparative study was carried out at Department of Pediatric Hematology and Oncology, Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka, Bangladesh from October 2021 to September 2022. The Institutional Review Board (IRB) of BSMMU approved this study. Total seventy (70) children, aged between 2 years to 18 years were enrolled following the selection criteria. Of them, 35 children had transfusion dependent thalassemia (cases) and another 35 were age and sex matched healthy children (controls). Diagnosed cases of children with

transfusion dependent thalassemia (TDT) who received at least 10 transfusions over last one year were included. Children having active infection, any other chronic disease and critically ill children were excluded from the study. Their demographic profile, detailed clinical history and relevant family history were recorded. A complete clinical assessment was performed and findings were noted accordingly. Then serum ferritin and serum lipid profile levels of all study population were done following standard procedure.

Study procedure

After selection of the study subjects informed written consent was taken from each of the participant's legal guardian. All study subjects were advised to come overnight fasting on the day of collecting blood samples. About 5 ml of fasting venous blood was collected in a plane test tube from every participant with strict aseptic precautions. Test tubes containing blood sample were kept in upright position for 30 minutes and then centrifuged at 3000 rpm for 15 minutes at room temperature (24°C - 26°C). Serum ferritin was measured by chemiluminescence immunoassay by LIAISON (Italy) analyzer and serum lipid profile (TC, HDL, LDL, TG) was measured by photometric method in a clinical chemistry analyzer (Atellica).

The study population were divided into two groups; aged 2 to 9 years and 10 to 18 years for proper evaluation of TG level, on the basis of changing the normal value of TG at these different age group [18]. Demographic data, clinical and laboratory findings along with thalassemia related information were recorded in a case record form. In every step proper precaution was taken to protect confidentiality of the participants.

Data analysis

All collected data were verified and compiled. Statistical analysis was performed with a windows-based software Statistical Package for Social Sciences (SPSS) version 26. Quantitative data were expressed as mean with standard deviation (SD) and qualitative data were presented as frequency with percentages. Data were analyzed by Chi-square test, unpaired t-test and Pearson correlation coefficient test. A p-value <0.05 was considered as statistically significant.

3. RESULTS

This study was intended to assess the lipid profile and their correlation with serum ferritin among transfusion dependent thalassaemic children. A Total of 70 children were evaluated, of them; 35 were diagnosed cases of transfusion dependent thalassemia (cases) and another 35 were age and sex matched children as controls. It was observed that almost two third (62.9%) of participants belonged to age 2-9 years in transfusion dependent thalassemia group and 20(57.1%) were this age group in controls. The mean age was 8.53 ± 3.28 years in transfusion dependent thalassemia group and that was

8.92±3.59 years in control group. More than half (51.4%) of participants were male in transfusion dependent thalassemia group and 15(42.9%) were male in control group. The difference was not statistically significant ($p>0.05$) between the groups (Table- 1). It was observed that almost three fourth (71.4%) of participants belonged to body mass index (BMI) 5th-85th percentile in transfusion dependent thalassemia group and 33(94.3%)

participants of control group were in BMI 5th-85th percentile. The difference was statistically significant ($p<0.05$) between the groups (Table- 1). Majority (85.7%) of the participants had normal blood pressure in transfusion dependent thalassemia group, while in control group 33(94.3%) participants were normotensive. The difference was not statistically significant ($p>0.05$) between the groups (Table- 1).

Table- 1: Baseline characteristics of the study population (N=70)

Characteristics	Transfusion dependent thalassemia group (n=35)	Control group (n=35)	p value
Age (years)			
Age groups	n (%)	n (%)	
2-9 years	22(62.9%)	20(57.1%)	
10-18 years	13(37.1%)	15(42.9%)	
Mean±SD	8.53±3.28 years	8.92±3.59 years	*0.637 ^{ns}
Range (Minimum-maximum)	3-15 years	2-17 years	
Sex			
Male	18(51.4%)	15(42.9%)	**0.472 ^{ns}
Female	17(48.6%)	20(57.1%)	
Body mass index (BMI)			
<5 th percentile	10(28.6%)	2(5.7%)	**0.008 ^s
5 th -85 th percentile	25(71.4%)	33(94.3%)	
85 th -95 th percentile	0(0.0%)	0(0.0%)	
>95 th percentile	0(0.0%)	0(0.0%)	
Blood pressure (mm Hg)			
Hypertensive	0(0.0%)	0(0.0%)	**0.232 ^{ns}
Normotensive	30(85.7%)	33(94.3%)	
Hypotensive	5(14.3%)	2(5.7%)	

s= significant, ns= not significant, p value reached from *Unpaired-t test and ** Chi-square test

Among the children with transfusion dependent thalassemia (TDT); 23 (65.7%) children had Hb E β -

Thalassemia and 12(34.3%) were β -Thalassemia major (Figure- 1).

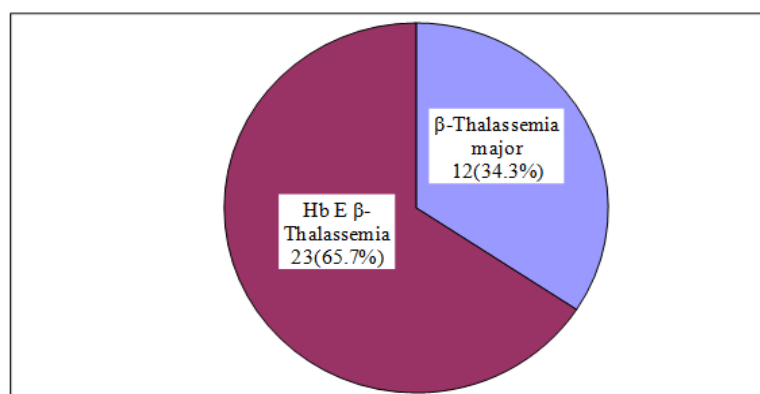


Figure- 1: Distribution of transfusion dependent thalassemia participants (n=35)

In this study, mean age at first diagnosis of β -Thalassemia major group was 1.58±0.8 years and that was 2.06±2.13 years in Hb E β -Thalassemia group. The mean duration of transfusion was 7.54±3.89 years in β -Thalassemia major group and 5.67±2.67 years in Hb E β -Thalassemia group. The difference was not statistically significant ($p>0.05$) between the groups (Table- 2).

Regarding the frequency of transfusion; all (100.0%) participants had every 4 weekly blood transfusions in β -Thalassemia major group and 82.6% participants had this frequency of blood transfusions in Hb E β -Thalassemia group. The difference was not statistically significant ($p>0.05$) between the groups (Table- 2).

Table- 2: Clinical profile of children with TDT (n=35)

Variables	β -Thalassemia major (n=12)	Hb E β -Thalassemia (n=23)	p-value
Age at first diagnosis (years)	1.58 \pm 0.8	2.06 \pm 2.13	*0.459 ^{ns}
Duration of blood transfusion (years)	7.54 \pm 3.89	5.67 \pm 2.67	*0.102 ^{ns}
Frequency of blood transfusion			
Every 3 weekly	0(0.0%)	4(17.4%)	**0.098 ^{ns}
Every 4 weekly	12(100.0%)	19(82.6%)	

ns= not significant, p value reached from *Unpaired-t test and **Chi-square test

The mean serum ferritin level was significantly higher in transfusion dependent thalassemia group than

control group (2735.9 \pm 1614.9 ng/ml versus 42.41 \pm 19.3 ng/ml, p<0.05) (Table- 3).

Table- 3: Distribution of study population according to ferritin level (N=70)

Ferritin (ng/ml)	Transfusion dependent thalassemias (n=35)	Controls (n=35)	p value
	n (%)	n (%)	
Mean \pm SD	2735.9 \pm 1614.9	42.41 \pm 19.3	0.001 ^s
Range (Minimum-Maximum)	517-6329	11.87-102.1	

s= significant, p value reached from Unpaired-t test

Among 35 TDT patients, 27(77.14%) children were taking chelating agents; of them 9(75.0%) children of β -Thalassemia major group and 18(78.3%) of Hb E β -

Thalassemia group. The difference was not statistically significant between the groups (p>0.05) (Table- 4).

Table- 4: Chelating agents taken by the children with TDT (n=35)

Taking chelating agents	β -Thalassemia major (n=12)		E β -Thalassemia (n=23)		p-value
	n	%	n	%	
Yes	9	75.0	18	78.3	0.827 ^{ns}
No	3	25.0	5	21.7	

ns= not significant, p value reached from Chi-square test

Among the TDT children; mean ferritin level was 2641.4 \pm 1625.8 ng/ml in chelator group and that was 2938.1 \pm 1444.1 ng/ml in non-chelator group. The

difference was not statistically significant between the groups (p>0.05) (Table- 5).

Table- 5: Comparison of ferritin level among chelator and non- chelator group (n=35)

Ferritin level (ng/ml)	Chelator group (n=27)	Non-chelator group (n=8)	p value
Mean \pm SD	2641.4 \pm 1625.8	2938.1 \pm 1444.1	0.645 ^{ns}
Range (Minimum-Maximum)	517-5780	1180-6329	

ns= not significant, p value reached from Unpaired-t test

The distribution of study population according to lipid profile levels is depicted in Table- 6. It was observed that one (2.9%) participant in TDT group and 5(14.3%) participants in control group belonged to total cholesterol (TC) level >170 mg/dl. The mean TC level was 107.3 \pm 22.17 mg/dl in TDT group and 149.09 \pm 20.78 mg/dl in control group. The difference was statistically significant (p<0.05) between the groups (Table- 6). Two (5.7%) of participants in TDT group and 2(5.7%) in control group belonged to low-density lipoprotein (LDL) cholesterol level >110 mg/dl. The mean LDL level was 58.7 \pm 18.4 mg/dl in TDT group and 86.51 \pm 21.47 mg/dl in control group. The difference was statistically

significant (p<0.05) between the groups (Table- 6). Majority (97.1%) of the participants in TDT group and 18(51.4%) in control group had high-density lipoprotein (HDL) cholesterol level <45 mg/dl. The mean HDL level was 22.7 \pm 7 mg/dl in TDT group and that was 44.89 \pm 10.17 mg/dl in control group. The difference was statistically significant (p<0.05) between the groups (Table- 6). In context of serum total triglycerides (TG); more than half (57.1%) participants in TDT group and 9(25.7%) in control group belonged to TG level >75 mg/dl, among 2-9 years participants. In 10-18 years age group; almost one third (31.4%) of participants in TDT group and 8(22.9%) in control group belonged to TG

level >90 mg/dl. The mean TG level was 135.1±43 mg/dl in TDT group, which was 87.97±30.47 mg/dl in control

group. The difference was statistically significant (p<0.05) between the groups (Table- 6).

Table- 6: Distribution of study population according to lipid profile levels (N=70)

Variables	Transfusion dependent thalassemias (n=35)	Controls (n=35)	p value
TC (mg/dl)	n (%)	n (%)	
<170*	34(97.1%)	30(85.7%)	
>170	1(2.9%)	5(14.3%)	
Mean±SD	107.3±22.17	149.09±20.78	0.001 ^s
Range (Minimum-Maximum)	75-168	117-204	
LDL (mg/dl)			
<110*	33(94.3%)	33(94.3%)	
>110	2(5.7%)	2(5.7%)	
Mean±SD	58.7±18.4	86.51±21.47	0.001 ^s
Range (Minimum-Maximum)	25-120	40-151	
HDL (mg/dl)			
>45*	1(2.9%)	17(48.6%)	
<45	34(97.1%)	18(51.4%)	
Mean±SD	22.7±7	44.89±10.17	0.001 ^s
Range (Minimum-Maximum)	12-45	27-70	
TG (mg/dl)			
For 2-9 years (n=42)			
<75*	2(5.7%)	11(31.4%)	
>75	20(57.1%)	9(25.7%)	
For 10-18 years (n=28)			
<90*	2(5.7%)	7(20.0%)	
>90	11(31.4%)	8(22.9%)	
Mean±SD	135.1±43	87.97±30.47	0.001 ^s
Range (Minimum-Maximum)	73-299	43-181	

*Reference limit, s= significant, p value reached from Unpaired-t test

In this study a significant positive correlation was found between serum ferritin and total cholesterol (TC) in TDT patients (r=0.383; p=0.023) (Figure- 2).

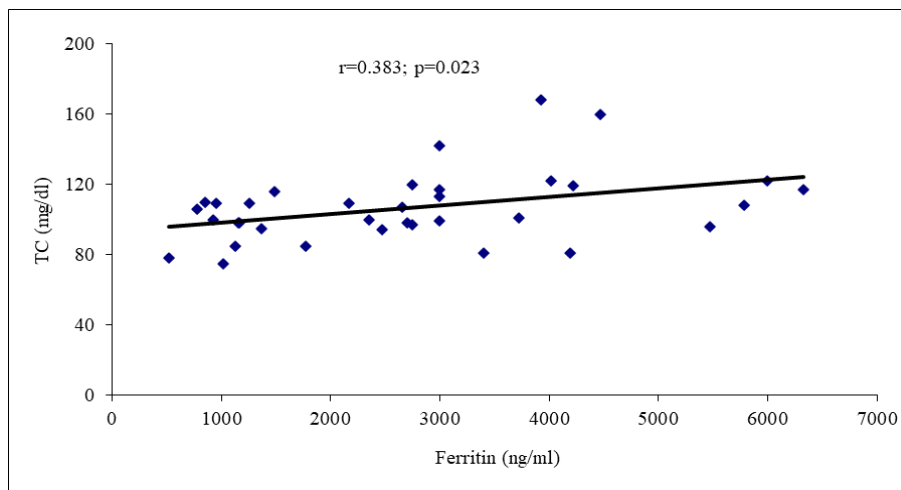


Figure- 2: Pearson correlation between serum ferritin with total cholesterol (TC) in TDT patients

There was a positive correlation observed between serum ferritin with high-density lipoprotein (HDL) cholesterol among patients with TDT, however

that was not statistically significant (r=0.107; p=0.541) (Figure- 3).

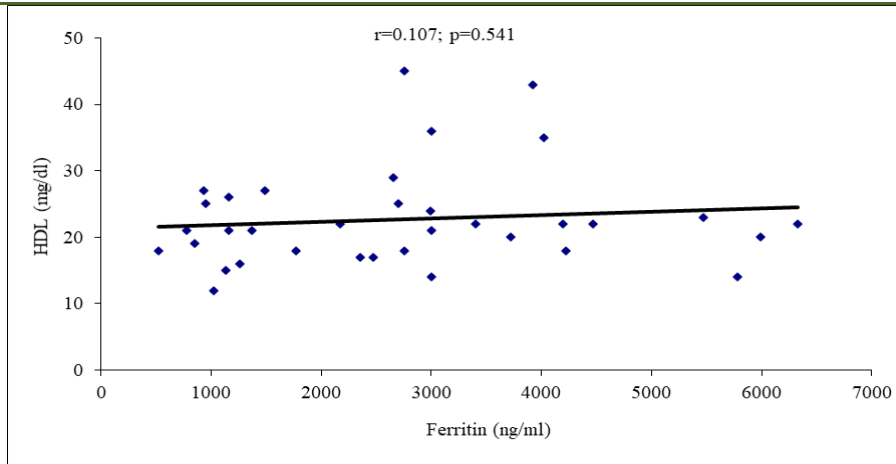


Figure- 3: Pearson correlation between serum ferritin with HDL cholesterol in TDT patients

Similarly, a positive correlation was observed between serum ferritin with low-density lipoprotein (LDL) cholesterol among patients with TDT, but which

was not statistically significant ($r=0.257$; $p=0.135$) (Figure- 4).

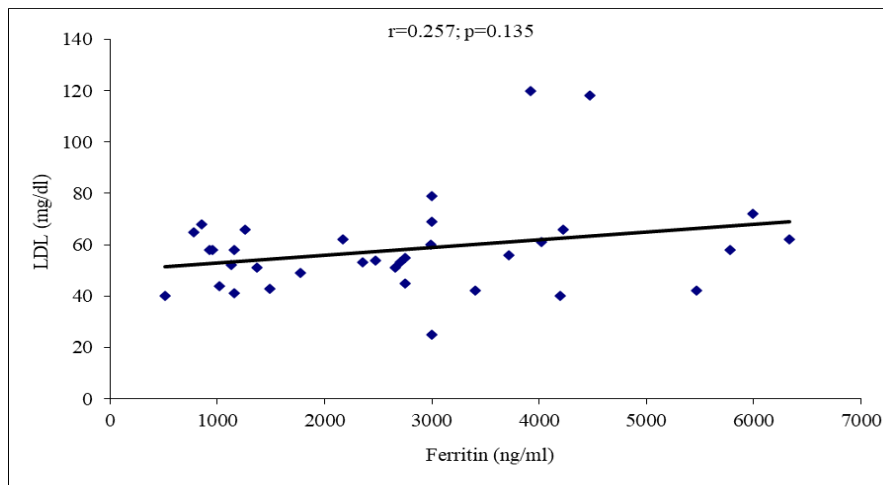


Figure- 4: Pearson correlation between serum ferritin with LDL cholesterol in TDT patients

Pearson correlation test revealed a significant positive correlation between serum ferritin with triglycerides (TG) in TDT patients ($r=0.386$; $p=0.021$) (Figure- 5).

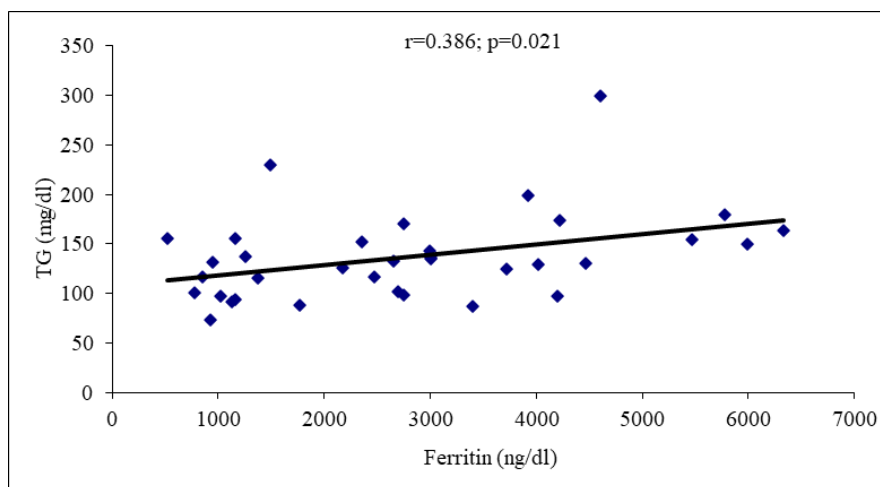


Figure- 5: Scatter diagram shows the correlation between serum ferritin with TG in TDT patients

4. DISCUSSION

Thalassemias are hereditary condition marked by aberrant hemoglobin synthesis, which is linked to inadequate hemoglobin production and excessive red blood cell destruction [19]. Transfusion-dependent thalassemia (TDT), the most severe type of the spectrum, includes- β -thalassemia major, non-deletional Hb H, and severe Hb E β -Thalassemia. These TDT patients require frequent blood transfusions to survive, which over time results in iron overload, that raises the non-transferrin-bound iron and labile iron pool, causing oxidative damage, persistent hypoxia, metabolic dysregulations, and cellular damage [20]. TDT is also linked to altered lipid levels due to oxidative stress, which can cause early atherosclerosis that increases the risk of cardiovascular disease and stroke [21]. This cross-sectional study was carried out with an aim to assess any alteration of lipid profile in children with transfusion dependent thalassaemias (TDTs) compared to healthy controls as well as to correlate lipid profile and serum ferritin in these children.

In this study, mean age was 8.53 ± 3.28 years (ranging from 3 to 15 years) in transfusion dependent thalassemia group and 8.92 ± 3.59 years (ranging from 2 to 17 years) in control group. The mean age was almost similar between the groups with no statistically significant difference ($p > 0.05$). Among the children with TDT; 65.7% children were labeled as Hb E β -Thalassemia and 34.3% were β -Thalassemia major in our study. These findings were consistent with a couple of previous study [5, 24]. In TDT group; 51.4% of participants were male. Similar observation regarding male predominance was also observed in several previous studies [14, 15, 17, 22]. However, Suman R *et al.* found female preponderance (56.4%) among their study subjects [9]. In TDT group 28.6% of participants belonged to BMI $< 5^{\text{th}}$ percentile. Patients with β thalassemia do not typically exhibit obesity; there are several reasons for this, such as endocrinopathies. The majority of the TDT patients in this study were underweight. In other research, these percentages were also smaller [23-24]. In a related study it was observed that 60.4% of β thalassaemic children had BMI $< 5^{\text{th}}$ percentile, which was higher than present study [25]. It was observed that 14.3% participants were hypotensive in TDT group and that was 5.7% in control group. The difference was not statistically significant between the groups ($p > 0.05$). In accordance, Gursel O *et al.* also found no significant difference in blood pressure between the groups [26]. Patients with thalassemia have decreased vascular resistance, which results in low or normal blood pressure despite their elevated cardiac output [27].

In this study, the mean age at first diagnosis was 1.58 ± 0.8 years in β -Thalassemia major group and that was 2.06 ± 2.13 years in Hb E β -Thalassemia patients. In contrast, Jaruratanasirikul S *et al.* observed that the mean

age of β -Thalassemia major at diagnosis was 3.2 ± 3.0 years [28]. Similarly higher mean age of β -Thalassemia major at the time of diagnosis was also observed in another study [29]. This present study revealed that the mean duration of blood transfusion was 7.54 ± 3.89 years in β -Thalassemia major group and that was 5.67 ± 2.67 years in Hb E β -Thalassemia group, which was comparable with a similar previous study [13]. In this study all (100.0%) of participants had received every 4 weekly blood transfusion in β -Thalassemia major group and that frequency was 82.6% in Hb E β -Thalassemia group. The mainstay of treatment for β -thalassemia is still routine blood transfusion therapy. There are clear transfusion recommendations for patients with β -thalassemia major, however there are no consistent transfusion protocols for patients with hemoglobin E β -thalassemia [30].

The mean ferritin level was 2735.9 ± 1614.9 ng/ml (ranging from 517 ng/ml to 6329 ng/ml) in TDT group, which was significantly higher than control group ($p < 0.05$). One previous study observed that all TDT cases had significantly increased levels of serum ferritin compared to the healthy controls ($p < 0.001$) [17]. This elevated level of serum ferritin indicates an existing iron overload in TDT cases, due to multiple blood transfusions and probably also due to intestinal hyperabsorption of iron [31]. Similarly, couple of related studies found a significant higher levels of ferritin values in TDT groups than those of the control groups ($p < 0.001$) [9, 14, 22]. In this study 75% of participants had taken chelating agent in β -Thalassemia major group and that was 78.3% in Hb E β -Thalassemia group. The mean serum ferritin level in non-chelator group was 2938.1 ± 1444.1 ng/ml and in chelator group it was 2641.4 ± 1625.8 ng/ml.

This study observed that 2.9% participant had total cholesterol (TC) level > 170 mg/dl in TDT group and that was 14.3% in control group. The mean TC level was significantly low in TDT group than control group (107.3 ± 22.17 mg/dl versus 149.09 ± 20.78 mg/dl, $p < 0.001$). Couple of related studies also reported a significant lower serum cholesterol level in TDT group [9, 14, 17, 22]. In this study, equally 5.7% participants in both groups had LDL cholesterol level > 110 mg/dl. The mean LDL cholesterol level was significantly low in TDT group compared to control group (58.7 ± 18.4 mg/dl versus 86.51 ± 21.47 mg/dl, $p < 0.001$). Similar findings were also observed in related studies [14, 15, 17, 22]. Ninety seven percent participants of this current study had HDL cholesterol level less than 45 mg/dl in transfusion dependent thalassemia group and that level was found among 51.4% participants in control group. The mean HDL cholesterol level was significantly low in TDT group than control group (22.7 ± 7 mg/dl versus 44.89 ± 10.17 mg/dl, $p < 0.001$). Similarly, Dey A *et al.* found that HDL cholesterol level in patients with thalassemia syndrome was significantly lower than

control group ($p < 0.001$) [17]. In vitro studies stated that there are oxidative interactions of unpaired hemoglobin chains with LDL ApoB, and this can cause oxidative modification of LDL cholesterol [32]. Such oxidation processes could conceivably alter the metabolic behaviors of both LDL and HDL cholesterol and result in increased uptake of the two modified lipoproteins by the already hyperplastic macrophage/monocyte system (scavenger pathway) [33-34]. In this context, Christina C *et al.* speculated that the decreased levels of enzymatic activities could play a role in determining the decrease of HDL observed in thalassaemic patients [35]. It is well known that low plasma levels of HDL represent an important independent risk factor for cardiovascular disease [36]. Among the study population, mean TG level was significantly elevated in TDT group compared to control group (135.1 ± 43 mg/dl versus 87.97 ± 30.47 mg/dl, $p < 0.001$). In accordance, one previous study observed that the mean TG level was 157.24 ± 33.04 mg/dl in TDT cases and 86.46 ± 12.263 mg/dl in controls, the TG levels were found to be significantly higher in TDT group ($p < 0.001$) [17]. These findings were also in agreement with the recent studies [9, 14, 15, 22]. The pathogenesis of these abnormalities can be caused by many mechanisms including plasma dilution because of anemia, accelerated erythropoiesis resulting in increased cholesterol uptake by macrophages and histiocytes of the reticulo-endothelial system, defective liver functioning because of iron overload, macrophage system activation with cytokine release and hormonal disturbances [37-39].

In this current study, a significant positive correlation was found between serum ferritin and TC ($r = 0.383$; $p = 0.023$). In contrast, Nandi S *et al.* revealed that serum TC had a significant negative correlation with ferritin ($r = -0.941$, $p < 0.05$) [14]. Similar findings regarding negative significant correlation of total cholesterol with serum ferritin were also observed in a couple of related studies, which differ from this present study [9, 40-41]. However, few studies found that TC was not correlated with ferritin levels [42-43]. This difference may be explained by racial and ethnic differences of study population. The current study observed that there was a positive but not statistically significant correlation between serum ferritin and HDL cholesterol ($r = 0.107$; $p = 0.541$). However, Nandi S *et al.* showed that serum HDL had a significant negative correlation with serum ferritin ($r = -0.751$, $p < 0.001$) [14]. This inverse correlation between high ferritin and low HDL cholesterol is corroborative with related previous studies [9, 41, 44]. Another study found that HDL cholesterol had no significant correlation with serum ferritin [15]. A positive correlation was found between serum ferritin and LDL cholesterol in this current study but that was not statistically significant ($r = 0.257$; $p = 0.135$). In this context, Nandi S *et al.* showed that serum LDL cholesterol negatively correlated with ferritin ($r = -0.964$, $p < 0.05$) [14]. Similar correlation was

also observed in other related studies, which differ with the current study [9, 41]. In this study, a significant positive correlation ($r = 0.386$; $p = 0.021$) was found between serum ferritin and TG. In this context, Nandi S *et al.* found that serum TG have a significant positive correlation with ferritin level ($r = 0.606$, $p < 0.05$) [14]. A couple of previous studies also showed a positive correlation of serum ferritin with TG [9, 15, 45].

5. CONCLUSION

This study concluded that lipid profile in transfusion dependent thalassaemic children show significantly lower levels of TC, LDL cholesterol, HDL cholesterol and higher TG compared to healthy controls. There is a significant positive correlation of TC and TG with serum ferritin; however, a positive but not significant correlation exist between serum ferritin with LDL cholesterol and HDL cholesterol in these children.

Limitations of the study

It was a single center study with a relatively small sample size. So that the results of this study may not reflect the exact picture of the country

Recommendation

A large population based multicenter study should be done to verify the findings of this study. Based on this present study, high TG and low HDL level raised concern about the cardiovascular risk in TDT children. So, lipid profile should be carried out routinely in all children with TDT.

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REFERENCES

1. Musallam KM, Taher AT. Mechanisms of renal disease in β -thalassemia. *Journal of the American Society of Nephrology*. 2012 Aug 1;23(8):1299-302.
2. Demosthenous C, Eleftheriou P, Apostolou C, Sarafidis P, Perifanis V, Vlachaki E. β -Thalassemia and renal complications. A narrative review of pathophysiologic mechanisms. *population*. 2018;11:12.
3. Colah R, Gorakshakar A, Nadkarni A. Global burden, distribution and prevention of β -thalassemias and hemoglobin E disorders. *Expert Review of Hematology*. 2010 Feb 1;3(1):103-17.
4. Olivieri NF, Pakbaz Z, Vichinsky E. Hb E/beta-thalassaemia: a common & clinically diverse disorder. *Indian Journal of Medical Research*. 2011 Oct 1;134(4):522-31.
5. Hossain MS, Raheem E, Sultana TA, Ferdous S, Nahar N, Islam S, Arifuzzaman M, Razzaque MA, Alam R, Aziz S, Khatun H. Thalassemsias in South Asia: clinical lessons learnt from Bangladesh. *Orphanet journal of rare diseases*. 2017 Dec;12:1-9.

6. Origa R, Porter J. Genetic basis, pathophysiology and diagnosis of thalassaemias. In: 2021 Guidelines: For the Management of Transfusion Dependent Thalassaemia (TDT)[Internet]. 4th edition 2023. Thalassaemia International Federation. Nicosia (Cyprus):22.
7. Viprakasit V, Ekwattanakit S. Clinical classification, screening and diagnosis for thalassemia. *Hematology/Oncology Clinics*. 2018 Apr 1;32(2):193-211.
8. Chuncharunee S, Teawtrakul N, Siritanaratkul N, Chueamuangphan N. Review of disease-related complications and management in adult patients with thalassemia: A multi-center study in Thailand. *PLoS One*. 2019 Mar 20;14(3):e0214148.
9. Suman R, Sanadhya A, Meena P, Singh J, Jain R, Meena S. Lipid profile in children of β -thalassemia major and their correlation with serum ferritin. *Int J Contemp Pediatr*. 2017 Mar;4(2):543-7.
10. Patel HV, Qari M, Mousa SA, Bloemen S, Laat BD, Hemker HC, Hajjar WM. Iron balance in β -thalassemia: Maintaining an antioxidant/oxidant ratio. *J Appl Hematol*. 2012 Jan 1;3(1):4-11.
11. Yaghobi M, Miri-Moghaddam E, Majid N, Bazi A, Navidian A, Kalkali A. Complications of transfusion-dependent β -thalassemia patients in Sistan and Baluchistan, south-east of Iran. *International journal of hematology-oncology and stem cell research*. 2017 Oct 10;11(4):268.
12. Hendarto A, Sari TT, Rahmartani LD, Widyasari A, Iskandar SD. Glucose and Lipid Profiles in Adolescents with Thalassemia Major and Its Association with Iron Overload in Specific Organs. *The Indonesian Biomedical Journal*. 2019 Aug 1;11(2):188-93.
13. Sherief LM, Dawood O, Ali A, Sherbiny HS, Kamal NM, Elshanshory M, Alazez OA, Alhady MA, Nour M, Mokhtar WA. Premature atherosclerosis in children with beta-thalassemia major: New diagnostic marker. *BMC pediatrics*. 2017 Dec;17:1-8.
14. Nandi S, Samanta S, Mondal T, Halder S. Study of lipid profile in β thalassemia major pediatric patients with multiple blood transfusion and its correlation with serum ferritin level in tertiary care hospital in Kolkata. *International Journal of Community Medicine and Public Health*. 2021 Apr;8(4):1778.
15. Daswani P, Garg K. Lipid profile in β -thalassemia major children and its correlation with various parameters. *Indian Journal of Child Health*. 2021 Jan 27;8(1):26-31.
16. Balcı YI, Ünal Ş, Gümrük F. Serum Lipids in Turkish Patients with β -Thalassemia Major and β -Thalassemia Minor. *Turkish Journal of Hematology*. 2016 Jan 1;33.
17. Dey A, Sandip C, Arya S. Correlation of serum lipid profile with serum iron, TIBC & ferritin levels in beta thalassemia major patients. *Eur J Biol and Med Sci Res*. 2016;4:17-26.
18. Shah AS, Wilson DP. Genetic Disorders Causing Hypertriglyceridemia in Children and Adolescents. In: *Endotext*. MDText.com, Inc., South Dartmouth (MA); 2000. PMID: 27809432.
19. Qurat-ul-Ain LA, Hassan M, Rana SM, Jabeen F. Prevalence of β -thalassemic patients associated with consanguinity and anti-HCV-antibody positivity—a cross sectional study. *Pak J Zool*. 2011 Mar 31;43(1):29-36.
20. Ghone RA, Kumbar KM, Suryakar AN, Katkam RV, Joshi NG. Oxidative stress and disturbance in antioxidant balance in beta thalassemia major. *Indian Journal of Clinical Biochemistry*. 2008 Oct;23(4):337-40.
21. Maioli M, Vigna GB, Tonolo G, Brizzi P, Ciccarese M, Donegà P, Maioli M, Fellin R. Plasma lipoprotein composition, apolipoprotein (a) concentration and isoforms in β -thalassemia. *Atherosclerosis*. 1997 May 1;131(1):127-33.
22. Sutay NR. Study of serum lipid profile in beta-thalassemia major patients. *J. Med. Sci. Clin. Res*. 2016;4:17-20.
23. Hashemi A, Ghilian R, Golestan M, Akhavan Ghalibaf M, Zare Z, Dehghani MA. The Study of Growth in Thalassemic Patients and its Correlation with Serum Ferritin Level. *IJPHO* 2021;1(4): 147-151.
24. Pemde HK, Chandra J, Gupta D, Singh V, Sharma R, Dutta AK. Physical growth in children with transfusion-dependent thalassemia. *Pediatric Health, Medicine and Therapeutics*. 2011 Feb 9:13-9.
25. Yousefian S, Mirialiabad G, Saleh R, Khedmati M. Association of Body mass index and serum ferritin level in pediatrics with Beta-thalassemia major disease. *Iranian Journal of Pediatric Hematology and Oncology*. 2022 Jan 10;12(1):34-40.
26. Gursel O, Kurekci AE, Tascilar E, Ileri T, Altun D, Tapan S, Kurt I, Kocaoglu M, Aydin A, Okutan V, Ozcan O. Premature atherosclerosis in children with β -thalassemia major. *Journal of pediatric hematology/oncology*. 2012 Nov 1;34(8):630-4.
27. Wood JC. Cardiac complications in thalassemia major. *Hemoglobin*. 2009 Jan 1;33(sup1):S81-6.
28. Jaruratanasirikul S, Wongcharnchailert M, Laosombat V, Sangsupavanich P, Leetanaporn K. Thyroid function in beta-thalassemic children receiving hypertransfusions with suboptimal iron-chelating therapy. *Journal-Medical Association of Thailand*. 2007 Sep 1;90(9):1798.
29. Najafipour F. Evaluation of endocrine disorders in patients with thalassemia major. *International Journal of Endocrinology and Metabolism*. 2008 Apr 30;6(2).
30. Mettananda S, Pathiraja H, Peiris R, Wickramarathne N, Bandara D, de Silva U, Mettananda C, Premawardhana A. Blood transfusion therapy for β -thalassemia major and hemoglobin E β -thalassemia: Adequacy, trends, and

- determinants in Sri Lanka. *Pediatric blood & cancer*. 2019 May;66(5):e27643.
31. Choudhary M, Bohra VD. Iron status of thalassemic children in south Rajasthan. *Int Jr Sci Res*. 2015 September;4(9):380-1.
 32. Altamentova SM, Marva E, Shaklai N. Oxidative interaction of unpaired hemoglobin chains with lipids and proteins: a key for modified serum lipoproteins in thalassemia. *Archives of biochemistry and biophysics*. 1997 Sep 1;345(1):39-46.
 33. Livrea MA, Tesoriere L, Maggio A, D'arpa D, Pintaudi AM, Pedone E. Oxidative modification of low-density lipoprotein and atherogenetic risk in β -thalassemia. *Blood, The Journal of the American Society of Hematology*. 1998 Nov 15;92(10):3936-42.
 34. Tesoriere L, D'Arpa D, Maggio A, Giaccone V, Pedone E, Livrea MA. Oxidation resistance of LDL is correlated with vitamin E status in β -thalassemia intermedia. *Atherosclerosis*. 1998 Apr 1;137(2):429-35.
 35. Christina C, Demosthenes B, Christos P. Distribution of serum lipids and lipoproteins in patients with beta thalassemia major; an epidemiological study in young adults from Greece. *Lipids in Health and Disease*. 2004;3:328-34.
 36. Tan K. Re-examining the high-density lipoprotein hypothesis. *Journal of Diabetes Investigation*. 2016 Jul;7(4):445.
 37. Deiana L, Garuti R, Pes GM, Carru C, Errigo A, Rolleri M, Pisciotto L, Masturzo P, Cantafora A, Calandra S, Bertolini S. Influence of β^0 -thalassemia on the phenotypic expression of heterozygous familial hypercholesterolemia: a study of patients with familial hypercholesterolemia from Sardinia. *Arteriosclerosis, thrombosis, and vascular biology*. 2000 Jan;20(1):236-43.
 38. Al-Quobaili FA, Abou Asali IE. Serum levels of lipids and lipoproteins in Syrian patients with beta-thalassemia major. *Saudi Med J*. 2004 Jul 1;25(7):871-5.
 39. Shalev H, Kapelushnik J, Moser A, Knobler H, Tamary H. Hypocholesterolemia in chronic anemias with increased erythropoietic activity. *American journal of hematology*. 2007 Mar;82(3):199-202.
 40. Mansi KM, Aburja TA. Lipid Profile in Jordanian Children with β -thalassemia Major. *UHOD: International Journal of Hematology & Oncology/Uluslararası Hematoloji Onkoloji Dergisi*. 2008 Jun 1;18(2).
 41. Anca V, Arica S, Ozer C. Serum lipid values in children with beta thalassemia major. *PediatTherapeut*. 2010;2(5):130-3.
 42. Shams S, Ashtiani MT, Monajemzadeh M, Koochakzadeh L, Irani H, Jafari F, Mohseni A. Evaluation of serum insulin, glucose, lipid profile, and liver function in β -thalassemia major patients and their correlation with iron overload. *Laboratory medicine*. 2010 Aug 1;41(8):486-9.
 43. Hartman C, Tamary H, Tamir A, Shabad E, Levine C, Koren A, Shamir R. Hypocholesterolemia in children and adolescents with β -thalassemia intermedia. *The Journal of pediatrics*. 2002 Oct 1;141(4):543-7.
 44. Mashaali JK, Obed FA, Thair NT. Lipid Profile in Iraqi Children with β -thalassemia Major. *Iraqi Journal of Hematology*. 2014 Jul 1;3(2):108-15.
 45. Hassanin A, Gindi HD, Wakeel MA, Kassas GM, Amer AF. Disturbances of lipid profile and serum ferritin levels in thalassemic children. *Curr Sci Int*. 2015;4(2):1781-3.