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Study of Dyslipidemia and its Association with Serum Ferritin and Amount of Blood Transfusion in β- Thalassemia Major Patients in a Tertiary Level Hospital

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Abstract

Introduction: Beta-thalassemia is thought to be the most common genetic blood condition in the world. Different kinds of Beta-thalassemia major have been shown to have lipid problems. The goal of this study is to evaluate the lipid profiles of beta-thalassemia major patients. The aim of the study was to study the association of dyslipidemia with serum ferritin levels and amount of blood transfusion among Beta thalassemia patients. ***Methods:*** This descriptive cross-sectional study was conducted at the Department of Medicine and Hematology, Sir Salimullah Medical College Hospital, Bangladesh. The study duration was 6 months, from January 2017 to July 2017. The targeted study sample size was 96, but due to the short duration of the study, a total of 40 patients were selected as the study population. ***Result:*** Hematological tests showed the mean hemoglobin level in the thalassemia group was 7.23 gm/dl, with a standard deviation of 1.23. Mean MCV, MCH, and MCHC in the thalassaemic group were significantly lower at 69.83 fl (SD8.34), 23.10 PGM (SD3.57), and 28.03 % (SD 2.58) compared to the normal range (P-value <0.001 in all parameters). Beta-thalassemia major patients had significantly lower high-density lipoprotein and low-density lipoprotein (LDL) (p<0.001) compared to the normal range. However, serum triglycerides levels of Beta-thalassemia patients (211.5±31.54 mg/dl) were significantly higher [p-value < 0.001].But total cholesterol level was not statically significant among participants (P-value 0.428). High levels of serum triglycerides were associated with high ferritin levels and an increased amount of blood transfusion. Low levels of HDL-C and LDL-C were associated with a high level of ferritin and an increased amount of blood transfusion. ***Conclusion:*** Our study revealed that there was a significant difference in various lipid levels between patients with beta-thalassemia major and normal values which may help physicians to design the therapeutic module for the treatment of such patients.

Keywords: Thalassemia, Ferritin, Serum Lipid, Dyslipidemia.

INTRODUCTION

Thalassemia is the most frequent kind of congenital chronic hemolytic anemia that needs regular blood transfusions to stay alive. Iron excess can induce oxidative stress and tissue damage, which can harm the heart, liver, and endocrine glands. Thalassemia is persistent hemolytic anemia caused by a hereditary hemoglobin abnormality. β-globulin chains are either absent or in limited supply in this illness [1]. According to the World Health Organization, roughly 1.5 percent of the world's population may be carriers of β thalassemia, and approximately 60,000 seriously afflicted newborns are born each year. Most of these people are from the Mediterranean, the Middle East, Central Asia, India, and southern China [2]. The Maldives has the world's highest thalassemia prevalence, with 18% of the population carrying the disease [3]. In Bangladesh, China, India, Malaysia, and Pakistan, the frequency is believed to vary between 3-8

percent [2]. People in Northern Europe and Africa have likewise reported a very low incidence [4]. Through frequent blood transfusions and increased iron absorption from the gastrointestinal system, patients with -thalassemia major are in danger of iron overloading in numerous organs. Iron excess can harm the heart, liver, and endocrine glands in particular. It has been shown that circulating low-density Lipoprotein-C (LDL-C) in thalassemia patients undergoes significant oxidative alteration, which might constitute a pathogenic event. The generation of free radicals is higher in patients with iron excess. Many scientific shreds of evidence have emerged in recent years demonstrating the negative impact of aberrant blood lipid levels, such as total cholesterol and other lipids and lipoproteins, on atherosclerotic disease [5]. It should be noted at this point that various other lifestyle-related variables, such as glucose intolerance, blood pressure levels, dietary habits, and smoking behaviors, may impact the association between blood lipids and atherosclerosis [6]. Severe iron overload and oxidative stress are the main causes of hypercholesterolemia in -thalassemia major [7, 8]. The low levels of TC, HDL-C, LDL-C, and TG in -thalassemia are due to significant liver damage. Furthermore, severe chronic liver disease is characterized by low total and LDL cholesterol levels, as well as a reduction in HDL cholesterol [9]. In our nation, no investigation on the lipid status of -thalassemia patients has been conducted. The goal of this study was to look at blood lipid levels in individuals with -thalassemia major, which might assist physicians in better assessing cardiovascular risk factors in these patients and building a therapy module for these patients in Bangladesh. It will also be beneficial to be aware of these findings in order to avoid needless testing in patients with beta-thalassemia major.

OBJECTIVE

General Objective

- To study the association of serum ferritin and dyslipidemia among β-thalassemia major patients
- To study the association between blood transfusion amount and dyslipidemia among β-thalassemia major patients

METHODS

This descriptive cross-sectional study was conducted at the Department of Medicine and Hematology, Sir Salimullah Medical College Hospital, Bangladesh. The study duration was 6 months, from January 2017 to July 2017. The targeted study sample size was 96, but due to the short duration of the study, a total of 40 patients were selected as the study population. Patients were selected from those who had β-thalassemia major attending the study hospital during the study period. Informed written consent was obtained from each participant prior to admission to the study, and strict confidentiality was maintained for patient information. Patients were informed of their right to withdraw from the study any time they wanted. Data collection was conducted using a pre-designed questionnaire. After data collection, data entry, processing, and analysis were performed using appropriate statistics.

Inclusion Criteria

- Patients suffering from β-thalassemia major.
- Age >12 years
- Patients who had given consent to participate in the study.

Exclusion Criteria

- Age ≤12 years
- Unable to answer the criteria question.
- Exclude those affected with other chronic diseases etc.

RESULTS

Table 1: Social-demographic characteristics of the participants (n=40)

Variable	Frequency	Percentage
Age		
≤15	9	22.50%
16-20	15	37.50%
21-25	9	22.50%
26-30	4	10.00%
>30	3	7.50%
Gender		
Male	22	55.00%
Female	18	45.00%
Consanguinity		
Present	10	25.00%
Absent	30	75.00%
Family History of Thalassemia		
Present	35	87.50%
Absent	5	12.50%

Among the participants, 37.50% of the participants were between the age range of 16-20 years, while 22.50% were under 16 years of age, and another 22.50% were between the age of 21-25 years. In total, 82.5% of the participants were under 26 years of age among the present study participants. 55% were male and 45% were female. Consanguinity was observed in 25% of the cases, but a family history of thalassemia was present among 87.50% of the participants.

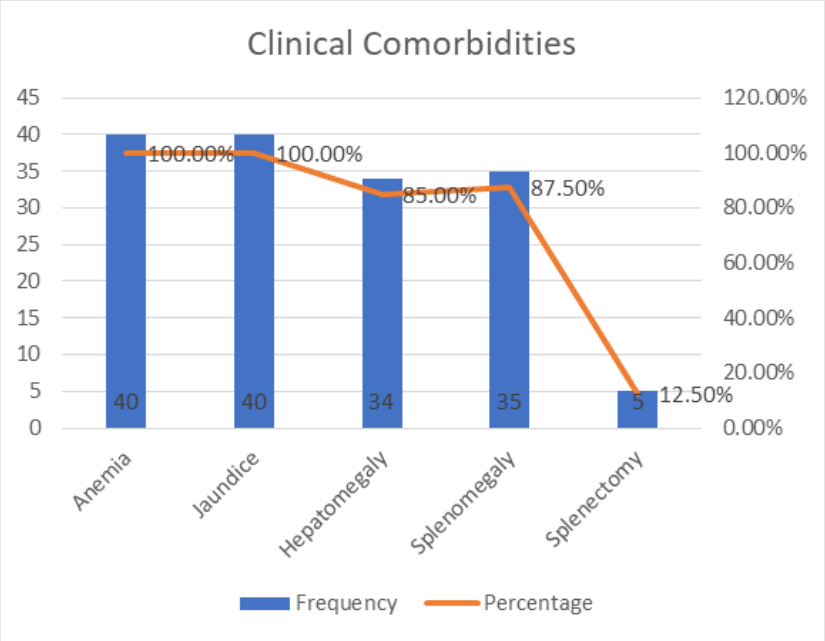

Figure 1: Incidence of clinical comorbidities among the participants (n=40)

Anemia and jaundice were present in all 100% of the participants. Hepatomegaly was observed in 85% of the participants. Splenomegaly was observed in 87.50% of the participants, while the remaining 12.50% had a splenectomy.

Table 2: Haematological parameters of the study population (n=40)

Haematological Parameters	Thalassemic Group (n=40)		P-value
	Mean	SD	
Haemoglobin (gm/dl)	7.23	1.23	0.001
MCV (fl)	69.83	8.34	0.001
MCH (pg)	23.1	3.57	0.001
MCHC (%)	28.03	2.58	0.001

The mean hemoglobin level in the thalassemia group was 7.23 gm/dl with a standard deviation of 1.23. Mean MCV, MCH, and MCHC levels were lower than the normal range. All of these parameters were statistically significant.

Table 3: Serum Lipid (mean±SD) levels Among participants (n=40)

Parameters (mg/dl)	Mean±SD	P-value
Total cholesterol	171.82±21.49	0.486
Triglyceride	211.5±31.54	<.001
HDL-C	35.63±5.43	<.001
LDL-C	73.05±8.75	<.001

Beta-Thalassemia major patients had significantly lower High–density lipoprotein cholesterol (HDL-C) and low–density lipoprotein cholesterol (LDL-C) compared to the normal range. However, Mean ± SD serum triglyceride levels were significantly higher compared to the normal range among the participants. Total cholesterol levels were within the normal range and were not statistically significant.

Table 4: Serum ferritin level among participants (n=40)

Serum ferritin level (ng/ml)	Frequency	Percentage
<1000	5	12.50%
1000-2000	26	65.00%
>2000	9	22.50%

Among the participants, serum ferritin levels were higher than normal in all patients. The majority (65%) had serum ferritin levels between 1000-2000 ng/ml, while 22.50% had serum ferritin levels higher than 2000 ng/ml and 12.50% had serum ferritin levels under 1000 ng/ml.

Table 5: Serum ferritin level with Lipid profile (mean±SD) level (n=40)

Parameters mg/dl	Serum ferritin level(ng/ml)			P-value
	<1000	1000-2000	>2000	
Total cholesterol	158±2.6	162±2.7	173±2.4	<0.001
Triglyceride	203±4.4	206±5.3	230±3.5	<0.001
HDL-C	44±3.4	40±2.6	33.25±2.7	<0.001
LDL-C	74±2.7	72±4.2	71±4.9	<0.001

Among serum ferritin <1000 participants, mean total cholesterol, TG, LDL-C, and HDL-C were 158±2.6, 203±4.4,74±2.7, and 44±3.4 mg/dl respectively. Among patients with serum ferritin levels between 1000-2000, mean total cholesterol, TG, LDL-C, and HDL-C were (162±2.7, 206±5.3, 72±4.2, 40±2.6 mg/dl respectively. Among patients with serum ferritin levels of >2000, mean (SD) total cholesterol, TG, LDL-C, and HDL-C were 173±2.4, 230±3.5, 71±4.9, 33.25±2.7 mg/dl respectively. Total cholesterol and triglyceride levels had significantly increased with increasing serum ferritin levels, while HDL-C and LDL-C levels had decreased significantly with increased serum ferritin levels.

Table 6: Amount of Blood transfusion with Lipid profile (Mean±SD) level (n=40)

Parameters(mg/dl)	Amount of Blood Transfusion			P-value
	<200 Unit	200-500unit	>500unit	
	(n=6)	(n=31)	(n=3)	
Total Cholesterol	162±3.4	166±3.8	173±5.2	<0.001
Triglyceride	189.6±3.4	238±3.6	270.5±5.4	<0.001
HDL-C	36±2.6	32.6±3.4	30.2±2.6	<0.001
LDL-C	75.3±3.8	73.2±4.5	69.1±2.8	<0.001

It was observed that mean TG and total cholesterol levels were higher with increased blood transfusion. Patients who got a transfusion of <200 units of blood had a mean(SD) of total cholesterol, TG, HDL-C, and LDL-C as 162±3.4, 189.6±3.4, 36±2.6, 75.3±3.8 g/dl respectively. Patients who received transfusion between 200-500 units had mean(SD) of total cholesterol, TG, HDL-C, and LDL-C as 66±3.8, 238±3.6, 32.6±3.4, 73.2±4.5 respectively. Patients who had received >500 units of blood transfusion had mean(SD) of total cholesterol, TG, HDL-C, LDL-C as173±5.2, 270.5±5.4, 30.2±2.6, and 69.1±2.8 respectively. These differences were statistically significant.

DISCUSSION

Among thalassemia, the β-Thalassemia gene has a widespread prevalence in the Mediterranean zone, Middle East, and Indian sub-continent including Bengal and parts of Southeast Asia [10]. The present study focused on the serum lipid status in β- Thalassemia major encountered in the department of medicine and hematology at Sir Salimullah Medical College and Mitford hospital. Among the present study participants, the male population was 55% and the female population was 45%, which was similar to the findings of another Bangladeshi study [9]. Consanguinity seemed to play an important role in the increasing prevalence of the problem, as observed in multiple studies [11]. Contradictory findings were also recorded, with only 7% of participants having consanguineous marriage in a study by Morshet *et al*., [12]. Our study had a 25% prevalence of consanguinity. Anemia and jaundice were common among all the participants of our study, and 85% had hepatomegaly or enlarged liver. Splenomegaly was observed in 87.50% of the participants, with 12.5% having a splenectomy. Hematological tests showed low Hb with a mean of 7.23±1.23 gm/dl. These results of low Hb among patients can be explained by the limited health education of the parents about the disease, so blood transfusion was used only when the patients showed clinical symptoms caused by severe anemia or simply just to sustain life [13, 14]. Other hematological parameters of participants were extremely variable compared to their standard range. Mean MCV, MCH, and MCHC in thalassemia patients were significantly lower than the normal range. These findings were similar to the study by Vichinsky *et al*., [15]. Beta-thalassemia major is one of the most common genetic disorders worldwide. Lipid abnormality has been frequently reported in thalassemia, but its pathophysiology is not clear [16-19]. In this study, we observed low HDL cholesterol and low LDL cholesterol with elevation lipoprotein cholesterol (LDL-C). However, Serum triglyceride levels of beta-thalassemia patients (211.5±31 mg/dl) were significantly higher. These findings were supported by the findings of various other studies [21-23]. Studies suggest that the risk for myocardial infarction is high when HDL cholesterol is Low, and the HDL cholesterol

levels of the present study thalassemia patients were significantly low [23]. In our study, we found that Triglyceride level was higher with a high level of serum ferritin (P-value < 0.01) and with an increased amount of blood transfusion (P-value <0.001). We also observed low levels of LDL-C and HDL-C with high ferritin levels (P-value <0.001) and with an increased amount of blood transfusion (P-value <0.001). Both values are statistically significant. But previously no study showed the relationship between TG, LDL-C, and HDL-C with serum ferritin level and amount of blood transfusion.

Limitations of the Study

The study was conducted in a single hospital with a small sample size. So, the results may not represent the whole community.

CONCLUSION

Our study revealed that there was a significant difference in various lipid levels between patients with beta-thalassemia major and normal values which may help physicians to design the therapeutic module for the treatment of such patients.

RECOMMENDATIONS

From this study, we may recommend that dietary modification is needed along with other modalities, regarding the proper management of patients with beta-thalassemia to prevent future cardiovascular risk. This study was done with small samples and for a short period of time. So it is recommended a further broad base multi-center study to validate these observations and explanation of this relationship as well as clarification of the exact mechanism and clinical consequences of lipid abnormalities in patients with beta-thalassemia.

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Conflict of interest: None declared

Ethical approval: The study was approved by the Institutional Ethics Committee

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