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Lipid Profile Abnormalities in ß-Thalassemia Patients with Multiple Blood Transfusions

Syeda Sabahat Haidar, Mehvish Sana, Rukhsana Tumrani, Farwa Shafqat

ABSTRACT

Objective: To determine lipid profile abnormalities in ß -thalassemia patients with multiple blood transfusions in tertiary care hospital.

Study design and setting: This cross-sectional study was conducted in Chemical Pathology section, Pathology department Sheikh Zayad Medical College and Hospital Rahim Yar Khan from 1st July 2022 to 31st October 2022.

Methodology: 110 patients aged 1 to 18 years from both genders enrolled in Thalassemia center of Sheikh Zayed Hospital with multiple blood transfusions were included in study using convenient sampling technique. Patients with cardiac disease, diabetes mellitus and family history of lipid disorders were excluded. Blood samples collected from thalassemia patients were subjected to estimation of serum total cholesterol, serum triglycerides, HDL-C, and LDL-C. Data was recorded on predesigned performa. Post stratification t test was applied and p value <0.05 was considered significant.

Results: Mean age of the patients was 7.77±3.846 years. Mean serum cholesterol, serum triglyceride, HDL-C and LDL-C were 89.15±20.33mg/dl, 211.00±77.78mg/dl, 21.01±6.554mg/dl and 29.79±17.02 respectively. Mean triglyceride and LDL-C level was higher in patients with weekly transfusion than patients undergoing monthly transfusion with statistically significant difference of triglycerides and LDL-C between two groups with p=0.002 and 0.023 respectively.

Conclusion: We found that frequent blood transfusion causes lipid profile abnormalities in thalassemia patients. Lipid profile abnormalities should be screened frequently in ß-thalassamia patients with multiple blood transfusions.

Keywords: Atherosclerosis, Blood transfusion, Iron overload, Lipid profile, ß-Thalassemia.

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INTRODUCTION:

Thalassemia is an inherited autosomal recessive microcytic hypochromic anemia resulting from hereditary defect in hemoglobin synthesis affecting production of alpha or ß globin chains. The results are disproportionate production of alpha or ß globin chains.[1] Individuals with thalassemia either have an absolute defect in synthesis of ß globin chains and therefore absence of ß chains called ß-thalassemia major (Cooley's anemia) or partially decreased production of ß chain called ß-thalassemia minor while thalassemia intermedia a group of patients with ß thalassemia in whom the clinical severity of the disease is somewhere between the mild symptoms of ß thalassemia trait and the severe manifestations of ß thalassemia major. The diagnosis is a clinical one made on the basis of the patient maintaining a satisfactory Hemoglobin level of at least 6-7 g/dl without the need for regular blood transfusions.[2] In ß-thalassemia major there is severe impairment in ß-globin chain production and this synthetic imbalance leads to ineffective erythropoiesis and hemolytic anemia making regular blood transfusion only means of survival for these individuals.[3] Thalassemia gene is carried by 3% population of the world. A higher thalassemia prevalence has been reported in Central Asia, Middle East, and Mediterranean countries.[4] Pakistan is estimated to have a carrier rate of 5-7%, with overall 9.8 million carriers in the population.[5] High frequency of this hemoglobin disorder compared with other monogenic diseases is mediated by high frequency of consanguineous marriages in many countries[3] including Pakistan. ß-thalassemia patients have significantly low levels of cholesterol associated with their disease and remains unaffected by age, gender, hemoglobin, or ferritin levels.[6]

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In transfusion dependent ß-thalassemia patients liver is the primary organ to deposit iron causing damage to both hepatocyte and reticulo-endothelial cells which may lead to liver fibrosis. Liver damage is evinced by elevated liver enzymes and triglycerides while serum total cholesterol, high density lipoprotein (HDL) and low density lipoprotein (LDL) are decreased.[7,8] The pathophysiology of hypocholesterolemia in thalassemia is uncertain, although various mechanisms have been suggested including increased cholesterol requirement associated with erythroid hyperplasia, plasma dilution attributable to anemia and high cholesterol consumption by the reticuloendothelial system.[7] Thalassemia is a condition of secondary iron overload. Frequent blood transfusions and increased iron absorption from gut both contribute to iron overload.[9] Iron overload can lead to many complications in thalassemia patients including lipid profile derangement.[10] In iron overload patients free radical production is increased through Fenton reaction. These free radicals accumulate in liver, heart, and other organs causing immense tissue damage. A high incidence of endothelial dysfunction, atherogenesis and thromboembolic event has been reported in thalassemia patients most probably due to abnormality in lipid profile related to transfusion iron overload in liver. There is also increased risk of cardiovascular complications and pancreatitis due to atherogenesis and high triglyceride level respectively.[10]

This study aims to observe the lipid profile abnormalities in ß-thalassemia patients so as to guide the pediatricians and staff of thalassemia center for routine screening of lipid abnormalities in these patients in order to prevent the cardiovascular complications due to lipid profile abnormalities and mortality due to these complications.

METHODOLOGY:

This cross-sectional study was conducted in Chemical Pathology section, Pathology department of Sheikh Zayed Medical College and Hospital Rahim Yar Khan for 4 months from 1st July 2022 to 31st October2022. 110 patients aged 1 to 18 years from both genders enrolled in Thalassemia center of Sheikh Zayed Hospital with more than 1 year of regular blood transfusions were included in study using convenient sampling technique after obtaining ethical approval from institutional review board (474/IRB/SZMC/SZH dated 11/6/2022). Informed consent was taken from patients and their parents. Patients with cardiac disease, diabetes mellitus. family history of lipid disorders and not willing to be included in study were excluded. Blood samples were collected in gel tubes which were centrifuged after 30 minutes of collection to obtain clear serum. Serum of each patient was subjected to estimation of serum total cholesterol, serum triglycerides and HDL-C. LDL-C concentrations were determined by Friedewald's formula. All tests were performed on Atellica CH 930 fully automated chemistry analyzer based on spectrophotometry. Age, gender, weekly or monthly transfusion status and all the test results were recorded on predesigned performa. Data was entered and analyzed using SPSS 20. Qualitative data was presented as frequency and percentage while quantitative data was given as mean and SD. Post stratification t-test was applied and p value <0.05 was taken as significant.

RESULTS:

One Hundred and Ten ß-thalassemia patients with multiple blood transfusions were included in study among which 60(54.5%) were males and 50(45.5%) were females. 77(70%) patients were in 1-9 years age group while 33(30%) were

Table 1: Lipid profile abnormalities in ß-thalassemia patients with respect to age

Lipid profile	1-9 years	10-18 years	p-value
Total cholesterol mg/dl	90±20	85±20	0.163
Triglyceride mg/dl	222±76	183±75	0.016
HDL-C mg/dl	21±7.6	20±2.5	0.458
LDL-C mg/dl	29±16	30±18	0.850

Figure 1: Transfusion frequency of patients

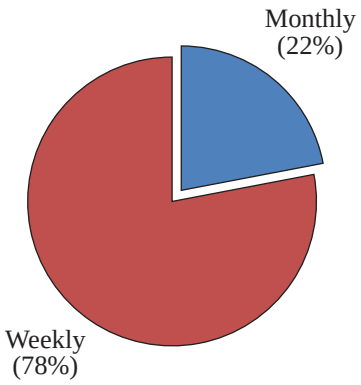

Table 2: Transfusion frequency and lipid profile abnormalities in ß-thalassemia patients

Lipid profile	Weekly Transfusion	Monthly Transfusion	p-value
T.cholesterol mg/dl	88±20	90±18	0.765
Triglyceride mg/dl	222±81	169±44	0.002
HDL-c mg/dl	20±7.0	21±4.6	0.712
LDL-c mg/dl	27±16	36±17	0.023

Table 3: Lipid profile derangement in ß-Thalassemia major patients

Lipid profile	(mean±SD)
T. cholesterol (mg/dl)	89.15±20.33
Triglyceride (mg/dl)	211.00±77.78
HDL-C (mg/dl)	21.01±6.554
LDL-C (mg/dl)	29.79±17.02

in 10-18 years age group. Mean age of the patients was 7.77±3.846 years. Mean triglyceride level in 1–9-year age group was 222±76 mg/dl, while in 10–18-year age group was 183 ±75 mg/dl with statistically significant difference between two groups (p=0.016) as shown in table 1 while difference of serum total cholesterol, HDL-C and LDL-C was statistically insignificant in two age groups. 86(78%) patients were on weekly transfusion while 24(22%) were on monthly transfusion as shown in figure 1. Mean triglyceride level in patients undergoing weekly transfusion was 222±81 mg/dl and in patients with monthly transfusion was 169±44 mg/dl with statistically significant difference of triglycerides between two groups (p=0.002). Mean LDL-C level in patients with weekly transfusion was 27±16 mg/dl and in patients with monthly transfusion was 36±17 mg/dl with statistically significant difference of LDL-C between two groups (p=0.023). Total cholesterol and HDL-C were slightly lower in patients undergoing weekly transfusion than monthly transfusion patients but difference was not statistically significant as shown in table 2. Overall High serum triglyceride and low serum cholesterol, HDL-C and LDL-C levels were observed in ß-thalassemia patients as compared to reference values of these analytes as shown in table 3.

DISCUSSION:

In our study ß-thalassemia patients had high triglyceride level while total cholesterol, HDL-C, LDL-C were low as compared to reference values of these analytes. Serum triglyceride was higher in 1-9 years age group as compared to 10-18 years age group and difference of serum triglyceride between these two age groups was statistically significant. The mean value of Triglyceride (mg/dl) of thalassemia patients in our study was (mean±SD) 211.00±77.78 mg/dl. Higher triglyceride level was observed in patients with weekly transfusion than monthly transfusion patients and difference was statistically significant (p=0.002). The mean serum total cholesterol, HDL-C and LDL-C of thalassemia patients in our study was 89.15±20.33 mg/dl, HDL-C 21.01±6.554 mg/dl and LDL-C 29.79±17.02 mg/dl respectively. A study conducted in Basrah, Iraq showed significantly lower serum total cholesterol, HDL-cholesterol and LDL-cholesterol and significantly higher serum triglyceride in ß-thalassemia major patients as compared to controls ($p<0.05$).[11] Saleh et al reported hypocholesterolemia, hypertriglyceridemia with low levels of HDL-C and LDL-C in ß-thalassemia major patients.[12] A study conducted in northwestern India reported lower total cholesterol and HDL-C in thalassemia patients as compared to controls ($p<0.001$ for both) while triglyceride was higher in thalassemia patients as compared to controls ($p<0.001$).[13] A higher total cholesterol/HDL ratio was also reported in this study.[13] Dyslipidemia was characterized by high triglyceride, low HDL and high cholesterol/HDL ratio in transfusion dependant patients in Eastern India.[14] Dey et al and Mashaali et al reported HDL-C value of 36.58±12.22 mg/dl which was on lower side of their reportable range.[15,16] Dyslipidemia in ß-thalassemia major patients irrespective of age and gender was reported in a Southern Pakistan study.[17] A study conducted in Swat, Pakistan showed high level of serum triglyceride and low level of serum cholesterol and HDL-C in thalassemia patients.[18] Findings of our study are in line with above given reports as hypertriglyceridemia, hypcholesterolemia, lower HDL-C and LDL-C were observed in our study. Inati et al conducted a study in Lebanon and reported altered lipid profile in ß-Thalassemia major patients. In this study lower levels of serum total cholesterol and LDL-C were observed in thalassemia major patients than healthy controls, while no significant difference was observed in serum triglycerides levels of thalassemia patients and controls.[19] A double blind randomized controlled trial of curcumin showed significant decrease in triglyceride as compared to placebo group ($p=0.038$).[20] Main mechanism proposed for this dyslipidemia was severe iron overload, accelerated erythropoiesis, oxidative stress and increased cholesterol utilization.[21] Liver failure due to iron overload, cytokine release, macrophage system activation and hormonal disturbance may also contribute to lipid abnormality.[22] HDL and LDL cholesterol are key components of the lipid profile. Several epidemiological studies have confirmed low HDL-C as a predictive biomarker for atherosclerotic cardiovascular diseases including ischemic heart disease and myocardial infarction.[23] Early identification of thalassemia patients with a altered lipid profile is essential to prevent thrombotic and atherogenic complications. Patients with altered lipid profile particularly hypertriglyceridemia and low HDL-C should be advised dietary and lifestyle modifications and if it is not controlled by these then lipid-lowering agents may be started. Increasing awareness of thalassemia in general population by awareness campaigns, earlier identification, increased blood donation and blood availability for transfusion, modern therapy in iron chelation and proper follow up makes this disease easier to handle.

CONCLUSION:

It is concluded that frequent blood transfusion causes lipid profile abnormalities in thalassemia patients. Lipid profile abnormalities should be screened frequently in ß-thalassamia patients with multiple blood transfusions as these patients are at risk of atherosclerosis and cardiovascular disease due to altered lipid profile particularly high triglyceride and low HDL-C. Therefore diagnosis, awareness and treatment of lipid profile abnormalities is helpful in these patients for prevention of cardiovascular events.

Authors Contribution:
Syeda Sabahat Haidar: Conception and design
Mehvish Sana: Manuscript writing, data analysis, interpretation
Rukhsana Tumrani: Data analysis and interpretation
Farwa Shafqat: Data collection

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