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Assessment of Some Biochemical Markers in Patients with Beta Thalassemia Major

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ABSTRACT

Background: *The hereditary state red blood cells are harmed by beta-thalassemia's poor hemoglobin (Hb) production. A reduced capacity to synthesis one or more globin chains is its defining feature. For patients with this illness to survive, multiple blood transfusions are necessary.* ***Objective****: to examine serum level of serum lipid profiles (Total cholesterol (TC), triglyceride (TG), high density lipoprotein (HDL), low density lipoprotein (LDL) and very low-density lipoprotein (VLDL.* ***Materials and Methods:*** *forty-five patients with β-thalassemia major and forty-five healthy control groups were involved in the present study. Serum lipid profile level in addition to BMI and CRP for both patient and control groups were measured.* ***Results****: Serum TC, HDL-C, LDL-C and BMI revealed significant decreasing in patients with β-t halassemia major as comparing with healthy subjects. The findings of TC, HDL-C, LDL-C and BMI which exhibited through this study are, (117.14 ± 14.22 vs 87.26 ± 11.85, P< 0.001), (25.09 ± 2.96 vs 32.15 ± 6.92, P< 0.001), (66.39 ± 14.83 vs 86.13 ± 19.57, P< 0.001) and (19.32 ± 3.26 vs 22.52 ± 3.61, P< 0.001) respectively. Serum level of TG, VLDL-C and CRP manifested significantly higher in patients than healthy subjects.* ***Conclusion****: In the current study, TC, HDL-C, LDL-C and BMI revealed significant decreasing in patients with β-thalassemia major as comparing with healthy subjects while Serum level of TG, VLDL-C and CRP manifested significantly higher in patients than healthy subjects*

Keywords: β-thalassemia, Lipid profile, Biochemical Markers.

Article Information

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INTRODUCTION

Thalassemia is an inherited blood condition characterized by decreased or missing synthesis of alpha- or beta-globin. The Greek words thalassa, which signifies the Mediterranean sea, and anemia, which means "weak blood," are combined to form the name of thalassemia. Another word that is infrequently used in literature is Cooley's anemia, which is named for Prof. Cooley Thomas, a pediatrician in the United States who first described the clinical characteristics of this sickness in individuals [(1)]. Individuals diagnosed a severe form of microcytic and hypochromic anemia, marked by an increase in red blood cells and a decrease in mean corpuscular hemoglobin (MCH) and mean corpuscular volume (MCV), is seen in people with thalassemia major. The severity of anemia is associated with the quantity of erythroblasts, which increases significantly following splenectomy [(2)]. Transfusion-induced myocardial ischemia causes myocardial disease, the most serious and potentially lethal effect of iron excess in beta-thalassemia. Indeed, it has been found that 71% of deaths in people with beta-thalassemia major are due to cardiac problems[(3)].

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Symptoms of Thalassemia

This disease is observed with the symptoms of severe and chronic anemia, lack of proper growth, enlarged liver and spleen, bone disorders especially visible changes in head and face bones with change of look **(4).** The type of defect and whether one or both genes are impacted determine how severe the condition is. Anemia can range from moderate to severe if both genes are impacted (5). Extramedullary hematopoiesis, or the formation of masses due to blood cell production outside the bone marrow, is another symptom that may manifest. The spleen, liver, lymph nodes, chest, and spine are the main locations for these masses, which may compress nearby tissues and result in a number of symptoms. Those who are affected may develop osteoporosis, leg ulcers, and a higher risk of forming blood clots in veins **(6).**

Clinical Diagnosis

Children under the age of two who exhibit microcytic anemia, moderate jaundice, and hepatosplenomegaly are clinically diagnosed as beta-thalassemia major (TM) **(7).** A patient with beta-thalassemia major will have microcytic hypochromic anemia, as shown by a complete blood count (CBC) with hemoglobin levels below 7 g/dl, a mean corpuscular volume (MCV) between 50 and 70 fl, and a mean corpuscular hemoglobin (MCH) between 12 and 20 pg. MCV 50 to 80 fl, MCH 16 to 24 pg, and Hb between 7 and 10 g/dl are the typical presentation of beta-thalassemia intermedia. Red cell numbers are frequently higher, MCV and MCH are lower, and the red cell distribution width (RDW) is usually low in beta-thalassemia minor. Thalassemia can be distinguished from other microcytic hypochromic anemias, such as iron deficiency anemia and sideroblastic anemia, where the RDW is usually quite high, by using the normal to slightly elevated RDW **(8).**

Laboratory Diagnosis of Thalassemia

A combination of laboratory tests, such as the assessment of red blood cell indices by an automatic hematology analyzer, Hb analysis, and measurement of HbA2 and HbF, are necessary for the diagnosis of thalassemia and abnormal hemoglobin. High-performance liquid chromatography (HPLC) and capillary zone electrophoresis (CE) systems are used to differentiate between thalassemia illnesses. These technologies provide highly accurate qualitative and quantitative analysis of Hb components **(9).** Certain thalassemia mutations can be found by DNA analysis, and point mutations have been found in a number of ways. Thalassemia can also be genotyped using real-time polymerase chain reaction (PCR) and melting curve analysis **(10).**

METHOD AND MATERIAL

The Study of design

Ninety patients and one healthy control are the number of samples that are collected in a case-control study design. The samples were gathered between April and July of 2023.

The study group included 45 patients with β-thalassemia major. The using ages in this study were in range 5-20 years which dependent on visiting patients in Al Zahra Teaching Hospital. Patients with β-thalassemia major were registered in the “Thalassemia Unit” in “Al Zahra Teaching Hospital” Najaf, Iraq. A questionnaire was designed to obtain the information of the detailed history about the present patients with β-thalassemia major, family history, weight, height, age and other anthropometric parameters are calculated on all enrolments. Diabetes mellitus, infection and inflammation, heart diseases were excluded from the study.

For the control group, forty-five healthy volunteers were chosen. They were matched to patients in terms of age and weight. None of the healthy volunteers displayed any symptoms

of infection or anemia, nor did they exhibit any overt systemic or chronic illnesses.

Blood Samples Collection

All samples of patients and healthy volunteers at five milliliters were drown from venous by using a disposable needle and plastic syringes. Five milliliters of blood from patients and healthy volunteers were drowned, allowed to coagulate for ten to fifteen minutes, and then centrifuged (at 4000 xg) for five minutes to separate the serum from the other blood components. The Serum was distributed into five Eppendorf Tubes and stored at (-20Cº) until time of analysis.

Measurement of Body Mass Index

The BMI values were calculated by equation: BMI=Weight (Kg)/Height (m2). It was calculated by electronic balance and height apparatus, the normal weight ranges 18.5to24.9 Kg/m2 and for overweight ranges 25to29.9 Kg/m2, when BMI with more than 30 Kg/m2, the person is absolutely obese, while BMI with more than 40 Kg/m2, the person is morbid.

Determination of serum Lipid Profile

Determination of serum Triglyceride Level

Triglyceride (TG) can be enzymatically hydrolyzed to glycerol according to the following reaction (Fossati and Prencipe 1982). The absorbance was measured at 500 nm.

Determination of serum Total Cholesterol Level

Following oxidation and enzymatic hydrolysis, total cholesterol (TC) is measured. In the presence of phenol and peroxidase, hydrogen peroxide and 4-aminophenazone combine to generate the indicator quinonimine. (Roeschlau, Bernt et al. 1974).

Determination of High-Density Lipoprotein-Cholesterol level (HDL-C).

HDL-C is dissolved by a particular detergent during the second phase, which also involves the activities of cholesterol oxidase and cholesterol esterase. The color of the reaction between peroxidase and 4-amino-antipyrine is related to the amount of HDL cholesterol. (Herrmann, Schütz et al. 1983).

Determination of Low-Density Lipoprotein-Cholesterol (LDL-C) and Very Low-Density Lipoprotein-Cholesterol (VLDL-C).

Low-density lipoprotein – cholesterol (LDL–C) was calculated using Friedwald equation (Friedewald, Levy et al. 1972), while VLDL-C has been calculated by T.G

LDL-C= TC – (HDL-C + VLDL-C) VLDL-C = TG/5

Determination of serum C-reactive protein (CRP) level

Specific kit for measuring CRP concentrations in serum was supplied by Elabscience Biotechnology Co., Ltd. A Catalog No: E-EL-H0043

RESULTS

General Characteristics

In this study, ninety of individuals suffering of β-thalassemia major were examined. The patients have been divided into 46.66% (n=21) males and 53,33% (n=24) females, while forty-five of healthy volunteers included through the study 48.88 % (n=22) males and 51.11% (n=23) females. Age of both patients and controls (range 5-16 years) were approximately matching. BMI and CRP have been calculated for patients and controls as represented in **fig.1**.

Through this study, mean and standard deviation for patients and control groups as well as male's and females' age, BMI and CRP have been calculated as shown in **table.1.** According to the obtained results, age demonstrated non-significant differences for two groups (patients and controls), while found significant difference of BMI and CRP of β-thalassemia patients ($P<0.001$) when it compared with the control subjects.

Table 1. General characteristics of the enrolled patients and control.

Parameter	Patients group (n=45) Mean ± S.D	Control group(n=45) Mean ± S.D	P-value
Age (year)	12.16 ± 3.83	11.80 ± 3.98	0.504 NS
BMI (Kg/m^2)	19.32 ± 3.26	22.52 ± 3.61	<0.001
CRP	3.60 ± 1.52	1.82 ± 0.78	<0.001
Males of β-thalassemia patients and control			
Age (year)	12.92 ± 3.49	11.38 ± 3.80	0.544
BMI (Kg/m^2)	19.19 ± 2.20	22.88 ± 3.25	<0.001
CRP	3.06 ± 1.18	1.58 ± 0.69	<0.001
Females of β-thalassemia patients and control			
Age (year)	12.13 ± 3.39	12.01 ± 3.96	0.698
BMI (Kg/m^2)	19.06 ± 2.32	222.18 ± 3.39	<0.001
CRP	3.58 ± 1.39	1.86 ± 0.66	<0.001

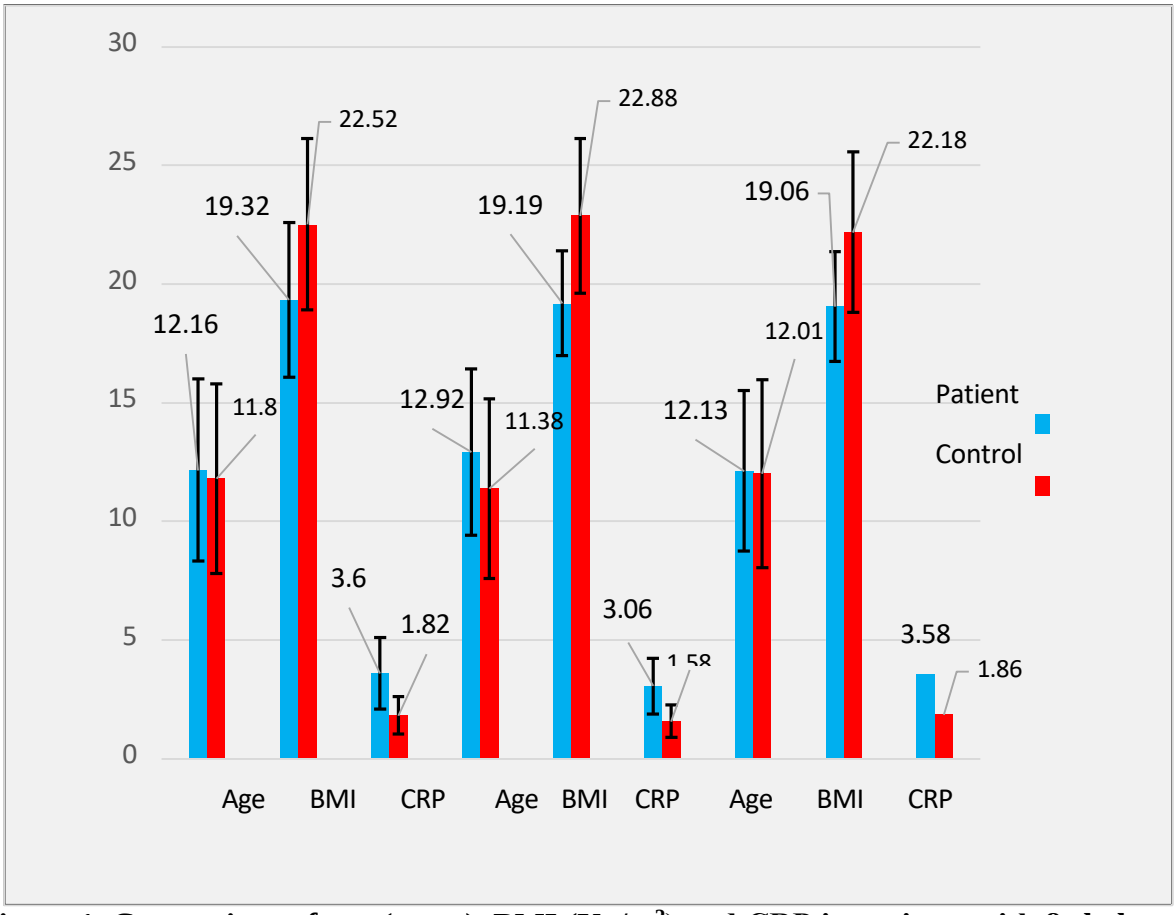

Figure 1. Comparison of age (years), BMI (Kg/m^2) and CRP in patients with β-thalassemia major.

Table 2. Comparison of lipid profile between β-thalassemia patient and control group.

Parameter	Patients group (n=45) Mean ± S.D	Control group (n=45) Mean ± S.D	P-value
HDL-C (mg/dL)	25.09 ± 2.96	32.15 ± 6.92	<0.001
VLDL-C (mg/dL)	25.65 ± 3.42	17.45 ± 2.37	<0.001
LDL-C (mg/dL)	66.39 ± 14.83	86.13 ± 19.57	<0.001
TC (mg/dL)	117.14 ± 14.22	135.73 ± 17.94	<0.001
TG (mg/dL)	128.25 ± 17.12	87.26 ± 11.85	<0.001

Data represented as Mean ±SD: standard deviation, NS= non-significant differences at (P>0.05). *=significant differences at (P< 0.05), **=significant differences at (P< 0.001).

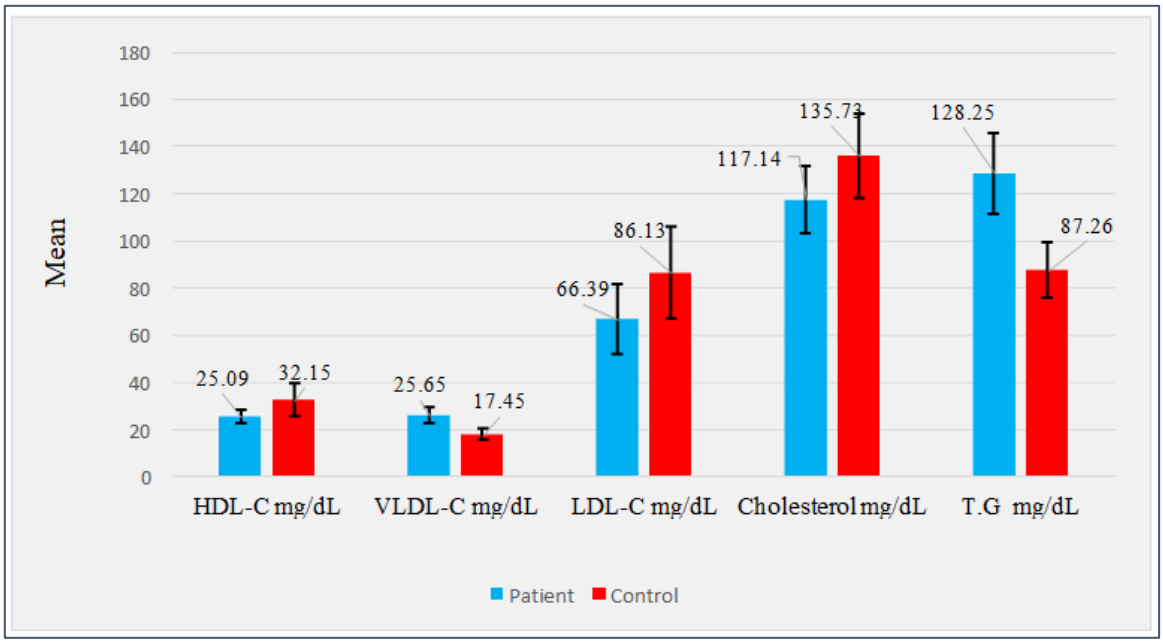

Figure.2. Comparison of lipid profile for mean of patient and control group.

Comparison of serum lipid profile levels between patients and control group.

The clinical parameters of lipid profiles such as TC, T.G, HDL-C, VLDL-C and LDL-C were evaluated in both BTM patients and control group as shown in tab**le 2 and fig 2.** Serum levels of TG and VLDL-C demonstrated statistically significant increasing, whereas TC, LDL-C and HDL-C revealed significant decreasing in patients with BTM as comparing with healthy subjects (P<0.001) as shown in **table 2**. According the sex, the comparison of lipid profile between male's patients and controls has been conducted in this study. Though **table.3**, patients with β- thalassemia have significant increasing in triglyceride and VLDL-C as comparing with control group, whereas HDL-C, LDL-C and cholesterol for BTM patients have significant decreasing when comparing with control group (P<0.001) as shown in **fig.3.**

Table 3. Comparison of lipid profiles between males' patients and control group.

Parameter	Patients group (n=21) Mean ± S.D	Control group (n=22) Mean ± S.D	P-value
HDL-C (mg/dL)	24.99 ± 2.70	33.28 ± 7.58	<0.001
VLDL-C (mg/dL)	25.59 ± 3.71	17.18 ± 2.47	<0.001
LDL-C (mg/dL)	69.34 ± 14.23	75.59 ± 14.45	0.06
TC (mg/dL)	119.93 ± 13.29	126.05 ± 12.63	0.044
TG (mg/dL)	127.98 ± 18.57	85.85 ± 12.36	<0.001

Data represented as Mean ±SD: standard deviation, NS= non-significant differences at (P>0.05). *=significant differences at (P< 0.05), **=significant differences at (P< 0.001).

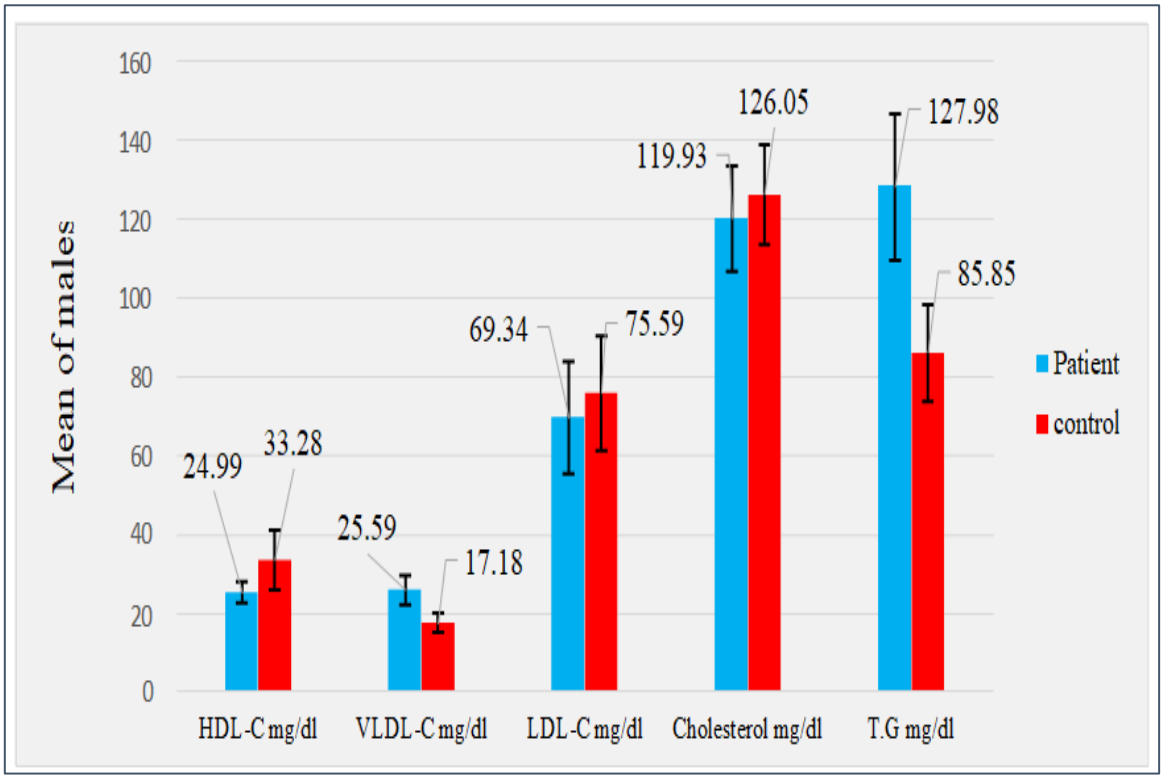

Figure. 3. Comparisons of lipid profile for mean value between of male's patient and control group.

As illustrated in **fig. 4**, lipid profile characteristics were also compared between the control group and female BTM patients. In this study, TG and VLDL-C for β-thalassemia patients have higher than healthy subjects, whereas cholesterol, LDL- C and HDL-C were lower in patients than control group (P<0.001) as shown in **table 4.**

Table 4. Comparison of lipid profiles between females' patients and control group.

Parameter	Patients group (n=24) Mean ± S.D	Control group (n=23) Mean ± S.D	P-value
HDL-C (mg/dL)	25.18 ± 3.18	31.08 ± 6.17	<0.001
VLDL-C (mg/dL)	25.69 ± 3.18	17.71 ± 2.27	<0.001
LDL-C (mg/dL)	63.90 ± 14.98	95.98 ± 18.72	<0.001
TC (mg/dL)	114.78 ± 17.57	144.78 ± 14.67	<0.001
TG (mg/dL)	128.48 ± 15.92	88.57 ± 11.39	<0.001

Data represented as Mean ±SD: standard deviation, NS= non-significant differences at (P>0.05). *=significant differences at (P< 0.05), **=significant differences at (P< 0.001).

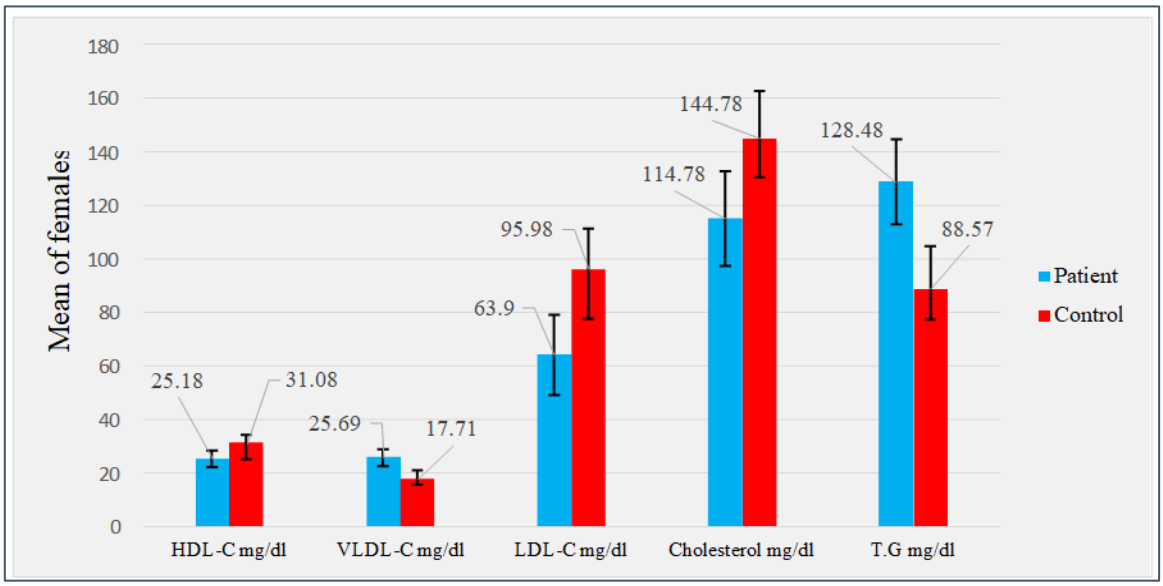

Figure 4. Comparisons of lipid profile for mean value between of male's patient and control group.

DISCUSSION

Serum levels of HDL-C, VLDL-C, LDL-C, cholesterol, and TG in BTM patients showed substantial differences (P<0.001) from the control group in the current investigation. The abnormalities of lipid profile in patients with BTM are likely occurred by the diminished hepatic efficiency due to anemia and iron overload, and accelerated erythropoiesis, with excess uptake of cholesterol by macrophages of the reticuloendothelial system leading to hypocholesterolemia, low plasma cholesterol and an increased uptake of LDL-C, while reduced extrahepatic lipolytic activity could account for the rise in the circulating triglyceride [(11)]. It appears that oxidative stress and extreme iron overload are the primary causes of hypocholesterolemia in BTM. [(12)] and [(13)]. According to Amendola and colleagues [(14)], increased bone marrow activity and increased cholesterol intake may be the cause of lipid abnormalities in BTM.

In TDT patients, dyslipidemia and its consequences have raised the risk of endothelial dysfunction, thromboembolic events, and early atherogenesis, The lipid

profile imbalance increases the risk of pancreatitis and cardiovascular and cerebrovascular effects because it increases atherogenesis and blood triglyceride levels. Lipid and carbohydrate metabolisms in BTM patients are further impacted by insulin resistance and liver damage from transfusional iron excess [(15)] and [(16)], While the change in the lipid profile is most likely the result of a hepatic disorder caused by anemia, iron overload, hormonal imbalances, and the rapid breakdown of HDL and LDL by activated monocytes and macrophages, the increase in circulating triglycerides may be caused by a decreased extrahepatic lipolytic action, according to a recent study by Ray and colleagues [(17)].

According the preceding studies, the mechanism of abnormalities in lipid profile for BTM were detected. These lipid profile abnormalities result from decreased hepatic production, as anemia and iron overload lower cholesterol, HDL-C, and LDL-C while lowering extrahepatic lipolytic activity in patients raises triglycerides [(18), (19),(20)]. One of the causes which lead to lipid abnormalities in BTM is iron overload that is associated with increased oxidative stress, lipid peroxidation and liver damage, may affect lipid synthesis and metabolism among patients with BTM [(21)]. According to another study, patients with BTM are more likely to experience thrombotic and atherogenic consequences; therefore, it is necessary to identify these patients with abnormal lipid profiles early on in order to prevent these complications [(22)]. The present findings are in agreement with previous studies which showed an increase in TG and VLDL-C, and decreasing in HDL-C, LDL-C and Cholesterol for BTM as comparing with control group [(23), (24)].

CONCLUSTION

Through this study, TG and VLDL-C exhibited a significant increasing in patients with β-thalassemia major, while TC, LDL and HDL appeared singnificant decrease in patients with β-thalassemia major as comparing with healthy participants. In other words, BMI revealed significant decreasing and CRP exhibited significant increasing in patients with β-thalassemia major as comparing with control group, whereas age revealed non-significant between patients and control groups.

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