Original article

Lipid Profile in Iraqi Children with ß-thalassemia Major

Jawad k.Mashaali Msc, bacteriology unit, National center of hematology/ Almustansiriya University

Fatma A. Obed Msc, Aphresis unit, National center of hematology/ Almustansiriya University

Noor Thair Tahir , National Diabetes Center / Almustansiriya University

ABSTRACT

Background: Thalassemia are group of genetic disorders in which production of normal hemoglobin (Hb) is partly or completely suppressed because of defective synthesis of one or more globin chains, vary from asymptomatic forms to severe or even fatal entities . People with thalassemia make less hemoglobin which results in mild or severe anemia present as microcytic anemia. thalassemias are classified according to which chain of the hemoglobin molecule is affected. In α thalassemias, α globin chain is affected, while in β thalassemia, production of the β globin chain is affected. Lipid abnormalities have been detected in different types of beta thalassemia, suggested mechanisms including plasma dilution due to anemia, accelerated erythropoiesis resulting in increased cholesterol uptake by macrophages and histiocytes of the reticuloen-dothelial system, defective liver functioning due to iron overload, macrophage system activation with cytokine release, and hormonal disturbances,

Objectives: The purpose of the study was to examine the blood lipid profile in children with beta-Thalassemia major in Iraq , and to determine the factors that affect it.

Material and Method: Blood lipid profiles of forty-five patients between the ages of three and ten years with beta-Thalassemia major who were receiving regular chelation therapy followed by from paediatric clinic of Ibn-albalady hospital were examined retrospectively. Blood lipid profiles of thirty healthy children were taken for use as the control group.

Results: Hb and Hct values of the group with Beta-Thalassemia major were significantly lower than the control group . Ferritin values in the group with Beta-Thalassemia major were found to be significantly higher than in the control group . Cholesterol, HDL-cholesterol, LDL-cholesterol levels were found to be significantly lower in patients with Beta-Thalassemia major than in the control group , while the triglyceride level was found to be higher .

Conclusion: lower total cholesterol, LDL-HDLcholesterol and high TG was found in BTM groups compared to healthy control participants. The suggested mechanisms for the decreases in lipids are increased erythropoiesis and cholesterol consumption, iron overload, hormonal change and oxidative stress in BTM.

Key words:-lipid, thalassemia, children

Introduction:

Thalassemia are the most common heterogeneous group of genetic disorders in which production of normal hemoglobin (Hb) is partly or completely suppressed because of defective synthesis of one or more globin chains, that vary widely in severity from asymptomatic forms to severe or even fatal entities [1,2].

People with thalassemia make less hemoglobin and have fewer circulating red blood cells than normal, which results in mild or severe anemia present as microcytic anemia.

Thalassemia is classified according to which chain of the hemoglobin molecule is affected. In α thalassemia, production of the α globin chain is affected, while in β thalassemia production of the β globin chain is affected. The β globin chains are encoded by a single gene on chromosome 11; α globin chains are encoded by two closely linked genes on chromosome 16[3].

There are>200 mutations for ß-thalassemia , about20 common alleles constitute80% of the known thalassemia worldwide:3% of population carry genes for ß-thalassemia .in united states 2000 persons have ß-thalassemia[4].

During the 2nd 6mo. Of life, infant with ß-thalassemia usually become symptomatic from progressive hemolytic anemia with cardiac decompensation .so transfusions are necessary beginning in 2nd month to 2nd yrs. of life according to the child ability to compensate for the degree of anemia .the classic presentation of children with severe anemia (Cooley's anemia) includes thalassemic facies, pathologic fracture, marked hepatosplenomegaly and cachexia.

Thalassemia can cause significant complications, including iron overload, bone deformities, cardiovascular illness and transfusion related infection like HBV, HCV AND HIV. However this same inherited disease of red blood cells may confer a degree of protection against malaria, which is or was prevalent in the regions where the trait is common. This selective survival advantage of carriers (known as heterozygous advantage) may be responsible for perpetuating the mutation in populations [5, 6].endocrinopathy, heart&liver disease, chelation therapy complication and bacterial infection are noticed as a complication of iron overload.

Lipid abnormalities have been detected in different types of beta thalassemia, and also in various hematological disorders including sickle cell disease, glucose-6-phosphate dehydrogenase (G6PD) deficiency, spherocytosis, aplastic anemia and myelodysplastic syndrome.[7-11] The pathogenesis of these abnormalities is not exactly clear, but there are many suggested mechanisms including plasma dilution due to anemia, accelerated erythropoiesis resulting in increased cholesterol uptake by macrophages and histiocytes of the reticuloendothelial system, defective liver functioning due to iron overload, macrophage system activation with cytokine release, and hormonal disturbances.[9,12].

The aim of this research is to assess the lipid profiles in Iraqi children with BTM and to compare the findings to those in healthy control participants.

Material and methods

The study group consisted of patients with thalassemia major (n = 45) selected Randomly from the patients referred to the thalassemia clinic in Ibn-al balady hospital. This study was conducted over a 3-month period (February-January-May 2014), 25female, 20male were diagnosed by clinical history, requirement for regular blood transfusions, and laboratory tests including complete blood count (CBC) and hemoglobin electrophoresis. All of the 45 patients studied were on iron chelation therapy. Exclusion criteria were having diabetes mellitus, renal failure and hereditary hyperlipidemia.

The control group consisted of 30 healthy participants matched for sex and age distribution. They selected from the children who referred for checkup. The age of participants in all tow groups was Between three to ten years. Serum lipid profile was determined in all patients and controls following overnight fasting. TC, triglycerides (TG) and HDL were determined enzymatically by using commercial analytical kits (randox&human-NM500) measured by CECIL 1011 analyzer (France). The levels of LDL-C were estimated by calculation using the formula of Friedewald and Levy[13]. LDL-cholesterol= (TC)-(TG/5)-(HDL cholesterol).VLDL=TG/5. Serum ferritin concentration was assayed using a commercial kit (monobind). Hemoglobin was assayed using hemolyzer5 (Germany). All results are expressed as means standard deviation (SD). Comparison between controls and thalassemic patients were performed by using Student's t-test. Relationships were considered significant if the corresponding *P* value < 0.05.

Result

In Table 1. It is clear from the results that a significant decreases. ($p<0.05$) of hemoglobin concentration in both male and females was noticed in comparison with control. serum ferritin concentration was significantly higher in both males and females (2368±1670, 2286±1600 respectively) in comparison with controls (58±39, 53±14 respectively).

Table 1. Hematological data of B-thalassemia major patients

Hematologic parameters	Patients (45)		Controls (30)		p
	Male (20)	Female (25)	Male (12)	Female (18)	
Hemoglobin (g/dl)	9.1±2.2	8.4±1.8	11.8±0.6	12±0.9	**p<0.05**
Hematocrit (%)	28±6	27±4	35±1.6	37±1.4	**P<0.05**
Ferritin (µg/L)	2368±1670	2286±1600	58±39	53±14	**P < 0.05**

Table2:- Serum lipids (mean± SD) levels of male and female children with ß-thalassemia major*

	Patients		Controls	
	Male (20)	Female (25)	Male (12)	Female (18)
Cholesterols (mmol/l)	3.127±1.09	3.2±o.8	4.8±1.8	4.64±1.4
Triglyceride (mmol/l)	2.4±o.8	2.81±o.6	1.7±o.8	1.06±0.14
HDL-Ch (mmol/l)	o.721±o.426	0.82±0.62	2.8±0.8	2.42±0.8
LDL-Ch (mmol/l)	1.808±0.82	1.63±o.8	2.9±0.6	2.5±0.6
VLDL-CH (mmol)	0.355±0.15	o.35±0.18	0.52±0.3	0.44±0.5

TC: total cholesterol (normal value 3.9-6.5); TG: triglycerides (normal value0.9-2.4); HDL-C: high-density lipoprotein cholesterol (normal value0.8-4.4); LDL-C: low-density lipoprotein cholesterol(normal value1.8-3.4);very low –density lipoprotein(normal value<0.53).
*p-value 0.03

patients with ß- thalassemia major had significantly lower total cholesterol (TC), high-density lipoprotein cholesterol (HDL-C) , low-density lipoprotein cholesterol (LDL-C)and very low-density lipoprotein compared with controls (p-value 0.03). serumTG levels of males and females patients (2.4±o.8,2.81±o.6respectively) were higher than in control males and females (1.7±o.8, 1.06±0.14respectively

Discussion

The aim of this research is to assess the lipid profiles in patients with BTM in iraq, and to compare the findings to those in healthy control participants. The majority of the patient had low total cholesterol levels, HDL cholesterol , LDL cholesterol and VLDL cholesterol levels.

In addition triglycerides levels were substantially high. The present findings are in agreement with those of Papanastasiuo et al, Hartman et al, and Amendola et al, who showed that TC and LDL-cholesterol levels were lower in persons with BTM than in the control group [14,15,16]. Papanastasiou et al., also found a positive correlation between age and triglycerides levels, while the present study observed no similar relation . Different results were obtained in studies in terms of explaining the serum lipid changes observed in patients with B-TM [17]. This alteration is likely due to diminished hepatic biosynthesis as of anemia and iron overload (high ferritin level), hormonal disturbances, and the quick cleaning of modified HDL and LDL (richer than triglyceride, poor, cholesterol ester) by activated monocytes and macrophages were held responsible. while a reduced extrahepatic lipolytic activity could account for the rise in circulating TG [18]. Some studies have suggested that low blood cholesterol values in patients with B-TM occur as a result of an increase of erythropoiesis and increase of LDL uptake by macrophage and histiocytes in reticuloendothelial system (RES)[19,20]. Giardini O et al, found that total phospholipids and its functions also decrease with the decrease of total cholesterol, and levels of serum lipid multiple unsaturated fatty acids decreased, Those changes appear as a result of excessive iron-loading and liver damage [21]. However in our study, results are not sufficient to clarify the subject. A positive correlation between triglyceride and serum ferritin levels in our study noticed, This also suggest us that it may be effective on blood lipid values as a result of excessive iron-loading. These results may support the hypothesis that both serum iron and serum triglyceride play role in LDL-C oxidation pathogenesis. Increased susceptibility of red-blood-cell lipids to auto-oxidation in thalassemia major has been documented [22,23]. Since auto oxidation may be initiated by free radicals, which are constantly formed in the normal red cell, and may be especially prevalent when unstable hemoglobin is present[24]. This suggests that the use of antioxidants (like vitamin E, ascorbic acid and xanthin oxidase inhibitors) may have a protective effect improving red

cell survival. Also, iron supplements and oxidative drugs should be avoided for the patients of β-thalassemia who receive regularly blood transfusions. Using appropriate iron chelators (deferoxamine and deferiprone) will eliminate oxidative red cell damage in β-thalassemia [25,26]

Because of the regular blood transfusions, all ß- thalassemia patients had abnormally very high levels of serum ferritin (2368±1670 in male, 2286±1600 in female µg/l) compared to the reference range (58±39, 53±14 µg/l respectively), indicating that these patients have iron over load, probably due to multiple blood transfusion, increased dietary iron absorption or inadequate chelating therapy with DFO [25]

Conclusions

In conclusion, lower total cholesterol, LDL-HDL cholesterol and high TG was found in BTM groups compared to healthy control participants. The suggested mechanisms for the decreases in lipids are increased erythropoiesis and cholesterol consumption in BTM, iron overload, hormonal change and oxidative stress in BTM. Awareness to these findings is helpful to avoid unnecessary evaluation in patients with beta-thalassemia. However more future researches are needed for confirmation and explanation of this relationship as well as clarification of the exact mechanism and clinical consequences of the decreases in lipids in patients with beta-thalassemia

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Correspondence to:
Jawad k.Mashaali MSc
Department of bacteriology
The national center of hematology
Almustansiriya university
Baghdad/Iraq