Lipid Profile in Jordanian Children with ß-thalassemia Major

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ABSTRACT

The aim of the present study was to investigate the lipid pattern in Jordanian children with Beta-thalassemia major (ß-TM). Twenty six transfusion dependent ß-TM patients, 14 males and 12 females, (mean age 9 ± 5 years) that undergo periodical blood transfusion and desferioxame as a chelating agent, were studied. Twenty controls of matched age and gender were also included in the study. ß-thalassemia major patients showed significantly lower total cholesterol, high-density lipoprotein cholesterol and low-density lipoprotein cholesterol when compared with control. Serum triglycerides levels of TM patients were found to be significantly higher than levels in control subjects. Our results revealed that lipid profile changed in patients with major ß-TM. Many factors such as iron overload, liver injury, hormonal disturbances and aging might cause these changes.

Key Words: ß-thalassemia major, Lipid profile, Cholesterol, Triglyceride, High-density lipoprotein, Low-density lipoprotein

ÖZET

ß-Talassemi Majör Hastası Ürdünlü Çocuklarda Lipid Profili

Bu çalışmanın amacı, ß-talassemi (ß-TM) majör hastası olan Ürdünlü çocuklarda lipid paternini incelemektir. Periyodik kan transfüzyonu yapılan ve desferoksamin tedavisi alan 14 erkek ve 12 kız (ortalama yaş=9±5) toplam 26 ß-TM hastasıçalışmaya alınmıştır. Yaş ve cinsiyet eşleştirilen 20 çocuk kontrol grubu olarak alınmıştır. Kontrol grubu ile karşılaştırıldığında, ß-TM hastalarında istatistiksel olarak anlamlı düzeyde düşük kolesterol düzeyi, yüksek yoğunluklu lipoprotein kolesterolü ve düşük yoğunluklu lipoprotein kolesterolü tesbit edilmiştir. Serum trigliserit düzeyleri kontrol grubuna göre ß-TM hastalarında anlamlı olarak daha yüksektir. Bulgularımız, majör ß-TM hastalarında lipid paterninin değiştiğini ortaya koymuştur. Demir yükü, karaciğer hasarı, hormonal bozukluklar ve yaşın bu değişiklikte rol oynayan faktörler olduğu düşünülmüştür.

Anahtar Kelimeler: ß-talassemi majör, Lipid profili, Kolesterol, Trigliserid, Yüksek yoğunluklu lipoprotein, Düşük yoğunluklu lipoprotein

INTRODUCTION

Thalassemia are the most common heterogeneous group of genetic disorders in which the 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). Patients with ß-thalassemia major may go through several complications as the transfusion-related infections like HBV, HCV, and HIV (3). Iron overload complication are also noticed that includes endocrinopathies, heart and liver diseases, chelation therapy complications (4) and bacterial infections. Thalassemic patients are also subjected to peroxidative tissue injury. It has been documented that circulating low density lipoprotein-C (LDL-C) in thalassemic patients show marked oxidative modification that could represent an event leading to pathogenesis. Free-radical production is increased in patients with iron overload. Iron-loaded patients have elevated plasma levels of thiobarbituric acid reactants and increased hepatic levels of aldehyde-protein adducts, indicating lipid peroxidation (5). During the past years many scientific evidences have raised the adverse effect of abnormal blood lipid levels, like total cholesterol and other lipids and lipoproteins, on atherosclerotic disease (6-8). At this point it should be mentioned that the relationships between blood lipids and atherosclerosis might be influenced by several other lifestyle-related factors, like glucose intolerance, blood pressure levels, dietary habits and smoking habits (9). Selimo et al., (10) suggested that both serum iron and triglycerides are involved in the pathogenesis of LDL-C oxidation. However, blood lipids in these patients have rarely been investigated (5). In this study we examined for the first time the lipid profile of the Jordanian thalassemic children.

PATIENTS AND METHODS

Patients

The study population included 26 patients with ß-TM major (12 females and 14 males) that undergo periodical blood transfusion and DFO as chelating agent. Patients are treated in Thalassaemia Unit at Princess Rahma Educational Hospital in Irbid –Jordan. All patients were tested for HBV, HCV using the immunological available kit. None of them revealed to have positive results. On the other hand, patients were also tested for HIV using immunological available kit. None of them showed positive results. The tested group aged from 4-14 years. The diagnoses of ß-TM major were made based on the clinical, hematological and hemoglobin electrophoresis profiles and the results of ß-globulin chain synthesis which is indicative sign of the presence of ß-TM major. Twenty controls (10 males and 10 females) of matched age and gender were also included in the study. All patients were interviewed and filled out standardized questionnaires during the first visit of study and their medical histories were obtained from the hospital files. All patients were transfusion dependent at a rate ranged from one to three times monthly. Also, all of them are treated with deseferal (S.C. administration of infusion of 2 grams or 2.5 grams using infusion pimp). None of the subjects was treated with vitamin E supplementation before the study.

Blood Collecting

Blood samples were drawn from the thalassemic patients (whom are free from HBV, HCV and HIV) in plain tubes and allowed to clot, then centrifuged to obtain serum using a bench top centrifuge (Cenformix). In addition to the 3ml venous blood samples in the plain tubes the control group were asked to give an additional 1 ml in EDTA tube for Hb test.

Methods

Serum lipid profile was determined after 12-14h of fasting, including: total cholesterol (TC), triglycerides (TG), high-density lipoprotein cholesterol (HDL-C) and low-density lipoprotein cholesterol (LDL-C). Standard hematological and biochemical procedures were used. TC, TG, LDL-C and HDL-C of all the subjects were evaluated using commercial analytical kits from Sigma (St. Louis, Mo, USA).

Serum ferritin concentration was assayed using a commercial kit from Bio System (S.A. Spain). ALT and AST activity were assayed according to Wroblewski and Karmen procedure using a commercial Kit (TECO DIAGNOSTICS, USA). Hemoglobin was assayed using a blood analyzer (BC-2800, MINDRAY AUTO HEMATOLOGY ANALIZER - China)

Table 1. Hematological and biochemical data of ß-thalassemia major patients

Hematologic parameters	Patients (26) *		Controls (20)*		
	Male (14)	Female (12)	Male (10)	Female (10)	P
Hemoglobin (g/dl)	9.3±2.6	8.6±1.2	11.9±0.7	12.1±0.9	P < 0.05
Hematocrite (%)	29 ±2.0 27±4.2	35±2.6	36±3.8	P < 0.05	
Ferritin (μg/L)	2418±1679	2376±1558	58 ± 32	52 ± 24	P < 0.05
AST (IU/L)	37.27±5.18	34.14±7.42	36.9±6.60	37.23±5.37	P < 0.05
ALT (IU/L)	33.66±8.05	32.62±12.53	34.85± 6.20	35.87±9.40	P < 0.05

* The number of the subjects
AST: aspartate aminotransferase; ALT: alanine aminotransferase

Statistical Analysis

All quantitative data were expressed as mean ± S.D. Statistical analyses were calculated using the ORIGIN and MINITAB software. ANOVA, student two sample t-tests, and the correlation analysis were used to compare the data.

RESULTS

Table 1 shows the hematological and biochemical results of the examined patients and the control. It is clear from the results that a significant decrease ($p<0.05$) of hemoglobin concentration in both males and females was noticed in comparison with controls. On the other hand, ferritin concentration was significantly higher in both males and females (2418 ± 1679, 2376 ± 1558 respectively) in comparison with controls (58 ± 32, 52 ± 24 respectively). The results of various lipid analyses of controls and thalassemic children are presented in Table 2. ß-thalassemia major patients had significantly lower total cholesterol (TC), high-density lipoprotein cholesterol (HDL-C) and low-density lipoprotein cholesterol (LDL-C) compared with controls ($p<0.05$).However serum TG levels of ß-TM males and females patients (148 ± 37, 136 ± 41 respectively) were significantly higher than in control males and females (92 ± 18, 84 ± 08 respectively) ($p<0.05$).

DISCCUSSION

Our study investigated the distribution of some blood lipids in the blood of Jordanian children with beta thalassemia major. It was found that the majority of the participants had low total cholesterol levels HDL cholesterol and LDL cholesterol levels. In addition, triglycerides levels were substantially high. Papanastasiou et al., (11) have shown that total cholesterol, HDL and LDL-cholesterol was significantly decreased, while triglycerides were significantly increased in the thalassaemic patients compared to the control subjects. They also found a positive correlation between age and triglycerides levels. The present study also observed similar results regarding blood lipids levels among our patients and the healthy controls from the general population of Jordan. Other study on beta thalassaemia major in patients from Italy found that these patients disclosed significantly lower total-cholesterol, LDL cholesterol, HDL cholesterol and higher triglycerides concentration (11). It appears, therefore, that many factors such as iron overload (high ferritin level), liver injury (disturbance of the ratio between AST and ALT), and hormonal disturbances affects lipids pattern among patients with major form of beta-thalassemia. Some authors suggested that accelerated erythropoiesis and increased uptake of LDL by macrophages and histiocytes of the reticuloendothelial system are the main determi-

Table 2. Serum lipids (mean± SD) levels of male and female children with ß-thalassemia major

	Patients		Controls		
Parameter	Male (14)	Female (12)	Male (10)	Female (10)	P
Triglycerides (g/dl)	148 ± 37	136 ± 41	92 ± 18	84 ± 08	P < 0.05
Cholesterol (g/dl)	109 ± 22	124 ± 32	179 ± 31	168 ± 45	P < 0.05
HDL-Ch (g/dl)	34 ± 13	38 ± 14	53 ± 5	49 ± 7	P < 0.05
LDL-Ch (g/dl)	58 ± 23	62 ± 28	136 ± 38	100 ± 17	P < 0.05

TC: total cholesterol; TG: triglycerides; HDL-C: high-density lipoprotein cholesterol;
LDL-C: low-density lipoprotein cholesterol

nants of low plasma cholesterol levels in beta thalassemia major (12,13). In addition, total serum phospholipids, their fractions and cholesterol were significantly lower among patients with thalassemia major (14). These changes were referred to hepatic damage and to iron overload. Furthermore, some serum lipid polyunsaturated fatty acids were significantly decreased among patients with beta thalassemia major as compared to normal controls. Since these alterations are a sign of lipid oxidation, the causes of this phenomenon were studied. These differences on blood lipids and lipoprotein levels could also attribute to the adherence of a heal their lifestyle by people with beta thalassemia, which could include consumption of healthy foods since childhood. However, a recent report (15) showed that adolescents with beta-thalassemia minor have significantly lower cholesterol levels than patients with beta thalassemia major. The investigators suggested that this has been related to their disorder and not influenced by age, gender, hemoglobin or ferritin levels. At this point it should be noted that the extrapolation of our findings into other populations with beta thalassemia major might be under scrutiny, since thalassemia is genetically oriented and various expressions of the related polymorphisms may be involved in the distribution of blood lipids and lipoprotein levels. Increased susceptibility of red-blood-cell lipids to autooxidationin thalassemia major has been documented (5,16). Since autooxidation 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 (17).

This study shows similar results in lipid profile of thalassemic patient that were observed by other studies, where significant decrease in total cholesterol and HDL-C were detected (18, 19). Triglycerides lipase activities (both hepatic and extrahepatic) were significantly lower in thalassemic patients. Christina et al. (19) speculated that the decreased levels of these enzymatic activities could play a role in determining the decrease of HDL-C observed in thalassaemic patients.

The present findings are in agreement with those found by other studies (20,21) as there is significant increase in plasma TG level, which is the same as detected by Pogana et al., (22). However other researchers did not find such differences (23). They also noted an increase in TG with increasing ferritin values and a positive correlation of the patients' TG with both age and oxidative LDL-C antibodies (24). A decrease in the amount of stored iron only known cause for a low serum ferritin result (25); while increased stored iron (overload) associated with raised serum ferritin levels (e.g. massive blood transfusion). Also liver disease or inflammation will result in high serum ferritin levels (26). Serum

ferritin, Hb and two liver enzymes activities were evaluated in our study in a sample of selected thalassaemic patients from the northern part of Jordan whom have ß-thalassemia major, and whom under regular blood transfusions and chelation therapy. Patients whom were infected with or suspected to be infected any sort of disease e.g. Hepatitis, HIV, Diabetes, were excluded from this study.

Because of the regular blood transfusions, all ß-thalassemia patients had abnormally very high levels of serum ferritin (2397 ± 1768 μg/l) compared to the reference range (7-140 μg/l), indicating that these patients have iron over load, probably due to multiple blood transfusion, increased dietary iron absorption or inadequate chelating therapy with DFO (9). Moreover, pretransfusion hemoglobin level was assayed for each individual and it was (8.9 ± 2.4).

In this study TG level could be correlated positively with the serum ferritin levels. These results might support the hypothesis that both serum iron and triglycerides are involved in the pathogenesis of LDL-C oxidation (10). Our results showed that LDL-C was significantly decreases in its values and it is in agreement with those found by other workers (30). Moreover Maioli et al., showed that LDL-C was influenced by both diagnosis and ferritin levels (12). In the present study we elicited a significant positive correlation between ferritin and TG a marker of disturbed lipid profile with abnormal iron overload and inadequate chelating therapy with DFO. Data analysis of our study showed that the lipid profile in TM patients is not influenced by age, sex, liver injury, hemoglobin or ferritin levels (Table 1); the higher erythroid bone marrow activity with the enhanced cholesterol consumption could be the dominant mechanism implicated in the lipid abnormalities of TM patients.

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