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IJPBS |Volume 2| Issue 2 |APRIL-JUNE |2012|106-112

LIPID ABNORMALITIES IN PATIENTS OF BETA THALASSAEMIA MAJOR

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BIOLOGICAL SCIENCES RESEARCH ARTICLE

RECEIVED ON 30-04-2012 ACCEPTED ON 10-05-2012

ABSTRACT

Beta thalassaemia is considered to be the most frequent hereditary blood disorder worldwide. Lipid abnormalities have been detected in different types of beta thalassaemia. In the present study clinically diagnosed 50 patients of beta thalassaemia major were included. Significant changes confirm that lipid abnormality occur in thalassaemic patients when total cholesterol, high density lipoprotein cholesterol, low density lipoprotein cholesterol and Serum triglycerides levels compared with normal healthy subjects. Many factors such as iron overload, liver injury, hormonal disturbance and ageing might cause these changes. Hence this study may focus on lipid abnormalities in beta thalassaemia major, which may help physicians to design the therapeutic module in the treatment of such patients.

KEYWORDS: *Beta thalassaemia major, Total Cholesterol (TC), Triglyceride (TG), High density lipoprotein (HDL), Low density lipoprotein (LDL)*

INTRODUCTION

Beta thalassaemia major is a very serious blood condition since individuals with it are unable to make enough healthy red blood cells and depend on blood transfusions all their life. It is the most prevalent type of thalassaemia as it is common in certain populations and causes severe anaemia in its homozygous state. Thalassaemia represents the most common single gene disorder causing a major public health problem. About 190 million people throughout the world have genetic mutations associated with different hemoglobinopathies and more than 90 million of them carry defective genes leading to thalassaemia. In India, every year more than 10,000 children are born with beta thalassaemia major.[1,2,3] It is the risk of an iron overloading in various organs, which is through repeated blood transfusion and increased iron absorption from the gastrointestinal tract. Iron overload may particularly cause injury to the heart, liver and endocrine glands. Iron-induced liver injury is often characterized by the development of fibrosis and eventually, cirrhosis. [4]

Beta thalassaemic patients who usually have a combination of chronic haemolytic anaemia, iron storage disease, myocarditis, and premature death especially due to heart failure may also have increased oxidation of lipids and abnormal lipoprotein concentrations. In beta thalassaemia major,

liver damage accounts for the low total cholesterol (TC),high density lipoprotein cholesterol (HDLc) and low density lipoprotein cholesterol (LDLc) serum levels.[5] Moreover, it is known that severe chronic liver disease is characterized both by low total and LDL cholesterol level and by decrease in HDL cholesterol.[6]

To the best of our knowledge no data are available on lipids serum concentrations in Indian patients with beta thalassaemia major. This lack of information prompted us to determine the lipids levels, in comparison to controls and evaluate its significance in Indian patients with beta thalassaemia major.

PATIENTS AND METHODS

The prevalence of beta thalassaemia major is high in tribal and non-tribal population in area around Dhule, Nandurbar and Jalgaon districts of Maharashtra. After clinical examination and confirmed diagnosis by physician 50 blood samples were randomly collected from-

Shri Bahusaheb Hire Government Medical College & Hospital, Dhule, ACPM Medical College and Hospital, Dhule and Navjeevan Blood Bank, Thalassaemia Center, Dhule (Maharashtra),during June 2010- Dec 2011. These patients were compared with healthy normal participants on the basis of age, sex, dietary conditions and life styles. Mean age of patients and participants was in range between 10 to 31 years. Exclusion criteria were having diabetes mellitus, hypothyroidism, hyperthyroidism, renal failure and hereditary hyperlipidemia. The levels of Hb, Iron, Cholesterol, Triglyceride, HDLc, LDLc, VLDLc, were measured by using latest techniques in clinical biochemistry laboratory.

METHODOLOGY AND TECHNIQUES

1. Iron - Dipyridyl method
2. Cholesterol - Enzymatic method
3. HDL Cholesterol-Phosphotungstate method
4. LDL Cholesterol - Friedewalds formula
5. VLDL Cholesterol- Friedewalds formula
6. Triglyceride- Enzymatic method
7. Phospholipid- Aldersberg's equation

The research protocol was approved by the ethics committee of ACPM Medical College and Hospital Dhule.

Statistical Analysis

The data obtained in our study was analyzed for its statistical significance using 'z' test. P value less than 0.05 was considered the level of significance.

RESULTS

The demographic and biochemical characteristics of patients with thalassaemia are shown in table-

Parameter	Group I (n= 50)	Group II (n= 50)
Age (Year)	23.1 ± 6.4	23.7 ± 7.1
Sex (Male/Female)	27/23	25 / 25
Hb (g/dL)	9.5 ± 2.8 ©	11.4 ± 0.2
Serum Iron (µg/dl)	165.55 ± 14.30 ©	112.14 ± 15.28
TC (mg/dL)	178.08 ± 24.24 ©	263.4 ± 32.15
TG (mg/dL)	205.18 ± 64.92 ©	122.86 ± 24.70
HDL-C (mg/dL)	39.5 ± 6.62 ©	48.76 ± 7.06
LDL-C (mg/dL)	98.10 ± 22.63 ©	188.29 ± 40.87
VLDL-C (mg/dL)	41.30 ± 12.98	24.57 ± 4.94
Phospholipids (mg/dL)	226.47 ± 21.57 ©	301.52 ± 31.27

Data are presented as means ± SD

Group I - Beta thalassaemia major patients, Group II – Controls

© Significant difference compared with controls (p < 0.05)

There are no significant differences between Group I and Group II regarding age or sex.

DISCUSSION

Beta thalassaemia major is one of the most common genetic disorders in tribal population of India. It results from a defect in β globulin chain production and ranges from clinically silent heterogeneous thalassaemia minor to severe transfusion-dependent thalassaemia major (TM). A significant increase serum iron proves patients have severe anemia due to ineffective erythropoiesis which is primary reason for iron overload and blood transfusion is secondary to it. Frequent blood transfusions have increased life expectancy and improved the quality of life for the patients with thalassaemia major, but it causes progressive iron overload, which is a major clinical complication of the treatment. Lipid abnormality has been frequently reported in thalassaemia, but its pathophysiology is not totally clear. [7-10] In this study, we observed low total serum cholesterol, low HDL-cholesterol and low LDL cholesterol with elevation of triglycerides in beta thalassaemia major patients, as compared to control subjects. Our results agree with previous findings with regard to the above altered

serum lipid pattern [11-13] in patients with beta thalassaemia major. This alteration is likely due to diminished hepatic biosynthesis as of anemia and iron overload, while a reduced extrahepatic lipolytic activity could account for the rise in circulating TG. [14]

The pathophysiology of hypocholesterolemia is obscure in these hematologic disorders, in which anemia is a common characteristic. The purposed mechanisms include increased erythropoietic activity resulting in increased cholesterol requirements, liver injury due to iron overload, and macrophage system activation with cytokine release. [15] It seems that the main mechanism of hypocholestrolemia in beta thalassemia major is severe iron overload and oxidative stress. The results reported by Ricchi et al [16] support this idea; they showed lower values of cholesterol in patients with a more severe genotype. Maioli and colleagues in their studies published from 1984 to 1997 suggested that liver damage, accelerated erythropoiesis, and an increased uptake of low-density lipoprotein (LDL) by macrophages and histiocytes of the reticuloendothelial system are the main determinants of low plasma cholesterol in thalassaemia.[17,18] In 1991 Goldfarb and colleagues found low plasma cholesterol and abnormality in structure and composition of lipoproteins in thalassaemia major.[19] They found that all 3 high-density lipoprotein (HDL) populations were enriched with TG and poor in cholesterol ester contents. It is said that anemia, activating the macrophage system and liver dysfunction, interrelates to the final serum lipoprotein pattern.

Our findings are also in agreement with those of Papanastasiuo et al,[20] Hartman et al,[21] and Amendola et al,[22] who showed that TC and LDL-cholesterol levels were lower in persons with beta thalassaemia major than the control group. In our study we found that serum TG was significantly higher in patients compared to controls. Increased concentrations of TG were observed in most published studies on lipid profiles of thalassaemic patients. [23] A recent study by Amendola and collagues in 2007 suggested that the higher bone marrow activity with enhanced cholesterol consumption could be the cause of lipid abnormality in thalassemia. [24]

On the contrary, when we focused our interest on HDL cholesterol we observed that thalassaemic patients had very low values. Studies suggest that risk for myocardial infarction is high when HDL cholesterol is low. [25] The later may highlight the importance of total-to-HDL cholesterol ratio for the evaluation of blood lipids and the prevention

of atherosclerotic disease. It has also been reported that the total cholesterol-to-HDL cholesterol ratio predicts coronary heart disease risk regardless of the absolute LDL- and HDL-cholesterol. we could suggest that thalassaemic patients are at much higher coronary risk than their matched controls, because of the low HDL cholesterol production, even if they are within normal values of total cholesterol. Bersot et al [26] suggested that in populations at risk for coronary heart disease caused by low HDL cholesterol, qualification of subjects for treatment based on the total to HDL cholesterol ratio thresholds (i.e. 3.5) identifies more high-risk subjects for treatment than other cholesterol threshold values alone.

Moreover, Maioli et al [27] suggested that accelerated erythropoiesis and increased uptake of LDL by macrophages and histiocytes of the reticuloendothelial system are the main determinants of low plasma cholesterol levels in beta thalassaemia major. In addition, Giardini et al [28] observed that total serum phospholipids, their fractions and cholesterol were significantly lower among patients with thalassaemia major. These changes were referred to hepatic damage and to severe anaemia, respectively. These differences on blood lipids and lipoprotein levels could also attribute to the adherence of a healthier lifestyle by people with beta thalassaemia, which could include consumption of healthy foods since childhood. Our results are also correlates with this and it is well known that phospholipid concentrations varies in the same direction as that of cholesterol.

CONCLUSION

In conclusion, our study revealed that thalassaemia patients had hypertriglyceridaemia, hypocholesterolemia and low HDL-cholesterol levels. It should be a motive for concern of better evaluation of the cardiovascular risk factors in these patients. Therefore awareness of lipid abnormality is helpful to avoid unnecessary evaluation in patients with beta thalassaemia.

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