Serum Fasting Lipid Profile of Children with β-Thalassemia Major in Peshawar, Pakistan

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ABSTRACT: Beta thalassemia (β-thalassemia) is one of the most common inherited disorder caused number of mutations in the beta globin gene. Most important problem encountered in thalassemic patients are diabetes. Vascular dysfunction with increased arterial stiffness and endothelial dysfunction has been found in patients with β-thalassemia. Endothelial dysfunction occurs in thalassemic children because of per oxidative tissue injury because of continuous blood transfusions. The aim of the study was to examine different lipid component levels in serum fasting of children having β-thalassemia major. A cross sectional study was carried out on 40 β-thalassemia patients. After examining the serum of patients show high value of high-density lipoprotein have significant decrease in their bilirubin content. While high value of high-density lipoprotein results in decrease of low-density lipoprotein content in serum. The age group 10-15 years was described as the highest risk group of β-thalassemia between the investigated populations. Our study revealed that deranged lipid profile is not uncommon in β-thalassemia patients irrespective of age and gender. Considerable deficiency of HDL and significantly high TC: HDL could be predictive for future coronary events. The study propose that lipid profile should be evaluated in these patients as low HDL and raised TC: HDL are important tools for coronary risk assessment. The exact mechanisms and clinical consequences of dyslipidaemia in β-thalassemia should be further investigated in larger prospective studies to represent the Pakistan population.

Keywords: Beta thalassemia, HDL, Lipoprotein, Globin

1. Introduction

β-thalassemia are hereditary blood disorder characterized by reduced beta globin synthesis result in less amount of hemoglobin (Hb) in red blood cells (RBCs) and reduced RBCs production. Mostly inherited as recessive traits. High prevalence has been reported in Mediterranean countries, Central Asia, Middle East, southern China, India, Africa and South America. In Cyprus highest carrier frequency 14% has reported. In Cyprus the high gene frequency of β-thalassemia is most likely associated to the selective pressure from Plasmodium falciparum malaria [1].

As per Thalassemia International Federation, just around 200,000 patients with thalassemia major are alive and enrolled as getting standard treatment around the globe. The most widely recognized combination of beta-thalassemia with abnormal Hb, which is most predominant in Southeast Asia where the bearer recurrence is around 50% [2]. Cholesterol is not only a fundamental element of cell membranes but also the principal precursor for steroid and sexual hormone biosynthesis. Furthermore, cholesterol, through its intermediary products such as farnesyl diphasphate and geranyl diphasphate, is involved in the regulation of Ras-protein intracellular signal transduction [3].

Therefore, we investigated the distribution of serum lipoprotein concentration in the samples of patients with β-thalassemia. We also evaluated the relationship between these biochemical parameters with maternal characteristic. The aim of the present study is to identify the relationship of biochemical
2. Methodology

The study was designed at the Department of Biotechnology, Bacha Khan University Charsadda. All the clinical samples were collected from the Pediatric Department of the Hospital.

2.1 Samples Collection

Blood was drawn for biochemical analysis from the subjects. To examine lipid profile accurately fasting about 9-12 hours before test is must. But sometimes it's done even in non-fasting condition. Laboratory work was performed at Biochemistry section, Department of pathology, Govt. Lady Reading hospital, Peshawar, Pakistan.

2.2 Sample Processing

In the very first step blood sample was allowed to stand for 45 minutes at room temperature. The samples were centrifuged at 1,500 xg for 30 minutes at 4°C. Cholesterol, triglyceride and HDL-cholesterol analyses were performed on a Hitachi 902 analyzer serviced by Roche Diagnostics, Indianapolis, IN. Cholesterol was measured enzymatically using the Cholesterol High Performance reagent, Roche Diagnostics. Triglycerides were analyzed enzymatically simultaneously with cholesterol using reagents from the same manufacturer. Triglyceride blanks were measured in CDC surveillance materials using the same reagent, but without lipase. Direct HDL-cholesterol reagent was obtained from Roche Diagnostics, and analyzed simultaneously with cholesterol and triglycerides. Specimens to be analyzed for cholesterol, triglyceride and HDL-cholesterol stored for up to 1 year at -80°C. The reaction condition was established by the Instrument Settings.

The process was start with placing a 100 ul aliquot of sample into the disposable sample cups on the instrument carousel using a disposable polyethylene transfer pipet. Samples were arranged on the carousel in the order in to be analyzed, as determined. Quality control samples were also placed into their assigned positions on the instrument. The results were obtained on the Hitachi printout and on real time to computer as a text file.

2.3 Statistical Analysis

The data was statistically analyzed by computer software program JMP, SAS (Version 7.0. SAS, USA).

3. Results

The total 40 subjects participated in the study. According to our results most cases of β-thalassemia major was recorded in children ranges from 10 to 15 years of age.

3.1 Lipid Profile

Correlation of the high-density lipoprotein by bilirubin content present in serum samples shows significant decrease in bilirubin content with increase in high density lipoprotein (Fig. 1).

3.2 Low Density Lipoprotein by Bilirubin

Correlation of the low-density lipoprotein by bilirubin content present in serum samples shows significant decrease in bilirubin content with increase in low density lipoprotein (Fig. 2).

3.3 Low Density Lipoprotein by High-density Lipoprotein

Correlation of the low-density lipoprotein by high density lipoprotein content present in serum samples shows significant increase in high density lipoprotein content with decrease in low density lipoprotein (Fig. 3).

3.4 Thin Layer Chromatography by Bilirubin

Correlation of the thin layer chromatography by bilirubin content present in serum samples shows significant decrease in bilirubin content with increase in thin layer chromatography (Fig. 4).
**Fig 1.** Correlation of HDL by Bilirubin

**Fig 2.** Correlation of LDL by Bilirubin

**Fig 3.** Correlation of LDL by HDL
4. Results

Lipid abnormalities have been reported in β-TM, but its pathophysiology is still not entirely defined. In the present study, we report serum lipid levels of children with β-thalassemia major. The results of the present study showed that the β-thalassemia patients had higher serum TLC and HDL, with lowered serum LDL and TLC: Bilirubin with respect to reference ranges. Decreased concentrations of cholesterol were observed in most published studies reported from Paris, France [4]. According to our study results, we have found a direct correlation between low density lipoprotein with high density lipoprotein in terms of lowering possibilities of coronary heart diseases in thalassemia patients was also reported by Zhenghui et al in 2014 associations between alanine aminotransferase (ALT), aspartate aminotransferase (AST) and major components of serum lipid profiles in a nationally representative sample of 23,073 individuals, who had no chronic viral hepatitis and were not taking lipid-lowering medications, from the National Health and Nutrition [5]. Our result was the same as Shah Sejal and his co-workers described that out of total 35 cases β-thalassemia Major was the most frequent (40%) followed by homozygous sickle cell disease (20%). More than one third cases (34.3%) were of 10 or more years of age while 31.4% cases were in 1-3 years of age group. Sex wise distribution showed male preponderance (74.3%). Religion wise majority were hindus (80%). Caste wise majority were of general category (83%). Pallor was found in all cases. Most of the cases showed hypochromia, microcytosis, Anisopoikilocytosis, polychromatophilia [6]. Total phospholipids and its functions also decrease with the decrease of total cholesterol. In the same study it was shown that the levels of serum lipid multiple unsaturated fatty acids decreased. Those changes appear because of excessive iron-loading and liver damage [7].

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. It seems that the main mechanism of hypocholesterolemia in BTM is severe iron overload and oxidative stress, but in β-thalassemia the major mechanism is accelerated erythropoiesis and enhanced cholesterol consumption. According to Taher A et al, the potential role of hypocholesterolaemia in the pathogenesis of some clinical aspects of thalassaemia has been rarely discussed. These include alternations in endocrine function, increased susceptibility to infections and vascular complications such as thrombophilia, which
affect thalassaemia major and intermedia patients in a different manner [8].

We determined a positive correlation between high density lipoprotein and low-density lipoprotein levels in our study. This also suggests that it may be effective on blood lipid values because of excessive iron-loading due to excessive iron-loading and decrease the efficacy of chelation therapy or its inadequately application. These results may support the hypothesis that both serum iron and serum triglyceride play role in LDL-C oxidation pathogenesis [5].

5. Conclusion

In conclusion, the concentration of some fractions of serum lipids which in thalassemia carriers are below the normal levels can potentially reduce the risk of cardiovascular diseases. The Lipid-lowering effect of beta-thalassemia trait in minor thalassemia raises the question as to whether this effect might slow down the progression of coronary diseases and delay the occurrence of myocardial infarction in these patients. The answer to this question requires more prospective studies on patients with beta thalassemia trait. The exact mechanisms and clinical consequences of dyslipidaemia in β-thalassemia should be further investigated in larger prospective studies to represent the Pakistan population.

References


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**Competing Interests:**
The authors declare that they have no competing interests.

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