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Research Article

Serum Lipid Profile and Nitric Oxide Levels in Beta-Thalassemia Patients

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Introduction

Beta thalassemia is an inherited disorder of blood which is characterized by decreased synthesis of beta chains of HbA (adult hemoglobin) [1]. It is also known as Cooley's anemis. The cause of decreased beta chain synthesis lies in alteration of its gene due to which alpha chains start accumulating. There occurs precipitation of alpha chains in erythroid precursors within bone marrow [2]. Approximately 5% of the world's populations are thalassemic and abnormal Hb carriers [3]. Beta thalassemia has major impact on lipid profile and lipoproteins levels. It is also associated with oxidative stress which can cause premature death due to cardiac complications [1].

The main therapy of this disease is blood transfusion along with chelation therapy (to remove iron overloading because of repetitive blood transfusions) although chelation therapy prevents iron overloading to some extend still there are chances of oxidative damage to cells because of the circulating free toxic iron which is not bound to transferring. It also promotes the production of reactive oxygen species (ROS) through Fenton reaction [2]. This study was planned to analyze lipid profile including TG, TC, HDL-C, LDL-C and VLDL-C along with nitric oxide levels to measure the oxidative stress in Haryana population.

Materials and Methods

The study was conducted on 50 thalassemia major patients (who were free from HBV, HCV and HIV) in age range of 1.5 to 30 years who were receiving regular chelation therapy followed from thalassemia ward of Pt B D Sharma, UHS, Rohtak. Out of 50 patients 18 were females and 32 were males. After taking informed consent blood samples were taken on an empty stomach in red vacutainers. In case of major consent was given by the patient but in case of minors consent was obtained from their parents. Samples were allowed to clot and serum was separated by centrifugation. Samples were analyzed on the same day for lipid profile, calcium, phosphorus and nitric oxide levels. All patients were subjected to detailed history regarding thalassaemia, start of blood transfusions, number of transfusions/month and chelation therapy.

Calcium, phosphorus, TG, TC, HDL-C, LDL-C and VLDL-C of all the subjects were evaluated using commercial analytical kits from Randox on Randox Suzuki auto analyzer. The NO level (measured as nitrite plus nitrate (NO(x)) concentration) was estimated by Griess reagent method [4]. Average values and standard deviations of results were calculated. Student t tests was used to compare both groups and $p<0.05$ was regarded as significant and $p<0.001$ as statistically significant.

Results

In table 1 shows various demographic and biochemical parameters of cases and controls. Hb and Hct values of the group with Beta-Thalassemia were significantly lower than those of the control group ($p<0.05$). As seen in (Table 1 and Figure 1).

Parameter	Cases (n=50)	Controls (n=50)	p value
Age (years)	1.5 - 30	Feb - 30	-
M : F	32:18:00	30:20:00	-
Hb (g/dL)	8.9 ± 2.7	11.6 ± 1.3	0.000**
Hematocrit (%)	28 ± 2.1	38 ± 3.0	0.030*
TG (mg/dL)	222.7 ± 73.8	132.7 ± 54.7	0.000**
TC (mg/dL)	107.7 ± 26.92	157 ± 60.42	0.000**
HDL (mg/dL)	31 ± 11.2	40.2 ± 11.2	0.021*
LDL (mg/dL)	51.5 ± 19.0	75.8 ± 46.9	0.001*
VLDL (mg/dL)	26.3 ± 10.8	42.7 ± 12.7	0.000**
NO (µM/L)	7.4 ± 4.32	35.23 ± 13.3	0.046**

All values are in Mean ± SD; *Significant; ** highly significant

Table 1: Table showing demographic and biochemical characteristics in cases and controls.

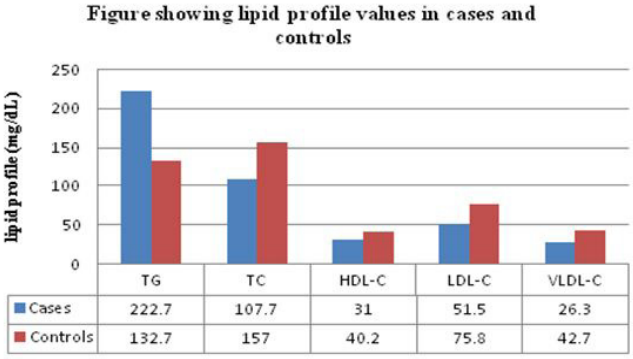

Figure 1: Figure showing lipid profile values in cases and controls.

TC, HDL-C, LDL-C and VLDL-C levels in patients with Beta-Thalassemia were found to be significantly lower than those of the control group ($p<0.001$), while the TG levels were found to be higher ($p<0.001$). The average total cholesterol values were measured in the group with B-TM and the control group as 107.7 ± 26.92 mg/dl, 157 ± 60.42 mg/dl ($p<0.001$), respectively; the average triglyceride values as 222.7 ± 73.8 mg/dl, 132.7 ± 54.7 mg/dl ($p<0.001$), respectively; the HDL-cholesterol values as 31 ± 11.2 mg/ dl, 40.2 ± 11.2 mg/dl ($p<0.05$), respectively. Average LDL and VLDL values were found as 51.5 ± 19.0 mg/dl, 75.8 ± 46.9 mg/dl ($p<0.05$); 26.3 ± 10.8mg/dl, 42.7 ± 12.7 mg/dl ($p<0.001$), respectively.

Discussion

Beta thalassaemia major is one of the most common genetic disorders in tribal population of India. The aim of this research was to study the lipid profile and NO in beta thalassemia patients in comparison with a group of age and sex matched healthy controls. TC, HDL-C, LDL-C and VLDL-C levels were found to be lower than those of healthy individuals. The present findings are in agreement with previous studies of Maioli M et al [5,6], Goldfarb AW et al [7], Cherchi GM et al [8] A B Patne et al [9], Papanastasiou A et al [10] and Arical V et al [3]. TG levels were found to be higher in cases in present study which are consistent with some studies [11,12] but contradict with others [13]. Nitric oxide levels were found to be decreased in these patients.

There are many possible reasons for explaining these types of changes. One main reason is transfusion induced iron overload and chelation therapy which damages the liver, heart and endocrine glands by iron catalyzed free radical damage via Fenton and Haber-Weiss reaction. Ineffective erythropoesis is the major reason for iron overload. Iron induced liver injury is characterized by the development of fibrosis and cirrhosis [9]. Liver damage results in deterioration of AST and ALT ratio. Activity of hepatic and extra hepatic lipase enzymes also decreases resulting in quick cleaning of modified HDL and LDL (rich in triglycerides and poor in cholesterol esters) by activated monocytes and macrophages. In addition hormonal disorders also produces such changes. [3,14] Accelerated erythropoesis in Beta Thalassemia, also results in increased cholesterol uptake by macrophages and histiocytes of the reticuloendothelial system. Cytokines play a major role in pathogenesis of thalassemia which in turn activates macrophage system which is also responsible for hypercholesterolemia [14]. Amendable and colleagues in 2007 suggested that the higher bone marrow activity with enhanced cholesterol consumption could be the cause of lipid abnormality in thalassaemia [15]. On the other hand when we look at HDL-C,its level decreases in thalassemia which raises the risk of Myocardial Ischemia (MI). So, beta thalassemia patients should be evaluated for cardiovascular risks and ratio of TC/HDL-C (>3.5) is a better marker than their absolute values.

Hyper production of ROS induces lipid per oxidation which is accompanied by generation of a large variety of potential genotoxic breakdown products like peroxyl radicals, alkoxyl radicals and aldehydes such as Malondialdehyde [16]. Oxidative damage to endothelial cells in thalassemia accelerates the destruction of NO, and limits the compensatory increase in NO production. Chronic hemolysis is well documented in hemoglobinopathies. The products of chronic hemolysis further exerts negative effect on NO and arginine production. Immature red cells and reticulocytes releases large amount of arginase which limits the availability of arginine for NO production. It further leads to endothelial dysfunctioning resulting in more pronounced NO reduction [17]. NO reacts with ROS to produce reactive nitrogen species. NO binds very rapidly to deoxyhemoglobin, forming a stable Hb (Fe+2)-NO complex. NO also reacts with and converts oxygenated hemoglobin to methemoglobin and nitrate (NO3-) [18]. Decreased NO levels promotes vasoconstriction and platelet aggregation which is again a risk factor for MI [19]. Lastly, increased oxidative stress in thalassemia uncouples Endothelial Nitric Oxide Synthase (e NOS) further decreasing the production NO (Figure 2).

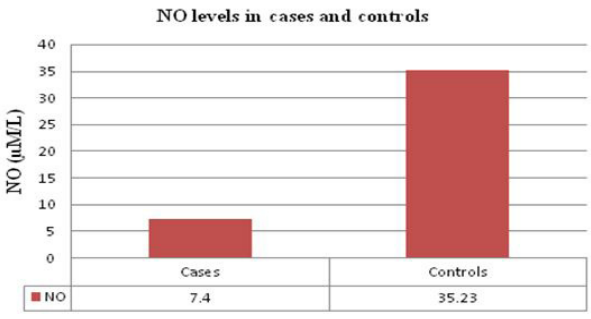

Figure 2: Figure showing NO levels in cases and controls.

Conclusion

Both altered lipid profile and decreased NO levels in beta thalassemia patients suggest an increased coronary risk. As this disease is associated with increased oxidative stress (mainly because of iron overload) which further promotes lipid per oxidation. So, early introduction of iron chelatory agents and antioxidants along with evaluation of cardiovascular risk factors can be beneficial in clinical practice.

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