Hypocholesterolaemia in Beta-Thalassaemia

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Abstract

Background: To assess the plasma total cholesterol of male and female β-thalassaemia patients. The plasma cholesterol of normal individual compared with the β-thalassaemia cases.

Methods: From October 2010 to March 2011, we enrolled 36 consecutive patients with β-thalassaemia that visited District Head Hospital, Balasore and Odisha every month for routine examinations. The sample was collected in the EDTA vial (5 ml), immediately centrifuged at 5000 rpm for 5 min and supernatant (plasma) collected in to the microcentrifuge tube and stored in -20ºC freezer for other biochemical experiment. We have used Infinite cholesterol kit. We also found 5 sickle patients and included them in our analysis.

Results: Of the 36 thalassaemic patients, 25 were males (12 ± 5.91 years) and 11 were females (9.08 ± 4.32 years) with comparison to 30 normal cases (15-35 years). Data analysis revealed that total cholesterol level, in case of normal (178.8.5 ± 31.1mg/dl), in thalassaemic cases (135.8.6 ± 29.3mg/dl) and in case of 5 sickle patients (143.3 ± 15.7mg/dl). The total cholesterol levels in case of normal is high than that of thalassaemic and sickle patients. In case of thalassaemia cases the low total cholesterol is 47.4 mg/dl. The expected values of total cholesterol is <200 mg/dl. In case of thalassaemia the values are too low than expected values. The ‘t’ test data revealed that there is comparison of two mean of the sample (normal and thalassaemic) is negligible small.

Conclusion: The present study revealed that the majority of males and females with beta-thalassaemia have their blood lipid levels within the normal range, and lower than the healthy individuals of the same age and population. Such low level of cholesterol in thalassaemic patients seems to reflect the inability of the organism to balance the increased cholesterol requirement for red cell membrane formation. It is conceivable that the availability of cholesterol, ordinarily used in steroid hormone synthesis to control hypercoagulability.

Keywords: Beta-thalassaemia; Mean; Standard deviation; ‘t’ test; Total cholesterol (TC)

Introduction

Thalassemia is among the most common genetic disorders worldwide; 4.83 percent of the world’s population carries globin variants, including 1.67 percent of the population who are heterozygous for α-thalassemia and β-thalassemia. In addition, 1.92 percent carries sickle hemoglobin, 0.95 percent carry hemoglobin E, and 0.29 percent carry hemoglobin C. Thus, the worldwide birth rate of people who are homozygous or compound heterozygous for symptomatic globin disorders, including α-thalassemia and β-thalassemia, is no less than 2.4 per 1000 births, of which 1.96 have sickle cell disease and 0.44 have thalassemias [1].

β-thalassemia can be broadly defined as a syndrome of inherited hemoglobin disorders characterized by a quantitative deficiency of functional β globin chains. Although it is defined as a reduction in the synthesis of β-globin, some forms result from structural hemoglobin variants that are ineffectively synthesized or are so unstable that they result in a functional deficiency of the β chains and a thalassemia phenotype [2]. Beta-thalassemia is a very serious blood disorder since individuals with it are unable to make enough healthy red blood cells and depend on blood transfusion throughout their life. However, quality and duration of life of transfusion-dependent thalassemic patients has been transformed over the last few years, with their life expectancy increasing well into the third decade and beyond with a good quality of life [3].

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 [4-6]. 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 and smoking habits [7]. In recent years, several authors reported a high incidence of endocrine abnormalities in children, adolescents and young adults suffering from thalassemia.

To the best of our knowledge, data regarding the distribution of blood lipid levels among patients with beta thalassaemia are lacking. Therefore, we investigated the distribution of glucose, protein, bilirubin, urea and total cholesterol in plasma samples of patients with beta-thalassaemia in district of Balasore, Odisha, India. Among these the total cholesterol profile gives the good result with comparison to the normal cases.

Total cholesterol (TC) consists largely of the cholesterol in LDL particles (LDL cholesterol) plus the cholesterol in high-density lipoprotein particle (HDL cholesterol). 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 diphosphate and geranyl diphosphate, is involved in the regulation of ras-protein intracellular signal transduction.

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Received January 24, 2012; Accepted February 09, 2012; Published February 15, 2012


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Material and Methods

Patients (belonged to various region of Odisha) with β-thalassaemia visited District Head Hospital, Balasore, Odisha every month for routine examinations were enrolled. Moreover, the selected sample can be considered as representative since there were only minor, insignificant, differences in sex and age distribution between the study population and the target population regarding the sex-age distribution. In addition to the β-thalassaemia cases we found some sickle patients who were also screened.

Among total cholesterol, other biochemical testing and quantification of the fetal hemoglobin (Hbf), sickle hemoglobin (Hbs), adult hemoglobin (HbA), through hemoglobin electrophoresis and molecular diagnosis for the detection of different type of mutation were also done.

From October 2010 to March 2011, we enrolled 36 consecutive patients with β-thalasemia that visited District Head Hospital, Balasore, and Odisha every month for routine examinations. The sample was collected in the EDTA vial (5 ml), immediately centrifuged at 5000 rpm at 5 min and supernatant (plasma) collected in to the micro centrifuge tube and stored in -20°C freezer for other biochemical experiment. We have used Infinite cholesterol kit. We also find that 5 number of sickle patients and include them in our analysis. All the experiments being done in the Department of Bioscience and Biotechnology, Fakir Mohan University, Balasore, Odisha, India.

By using Infinite cholesterol kit and it is based on the principle:

Cholesterol esterase hydrolyses cholesterol esters into free cholesterol and fatty acids. In the second reaction cholesterol oxidase converts cholesterol to cholest-4-en-3-one and hydrogen peroxide. In presence of peroxydase, hydrogen peroxide oxidatively couples with 4-aminoantipyrine and phenol to produce red quinoneimine dye which has absorbance maximum at 510 nm. The intensity of the red colour is proportional to the amount of total cholesterol in the specimen [8,9]. Continuous variables were analysed as:

mean values ± standard deviation

Results

Of the 36 thalassemic patients, 25 were males (12 ± 5.91 years) and 11 were females (9.08 ± 4.32 years) with comparison to 30 normal cases (15-35 years).

The β-thalassemia cases have the hemoglobin (7.9 ± 2.3%). The patients were subjected to blood transfusion every 15-21 days interval. The total cholesterol (TC) profile of the patients with respect to the normal cases has been calculated. We have made comparison of mean and standard deviation between the normal, thalassemia patients and also in sickle cell disease (Table 1). The Table 1 suggest the result of total plasma cholesterol level is as much as low in case of patients having 201.3 mg/dL. The range of the total plasma cholesterol profile in case of normal and thalassaemic cases is 178.9 ± 31.1 mg/dL and 135.8 ± 29.3 mg/dL. The range of total plasma cholesterol in thalassaemic patients was significantly lower than in control cases.

We have made the comparison of total cholesterol (TC) of the β-thalassaemic patients with respect to the normal cases (n=30), Y-axis taken as TC values and X-axis taken as no. of cases (Figure 1). The sample size of sickle cell patients (n=5) is very small so it is not taking into consideration.

Discussion

In this study the total plasma cholesterol profiles in beta thalassaemic patients of Balasore District were evaluated. Majority of the participants had abnormal total-cholesterol levels; on the contrary to the normal cases.

A recent report from a study, which enrolled a representative and adequate sample of the general healthy population from Greece, suggested that roughly 25% patients had high total-cholesterol [10]. Based on the previous report it could be speculated that patients with beta -thalassemia have lower total-cholesterol levels as compared to healthy individuals of the same age. Studies suggest that even for those with normal levels of total-cholesterol, risk for myocardial infarction is high when HDL-cholesterol is low [11,12]. In another report, beta thalassemia major patients showed significantly lower cholesterol compared with the control, also serum triglycerides levels of thalassemia major patients were significantly higher than in control [13]. Our report shows that there is abnormal decrease in the total plasma cholesterol of beta thalassaemia patients with that of the normal cases that we have screened with same age groups.

In this report the Figure 1 suggests that the comparison of the total plasma cholesterol level with the normal with same age groups. This shows that the total plasma cholesterol level is as much as low in case of patients having 47.433 mg/dL and higher among the thalassaemic patients having 201.3 mg/dL. The range of the total plasma cholesterol level is 31.1–29.3 mg/dL. The range of the total plasma cholesterol level is as much as low in case of patients having 201.3 mg/dL and higher among the thalassaemic patients having 201.3 mg/dL. The range of the total plasma cholesterol level is 31.1–29.3 mg/dL.

Table 1: shows the comparison of mean of the total plasma cholesterol among the normal, β thalassemia and sickle patients.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>normal</th>
<th>β thalasemia</th>
<th>Sickle cell disease</th>
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</thead>
<tbody>
<tr>
<td>Number</td>
<td>n=30</td>
<td>n=36</td>
<td>n=5</td>
</tr>
<tr>
<td>Total cholesterol (TC) in mg/dL</td>
<td>178.9±31.1</td>
<td>135.8±29.3</td>
<td>143.3±15.7</td>
</tr>
<tr>
<td>Age in years</td>
<td>15-35</td>
<td>21.0±10.2</td>
<td>-</td>
</tr>
<tr>
<td>Range of TC in mg/dL</td>
<td>83.4–211.3</td>
<td>47.4–201.3</td>
<td>-</td>
</tr>
</tbody>
</table>

Table 2: calculation of ‘t’ test among the normal cases (n=30) and thalassaemia cases (n=36) with the significance level at 0.05.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Comparison of normal and thalassaemia cases</th>
</tr>
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<tbody>
<tr>
<td>Significance level</td>
<td>0.05</td>
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<tr>
<td>Number of cases (µ)</td>
<td>86-2=64</td>
</tr>
<tr>
<td>Cal t</td>
<td>0.356</td>
</tr>
<tr>
<td>Tab t</td>
<td>1.96</td>
</tr>
<tr>
<td>Remarks</td>
<td>Cal t &lt; tab t</td>
</tr>
</tbody>
</table>

Figure 1: Comparison of total cholesterol (TC) of the β thalassaemic patients with respect to the normal cases (n=30), Y-axis taken as TC values and X-axis taken as no. of cases.
falls in between 47.4–201.3 mg/dL in thalassaemic patients whereas the range falls in 83.4–211.3 mg/dL in case of normal cases. The mean of total plasma cholesterol of beta thalassaemia cases is 135.8 ± 29.3 mg/dL where n is 36 and in case of normal i.e. 178.9 ± 31.1mg/dL where the n is 30. This data shows total plasma cholesterol level of beta thalassemia patients decreased with that of normal. We have calculated the student t test (Table 2) with the comparison of two mean between the samples (normal and thalassaeemia) at the significance level (0.05) at n=64, calculated t is 0.356 and tabulated t is 1.96 then the level of difference is not significant. Null hypothesis is accepted. So the difference of mean of the two cases is negligible small.

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 [14]. Based on the previous report it could be speculated that patients with β-thalassaemia have lower total-cholesterol levels as compared to healthy individuals of the same age. Such low levels of cholesterol in thalassaemic patients seem to reflect the inability of the organism to balance the increased cholesterol requirement for red cell membrane formation; thus it is conceivable that the availability of cholesterol, ordinarily used in steroid hormone synthesis to control infection and to control hypercoagulability, could be at in part reduced [15].

Conclusion

The present study revealed that the majority of males and females with beta thalassaemia have their blood cholesterol levels within the normal range, and lower than the healthy individuals of the same age and population. Hypocholesterolaemia in the absence of a cholesterol metabolism genetic disorder is a constant clinical feature of patients with severe thalassaemia. Further studies are needed to better elucidate the relationship between Hb and cholesterol level and other parameter of erythropoietic activity, such as soluble transferrin receptor, reticulocyte count and extramedullary erythropoiesis in patients affected by thalassaemia.

Acknowledgement

The authors are highly indebted to the Department of Science and Technology, Govt. of Odisha for providing financial support for the project work. Our thanks also to the Vice Chancellor of Fakir Mohan University, for his encouragement and support to carry out the project work in the department. Special thanks to all the thalassaemic and sickle cell patients and health centers that voluntarily provided us the blood samples for the study.

References