**Study of lipid profile parameters abnormalities in patients with sickle cell disease from single centre study in central India**

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**ABSTRACT**

**Background:** Metabolism of lipids and lipoproteins is being altered in patients with sickle cell disease (SCD). It has been postulated that the hypocholesterolemia in SCD might be due to increased cholesterol utilization and decreased circulation. Hemolytic stress can be associated with a significant reduction in plasma lipid concentration.

**Methods:** This prospective observational study was conducted from February 2016 to October 2017 at MGM Medical College and MY Hospital Indore, MP, which included 50 SCD patients and 50 healthy, age, and sex matched controls.

**Results:** Total Cholesterol (TC) was less than 200mg/dl in 48 SCD patients with mean TC levels was 115.3mg/dl and it more than 200mg/dl in 2 SCD patients only with mean TC was 211mg/dl. This was statistically significant low as compare to controls (p value=0.001060). HDL was less than 60mg/dl in 47 SCD patients with mean HDL was 33.74mg/dl and more than 60mg/dl in 3 SCD patients with mean HDL was 105.6mg/dl and it was statistically significantly low in SCD patients(p value=0.001787). Tryglyceride (TG) was more than 150mg/dl in 27 SCD patients and it was less than 150mg/dl in 23 SCD patients. TG was statistically significantly high in SCD patients (p value=0.011303). LDL was less than 60mg/dl, 60-130mg/dl, and more than 130mg/dl in 25, 21, and 4 SCD patients respectively. This increase in LDL in SCD patients was statistically significant (p value 0.018977).

**Conclusions:** It was evident from this study that dyslipidemia characterized by low HDL and TC was present among the SCD patients who participate this study. Further study in large number of SCD patients and controls may help to confirm or exclude the above correlation of SCD with derangement in lipid profile.

**Keywords:** Cholesterol, Dyslipidemia, Hypcholesterolemia, Haemolysis, Hypertryglyceridemia, Sickle cell disease

**INTRODUCTION**

It has been postulated that the hypocholesterolemia in Sickle Cell Disease (SCD) might be due to increased cholesterol utilization and decreased circulation. Hemolytic stress could be associated with a significant reduction in plasma lipid concentration.12 Metabolism of lipids and lipoproteins is being altered in patients with SCD. Decreased red cell volume in these patients leads to increased plasma volume and dilution of plasma constituents including lipids and lipoproteins or the down regulation of cholesterol biosynthesis which occurs through the rate-limiting enzyme of βhydroxymethyl–glutaryl – CoA reductase or 25 decrease dietary intake of cholesterol or decrease activity of lecithin: cholesterol acyltransferase (LCAT).3,4

Another suspected cause was increase in the rate of exchange between plasma cholesterol and RBC membrane cholesterol.5 Increased hepatobiliary excretion.
of cholesterol and bile salts, increased conversion of cholesterol to bile salts, decreased reabsorption of cholesterol and bile salts in the small intestine, and down regulation of cholesterol biosynthesis pathway was put forward the explanation for hypcholesterolemia in SCD. It is also proposed that hypcholesterolemia in SCD might be induced by HbS gene.

In previous work and established projects the cholesterol levels were significantly low because cholesterol was utilized in excess in erythropoietic activity. However it is also hypothesized that cholesterol is largely conserved by entero-hepatic circulation, at least in healthy symptomless individuals. RBCs membranes synthesized by recycled cholesterol from hemolysed RBCs. The abnormal viscoelastic properties of oxygenated sickled cells; irreversibly correlate to abnormal property of the red cell membrane which affect the plasma lipid profile. In sickle cell disease alteration in the lipid metabolism becomes pronounced; especially in vasooclusive crisis.

In SCD, there exists an alteration in the distribution of membrane lipids, with exposure of phosphatidyl serine (PS) in some red cells in circulation. This distorts the membrane and consequently exposes and activates cell adhesion receptors as well as the binding sites of certain enzymes like promthrombinase. It also initiates apoptosis of red cells and its removal by the splenic macrophages. The concentration of the membrane lipids differs across various locations on the membrane, with some regions showing increased concentration of certain fatty acids. These areas are known as “rafts” or “microdomains”.

With above mentioned background this study was planned to look for lipid profile derangement in SCD patients and its effects in these patients and we tried to correlate these biochemical changes in these patients.

METHODS

This prospective observational study was conducted from February, 2016 to October, 2017 at MGM Medical College and MY Hospital Indore, MP, which included 50 SCD patients and 50 healthy, age, and sex matched controls.

Clinical history of the patients

The information of patients regarding to study as name, age, gender, weight, marital status, occupation, address and disease related history was achieved by the conversation and questionnaire with the patients.

Laboratory examination

Blood sample of the patients was collected for the laboratory examination such as haemoglobin electrophoresis, total blood count, lipid profile, LDH etc. These tests were done in the laboratory of MGM Medical College and MY Hospital, Indore, MP.

Inclusion criteria

All SCD patients who were diagnosed and with/without treatment for SCD and not on any lipid lowering drugs.

Exclusion criteria

All patients on lipid lowering drugs for coronary artery disease, cerebro-vascular accident or any other cause of hyperlipidemia.

Statistical analysis

For the present study, statistical analysis required was done by the statistician accordingly the appropriate tests were applied. For analysis, statistical software SPSS latest version 20.0 was used. A p value of <0.05 was considered as statistically significant.

RESULTS

This prospective observational study was conducted from February, 2016 to October, 2017 at MGM Medical College and MY Hospital Indore, MP, which included 50 SCD patients and 50 healthy age and sex matched controls.

Table 1: Comparison of various parameters of lipid profile between cases and controls.

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Number of patients</th>
<th>Mean value</th>
<th>Number of controls</th>
<th>Mean value</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total cholesterol (mg/dl)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;200</td>
<td>48</td>
<td>115.33</td>
<td>36</td>
<td>160.2</td>
<td>0.001060</td>
</tr>
<tr>
<td>≥200</td>
<td>2</td>
<td>211.4</td>
<td>14</td>
<td>244.5</td>
<td></td>
</tr>
<tr>
<td>HDL (mg/dl)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;60</td>
<td>47</td>
<td>33.7</td>
<td>35</td>
<td>45.6</td>
<td>0.001787</td>
</tr>
<tr>
<td>≥60</td>
<td>3</td>
<td>105.7</td>
<td>15</td>
<td>106.4</td>
<td></td>
</tr>
<tr>
<td>Triglycerides (mg/dl)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;150</td>
<td>23</td>
<td>87.2</td>
<td>11</td>
<td>98.5</td>
<td>0.011303</td>
</tr>
<tr>
<td>≥150</td>
<td>27</td>
<td>204.8</td>
<td>39</td>
<td>230.4</td>
<td></td>
</tr>
<tr>
<td>LDL (mg/dl)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;60</td>
<td>25</td>
<td>33.8</td>
<td>18</td>
<td>40.0</td>
<td>0.018977</td>
</tr>
<tr>
<td>60-130</td>
<td>21</td>
<td>88.9</td>
<td>17</td>
<td>94.5</td>
<td></td>
</tr>
<tr>
<td>&gt;130</td>
<td>4</td>
<td>200.2</td>
<td>15</td>
<td>170.8</td>
<td></td>
</tr>
</tbody>
</table>
As shown in table 1, Total Cholesterol(TC) was less than 200mg/dl in 48 SCD patients with mean TC levels was 115.3mg/dl and it was more than 200mg/dl in 2 SCD patients only with mean TC was 211mg/dl. This was statistically significant low as compare to controls (p value=0.001060). HDL was less than 60mg/dl in 47 SCD patients with mean HDL was 33.74mg/dl and more than 60mg/dl in 3 SCD patients with mean HDL was 105.6mg/dl and it was statistically significantly low in SCD patients (p value=0.001787). Triglyceride (TG) was more than 150mg/dl in 27 SCD patients and it was less than 150mg/dl in 23 SCD patients. TG was statistically significantly high in SCD patients (p value=0.011303). LDL was less than 60mg/dl, 60-130mg/dl, and more than 130mg/dl in 25, 21, and 4 SCD patients respectively. This increase in LDL in SCD patients was statistically significant (p value 0.018977).

As shown in table 2, p value for Hemoglobin is found to be 0.806 i.e. there is no effect of decreased TC on haemoglobin. On pearson, correlation test, r value is found to be 0.036 i.e. there is significant negative correlation between TC and haemoglobin.

**Table 2: Comparison of total cholesterol with average hemoglobin levels.**

<table>
<thead>
<tr>
<th>Hemoglobin (in gm%)</th>
<th>Decreased TC</th>
<th>Normal TC</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt;12</td>
<td>1</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>8-12</td>
<td>27</td>
<td>2</td>
<td>29</td>
</tr>
<tr>
<td>4-8</td>
<td>20</td>
<td>0</td>
<td>20</td>
</tr>
</tbody>
</table>

As shown in table 3, p value for WBC is found to be 0.175 i.e. there is no effect of decreased TC on WBC. On Pearson, correlation test, r value is found to be 0.195 i.e. there is significant negative correlation between TC and WBC.

**Table 3: Comparison of total cholesterol with total leucocyte count (TLC).**

<table>
<thead>
<tr>
<th>TLC</th>
<th>Decreased TC</th>
<th>Normal TC</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;4000</td>
<td>1</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>4000-11000</td>
<td>29</td>
<td>2</td>
<td>31</td>
</tr>
<tr>
<td>&gt;11000</td>
<td>18</td>
<td>0</td>
<td>18</td>
</tr>
</tbody>
</table>

**DISCUSSION**

We found a significant decrease in TC levels in SCD patients compared to control. HDL cholesterol in SCD patients is significantly lower than that of control subjects. It is the same for other authors’ studies. Serum LDL cholesterol levels in SCD is significantly lower than the controls. Some of the workers have shown that the plasma total cholesterol of SCD, was significantly lower in comparison to normal control. It has been postulated that the hypocholesterolemia in SCD might be due to increased cholesterol utilization and decreased circulation. Hemolytic stress could be associated with a significant reduction in plasma lipid concentration. Metabolism of lipids and lipoproteins is being altered in patients with SCD. Decreased red cell volume in these patients leads to increased plasma volume and dilution of plasma constituents including lipids and lipoproteins or the down regulation of cholesterol biosynthesis which occurs through the rate-limiting enzyme of β hydroxymethyl - glutaryl - CoA reductase or decrease dietary intake of cholesterol or decrease activity of lecithin: cholesterol acyltransferase (LCAT).

The preferred lipoprotein by human LCAT is HDL. LCAT catalyzes the esterification of plasma cholesterol and prefers the lecithin molecules of the major HDL phospholipid, which contains polyunsaturated fatty acids. The reduction of HDL concentration and n-3 polyunsaturated fatty acids in serum phospholipids of sickle cell anemia has been reported in Nigeria. Also, a significant decrease of polyunsaturated fatty acids in erythrocyte of SCD patients was found. It was suggested that the elongation and desaturation of fatty acids be disrupted in sickle cell disease. Another suspected cause was increase in the rate of exchange between plasma cholesterol and RBC membrane cholesterol. Increased hepatobiliary excretion of cholesterol and bile salts, increased conversion of cholesterol to bile salts, decreased reabsorption of cholesterol and bile salts in the small intestine, and down regulation of cholesterol biosynthesis pathway was put forward the explanation for hypocholesterolemia in SCD. There is markedly derangement in levels of Haemoglobin and erythropoietin. As a result of above findings there is increased rate of erythropoiesis which is the main factor for increased cholesterol utilization.

In previous work and established projects the cholesterol levels were significantly low because cholesterol was utilized in excess in erythropoietic activity. However it is also hypothesized that cholesterol is largely conserved by entero-hepatic circulation, at least in healthy symptomless individuals. RBCs membrane is synthesized by recycled cholesterol from hemolysed RBCs. Triglyceride-rich VLDL-C particles availability may play an important role in lipid oxidization in SCD patients. The increase of triglycerides probably contributes to an increase in the hepatic production of VLDL-C, increasing the number of receptors for LDL-C that is extensively metabolized, decreasing its serum levels. However, the role of cholesterol and triglycerides and the regulation of assembly and production of VLDL-C are poorly understood. Low levels of HDL-C are an important cardiovascular risk factor, and HDL-C and apolipoprotein I have been shown to decrease lesions and improve vascular reactivity in animal models of atherosclerosis and in humans; these changes may be due to the reduction of oxidized lipids and the enhancement of reverse cholesterol transport. Patients with lower HDL-C levels were also likely to have had more blood transfusions; this
can be linked with a more severe clinical course of disease, once that it is a therapeutic strategy used to prevent several clinical symptoms, such as stroke.

In this study, there were 1 patients having Hb (gm%) >12 range. There were 20 patients having Hb (gm%) 4-8 range. Out of them 20 patients were having decreased cholesterol and no patients were having normal TC. There were 29 patients having Hb(gm%) 8-12 range. Out of them 27 patients were having decreased cholesterol and 2 patients were having normal TC. In this study, p value for decreased cholesterol is found to be 0.8061 i.e. there is no significant effect of decreased cholesterol. On Pearson’s correlation test, r value is found to be 0.036 i.e. there is significant negative correlation between Hb and decreased cholesterol. In this study, there were 1 patients having WBC 11000 range. Out of them 18 patients were having decreased cholesterol and none of patients were having normal TC. There were 31 patients having 4000-11000 range. Out of them 29 patients were having decreased TC and 2 patients were having normal TC. In this study, p value for decreased cholesterol is found to be 0.175 i.e. there is no significant effect of decreased TC. On Pearson’s correlation test, r value is found to be 0.195 i.e. there is significant negative correlation between WBC and decreased TC.

CONCLUSION

It was evident from this study that dyslipidemia characterized by low HDL and TC was present among the SCD patients who participate this study. Further study in large number of SCD patients and controls may help to confirm or exclude the above correlation of SCD with derangement in lipid profile.

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Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

REFERENCES
