SERUM LIPID PROFILES DURING ONSET AND REMISSION OF STEROID SENSITIVE NEPHROTIC SYNDROME IN CHILDREN

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ABSTRACT

Aims

To study the levels of serum cholesterol, serum triglycerides, LDL (Low density lipoprotein), VLDL (Very low density lipoprotein) and HDL (High density lipoprotein) in nephrotic syndrome at the onset and during remission in first episode and relapse cases.

Materials and Methods

A prospective study which included 50 children with steroid sensitive nephrotic syndrome, aged between 2-12 years. Out of which 35 children were presented as first episode, and 15 children as relapse cases. They were clinically examined and lipid profile was done at the onset and during remission. 30 age matched controls without liver and kidney disorders were taken as controls.

Results

There was significant (p < 0.005) increase in mean serum cholesterol, Triglycerides, LDL and VLDL. However, there was no significant (p = 0.234) change in HDL cholesterol when compared to controls. In first episode of nephrotic syndrome cases lipid levels (serum cholesterol, triglycerides, LDL, VLDL) were decreased significantly during remission, whereas in relapse cases lipid levels were significantly higher even during remission. There was an inverse correlation between albumin and cholesterol. The correlation was statistically highly significant (p = 0.000).

Conclusion

The present study shows that in nephrotic syndrome, there is generalized hyperlipidemia. This was significantly higher in relapse cases compared to first episode. Lipid profiles reaches normal during remission in first episode, whereas in relapse cases it was significantly higher even during remission. Hence there is a rationale for treatment.

KEY WORDS: Nephrotic Syndrome, Cholesterol, LDL, VLDL, HDL.
INTRODUCTION

Childhood nephrotic syndrome (NS) is a chronic glomerular disease, characterized by minimal change disease in the majority of cases [1]. Hyperlipidemia is an important characteristic of idiopathic nephrotic syndrome in children and is usually observed during the active phase of the disease and disappears with the resolution of the proteinuria [2]. The persistence and severity of lipid changes in serum correlates well with the duration and frequency of the relapses, even during the remission, which leads to increased risk of atherosclerosis in later life and the development of progressive renal injury [3]. Hence close monitoring of lipid levels during remission of nephrotic syndrome is necessary to select high risk patients. It has been noted that certain factors like diet, malnutrition, genetic traits are known to alter the frequency and severity of lipid pattern. The Indian patient has a different dietary, constitutional and genetic background. Hence we undertook a study to determine the spectrum of lipid abnormalities (serum cholesterol, serum triglycerides, LDL, VLDL and HDL) in nephrotic syndrome at the onset and during remission.

MATERIALS AND METHODS

It is a prospective study done in Basaveshwara Medical College and Hospital, Chitradurga during period of June 2010 to October 2013. 50 children in the age group of 2-12 years with typical features of nephrotic syndrome were included in the study. Children with prior history diabetes mellitus, hypothyroidism, familial hypercholesterolemia, steroid resistance at 4 weeks of steroid therapy, features which make minimal change disease less likely were excluded from study. Ethical clearance was sorted from institute ethical clearance committee. Written informed consent was taken from the subjects prior to enrollment of study. Data was collected by using pre-tested proforma meeting the objectives of the study.

Children with edema, low serum albumin (<2.5gm/dl) and urinary protein of more than 40mg/m²/hr or 3+/4+ protein were considered as nephrotic syndrome or relapse. Patients were considered in remission when urine albumin was nil or trace or proteinuria less than 4 mg/m²/hr for three consecutive days. Thirty age-matched controls without liver and kidney disorders were also enrolled in the study. Detailed history was taken and thorough clinical examination was done. Blood was collected in fasting state in the early morning and the samples were analysed for serum total proteins, serum albumin, serum globulin, blood urea, serum creatinine, and lipid profile (total cholesterol, triglycerides, LDL, VLDL, HDL).

Lipid profile was measured at the admission to the hospital and again in remission. Serum protein was estimated by modified Lowry’s method [4], serum albumin was estimated by Biuret method [5], urinary proteins were estimated by Ebschsalbuminometer. Blood urea was estimated by Diacetylmonoxime method [6], serum creatinine was estimated by Jaffes method [6], Serum total cholesterol was measured by cholesterol oxidase phenol amino antipyrine method (CHOD-PAP) [7], serum triglycerides were estimated by acetyl acetone method [8], LDL cholesterol was estimated by ammonium ferrothiocyanate method [9], VLDL cholesterol was measured by enzymatic method, Serum HDL Cholesterol (HDL) was measured by phosphotungstate method [6]. Statistical analysis was done by contingency coefficient test, descriptive statistics, independent sample t test, chi-square tests. SPSS-15 was used for analysis.

Treatment protocol

First episode: 60mg/m²/day daily (maximum dose 80mg divided into 2-3 doses) prednisolone for 6 weeks, followed by 40mg/m²/day alternate day as a single morning dose for 6 weeks.

Relapse cases: 60mg/m²/day daily (maximum dose 80mg divided into 2-3 doses) prednisolone until child enters remission, followed by 40mg/m²/day alternate day as a single morning dose for 6 weeks [1].

RESULTS

50 children with clinical diagnosis of nephrotic syndrome were enrolled in the study. Out of which, 35 were first episode and 15 were in relapse. In relapse cases 9 were infrequent relapses and 6 were frequent relapses. A total of 30 age matched controls were enrolled in the study. In the study group, age ranged between 2-12 years with mean age being 6.4 years. Whereas the control group aged between 2-12 years, with mean age being 6.6 years. 3 patients were in less than 2 years age, 37 patients were in 2-6 years, and 10 patients were more than 6 years age. There was preponderance in male gender (60%).

<table>
<thead>
<tr>
<th>Lipids</th>
<th>Cases (Mean ± SD)</th>
<th>Controls (Mean ± SD)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cholesterol</td>
<td>420.32 ±122.69</td>
<td>175.37 ± 18.32</td>
<td>0.000</td>
</tr>
<tr>
<td>Triglycerides</td>
<td>297.9 ± 93.09</td>
<td>94.1 ± 19.39</td>
<td>0.000</td>
</tr>
<tr>
<td>LDL</td>
<td>323.75 ±100.98</td>
<td>107.33 ± 16.10</td>
<td>0.000</td>
</tr>
<tr>
<td>VLDL</td>
<td>61.79 ± 19.78</td>
<td>24.00 ± 9.52</td>
<td>0.000</td>
</tr>
<tr>
<td>HDL</td>
<td>49.5 ± 20.10</td>
<td>51.2 ± 21.3</td>
<td>0.234</td>
</tr>
</tbody>
</table>
Table 1 shows that there was statistically significant increase in serum cholesterol, triglycerides, LDL and VLDL in nephrotic syndrome patients when compared to controls (p <0.005) but HDL value was not significant (p = 0.234).

### Table 2: Comparison of lipid profile at the onset and during remission in first episode nephrotic syndrome

<table>
<thead>
<tr>
<th>Lipids</th>
<th>Number of patients</th>
<th>Mean (mg/dl)</th>
<th>Standard Deviation</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>At the onset</td>
<td>During remission</td>
<td>At the onset</td>
</tr>
<tr>
<td>Cholesterol</td>
<td>35</td>
<td>372.82</td>
<td>282.74</td>
<td>106.20</td>
</tr>
<tr>
<td>Triglycerides</td>
<td>35</td>
<td>273.37</td>
<td>178.15</td>
<td>84.20</td>
</tr>
<tr>
<td>LDL</td>
<td>35</td>
<td>289.72</td>
<td>191.46</td>
<td>90.18</td>
</tr>
<tr>
<td>VLDL</td>
<td>35</td>
<td>57.24</td>
<td>47.19</td>
<td>18.86</td>
</tr>
<tr>
<td>HDL</td>
<td>35</td>
<td>49.33</td>
<td>54.75</td>
<td>20.20</td>
</tr>
</tbody>
</table>

Table 2 shows that in first episode of nephrotic syndrome cases lipid levels (serum cholesterol, triglycerides, LDL, VLDL) were decreased significantly during remission and were statistically significant. But HDL was increased during remission and was not statistically significant.

### Table 3: Comparison of lipid profile at the onset and during remission in relapse cases

<table>
<thead>
<tr>
<th>Lipids</th>
<th>Number of patients</th>
<th>Mean (mg/dl)</th>
<th>Standard Deviation</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>At the onset</td>
<td>During remission</td>
<td>At the onset</td>
</tr>
<tr>
<td>Cholesterol</td>
<td>15</td>
<td>531.17</td>
<td>407.98</td>
<td>80.58</td>
</tr>
<tr>
<td>Triglycerides</td>
<td>15</td>
<td>355.14</td>
<td>262.44</td>
<td>89.97</td>
</tr>
<tr>
<td>LDL</td>
<td>15</td>
<td>403.17</td>
<td>305.66</td>
<td>79.29</td>
</tr>
<tr>
<td>VLDL</td>
<td>15</td>
<td>72.40</td>
<td>64.85</td>
<td>18.26</td>
</tr>
<tr>
<td>HDL</td>
<td>15</td>
<td>49.82</td>
<td>55.06</td>
<td>20.23</td>
</tr>
</tbody>
</table>

Table 3 shows that in relapse cases lipid levels (serum cholesterol, triglycerides, LDL, VLDL) were significantly higher even during remission and were statistically significant. But HDL was increased during remission and was not statistically significant.

### Table 4: Comparison of serum albumin and serum cholesterol

<table>
<thead>
<tr>
<th>Albumin (g/dl)</th>
<th>Number of cases</th>
<th>Mean total cholesterol (mg/dl)</th>
<th>Standard deviation</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>1-1.5</td>
<td>6</td>
<td>569.11</td>
<td>138.37</td>
<td>0.000</td>
</tr>
<tr>
<td>1.6-2</td>
<td>23</td>
<td>445.65</td>
<td>120.78</td>
<td></td>
</tr>
<tr>
<td>2.1-2.5</td>
<td>21</td>
<td>350.07</td>
<td>59.04</td>
<td></td>
</tr>
</tbody>
</table>

The Table 4 shows an inverse relation between serum albumin and cholesterol. The p-value (0.000) was highly significant.

**DISCUSSION**

In the present study there was significant rise in total cholesterol, triglycerides, LDL, VLDL, when compared with controls. This is in accordance with the work done by various authors [10][11][12][13]. The mean serum cholesterol in relapse cases (mean = 531.17) was significantly higher than first episode nephrotic syndrome cases (mean = 372.82). Arije A et al also observed persistent rise in serum lipids in frequent relapse cases [14]. We noticed that the degree of serum lipid increase was not that high as reported by western workers. In our study the mean total cholesterol was 420.32 and the highest value was 703.9. Milne M reported that the total cholesterol in nephritic syndrome may be higher than 1000mg/dl [15]. Dnyanesh DK et al in his study observed that the mean total cholesterol was 422.61mg/dl and the highest value was 676mg/dl [16]. Thus we observed low serum lipids in Indian children. This difference in the lipid pattern could be due to different dietetic patterns of Indian children as regards to the carbohydrate and fat content of the diet. In our study HDL was normal in 52% of cases, decreased in 22%, increased in 26% of cases. The results of HDL have been variable in different studies, with high [12][17], low [13], and normal [10][18] levels of HDL cholesterol being reported.

The present study shows that lipid profile in first episode of nephrotic syndrome reaches normal value during remission, whereas in relapse cases, there is persistent elevation in the lipid profiles even during the remission. Merouani A et al observed hyperlipidemia during the active phase of the disease and disappeared with resolution of the proteinuria and was persistently abnormal in
frequently relapsing children [2]. Mahmud S et al observed that children with frequently relapsing nephrotic syndrome have prolonged periods of hypercholesterolemia and concluded that serum cholesterol may be regarded as predictor of relapse in childhood idiopathic nephrotic syndrome [19].

Relation between serum albumin and serum lipids

In our study, we observed an inverse correlation between albumin and cholesterol. The correlation was statistically highly significant (p=0.000). Krishnaswamy D et al found the correlation is not statistically significant [20]. Thomas EM et al found inverse correlation between serum cholesterol and albumin [21]. It is due to hepatic lipoprotein synthesis is stimulated in response to hypoalbuminemia, low oncotic pressure and urinary albumin loss.

CONCLUSION

The present study shows that in nephrotic syndrome, there is generalized hyperlipidemia (except HDL). This was significantly higher in relapse cases compared to first episode. Lipid profiles reaches normal during remission in first episode, whereas in relapse cases it was significantly higher even during remission.

Close monitoring of lipid levels during the remission of the nephritic syndrome especially in those with frequent relapses, is necessary to select the high risk patients. This will help in preventing the development of atherosclerosis and chronic renal failure. Prospective controlled studies in children evaluating efficacy and safety of lipid lowering drugs are needed.

REFERENCES