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SERUM LIPID PROFILES DURING ONSET AND REMISSION OF STEROID SENSITIVE NEPHROTIC SYNDROME IN CHILDREN: A PROSPECTIVE CASE CONTROL STUDY

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ABSTRACT

To study the levels of serum cholesterol, serum triglycerides, HDL, LDL and VLDL in nephrotic syndrome at the onset and during remission. 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. Thirty children aged matched controls without liver and kidney disorders were taken as controls. There was significant (p <0.005) increase in mean serum cholesterol, Triglycerides, LDL and VLDL. However, there was no significant (p value 0 .234) change in HDL cholesterol. In relapse cases of nephrotic syndrome there was significantly higher serum cholesterol (p <0.005), Triglycerides (p =0.003), LDL (p =0 .000) and VLDL (p = .011) when compared to first episode. The present study shows that in nephrotic syndrome, there is generalized hyperlipidemia. Generalized hyperlipidemia was significantly higher in relapse cases compared to other cases.

KEYWORDS : Nephrotic Syndrome, Cholesterol, Cholesterol, HDL, Cholesterol LDL, Hypercholesterolemia

Childhood nephrotic syndrome (NS) is a chronic glomerular disease, characterized by minimal change disease in the majority of cases (Bagga and Mantan, 2005). 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 (Merouani et al., 2003). The persistence and severity of lipid changes in serum correlates well with the duration and frequency of the relapses, even during the remission in patients of the nephrotic syndrome. The intensity of hyperlipidemia is usually related to the severity of proteinuria and hypoalbuminemia. Hyperlipidemia increases risk of atherosclerosis and may also be important in the development of glomerulosclerosis and progressive renal injury. It may be possible to control it by using lipid lowering drugs (Wheeler and Bernard, 1994). In addition to these quantitative changes, the lipoprotein composition is markedly changed, with a higher ratio of cholesterol to triglycerides in the (apo-B containing) lipoproteins and an increase in the proportion of cholesterol, cholesterol ester, and phospholipids compared with proteins. Apart from this, evidence has clearly shown that certain factors like diet, body fat, race, genetic traits are known to alter the of serum lipid levels. Indian patients have different dietary, constitutional and genetic background and further there paucity of data in this region. Hence, we undertook this study to study the level of serum cholesterol, serum triglycerides, LDL, VLDL and HDL at the onset and remission of nephrotic syndrome and to compare it with controls.

MATERIALS AND METHODS

50 Patients with diagnosis of nephrotic syndrome in Basaveshwara Medical College Hospital and Research Centre, Chitradurga, India during period of June 2010 and October 2014 were enrolled. Children in the age group of 2-12 years with typical features of nephrotic syndrome were included in the study. Children with edema, low serum albumin and urinary protein of more than 40mg/m/hr or 3+/4+ protein were considered as having nephrotic syndrome. Patients were considered in remission when urine albumin was nil or trace or proteinuria less than 4 $mg/m^2/hr$ for three consecutive days. 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. In this study, 30 age-matched controls were enrolled from outpatient

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clinic of same institute. These children had come for either routine follow up of other illness or minor illness and had no significant renal or liver disease.

Collection of Data

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. Data was collected at the time of admission to hospital and again during remission of nephrotic syndrome. Detailed history was taken and thorough clinical examination was done. All cases were investigated with serum albumin, urine routine and 24 hours urinary protein. Serum lipid profiles were collected in both cases and controls. Samples were collected during fasting state and in early morning hours.

Serum total cholesterol was measured by cholesterol oxidase phenol amino antipyrine method (CHOD-PAP) method (Ohta and Matsuda 1981), serum triglycerides were estimated by acetyl acetone method (Alexander et al., 1974), LDL cholesterol was estimated by ammonium ferrothiocyanate method(Vaziri 2003), VLDL cholesterol was measured by enzymatic method , Serum HDL Cholesterol (HDL) was measured by phosphotungstate method .

Statistical Analysis

Statistical analysis was done by calculating frequency, mean, standard deviation, chi-square tests. SPSS-15 was used for analysis.

RESULTS

Total of 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. A total of 30 age matched controls were enrolled in the study. Serum lipid profiles were collected both during onset and remission. We had 2(6%) patients in less than 2 years, 37 patients in 2-6 years, and 5 patients in more than 6 years age group. There was preponderance in male gender (60%).

Table 1 compares the serum lipid profiles of all three groups of subjects. There was statistically significant increase in serum cholesterol, triglycerides, LDL and VLDL in nephrotic syndromes when nephrotic syndrome patients were compared to controls (p value <0.005). But HDL levels did not show any significant increase in both groups (p value 0.234). There was significant increase in lipid profiles in all parameters (p value <0.005) except for HDL (p value 0.426) when compared between onset and remission of first episode nephrotic syndrome Figure 2.

Table 1 : Comparison of Lipid Profiles in Different Studied Groups

	Number	Total Cholesterol Mean (SD)	Triglycerides Mean (SD)	Low density lipoprotein Mean (SD)	Very low density lipoprotein Mean (SD)	HDL Mean (SD)
First Episode						
Onset	35	372.82 * (106.20)	273.37* (84.20)	289.72 * (90.18)	57.24 * (18.86)	49.33$ (20.20)
Remission	35	282.74* (47.50)	178.15* (49.43)	191.46* (52.96)	47.19* (17.24)	54.75$ (17.17)
Relapse						
Onset	15	531.17* (80.58)	355.14* (89.97)	403.17* (79.29)	72.40* (18.26)	49.82 # (20.23)
Remission	15	407.98* (96.25)	262.44* (74.09)	305.66* (79.89)	64.85* (17.24)	55.06 # (15.15)
Controls						
	30	175.37* (18.32)	94.10* (19.39)	107.33* (16.10)	24* (9.52)	54.16 @ (9.61)

All Values are in mg/dl, Degrees of Freedom 48, P value- $0.426, # 0.566, @ 0.234, *<0.005.

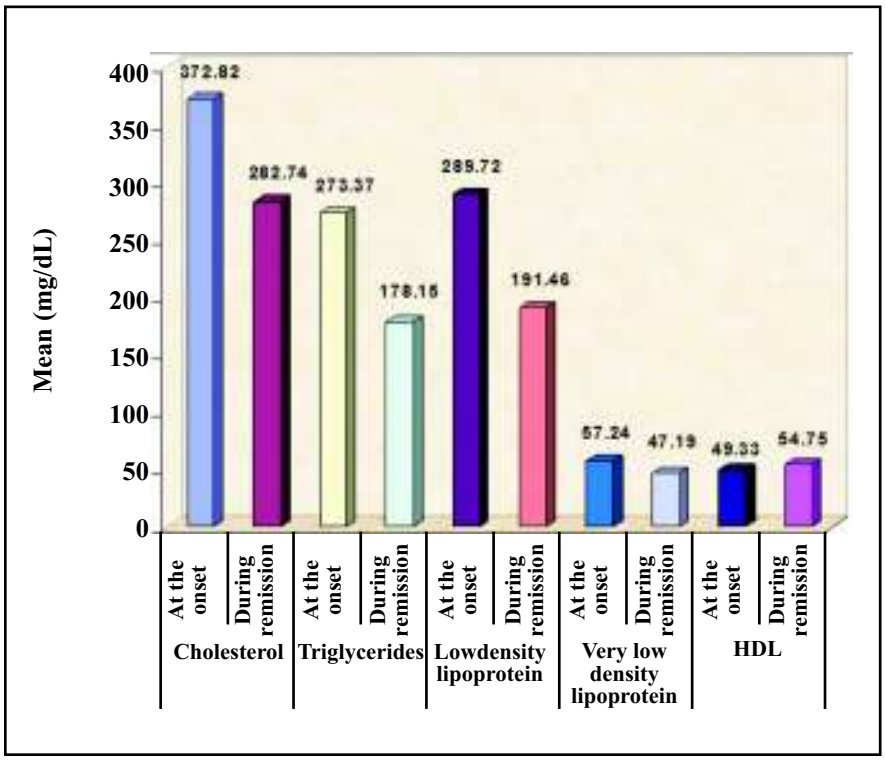

Figure 1: Comparison of Lipid Profile at the Onset And During Remission in First Episode Nephrotic Syndrome

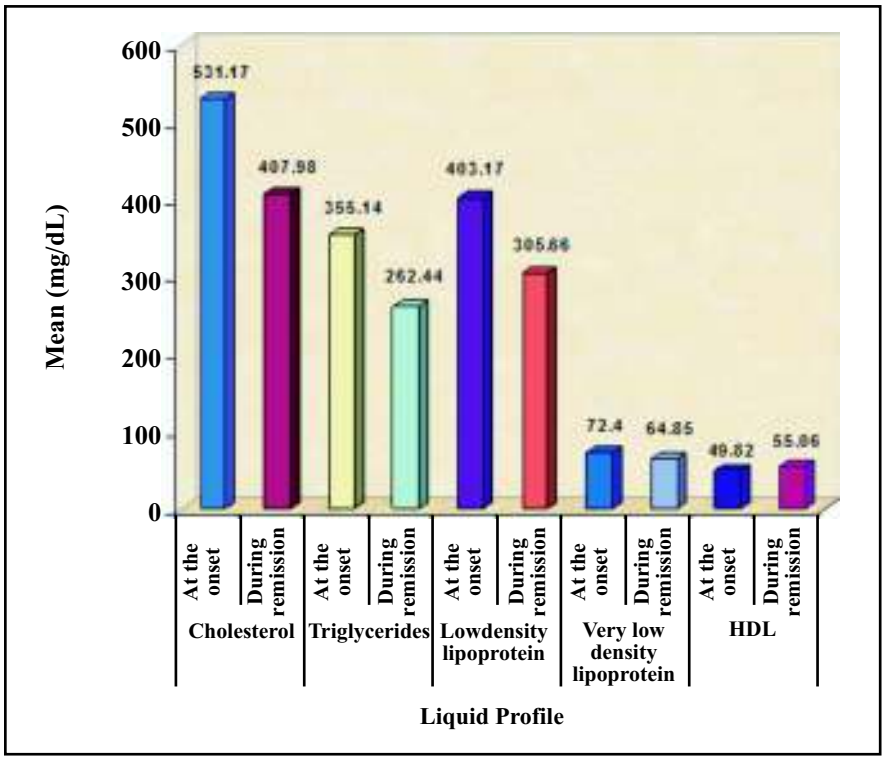

Figure 2 : Comparison of Lipid Profile at the Onset and During Remission in Relapse

Figure 2 Shows the mean lipid profiles at onset and remission in relapse. Mean values of lipid profiles in relapse at onset and remission had shown significantly increased values (p value 0.005) in cholesterol, triglycerides, LDL and VLDL during onset when compared to remission. But there was no significant increase in HDL levels (p value 0.566). (figure 1).

DISCUSSION

In our study, we have seen hyperlipidemia among all nephrotic syndrome patients when compared to controls. This is in accordance with the work done by various authors (5-8). Hyperlipidemia is secondary to defective regulatory response of 3- hydroxyl-3-methylglutararyl-coenzyme A (HMG-COA) reductase and hepatic cholesterol 7alpha-hydroxylase in nephrotics (Vaziri, 2003). These enzymes are rate limiting enzymes in cholesterol biosynthesis and catabolism to bile acids in humans. There was also an increased level of triglycerides in nephrotics when compared with control. This is in agreement with the previous report. This hypertriglyceridaemia is attributed to down regulation of lipoprotein lipase as found in nephrotics skeletal muscle, myocardium and adipose tissue, which is the principal sites of fatty acids consumption and storage(Vaziri, 2003). Both increased production of Apo B containing lipoproteins (VLDL+LDL) and impaired catabolism have been suggested to contribute to the hyperlipidemia. It is assumed that hepatic lipoprotein synthesis is stimulated in response to hypoalbuminemia, low oncotic pressure and urinary albumin loss (Keane and Kasiske, 1990). Decreased renal clearance of mevalonate provided a substrate for hepatic lypogenesis (Short and Durrington, 1990). On the other hand decreased catabolism of LDL-C by the receptor mediated pathway may also be involved in the pathogenesis of nephrotic hyperlipidemia (Warwick et al., 1990). Increased intracellular cholesterol may reduce the number of LDL receptors on the liver cell surface. Uptake of LDL-C by the liver, the major pathway of LDL-C removal from the plasma, may thereby be decreased (Warwick GL et al 1990). In our study HDL-C is normal in 52%, decreased in 22%, increased in 26% of cases. The results of HDL- C measurements have been variable in different studies, with high (Jensen H., 1990), low and normal (Joven et al., 1990)(5, 15) levels of HDL cholesterol being reported. Increased LDL-C and decreased HDL-C are strong risk factors for accelerated atherosclerosis (Olbricht, and Koch, 1992; Allain et al., 1974; Appel et al., 1995).

CONCLUSION

We therefore suggest that full lipid panel should be included in the investigation of suspected nephrotics to complement early diagnosis of the syndrome and to prevent further complications that could arise from the nephrotic syndrome. Prospective controlled studies in children evaluating efficacy and safety of lipid lowering drugs are needed.

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