International Journal of Contemporary Pediatrics
Sreenivasa B et al. Int J Contemp Pediatr. 2016 Nov;3(4):1297-1300
http://www.ijpediatrics.com
pISSN 2349-3283 | eISSN 2349-3291
DOI: http://dx.doi.org/10.18203/2349-3291.ijcp20163664

Original Research Article

Comparative study of lipid profile abnormalities in first episode and relapse cases of childhood nephrotic syndrome

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Received: 28 June 2016
Accepted: 05 August 2016

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ABSTRACT

Background: Nephrotic syndrome (NS) is an important chronic renal disease in children, characterized by minimal change disease in the majority of cases. The objective was to study the levels of serum cholesterol, serum triglycerides, LDL VLDL and HDL in nephrotic syndrome at the onset and during remission in first episode and relapse cases.
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 statistically significant increase in serum cholesterol, triglycerides, LDL and VLDL in nephrotic syndrome patients when compared to controls ($P \leq 0.005$), but HDL value was not significant ($P = 0.234$). In first episode of nephrotic syndrome cases serum lipids decreased significantly during remission, but HDL was increased during remission and it was not statistically significant, whereas in relapse cases even during remission serum lipids were significantly higher but HDL increase was not statistically significant. There was an inverse correlation between albumin and cholesterol. The correlation was statistically highly significant ($P = 0.000$).
Conclusions: 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. Hence there is a rationale for treatment.

Keywords: Cholesterol, Lipoprotein, Nephrotic syndrome

INTRODUCTION

Nephrotic syndrome (NS) is an important chronic renal disease in children, 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 in children with nephrotic syndrome. An attempt was also made to correlate the degree of proteinuria and hypoproteinemia, with the rise in serum lipid values in cases of nephrotic syndrome.

METHODS

Patients with diagnosis of nephrotic syndrome in Basaveshwara medical college hospital, Chitradurga, Karnataka, India during period of May 2012 to March 2015 fulfilling the inclusion and exclusion criteria were included in the study. 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 preform meeting the objectives of the study.

Children with edema, low serum albumin and urinary protein of more than 40 mg/m/hour 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/m^2/hour for three consecutive days. 30 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, serum albumin was estimated by Biuret method, urinary proteins were estimated by Esbachs albuminometer.[4,5] Blood urea was estimated by Diacetyl monoxime method, serum creatinine was estimated by Jaffes method.[6] Serum total cholesterol was measured by cholesterol oxidase phenol amino antipyrine method (CHOD-PAP) method, serum triglycerides were estimated by acetyl acetone method, LDL cholesterol was estimated by ammonium ferrothiocyanate method, VLDL cholesterol was measured by enzymatic method, Serum HDL Cholesterol was measured by phosphotungstate method.[6-9] Statistical analysis was done by contingency coefficient test, descriptive statistics, independent sample t-test , chi-square tests. SPSS-16 was used for analysis.

Treatment protocol

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

Relapse cases

60 mg/m^2/day daily (maximum dose 80 mg divided into 2-3 doses) prednisolone until child enters remission, followed by 40 mg/m^2/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. 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.

Table 1: Serum lipids in nephrotic syndrome.

Lipids	Cases (n = 50) mean±sd	Controls (n = 30) mean±sd	p value
Total cholesterol	420.32±122.69	175.37±18.32	0.000 (HS)
Triglycerides	297.9±93.09	94.1±19.39	0.000 (HS)
LDL	323.75±100.98	107.33±16.10	0.000 (HS)
VLDL	61.79±19.78	24.00±9.52	0.000 (HS)
HDL	49.5±20.10	51.2±21.3	0.234 (NS)

HS = highly significant; NS= not significant.

There was preponderance in male gender (60%) and 40 % females. There was statistically significant increase in serum cholesterol, triglycerides, LDL and VLDL in nephrotic syndrome patients when compared to controls ($P \leq 0.005$), but HDL value was not significant ($P = 0.234$) (Table 1). In first episode of nephrotic syndrome cases serum lipids decreased significantly during remission, but HDL was increased during remission and it was not statistically significant, whereas in relapse cases even during remission serum lipids were

significantly higher but HDL increase was not statistically significant (Table 2). The mean value of serum albumin in study group was 2.00 g/dl while in control group it was 4.19 g/dl. The P-value (0.000) was highly significant (Table 3). Hyperlipidemia is most marked when serum albumin is low, and the correlation is statistically significant (Table 4).

Table 2: Comparison of lipid profiles at the onset and during remission in nephrotic syndrome first episode and in relapse.

	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.

Table 3: Mean serum albumin (g/ld.) in study and control groups

	Number	Mean	SD	Significance
Study group	50	2.00	0.31	0.000
Control group	30	4.19	0.25	

Table 4: Comparison of serum albumin and serum cholesterol.

Albumin (g/dl)	Number of cases	Mean total cholesterol (mg/dl)	SD	p-value
1-1.5	6	569.11	138.37	0.000 (HS)
1.6-2	23	445.65	120.78	
2.1-2.5	21	350.07	59.04	

HS = 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.[10-13] The mean serum cholesterol in relapse cases (mean = 531.17) was significantly higher than first episode nephrotic syndrome cases (mean = 372.82). Arije 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 mg/dl and the highest value was 703.9 mg/dl. Miline reported that the total cholesterol in nephrotic syndrome may be higher than 1000mg/dl.[15] Dnyanesh et al in his study observed that the mean total cholesterol was 422.61 mg/dl and the highest value was 676 mg/dl.[16] Thus we observed low serum lipids in Indian children .This difference in the lipid pattern could be due to different dietic patterns of Indian children as regards to the carbohydrate and fat content of the diet. In our study HDL - C was normal in 52% of cases, decreased in 22%, increased in 26% of cases. The results of HDL-C have been variable in different studies, with high, low and normal levels of HDL cholesterol being reported.[10,12,13,17,18]

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 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] In relapse cases serum lipids were higher probably due to persistence of hyperlipidemia of previous episode. In our study, we observed an inverse correlation between albumin and cholesterol.

The correlation was statistically highly significant (p = 0.000). Krishnaswamy et al found the correlation is not statistically significant.[20] Thomas et al found 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. Prospective controlled studies in children evaluating efficacy and safety of lipid lowering drugs are needed.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: Not required

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Cite this article as: Sreenivasa B, Manjunatha B, Joseph N. Comparative study of lipid profile abnormalities in first episode and relapse cases of childhood nephrotic syndrome. Int J Contemp Pediatr 2016;3:1297-1300.