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ORIGINAL RESEARCH

EVALUATION OF SERUM LIPID PROFILE IN CHILDREN WITH NEPHROTIC SYNDROME: A PROSPECTIVE COHORT STUDY FROM NORTH INDIA

[1]Deepali Bangalia, [2]Satyendr Sonkariya, [3]Chethan C.S., [4]Laxman Singh Charan, [5]Anil Kumar Jain

[1,2,3]MD Pediatrics, [4]Assistant Professor, [5]Senior Professor, Department of Pediatrics, Jawaharlal Nehru Medical College, Ajmer, Rajasthan, India

Correspondence:
Laxman Singh Charan
Assistant Professor, Department of Pediatrics, Jawaharlal Nehru Medical College, Ajmer, Rajasthan, India
E-mail: drlaxmansinghcharan@gmail.com

ABSTRACT

Background: Nephrotic syndrome is a collection of clinical findings due to kidney damage. This includes protein in urine, low blood albumin levels, high blood lipids, and significant edema. The main cause of hyperlipidemia in patients with NS is probably increased hepatic lipogenesis, a non-specific reaction to falling oncotic pressure secondary to hypoalbuminemia. Hyperlipidemia is usually observed during the active phase of the disease and disappears with resolution of proteinuria. However, it may persist in some cases, leading to increased risk of atherosclerosis in later life and development of progressive renal injury. The current study was carried out to evaluate dyslipidemia in children with nephrotic syndrome.

Methods: This prospective cohort study was carried out at outpatient and inpatient units of Department of Pediatrics, JLN Medical College, Ajmer, Rajasthan, India during January 2020 to December 2020. A total of 60 consecutive children aged between one year and 18 years with newly diagnosed nephrotic syndrome or presenting with relapse of the disease. All patients were routinely monitored with daily weight, BP, abdominal girth, intake/output chart and urine albumin. Patients previously diagnosed with nephrotic syndrome with relapse were also admitted. Serum lipid profile was done by standard methodsat three points of time: during disease activity, after attainment of remission and two weeks after completion of steroid therapy in steroid responsive nephrotic syndrome.

Results: Lipid parameters including mean total cholesterol, Triglyceride, LDL and VLDL were elevated at admission and these levels reduced significantly at remission and at completion of steroid therapy (All p values<0.001). There was significant elevation of mean total cholesterol level in case of relapse as compared to the first

episode of nephrotic syndrome (p=0.048), however, LDL, VLDL and HDL were not significantly different. There was significant elevation of total cholesterol level at admission in subsequent relapses as compared to first episode of nephrotic syndrome (p=0.01).

Conclusion: In children with nephrotic syndrome, lipid parameters including mean total cholesterol, Triglyceride, LDL and VLDL were elevated at admission and these levels reduced significantly at remission and at completion of steroid therapy. Total cholesterol level was significantly elevated in children with relapse as compared to those with first episode of nephrotic syndrome.

Keywords: Nephrotic Syndrome, Lipid profile, Relapse, Dyslipidemia.

INTRODUCTION

Nephrotic syndrome is the clinical manifestation of glomerular disease associated with massive (nephrotic range) proteinuria, hypoalbuminemia (<2.5 g/dl), generalized edema, and hyperlipidemia (cholesterol >200 mg/dl). Nephrotic range proteinuria is defined as proteinuria >1g/m^2 /24 hours or >40 mg/m^2 /hours.[1] Nephrotic syndrome is usually accompanied by retention of water and sodium. The degree to which this occurs can vary between slight edema in the eyelids, to affecting the lower limbs, to generalized swelling, anasarca.[2] Lipiduria (lipids in urine) can also occur but is not essential for the diagnosis of nephrotic syndrome. Hypoproteinemia stimulates protein synthesis in the liver, resulting in the overproduction of lipoproteins. Lipid catabolism is decreased due to lower levels of lipoprotein lipase, the main enzyme involved in lipoprotein breakdown. Cofactors, such as apolipoprotein C2 may also be lost by increased filtration of proteins. The main cause of hyperlipidemia in patients with NS is probably increased hepatic lipogenesis, a non-specific reaction to falling oncotic pressure secondary to hypoalbuminemia. Both increased synthesis and decreased clearance of lipoproteins may contribute to the hyperlipoproteinemia which frequently complicates NS with increased levels of total and LDL cholesterol as the most characteristic abnormality. Hyperlipidemia is usually observed during the active phase of the disease and disappears with resolution of proteinuria. However, it may persist in some cases, leading to increased risk of atherosclerosis in later life and development of progressive renal injury.[3] Hence close monitoring of lipid levels during remission of nephrotic syndrome is necessary to select high risk patients.[4] Current study is designed to study the spectrum of serum lipid profile abnormalities in children with nephrotic syndrome.

MATERIALS & METHODS

This prospective cohort study was carried out at outpatient and inpatient units of Department of Pediatrics, JLN Medical College, Ajmer, Rajasthan, India – a tertiary care teaching institute, between January 2020 and December 2020. All consecutive children aged between one year and 18 years with newly diagnosed nephrotic syndrome or presenting with relapse of the disease were enrolled after obtaining informed consent. Children with family history of hyperlipidemia/ infantile stroke or historyof hepatobiliary disorders, hepatitis, renal tubular acidosis/chronic kidney disease were excluded. All newly diagnosed cases were admitted as inpatients. Detailed history was taken, and thorough general and systemic examination was done. Standard investigations like urine analysis for albumin, hyaline casts and RBC's, serum

protein, serum albumin, blood urea, serum creatinine, Mantoux test, X-ray chest, USG abdomen, Urine C&S were done. All patients were routinely monitored with daily weight, BP, abdominal girth, intake/output chart and urine albumin. Patients previously diagnosed with nephrotic syndrome with relapse were also admitted. Serum lipid profile was done by standard methodsat three points of time: during disease activity, after attainment of remission and two weeks after completion of steroid therapy in steroid responsive nephrotic syndrome. Automated Absorption Spectrophotometry (Beckman - Coulter) was used for the estimation of total cholesterol (TC), triglycerides (TGL) and high-density lipoprotein (HDL). Low density lipoprotein (LDL) and very low-density lipoprotein (VLDL) were estimated using standard formula.

STATISTICAL ANALYSIS

Quantitative data was expressed in mean $\pm$ standard deviation and differences between two groups were compared using Unpaired t test. Qualitative data were expressed in percentage, and difference between proportions was tested by chi square test. P value less than 0.05 was considered statistically significant. Statistical package for social sciences version 23 was used for the analysis.

RESULTS

A total of 60 patients with nephrotic syndrome were included in the study. The mean age was 6.6±3.3 years with majority (60%) of the patients from age group 5-10 years (Figure 1). There was preponderance of males (56%). Mean age at first episode was 5.2±2.5 years. Majority of the children (n=40, 75%) had first episode of nephrotic syndrome at admission while rest 25% children had relapse. In the current study, all 60 patients had oedema and facial puffiness; 50 patients had abdominal distension, and 23 patients had urinary complaints. 57 patients had pedal edema and 46 patients had anasarca.

Lipid parameters including mean total cholesterol, Triglyceride, LDL and VLDL were elevated at admission and these levels reduced significantly at remission and at completion of steroid therapy (all p value <0.001). There was no significant difference in HDL level at admission, at remission and at completion of steroid therapy (p=0.6) (Table 1). There was a significant elevation of mean total cholesterol level in case of relapse as compared to the first episode of nephrotic syndrome (p=0.048); however, LDL, VLDL and HDL were not significantly different (Table 2). There was significant elevation of total cholesterol level at admission in subsequent relapses as compared to first episode of nephrotic syndrome (p=0.01) (Figure 2). However, there was no significant elevation at remission and at completion of steroid therapy in subsequent relapses as compared to first episode (p>0.05).

Figure 1: Demographic distribution

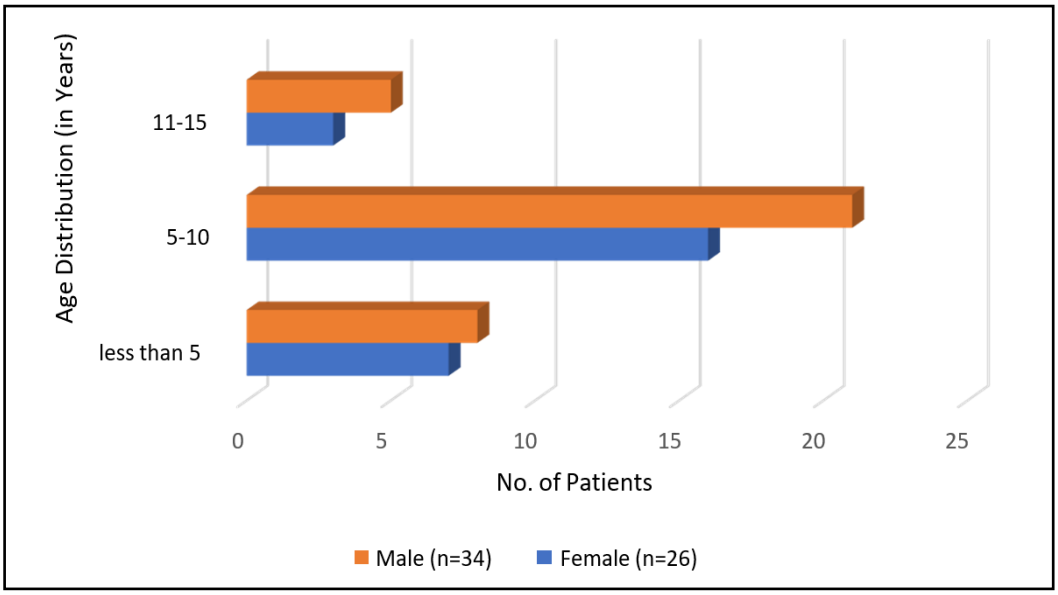


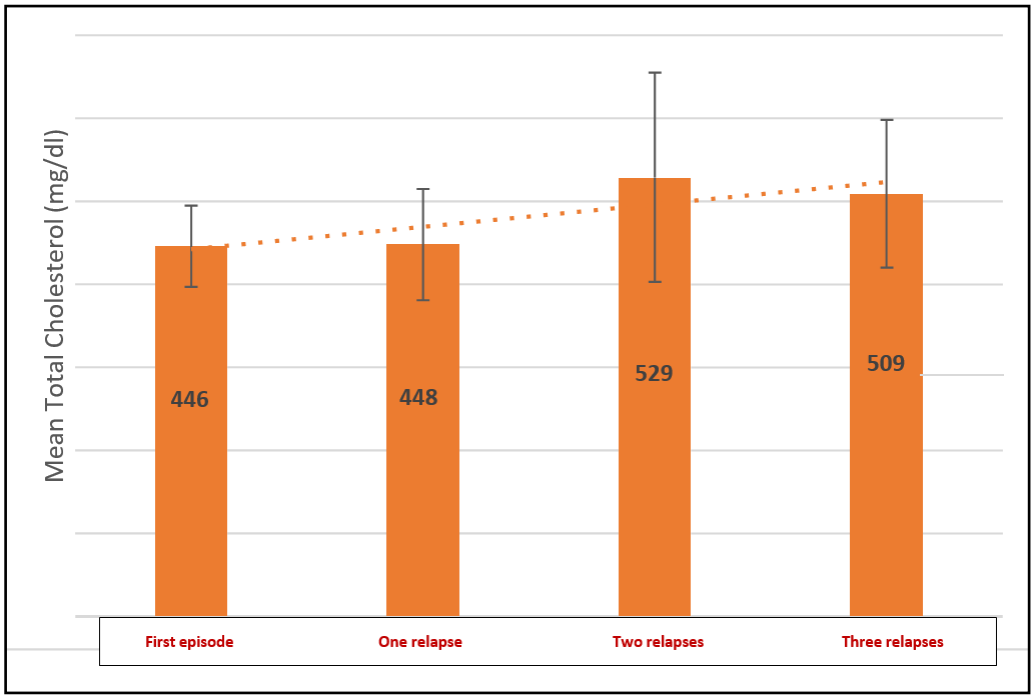
Table 1: Spectrum of lipid profile in nephrotic syndrome

Lipid parameter	At admission (Mean±SD)	At remission (Mean±SD)	At completion of steroid therapy (Mean±SD)	P value
Total cholesterol (mg/dl)	462±73	336±50	179±17	<0.001
Triglyceride(mg/dl)	285±74	200±46	94±14	<0.001
LDL (mg/dl)	277±91	191±48	89±17	<0.001
HDL (mg/dl)	52±8	50±5	52±5	0.6
VLDL (mg/dl)	66±13	49±8	33±6	<0.001

Table 2: Comparison of lipid parameters between first episode and relapse

Lipid parameter		At admission (Mean±SD)	P value
Total cholesterol(mg/dl)	First episode	446±49	0.048
	Relapse	509±109	
LDL (mg/dl)	First episode	277±73	0.907
	Relapse	274±133	
HDL (mg/dl)	First episode	52±9	0.385
	Relapse	50±4	
VLDL (mg/dl)	First episode	67±13	0.113
	Relapse	61±13	

Figure 2: Mean cholesterol level at admission



DISCUSSION

Lipoproteins are the major carriers of lipids in blood, and they participate in three major pathways that are responsible for the generation and transport of lipids within the name, the exogenous pathway, the endogenous pathway, and the reverse cholesterol transport pathway. Lipid and lipoprotein metabolism is altered in nephrotic syndrome.[5] The current study was carried out to evaluate dyslipidemia in children with nephrotic syndrome. The age of study subjects ranged between 1 and 15 years and a mean of 6.7±3.3 years. Majority (60%) of patients were in the age group of 5-10 years, followed by 13 % patients in the age group 11-15 years. The mean age was like that reported in other studies. In a study by Sahana et al, mean age at presentation was 7.4 years.[6] In their study, 65% of the subjects belonged to 6–12 years age followed by 1–5 years (31%). Pandya and Mehta reported mean age as 4.08 years and Kiran and Kumar reported the mean age at presentation as 6.7 years.[7,8] There were 34 (56%) males and 26 (34%) females with a male-female ratio of 1.3:1 (male preponderance). Sahana found that 76% of the subjects were males while 24% were females with male to female ratio of 3.27:1 suggesting a male preponderance.[6] Pandya and Mehta and Kiran and Kumar also observed male predominance in their studies.[7,8] The distribution of male and female patients in various age groups (p=0.5) was similar in thecurrent study.

In current study there was significant rise in total cholesterol level in patients in relapse phase of nephrotic syndrome (mean = 462 mg%, SD=73 mg%) as compared to total cholesterol in patients in remission phase (mean = 336 mg%, SD=50 mg%) and total cholesterol after completion of steroid therapy (mean=179 mg%, SD=17 mg%) and this difference was statistically significant ($p<0.001$). Similarly, LDL cholesterol ($p<0.001$), triglycerides ($p<0.001$) and VLDL cholesterol ($p<0.001$) levels were significantly high in relapse phase as compared to that in remission phase and after completion of steroid therapy. However, there was no significant difference in HDL cholesterol level before and after steroid therapy in

current study. This significant difference was observed in all three age groups (<5 years, 5-10 years, and 11-15 years) and in both males and females (all p value<0.001). Arije et al in his study on plasma lipids and lipoproteins cholesterol distributions in nephrotic syndrome patients duringshort term steroid treatment, had similar observations in his study.[9] We noticed that the degree of lipid increase was not that high as reported by Western studies. Milne reported that the total cholesterol in nephrotic syndrome may be higher than 1000 mg%.[10] In our study the mean total cholesterol was 462 mg%. Banerjee et al in his study observed that the mean total cholesterol was 341mg% and the highest value was 641mg%.[11] Thus, we observed low serum lipids in Indian children. Merouni et al observed hyperlipidemia during the active phase of the disease and it disappeared with resolution of the proteinuria while being persistently abnormal in frequently relapsing children.[12] Tsukahara et al observed that children with frequently relapsing nephrotic syndrome have prolonged periods of hypercholesterolemia.[13] Querfeld used statins in his study and observed 30-40% reduction in the total cholesterol.[14] Buyokcelik et al observed significant reduction in the total cholesterol with statins in adultpatients with nephrotic syndrome.[15]

Methodological weaknesses, small sample size and variability in the definition of abnormal lipid parameters across studies are few limitations.

CONCLUSION

In children with nephrotic syndrome, lipid parameters including mean total cholesterol, Triglyceride, LDL and VLDL were elevated at admission and these levels reduced significantly at remission and at completion of steroid therapy. Total cholesterol level was significantly elevated in children with relapse as compared to those with first episode of nephrotic syndrome.

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