

CORRELATION BETWEEN SERUM ALBUMIN AND SERUM LIPID PROFILE IN CHILDHOOD NEPHROTIC SYNDROME- A CROSS SECTIONAL STUDY

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ABSTRACT

Background and objectives: Hyperlipidemia is more commonly seen during the active phase of the disease and disappears after proteinuria is resolved. Renal damage may be exacerbated by hyperlipidemia. As a result, the goal of this study was to identify lipid abnormalities and see if there was a link between blood lipid and serum albumin levels in people with nephrotic syndrome.

Materials and methods: A prospective study of 30 children with nephrotic syndrome who were admitted to pediatric wards for the first time. A total of 30 children with nephrotic syndrome and 10 children without liver or renal problems were included in the research group.

Results: There was a statistically significant direct relationship between total cholesterol and LDL cholesterol (low-density lipoproteins) ($p=0.001$). There was a substantial reduction in the mean values of pretreatment total cholesterol and LDL cholesterol after 4 weeks of steroid therapy in first episode nephrotic syndrome ($p=0.001$). There was a highly significant reduction in the mean levels of pretreatment total cholesterol and LDL Cholesterol ($p=0.001$) at the end of steroid treatment (8 weeks) in first episode nephrotic syndrome. There was also a significant decrease in mean pretreatment triglycerides ($p=0.016$).

Conclusion: Even after stopping steroid therapy, there was no significant reduction in baseline total cholesterol, LDL cholesterol, VLDL (very low-density lipoproteins) cholesterol, or triglycerides in patients with relapsed nephrotic syndrome.

Keywords: Hyperlipidemia, Nephrotic Syndrome, Steroid resistant.

INTRODUCTION

One of the most prevalent findings in Nephrotic Syndrome patients is an increase in lipid levels. When there is an increase in cholesterol levels, this is a symptom of Nephrotic Syndrome¹. However, the pathophysiological reason of the rise in lipid levels has not been fully addressed. Various researchers have documented an increase in lipoprotein synthesis, a decrease in albumin levels, and a decrease in lipid levels. Lipoprotein lipase is a lipoprotein lipase enzyme that is active. In most situations, lipid levels fall, but in certain circumstances, lipid levels persist after the edema has

subsided. Lipid levels rise during the active phase of Nephrotic Syndrome, then return to normal as proteinuria subsides. However, in certain situations, there is a rise in lipid levels, which can lead to the illness Atherosclerosis in adulthood. As a result, during remission of Nephrotic Syndrome, it is critical to keep a careful eye on lipid levels and to identify individuals with a high risk of Nephrotic Syndrome.^{1,2}

Lipoproteins play a key role in the transport of lipids, and changes in lipoprotein fractions may contribute to a rise in cholesterol levels in Nephrotic Syndrome. Hypercholesterolemia is caused by a rise in LDL cholesterol, VLDL cholesterol, and triglycerides, as well as a normal or low HDL cholesterol level. However, the increase in cholesterol levels in Indian children is not as large as it is in western children. Renal damage can occur when cholesterol levels are too high. Other experimental investigations have found that lowering cholesterol levels delays the course of diseases such as glomerular and tubulointerstitial diseases. The purpose of this study is to look at the changes in serum lipids in people who have Nephrotic Syndrome. To determine if there is a link between serum albumin and serum lipids. Pathophysiology of lipoprotein abnormalities in Nephrotic Syndrome.^{3,4}

MATERIALS AND METHODS

From January 2019 to October 2020, a prospective research was conducted on 30 children with nephrotic syndrome who were hospitalized for the first time to the pediatric wards of sree mookmabika hospital. All forms of nephrotic syndrome were covered in the research. The control group consisted of ten children who did not have any liver or kidney disorders.

Method of collection of Data:

Before starting steroid therapy (ISKDC-International Study of Kidney Disease in Children, Regimen), after one month of steroid therapy, and at the end of therapy, the 30 nephrotic syndrome cases were clinically evaluated, and the following investigations were conducted in each instance.

Inclusion Criteria: Nephrotic syndrome affects all infants and children aged 0 to 12 years old.

Exclusion Criteria: Children with liver disorders, Kwashiorkor oedema, CCF (congestive cardiac failure) oedema, and kidney diseases other than nephrotic syndrome.

Treatment Protocol: International study group on kidney diseases in children (ISKDC) regimen. Prednisolone 60 mg/m²/day in three split doses for four weeks, then prednisolone 40 mg/m² on alternate days for another four weeks.

Steroid resistant: Failure to achieve response despite 4 weeks of steroid therapy.⁵

Relapse: Urinary protein 3+ or more on 3 consecutive days with or without edema, while in remission.

Serum total cholesterol: was measured by enzymatic method.

Normal serum cholesterol: 150- 250 mg/dl

Serum HDL (High density lipoproteins)cholesterol: was measured by Phosphotungstate method.

Normal HDL – Cholesterol: 30 – 70 mg/dl.

Serum LDL cholesterol: The value of LDL cholesterol was calculated as follows.⁶

LDL cholesterol may be estimated using Friedewald's equation if the value of Triglycerides is known.

LDL – chol mg/dl: Total CHOL – TRIGLYCERIDES – HDL – CHOL

Serum Triglycerides: was measured by enzymatic colorimetric method.⁷

NormalSerumTriglycerides:

Male: 60- 165mg/dl

Female: 40- 140mg/dl

Serum VLDL: The enzyme technique was used to determine the results.

SerumAlbumin: The photometric method was used to determine the results. 3.5–5.0 gm/dl is considered normal.

The Mann Whitney ‘U’ test, Wilcoxon signed rank sum test, and Pearson correlation test were used to analyze the data.

RESULTS

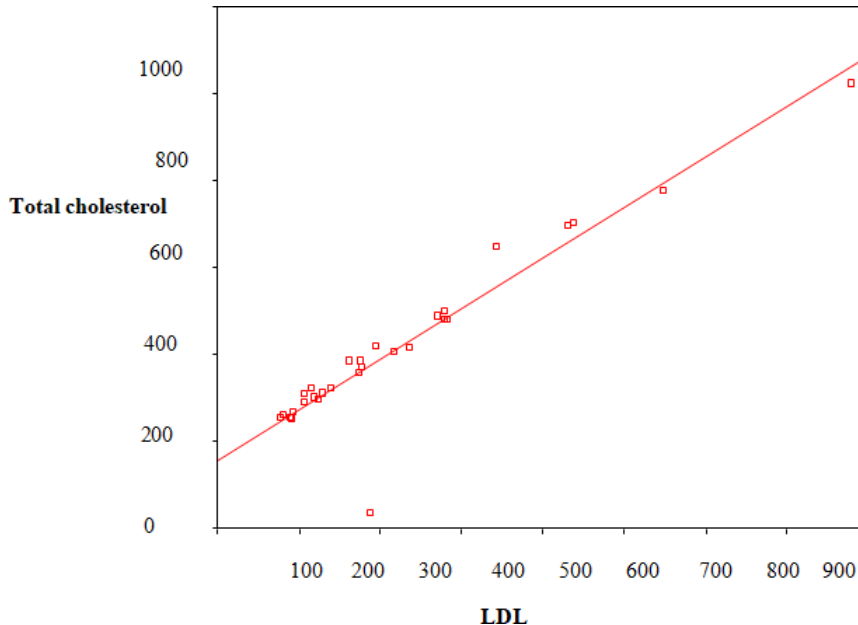
The age distribution revealed that 73.3% of the children were under the age of six, with the remainder falling between the ages of seven and twelve. Males outnumber females in this research. The male-to-female ratio is one-to-five.

Table 1: Serum lipids in nephrotic syndrome

Lipids	Controls		Study group		P- value
	Range(mg%)	Mean (mg%)	Range (mg%)	Mean (mg%)	
TotalCholesterol	151-250	190.10	253 – 676	422.61	P = 0. 001
LDL Cholesterol	86-170	119.50	190 – 577	319.10	P = 0.001
VLDL cholesterol	36-50	43.30	23 – 107	54.53	P = 0.001
HDL cholesterol	45-54	48.30	26 –70	45.56	P = 0. 078
Triglycerides	76-120	92.70	113 – 555	284.06	P = 0.001

There were ten controls in all. They ranged in age from 2.5 to 12 years old. All of the patients' renal functions were normal. The lipids in the controls are summarized in table 2 and figure 2. Total cholesterol, LDL cholesterol, VLDL cholesterol, and triglycerides were all substantially higher in this study than in the controls (P = 0. 001). HDL cholesterol, on the other hand, shows no statistically significant decrease (P = 0.078).

Figure-1: Scatter diagram showing correlation between total and LDL cholesterol



According to the scatter figure above, total serum cholesterol has a strong positive association with LDL cholesterol in nephrotic syndrome.

Table-2: Comparison of serum albumin and serum cholesterol

Albumin (g%)	Mean (mg%)	SD	P value
Serum albumin and serum cholesterol			
1 – 1.5	516.66%	292.13	0.537
1.6 – 2.0	362.55%	146.72	
2.1 – 2.5	336.25%	191.91	
serum albumin and HDL cholesterol			
1- 1.5	42.13%	3.014	0.537
1.6- 2.0	45.21%	4.013	
2.1- 2.5	45.27%	3.097	
serum albumin and serum VLDL-cholesterol			
1- 1.5	79.51%	21.17	0.57
1.6- 2.0	66.04%	23.85	
2.1- 2.5	59.19%	19.79	
Study	2.52%	3.39	0.001
Control	4.03%	0.15	

The table indicates that serum albumin and cholesterol have an inverse relationship. However, the correlation ($P=0.537$) is not statistically significant.

When serum albumin was between 1 and 1.5 gm%, the mean HDL cholesterol was 42.13 mg%, and when albumin was between 2.1 and 2.5 gm%, the mean HDL cholesterol was 45.27 mg%. However, the link was not statistically significant ($p=0.537$).

In our research, we discovered an inverse relationship between serum albumin and VLDL cholesterol. The correlation, however, was not statistically significant.

The serum albumin in nephrotic syndrome is significantly lower than in controls ($P = 0.001$), as seen in this table. In this study more than 90% cases were steroid sensitive.

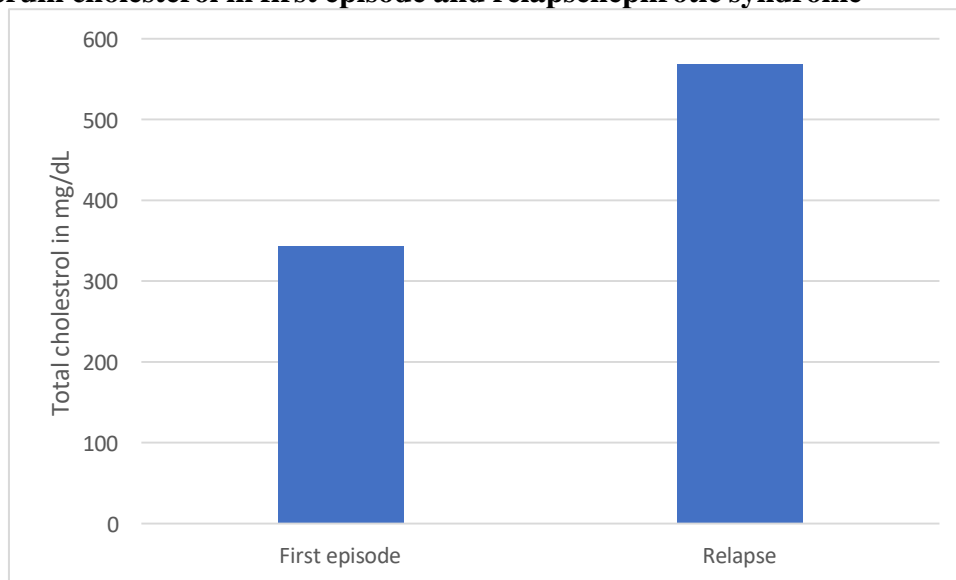
Table-3: serum albumin in response to steroid treatment paired differences

	Mean	SD	Z	P value
Sr Alb1 – Sr Alb2	- 0. 9667	3. 37	4. 169	0. 001
Sr Alb1 – Sr Alb3	- 1. 5367	3. 43	4. 170	0. 001
Sr Alb2 – Sr Alb3	- 0. 5700	0. 37	4. 629	0. 001

(Sr Alb1=Serum albumin before treatment, Sr Alb2 = Serum albumin after 1 month, Sr Alb3=Serum albumin at end of treatment).

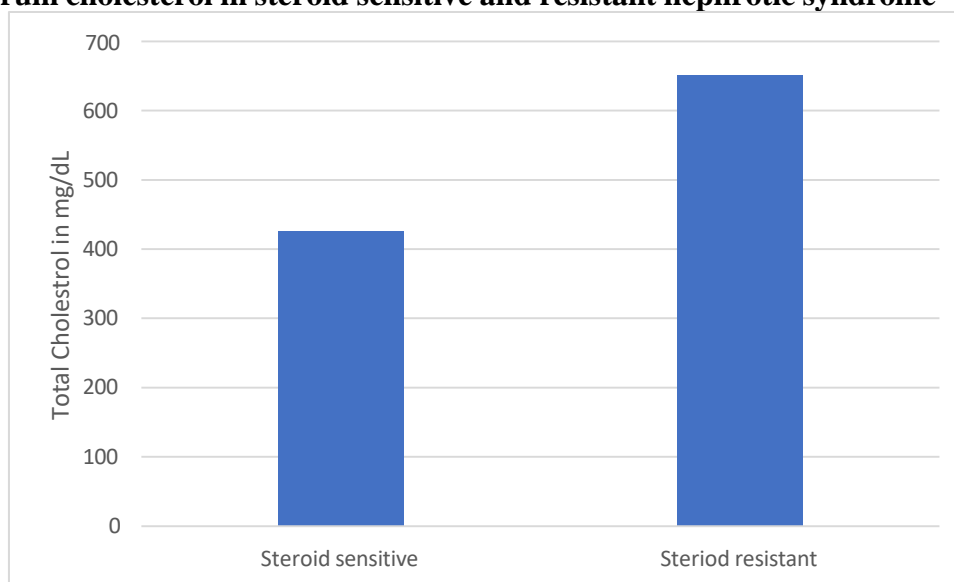
After steroid therapy, serum albumin gradually rises to normal levels. ($P = 0.001$)

Figure-2: Serum cholesterol in first episode and relapsenephrotic syndrome



In relapse cases, the mean serum cholesterol level was 568.52 mg%, which was significantly higher than the mean cholesterol in the first episode (mean= 343.4 mg%, $P = 0.001$).

Figure-3: serum cholesterol in steroid sensitive and resistant nephrotic syndrome



The mean cholesterol level in steroid resistant patients was much higher than in steroid sensitive cases ($p=0.001$ VHS), according to this study.

Table-4: Response of cholesterol to steroid therapy

Total Cholesterol	Mean			P Value
	Before Treatment	After 1month	End of Treatment	
1 st Episode	343.40	201.77	166.27	0.001
1 st Relapse	510.14	482.00	401.71	
3 rd Relapse	627.00	592.60	623.60	

At the completion of steroid therapy, serum cholesterol levels in the first episode of nephrotic syndrome return to normal. However, in the case of relapses, cholesterol levels remain elevated and are strongly associated to the number of relapses. ($P=0.001$)

Table-5: Lipid profile in first episode and relapse nephrotic syndrome after 4 weeks of treatment

Lipids	Mean(mg/dl)	SD	P value
First episode nephrotic syndrome after 4 weeks of treatment			
Total Chol	201.77	41.341	0.001 VHS
LDL Chol	151.13	37.173	0.001 VHS
VLDL Chol	52.51	5.243	1.078 NS
HDL Chol	45.98	3.023	0.518 NS
Triglycerides	231.19	20.177	0.537 NS
Relapse episode nephrotic syndrome after 4 weeks of treatment			
Total	541.00	102.141	0.001
LDL	337.04	81.723	0.001
VLDL	64.01	11.341	0.001
HDL	44.21	3.143	0.527
Triglycerides	351.13	30.321	0.001

After 4 weeks of steroid treatment, there was a significant reduction in pretreatment mean total cholesterol (mean=201.77mg%, p=0.001) and mean LDL cholesterol (mean=151.13mg %, p=0.001), but no significant change in HDL cholesterol, VLDL cholesterol, or triglyceride level in patients with first episode nephrotic syndrome.

Even after 4 weeks of steroid therapy, there was no significant improvement in pretreatment total cholesterol, LDL cholesterol, HDL cholesterol, VLDL cholesterol, or triglycerides in patients with relapsed nephrotic syndrome.

Table-6: Posttreatment lipid profile in first episode and relapse in nephrotic syndrome

Lipids	Mean (mg %)	SD	P value
Posttreatment lipid profile in first episode nephrotic syndrome			
Total cholesterol	166.27	33.1815	0.001
LDL cholesterol	112.17	22.6090	0.001
VLDL cholesterol	49.05	5.2715	0.060
HDL cholesterol	48.23	3.0203	0.070
Triglycerides	171.41	31.8607	0.016
Post-treatment lipid profile in relapse nephroticsyndrome			
Total cholesterol	537.00	112.131	0.001
LDL cholesterol	325.34	88.027	0.001
VLDL cholesterol	63.78	12.013	0.001
HDL cholesterol	43.17	3.132	0.560
Triglycerides	324.13	57.107	0.001

There was a statistically highly significant reduction in the mean levels of pretreatment total cholesterol (mean= 166.27mg %, p=0.001) and LDL cholesterol (mean= 112.17mg %, p=0.001) after the end of steroid therapy in first episode nephrotic syndrome. The amount of mean triglycerides was also reduced significantly (mean=171.41mg%, p=0.016). The average VLDL cholesterol level did not change much. However, there was a small but statistically significant rise in mean HDL cholesterol. Even after stopping steroid therapy, there was no significant reduction in baseline total cholesterol, LDL cholesterol, VLDL cholesterol, or triglycerides in patients with relapsed nephrotic syndrome. There was also no significant increase in HDL cholesterol.

DISCUSSION

Our study included 50 children with nephrotic syndrome, ranging in age from 0 to 12 years, as well as 10 healthy children with no liver or kidney problems who served as controls. Cholesterol levels increased significantly in this research, especially LDL cholesterol, although HDL cholesterol levels remained within acceptable ranges. We discovered that mean serum cholesterol in relapse cases was significantly higher than in first-episode nephrotic syndrome patients, and that mean serum cholesterol in steroid persistent cases was higher than in steroid sensitive cases. In frequent relapse patients, Arije et al found a persistent rise in serum lipids. We discovered that lipid increases in the land were not as great as those reported by western researchers.⁸

According to Milne, total cholesterol in nephrotic syndrome can be beyond 1000 mg%, however the mean total serum cholesterol in our study is 422.6 mg% and the maximum value is 676 mg%. According to Banerjee et al research, the average total serum cholesterol level is 341 mg/dL, with a highest value of 641 mg/dL. Low serum lipids were found in the Indian population. The positive association between total cholesterol and LDL cholesterol was statistically significant in our

study, with a p value of 0.05. A significant connection between LDL cholesterol and total cholesterol was also discovered by David et al.^{3,9,10}

In this study, we discovered that there is a strong negative relationship between albumin and cholesterol; when albumin is between 2 and 5, mean serum cholesterol is 336.25 mg%. Thomas et al. found a correlation between serum albumin and serum cholesterol, but no correlation between cholesterol, albumin globulin, or total protein. They used an experimental model in which they ligated ureters to stop protein loss in the urine and saw a drop in serum lipids. They found comparable findings with IV albumin infusion, which also revealed serum lipids.¹¹

Banerjee et al. found a correlation between the severity of hypoalbuminemia and hyperlipidemia, and the current investigation found the same result. We observed a relation between serum HDL cholesterol and albumin in our research. When blood albumin was too low in our investigation, serum HDL cholesterol was likewise too low. However, when albumin levels are between 2.1- 2.5 gm%, The average HDL cholesterol level is 45mg%. However, the connection is statistically insignificant. Similar findings were made by Mallik et al. We found an inverse relationship between albumin and serum VLDL cholesterol in our investigation, although it was not statistically significant.^{10,12}

In our current study, 90% of the patients are steroid responsive, with the remaining 10% being steroid resistant. Prednisolone short-term high-dose prednisolone is used in all instances, according to the (ISKDC) regimen. In our research, we discovered that first-episode nephrotic syndrome and recurrence patients had distinct responses. Before commencing therapy, blood cholesterol levels in first-episode nephrotic syndrome patients are high (mean=343.4 mg%). However, at the conclusion of the 8-week treatment period, serum cholesterol had returned to normal levels (p=0.001).

By the end of four weeks of high-dose prednisolone therapy, we noticed in a first-episode nephrotic syndrome case. Pretreatment total blood cholesterol (201.77 mg%) and mean LDL (151.11) levels were significantly lower [p=0.001]. However, there were no significant changes in HDL cholesterol, VLDL cholesterol, and triglycerides.

Arije et al. found that when short-term prednisolone therapy was given, mean pretreatment cholesterol and LDL levels were considerably lower at 4, 8, and 12 weeks of treatment. However, HDL cholesterol did not change substantially during therapy, but in the event of relapses, there was no significant change in lipid reduction by the end of relapses, and these lipid levels remained chronically high (p=0.001). In first-episode nephrotic syndrome, there was a statistically significant reduction in pretreatment total cholesterol, triglyceride levels, and LDL cholesterol at the conclusion of steroid therapy after 8 weeks of treatment. However, there were no significant increases in mean VLDL cholesterol. We also saw a little rise in mean HDL cholesterol, which was not statistically significant.⁸

Merouani et al reported hyperlipidemia only during the active phase of the disease, which returns to normal following proteinuria resolution, and chronically high lipid levels in often relapsing nephrotic syndrome patients. As a result, he recommended that patients with nephrotic syndrome be monitored, especially if they have a high risk of relapse.¹³

When Querfeld et al took statins, they saw a 30-40% reduction in total cholesterol. Treatment with lipid-lowering medications, on the other hand, has not been proved to be beneficial in children. Lipid-lowering medications, on the other hand, have been shown to be safe and effective in adults.¹⁴ According to Hari P et al. children with steroid resistant nephrotic syndrome are exposed to various cardiovascular risk factors, predisposing them to accelerated atherosclerosis, the risk of accelerated atherosclerosis in children with steroid sensitive nephrotic syndrome is minimal.¹⁵

Antipsk monoclonal antibodies and other treatments targeting the molecular mechanism of lipid transport disturbed in nephrotic syndrome have recently been approved for the treatment of dyslipidemia in nephrotic syndrome.

CONCLUSION

According to our findings, nephrotic syndrome is characterized by widespread hyperlipidemia and hypoalbuminemia. Although hyperlipidemia is more prominent when serum albumin is low, there is no definitive link between the degree of hypoalbuminemia and lipid rise.

The current study also demonstrates that after the end of steroid therapy, blood cholesterol levels in the first episode of nephrotic syndrome return to normal. In cases of recurrence, however, cholesterol levels remain elevated, perhaps predisposing to the development of atherosclerosis and the progression of chronic renal failure. As a result, there is a justification for therapy. Treatment with lipid-lowering medications, on the other hand, has not been proved to be beneficial in youngsters. More prospective control trials in children are needed to assess the effectiveness and safety of lipid-lowering medications.

FINANCIAL SUPPORT AND SPONSORSHIP:

Nil.

CONFLICTS OF INTEREST:

There are no conflicts of interest

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