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Original research article

Comparison of Serum Lipid Levels with Serum Albumin in Nephrotic Syndrome in Children

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Abstract

Background: A common nephrotic syndrome finding is the presence of hyperlipidemia. Total cholesterol, LDL, VLDL, and low or normal HDL levels have all increased. Typically, hyperlipidemia is seen when the disease is active and goes away when the proteinuria goes away. However, it may recur and raise the risk of developing atherosclerosis in later life in recurrent cases. We in the current study tried to correlate the severity of nephrotic syndrome and dyslipidemia in pediatric cases presenting to our hospital.

Methods: A pre-validated proforma was used to record the information from the person. Following the parental agreement, clinical information was gathered and recorded in the proforma, including the patient's age, sex, presenting complaints, pharmacological history, and type of nephrotic syndrome (episode, recurrence, SDNS, SRNS, or remission). Blood samples for the patients' lipid profiles and serum albumin were taken after obtaining their medical histories and performing a clinical examination.

Results: The lipid profile of the cases of nephrotic syndrome in the study showed total cholesterol, LDL, VLDL, and Triglycerides were significantly higher in the cases as compared to controls all the values were ($p = <0.05$). In cases of first episode nephrotic syndrome after 6 weeks of steroid treatment, there was a significant reduction in the levels of lipids from the pre-treatment mean total cholesterol reduced to 213.0 ± 33.18 mg/dl. Similarly, the LDL-C levels were reduced to mean levels of 124.76 ± 22.60 mg/dl. The VLDL levels were reduced to 42.61 ± 5.27 mg/dl. The HDL levels were increased to 48.23 ± 3.02 mg/dl. The levels of triglycerides were reduced to 104.19 ± 31.8 mg/dl.

Conclusion: In pediatric nephrotic syndrome cases there is a significantly increased serum lipid profile. The lipid profile parameters were negatively correlated with serum albumin levels except HDL with weak positive correlation. After 6 weeks of steroid treatment in the first episode of nephrotic syndrome, there was a significant reduction in the mean levels of pre-treatment total cholesterol and LDL cholesterol. In the relapse nephrotic syndrome cases at the end of steroid treatment, there was no significant reduction in the mean levels of total cholesterol, LDL-C, VLDL-C, and triglycerides.

Keywords: Lipid profile, Nephrotic syndrome, Steroid-Resistant Nephrotic Syndrome (SRNS), Steroid-Dependent Nephrotic Syndrome (SDNS)

Introduction

Nephrotic syndrome is a common problem in the pediatric age group. It is 15 times more common in children as compared to adults. The majority of affected children have steroid-sensitive minimal change nephrotic syndrome. The characteristic features of nephrotic syndrome are heavy proteinuria, hypoalbuminemia, edema, and hyperlipidemia. [1] The incidence of nephrotic syndrome varies widely based on age, race, and geography. The worldwide annual incidence in children below 16 years is 1-3/1,00,000 children. Few studies specifically compare differences in incidence by ethnicity because the incidence is higher in some ethnic groups, particularly South Asians and Africans, which may indicate environmental and/or genetic influences on disease. [2, 3] Some reports have used physician-reported questionnaires that lack follow-up or patient-level data and diverse treatment plans that affect outcomes. [2, 4] International study of kidney disease in children (ISKDC) found a minimal change in disease in 76.6% of children with primary nephrotic syndrome. There is a male preponderance in children with male to female ratio of 2:1. [5] Several agents and conditions have been reported to be associated with an idiopathic nephrotic syndrome such as infections, heavy metals, drugs (Gold, Lithium, Mercury, Ampicillin), AIDS, Allergy, (Pollen, Fungi, Coco, Milk, House Dust, Bee sting) Vaccinations and malignancies. [6] Dyslipidemia has been recognized finding in nephrotic syndrome. Hypercholesterolemia was described as a feature of nephrotic syndrome. [7] Although pathophysiological aspects of hyperlipidemia have been completely identified, hypoalbuminemia, increased lipoprotein synthesis, and decreased lipoprotein lipase activity has been described in some studies. [8] Some degree of correlation between lipids and serum albumin has been suggested by Thomas et al., [9] and between lipidemia and edema by Peters et al., [10] Generally when edema regresses lipid levels fall but, in some cases, it may continue to persist even after the edema has disappeared. Hyperlipidemia is usually observed during the active phase of the disease and disappears with the resolution of proteinuria. However, it may persist in some cases, leading to an increased risk of atherosclerosis in later life. Hence close monitoring of lipid parameters during remission of nephrotic syndrome is necessary for certain high-risk patients. Lipoproteins play an important role in the transport of plasma lipids, there is an increase or alteration in various fractions may be responsible for hypercholesterolemia in nephrotic syndrome. [11] there is increased total cholesterol, LDL cholesterol, VLDL cholesterol, Triglycerides, and normal or low HDL cholesterol. [11] However, in Indian children, the degree of hyperlipidemia is not high as in western counterparts. [12] More recently it has been expressed that hyperlipidemia may contribute to renal injury. [13] Experimental studies have demonstrated that the reduction of plasma lipid levels can slow the progression of glomerular and tubulointerstitial disease. [14]

With this background, we undertook the current study to determine whether any correlation exists between serum lipids and serum albumin.

Materials and Methods

This cross-sectional study was done in the Departments of Pediatrics and Biochemistry, Kakatiya Medical College, and MGM Hospital, Warangal. Institutional Ethical approval was obtained for the study. Written consent was obtained from the parents or guardians of the children included in the study after explaining the nature of the study in the local language.

Inclusion criteria

1. All cases diagnosed with nephrotic syndrome
2. Aged from 1 to 10 years.
3. New and old cases which include relapses,
4. Steroid-dependent Nephrotic syndrome
5. Steroid Resistant Nephrotic syndrome and remission

Exclusion criteria

1. Family history of hyperlipidemia
2. History of thyroid dysfunction
3. Children with other causes of hypoproteinemia
4. Liver diseases and malnutrition
5. Unwilling to participate in the study voluntarily

A pre-validated proforma was used to record the information from the person. Following the parental agreement, clinical information was gathered and recorded in the proforma, including the patient's age, sex, presenting complaints, pharmacological history, and type of nephrotic syndrome (episode, recurrence, SDNS, SRNS, or remission). Blood samples for the patients' lipid profiles and Serum albumin were taken after obtaining their medical histories and performing a clinical examination. The photometric analysis for testing serum albumin, the Phosphotungstate method for measuring HDL, the enzymatic calorimetric method for measuring LDL and triglycerides, and the enzymatic method for measuring serum cholesterol and VLDL.

***Statistical analysis*:**

The data was collected and uploaded on an MS Excel spreadsheet and analyzed by SPSS version 22 (Chicago, IL, USA). Quantitative variables were expressed on mean and standard deviations and qualitative variables were expressed in proportions and percentages. Mann Whitney U test and Wilcoxon signed rank sum test was used to find the difference between two proportions values of <0.05 were considered as significant.

Results

A total of n=30 cases were included in the study with n=10 samples taken from normal cases acting as controls. Out of n=30 cases n=18(60%) were males and n=12(40%) were females. The male-to-female ratio was 3: 2. The mean age of the cases in the study was 5.5 ± 1.5 years. In the control samples, n=6 samples were obtained from males and n=4 samples were obtained from females the age of the controls varies from 1 – 6 years. All the lipid parameters were found to be within the normal range in controls depicted in table 1.

Table 1: showing the lipid parameters recorded in controls

Lipid	*Range*	*Mean*
Total Cholesterol (mg/dl)	151 - 250	189
LDL Cholesterol (mg/dl)	86 - 170	97.4
VLDL (mg/dl)	36 - 50	43.6
HDL (mg/dl)	45 - 54	48

Serum triglycerides (mg/dl)	76 - 120	97.7

The lipid profile of the cases of nephrotic syndrome in the study showed all the parameters were increased as compared to the normal controls. Statistical analysis by Mann Whitney U test found total cholesterol, LDL, VLDL, and Triglycerides were significantly higher in the cases as compared to controls all the values were (p = <0.05). However, the HDL cholesterol although found to be less in nephrotic syndrome cases the p values were 0.078 and hence considered not significant.

Table 2: showing the lipid parameters recorded in Nephrotic syndrome cases

Lipid	*Range*	*Mean*	*Std Dev*
Total Cholesterol (mg/dl)	253 – 601	397.1	115.48
LDL Cholesterol (mg/dl)	152 – 468	291.1	102.3
VLDL (mg/dl)	42 – 103	67.43	19.3
HDL (mg/dl)	31 – 56	38.5	8.66
Serum Triglycerides (mg/dl)	132 - 480	264.23	117.2

The cases of nephrotic syndrome showed low levels of serum albumin with mean albumin levels of 1.70 gm/dl in the controls the mean serum albumin levels were 4.03 gm/dl. Statistical comparison between the two revealed the p values =0.0125 which is significant details given in table 3.

Table 3: Comparison of serum albumin levels in the cases and controls of the study

Group	*Range (gm/dl)*	*Mean (gm/dl)*	*SD (gm/dl)*	*P values*
Study	1.1 – 2.8	1.70	0.35	0.0125*
Control	3.9 – 5.3	4.03	0.14	

* Significant

A total of n=8 cases were present with a mean serum albumin range of 1.0 – 1.5 gm/dl the same cases had the mean serum total cholesterol levels of 516.66 mg/dl the Pearson correlation coefficient 'r' values were -0.514 which indicated inverse relation between the two the p values were (<0.05) significant. Similarly, n=13 cases in with mean serum albumin levels of 1.6 – 2.0 gm/dl the mean serum total cholesterol levels were 36.2.55 mg/dl in this category. The coefficient correlation 'r' was -0.224. The third group n=9 cases with mean serum albumin levels of 2.1 – 2.5 gm/dl. The mean total cholesterol in this group was 336.25 mg/dl and the correlation coefficient 'r' was -0.145 depicted in table 4.

Table 4: Correlation between serum albumin and serum Total cholesterol in cases of nephrotic syndrome

Frequency	*Range of Serum albumin (gm/dl)*	*Mean Serum Total cholesterol (mg/dl)*	*r values*
8	1.0 – 1.5	516.66	- 0.514*
13	1.6 – 2.0	362.55	- 0.224
9	2.1 – 2.5	336.25	-0.145

* Significant

The mean serum HDL-C was lowest in the cases with low mean serum albumin levels. Similarly, the mean serum HDL-C values did not significantly change with groups where the mean serum albumin was slightly higher as depicted in table 5.

Table 5: Correlation between serum albumin and HDL cholesterol in cases of nephrotic syndrome

Frequency	*Range of Serum Albumin (gm/dl)*	*Mean Serum HDL cholesterol (mg/dl)*	*r values*
8	1.0 – 1.5	42.13 ± 3.014	+0.235
13	1.6 – 2.0	45.27 ± 4.013	+0.354
9	2.1 – 2.5	45.27 ± 3.097	+0.451

The correlation between serum albumin and VLDL was calculated which showed a weak negative correlation between the serum albumin and VLDL cholesterol. The p values were not found to be significant given in table 6.

Table 6: Correlation between serum albumin and VLDL cholesterol in cases of nephrotic syndrome

Frequency	*Range of Serum Albumin (gm/dl)*	*Mean Serum VLDL cholesterol (mg/dl)*	*r values*
8	1.0 – 1.5	79.51 ± 21.17	-0.121
13	1.6 – 2.0	66.04 ± 23.85	-0.154
9	2.1 – 2.5	59.19 ± 19.79	-0.251

Out of the total cases n= 21 cases were the first episode of nephrotic syndrome and n=9 cases were relapses. The serum albumin was found to increase gradually in response to steroid treatment and the normal values of serum albumin were reached following 6 weeks of steroid therapy. In cases of first episode nephrotic syndrome after 6 weeks of steroid treatment, there was a significant reduction in the levels of lipids from the pre-treatment mean total cholesterol reduced to 213.0 ± 33.18 mg/dl. Similarly, the LDL-C levels were reduced to mean levels of 124.76 ± 22.60 mg/dl. The VLDL levels were reduced to 42.61 ± 5.27 mg/dl. The HDL levels were increased to 48.23 ± 3.02 mg/dl. The levels of triglycerides were reduced to 104.19 ± 31.8 mg/dl.

In n=9 cases of relapse nephrotic syndrome after the end of steroid treatment, there was no significant reduction in the mean levels of lipids. The mean post-treatment levels of total cholesterol were 385.2 ± 112.13 mg/dl. Similarly, the mean levels of LDL-C were 278.0 ± 88.02 mg/dl. The mean levels of VLDL were 65.00 ± 12.01 mg/dl. The serum HDL levels remained low at 42.22 ± 3.13 mg/dl. The mean triglyceride levels were 245.68 ± 57.10 mg/dl the data shows very little improvement in the relapse cases following steroid therapy.

Discussion

The main lipid carriers in the blood are lipoproteins, which take part in the three main pathways, the exogenous pathway, the endogenous pathway, and the reverse cholesterol transport system, that generate and transport lipids. Nephrotic syndrome, whether or not associated with chronic renal disease, alters lipid and lipoprotein metabolism (CKD). [15] The degree of proteinuria correlates with the degree of disturbed lipid metabolism in the nephrotic syndrome. In particular, the plasma concentrations of triglycerides, very low-density lipoprotein (VLDL), intermediate-density lipoprotein (IDL), and lipoprotein (a) all of which contain apolipoprotein B (ApoB) are all increased in nephrotic syndrome. [16] The healthy children have high levels of high-density lipoprotein (HDL), cholesterol, and the contents of ApoA-I and ApoA-II apolipoproteins. Warwick et al., [17] have demonstrated significant reduction of rate of

catabolism of apo (B) the principal apoprotein constituent of LDL in cases of Nephrotic syndrome. This study included pediatric cases diagnosed with nephrotic syndrome aged from 2 – 6 years and samples from normal children were taken as controls. This study found the incidence of nephrotic syndrome is more common in males as compared to females the ratio in this study was 3:2 the mean age of the cases in the study was 5.5 ± 1.5 years. Ahoui S et al., [18] in a similar study found the majority of children affected with the disease were in the 5-10 years age group (53.12%). There were 24 males (61.54%) out of the 39 children, representing a sex ratio of 1.60. In this study, there was a significant rise in total cholesterol levels mean value of all lipid parameters was higher and that of HDL levels remained slightly decreased. It was observed that the mean serum cholesterol levels in n=9 relapse cases were significantly higher as compared to the first episode nephrotic syndrome cases (n=21). Arije et al., [19] in a similar study observed the increase in serum lipids was higher in relapse cases as compared to first-episode cases. The increase in lipid parameters in this study was lesser as compared to Miline et al., [20] reported the mean levels of total cholesterol in pediatric nephrotic syndrome may be higher up to 1000 mg/dl. In the current study, we found the lowest cholesterol levels of 397.0 mg/dl and the highest value of 601.0 mg/dl. Banarjee et al., [21] in their study of Indian children observed that the lowest mean total cholesterol levels were 341 mg/dl and the highest was 641 mg/dl in concordance with the observation of the current study. There was a positive correlation between serum total cholesterol and LDL-C which were statistically significant. David et al., [11] in their study of nephrotic syndrome in children found a positive correlation between total cholesterol and LDL Cholesterol, and the p-values were significant. Benakappa et al., [12] have also reported similar observations in their study. There was an inverse correlation between serum albumin and cholesterol which was significant at albumin levels in the 1.0 – 1.5 gm/dl range (table 4). Heyman et al., [22] found there was no correlation between the development of hyperlipidemia and hypoalbuminemia and postulated that the severity of hyperlipidemia is related to the amount of nephrotic kidney tissue present. Thomas et al., [9] found that a negative correlation exists between serum cholesterol with serum albumin levels however, they did not find a correlation between serum cholesterol and globulin and total protein levels. In an experimental model Friedman et al., [23] found when ligation of ureters was done in animals to stop the urinary protein loss there was a fall in serum lipids. Similar results were also obtained by IV infusion of albumin. This study demonstrated that a positive correlation exists between serum albumin and HDL cholesterol although the values were not found to be significant (table 5). In their study, Yokoyama H, et al., [24] predicted that albumin would have a positive connection with HDL and a negative correlation with blood cholesterol. In their investigation, Niaudet P et al., [25] found a link between albumin and cholesterol that was detrimental. Nevertheless, the correlation is unimportant (P> 0.01). In this study, we found a significant response to steroid therapy in first-episode nephrotic syndrome cases with lowering of lipid parameters and increase of HDL-C the values of decrease were significant. Serum cholesterol levels were noticeably higher in relapse cases which were steroid-resistant individuals. In steroid-resistant nephrotic syndrome, LDL levels are significantly higher compared to the first episode and steroid-dependent nephrotic syndrome as reported in other studies. [26, 27] Even when they are in remission, children with often relapsing nephrotic syndrome had elevated serum cholesterol levels. Additionally, they demonstrated a bad association between albumin and LDL, and VLDL. [27]

Conclusion

The present study within its limitations found that pediatric nephrotic syndrome significantly increased the serum lipid profile. To properly manage the disorder, it is necessary to monitor the lipid profile in nephrotic syndrome. The lipid profile parameters were negatively correlated with serum albumin levels except HDL with weak positive correlation. After 6 weeks of steroid

treatment in the first episode of nephrotic syndrome, there was a significant reduction in the mean levels of pre-treatment total cholesterol and LDL cholesterol. In the relapse nephrotic syndrome cases at the end of steroid treatment, there was no significant reduction in the mean levels of total cholesterol, LDL-C, VLDL-C, and triglycerides.

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