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A Clinical Study to Evaluate the Lipid Profile in the Age Group of 1 to 12 Years with Primary Nephrotic Syndrome

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Abstract: ***Introduction: Nephrotic syndrome is a clinical state characterized by massive proteinuria, hypoalbuminemia and edema. This study is made to collate the effectiveness of lipid profile by follow up of patients of nephrotic syndrome. Objectives: To evaluate the serum level of total cholesterol, triglycerides, HDL, LDL, VLDL levels in children (aged 1 - 12years) with primary nephrotic syndrome for a period of 12 weeks duration. Methods: This prospective study was performed on 50 children with primary nephrotic syndrome who are attending to paediatric OPD of Katuri medical college & Hospital, Chinakondrupadu, Guntur. They were clinically examined and lipid profile was done at the onset of disease and on follow up at the 6th and 12th weeks. Results: The present study consists of 50 cases of children with idiopathic nephrotic syndrome aged between 1 and 12 years. Among the patients involved in the study, all patients were followed up at 6 & 12 week visits. Among 50 cases studied, the maximum number of cases were in the age group of 36 to 60 months (62%), male to female ratio was 3: 1, facial puffiness and edema was present in 90% of cases and decreased urine output in 10% cases. Hypoprotenemia and hypoalbuminaemia was present in all 100% cases. Hypercholesterolemia, hypertriglyderidemia, elevated LDL, VLDL was seen in all cases (100%). The p - value was <0.05. The mean cholesterol, triglyceride level, LDL, VLDL levels were significantly higher in relapse cases compared to the 1st episode of nephrotic syndrome. Conclusion: The present study shows that in nephrotic syndrome, there is hyper - lipidemia in all cases but it was significantly higher in cases of relapse compared to the 1st episode of nephrotic syndrome.***

Keywords: Serum cholesterol, serum triglycerides, serum albumin, serum globulin, serum LDL, serum VLDL, nephrotic syndrome

1. Introduction

- Nephrotic syndrome is a clinical state characterised by massive proteinuria (>40mg/m2/hr; 1gm/m2/day), hypo - albuminaemia (serum albumin <3gm/dl) and edema[1].
- Primary nephrotic syndrome is unassociated with any systemic disease. It accounts for 90% of childhood cases. Secondary nephrotic syndrome occurs as a part of a systemic disease or is related to any drug or toxin ingestion.
- Associated with systemic disease: SLE, anaphylactoid purpura, sickle cell disease, bergers IgA nephropathy, PIGN, syphilis, malaria, hepatitis, DM, lymphoma, schistosomiasis, toxoplasmosiss, cyotmegalovirus, AIDS, amyloidosis.
- Associated with drugs: NSAIDs, pencillamine, gold, tridone, heroine.
- Associated with toxins or allergens: bee sting, vaccination, food allergy.
- Massive proteinuria is the basic abnormality leading to hypo - albuminaemia.
- The patho - physiology of hyper - lipidemia in nephrotic syndrome is complex. Hyper - lipidemia and other abnormalities such as raised plasma aldosterone and ADH levels are prominent in patients having massive proteinuria and anasarca. The prevailing view is that the hepatic synthesis of both lipids and apolipoproteins is increased and that the clearance of chylomicrons and VLDL is reduced[2]. Persistent hyperlipidemia increases the risk of atherosclerosis and may also be important in the development of glomerulosclerosis and progressive renal injury[3].
- Lipoproteins play an important role in the transport of plasma lipids: their alteration or increase in various fractions may be responsible for hypercholesterolemia in nephrotic syndrome. There is increased total cholesterol, LDL, VLDL, IDL & lipoprotein A. HDL levels are reduced or unchanged, and there is a decreased HDL/LDL ratio (ideal 0.4).

2. Methodology

All children with primary nephrotic syndrome at onset or with relapse within the inclusion criteria were studied. The sample population was recruited from the outpatient clinic and inpatients wards. They were further categorized into onset, remission, relapse. The recruitment was completed within 8months of starting.

1) **Study design:** prospective study
2) **Sample size:** 50 children who are diagnosed as primary nephrotic syndrome.
3) **Duration of study:** 8 months.
4) **Method of collection of data:**
5) **Inclusion criteria**
   All children with primary nephrotic syndrome between 1 and 12 years of age attended outpatient and inpatient clinic at Katuri Medical College & Hospital, Chinakondrapadu, during the years 2022 and 2023.
6) **Exclusion criteria:**
   - Age < 1 year or > 12 years, steroid resistant nephrotic syndrome, secondary nephrotic syndrome, moderate to severe renal failure (GFR<90ml/min), sick child with NS requiring ICU care or IV antibiotics, already on corticosteroids for >2 weeks before recruitment,

children already on hyperlipidemic drugs, family history of hyperlipidemia.
- All children with primary nephrotic syndrome at onset or relapse, in the age group >1year and <12years attending the paediatric outpatient or inpatient wards at Katuri Medical College & Hospital were included in the study.
- ISPN 2021 criteria was used for the diagnosis of nephrotic syndrome in children.
- Spot urinary protein/creatinine>2.0; serum albumin <3mg/dl; serum cholesterol>200mg/dl.

Statistical analysis:
Data was collected using pre tested proforma meeting the objectives of the study. The observations and results were tabulated accordingly and data was analysed using the SSPS version 16. All P values <0.05 were considered to be statistically significant.

3. Results

Table 1: Mean Age at onset and recruitment

Mean age at	Mean age in months
Onset	51.28
Recruitment	51.28
Standard Deviation	± 19.71

Table 1 shows mean age at onset and recruitment. The mean age of recruitment was about 51 months, and the mean age on onset also corresponds to 51 months age group with a SD of 19.71months.

Table 2: Distribution of various parameters at onset

Component	Minimum	Maximum	Mean	Std. Deviation
Age in months	24	100	51.28	19.711
Total Protein	2.7	5.3	4.03	0.6754
Albumin	1.1	2.5	1.928	0.378
Total Cholesterol	169	575	358.44	90.030
Triglycerides	82	655	245.68	128.260
HDL	22	79	54	13.371
LDL	71.6	42.7	252.11	88.1774
VLDL	11.5	137	45.848	25.397

Table 2 shows the distribution of various parameters at the onset of disease. The mean of various parameters at the onset was as follows: total protein:4.03+/ -0.67, albumin: 1.92+/ -0.37, total cholesterol: 358+/ -90.30, triglycerides: 245+/ -128.2, HDL: 54+/ -133, LDL: 252.11+/ -128 & VLDL: 45.848+/ -25.39

Table 3: Distribution of various parameters at 6 weeks follow up

Component	Minimum	Maximum	Mean	Std. Deviation
Total Protein	4.1	7.6	6.312	.7347
Albumin	2.1	4.1	3.264	.5310
Total Cholesterol	100	365	187.90	68.151
Triglycerides	40	294	118.68	64.675
HDL	30	285	60.58	36.102
LDL	15.8	245.0	108.596	55.0004
VLDL	9.0	58.0	19.778	9.3250

Table 3 shows the distribution of various parameters at 6 weeks follow up. The mean of various parameters at the onset was as follows: total protein: 6.3+/ -0.73, albumin: 3.29 +/ -0.53, total cholesterol: 187.90+/- 68, triglycerides: 118.68+/ -64.67, HDL: 60.5+/ -36, LDL: 108.59+/ -55 & VLDL: 19.77 +/ -9.32

Table 4: Distribution of various parameters at 12 weeks follow up

Component	Minimum	Maximum	Mean	Std. Deviation
Total Protein	4.0	7.3	6.068	.7622
Albumin	2.1	4.0	3.008	.5225
Total Cholesterol	100	386	186.82	83.426
Triglycerides	36	271	118.34	67.429
HDL	27	84	49.16	11.739
LDL	16	272	118.52	65.491
VLDL	9.0	78.0	24.532	12.6844

Table 4 shows the distribution of various parameters at 12 weeks follow up. The mean of various parameters were as follows: total protein: 6.0+/ -0.76, albumin: 3.0 +/ -0.52, total cholesterol: 186.82+/- 83.426, triglycerides: 118.34+/ -67.429, HDL: 49.16+/ -11.7, LDL: 118.52+/ -65.4 & VLDL: 24.5+/ -12.6

Table 5: Lipid profile analysis at recruitment and follow up

Mean Values of/ at	Cholesterol (mg/dl)	Triglycerides (mg/dl)	LDL (mg/dl)	VLDL (mg/dl)	HDL (mg/dl)	Total Protein (mg/dl)	Albumin (mg/dl)	HDL/ LDL
Recruitment Visit	358.44± 90.030	245.68± 128.260	252.112± 88.17	45.848± 25.39	54± 13.37	4.32± 0.67	1.928± 0.37	0.21
At 6 wks visit	187.90± 68.15	118.68± 64.675	108.596± 55	108.59± 55	60.68±36.102	6.312± 0.73	3.264± 0.5310	0.55
At 12 wks visit	186.82± 83.42	118.34± 67.42	118.52± 65.49	24.532± 12.684	49.16± 11.73	6.068± 0.762	3.008 ± 0.522	0.41
P value (onset & 12 wks)	P = 0.003	P =0.004	P = 0.002	P =.0145	P = 0.645	P= 0.057	P = 0.046	

Table 5 shows lipid profile analysis at the recruitment and at follow up. In our study, those who had high values at recruitment, the mean serum total cholesterol, LDL, VLDL, Triglycerides compared to those on follow up at 6th and 12th weeks and P value compared between onset and 12 weeks shows statistically significant ($p<0.05$) expect in HDL ($p>0.05$) and HDL/ LDL ratio is variable. However, there is no significant change seen in HDL with onset and follow up.

Table 6: Distribution of Lipid profile in remission and relapse cases based on lipid profile norms in India children

Cut- offs based on Indian Child norms	Remission (N= 37)		Relapse (N= 13)	
	No.	%	No.	%
Total Cholesterol				
<190mg/dl	21	57%	0	0%
>190 mg/dl	16	43%	13	100%
Triglycerides				
<150mg/dl	36	97%	1	7%
>150mg/dl	1	3%	12	93%
HDL				
<20mg/dl	Nil	0%	Nil	0%
>20mg/dl	37	100%	13	100%
LDL				
<130mg/dl	35	94%	0	0%
>130mg/dl	2	6%	13	100%

Table 6 shows the distribution of Lipid profile in remission and relapse cases based on lipid profile norms in India children

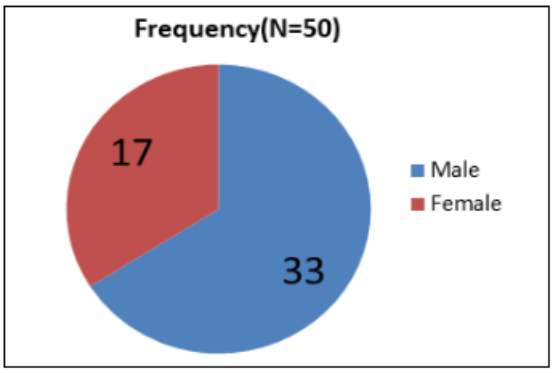

Figure 1: Gender distribution of the study population

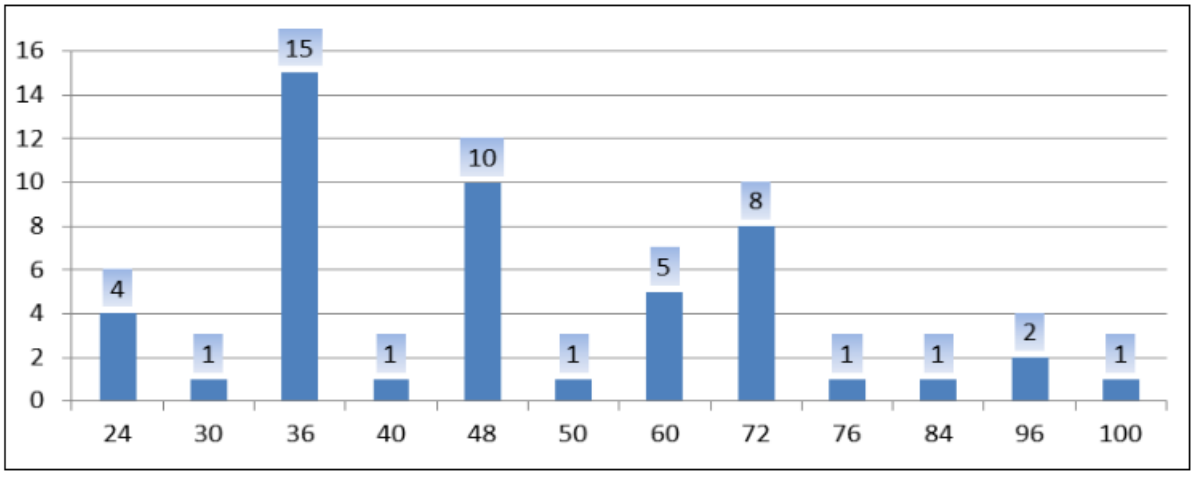

Figure 2: Age distribution of the sample

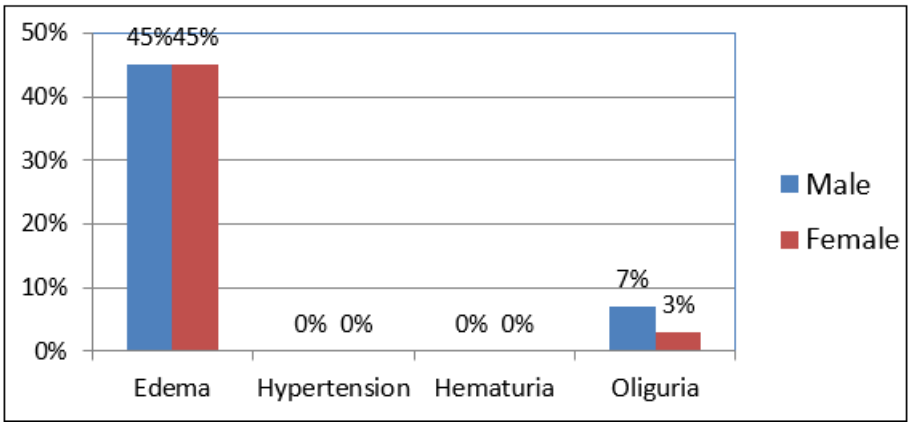

Figure 3: Type of presentation

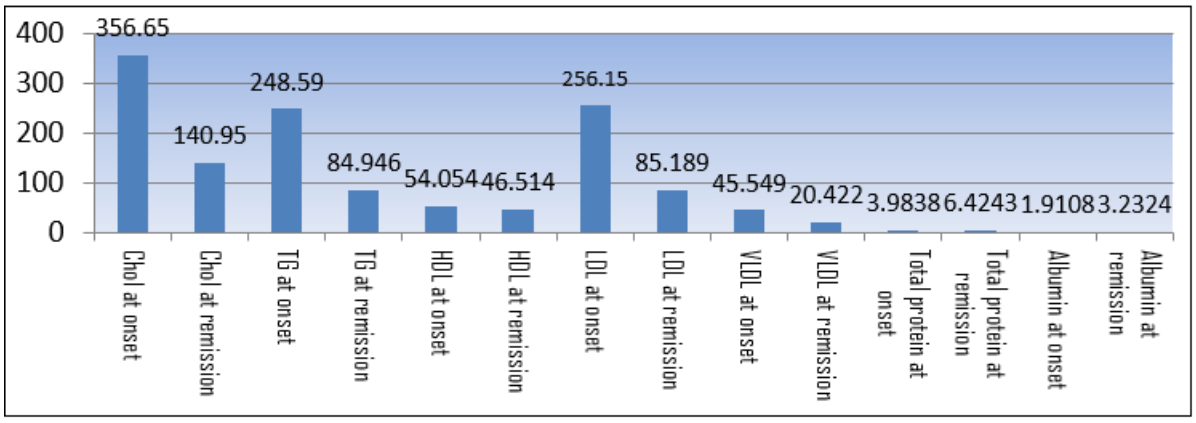

Figure 4: Comparison of variables at onset and remission in the 1st episode

4. Discussion

The present study consists of 50cases of children with idiopathic nephrotic syndrome aged between 1 & 12 years. Among the patients involved in the study, all patients completed their 6th & 12th week follow - up visits.

Age & sex distribution of cases:
The mean age of children in our study was 4.25years with a male preponderance (3: 1). Orth S et al.4 also reported a higher incidence in children with male preponderance (2: 1). In a study done by Indumati et al.5 among 20 cases of nephrotic syndrome, 12 cases were in between 1 to 4years, 5 cases were between 5 to 9years, & the mean age of presentation was 5.85 years.

Common presentation:
Among 50 cases of nephrotic syndrome, 40 children presented with oedema (90%), 5 children presented with decreased urine output (10%). Vidhi Sahni et al.6 in their study among 35 children of 1 to 8 years, showed the most common presentation is oedema (80%), followed by decreased urine output (62.85%) & by abdominal distension (31.42%).

Investigations:

Urine analysis:
Out of 50 patients, 24 (48%) patients had moderate proteinuria & 26 (56%) had severe proteinuria. Shah et al.7 reported 74% of cases of severe proteinuria & 26% with moderate proteinuria. But Balgopal et al. reported 18.4% of severe proteinuria, 38.15% of moderate, 44.73% of mild, and 11.8% of cases with traces of proteinuria.

Lipid profile assay:

- In our study there were high levels of total cholesterol (358.44±90.30mg/dl), LDL cholsterol (252.112±88.17mg/dl), VLDL cholesterol (45.84±25.39mg/dl), triglycerides (245.68±128.60mg/dl) at recruitment compared to the mean serum cholesterol, LDL, VLDL, triglycerides of those on follow up at 6th & 12th week. However, serum HDL cholesterol (54±13.37mg/dl) did not have any significant change between the time points.
- Mehta et al. (1985) [8] studied 22 cases of nephrotic syndrome and observed hypercholesterolemia in 100%, hypertriglyceridemia in 100%, elevated LDL in 100%, and elevated VLDL in 80% of cases. The values of HDL were normal in 88% and decreased by 12%.
- Appel GB et al (1985) [9] observed that mean total plasma cholesterol was 302 + 100 mg/dL and LDL cholesterol was 215 ± 89 mg/dL, were elevated in most patients, but the HDL level was normal or low (46 ± 18 mg/dL) in 95 percent of the patients.
- We observed that in relapse, the mean serum Triglycerides (213.38139.65 mg/dL and P - value 0.003) and mean Low - density serum lipoprotein (213.38+35.59 mg/dL and P - value 0.009) are significantly elevated compared to remission.
- Tsukahara et al[10] observed that children with frequently relapsing nephrotic syndrome have prolonged periods of hypercholesterolemia. There is a rationale for treatment since dyslipidemia may contribute to the development of atherosclerosis and the progression of chronic renal failure.
- Merouani et al. (2003) [11] observed hyperlipidemia during the active phase of the disease and disappeared with the resolution of the proteinuria and was persistently abnormal in frequently relapsing children and suggested close monitoring of lipid levels during the remission of nephrotic syndrome, especially in those with frequent relapses, to select high - risk patients.
- Chowdary et al. (1977) [12] studied 25 cases of nephrotic syndrome andreported that 96% of cases had hypercholesterolemia, 100% had raised LDL levels.
- Similarly, Western workers studied and reported hyperlipidemia in nephrotic syndrome cases with variations in HDL levels, HDL levels may be decreased, normal or higher.
- Merouani et al. (2003) [13] observed hyperlipidemia during the active phase of the disease and disappeared with the resolution of the proteinuria and was persistently abnormal in frequently relapsing children and suggested close monitoring of lipid levels during the remission of nephrotic syndrome, especially in those with frequent relapses, to select high - risk patients.
- Querfeld used statins in his study and observed a 30 - 40% reduction in total cholesterol. However, the benefits of treatment with lipid - lowering drugs have not been proven in children. Short - term studies in adults have documented the safety and efficacy of lipid - lowering agents.
- Buyokcelik et al. observed a significant reduction in the total cholesterol with statins in adult patients with

nephrotic syndrome[14]. Prospective controlled studies in children evaluating efficacy and safety of lipid - lowering drugs are needed.

- Abnormalities of lipid metabolism in NS include hypertriglyceridemia and hypercholesterolemia due to elevated apolipoprotein B - containing lipoproteins, decreased lipoprotein lipase and hepatic lipase activity, increased hepatic PCSKS levels, and reduced hepatic uptake of high - density lipoprotein[15].

Serum proteins:

- In this present study, the mean total protein at onset 4.032+0.6754 and mean serum albumin levels are 1.928+0.3780 compared with after 12 weeks of completion of follow up shows significant changes (p - values <0.05).66
- Katiyar et al. (1976) [16], Chowdary et al. (1977) [17] and Bhandari et al. (1980) [18] reported hypoproteinemia and hypoalbuminemia with normal globulin levels. Bhandari et al. (1980) [18]observed that mean values for total proteins were 4.49 +0.84 g/dL, for Serum albumin 1.85 ±0.52 g/dL and Serum globulin 2.70 ± 0.58 g/dL.
- Our study showed that the time taken for normalization of values for Total cholesterol was 3 months in 74% of children, Triglycerides 3 months in 74%, LDL in 3 months in 70%, VLDL 3 months in 90%, Albumin 3 months in 80% children.
- Heavy glomerular proteinuria (nephrotic syndrome) and advanced chronic kidney disease (CKD) can elicit profound changes in the structure and function of HDL HDL abnormalities in nephrotic syndrome impair reverse cholesterol transport and consequently promote foam cell formation, atherosclerosis, and glomerulosclerosis. HDL abnormalities in nephrotic syndrome are largely due to lecithin - cholesteryl acyltransferase (LCAT) deficiency caused by urinary losses. elevated plasma cholesterol ester transfer protein levels, hypoalbuminemia, and/or reduced expression levels of hepatic HDL docking receptor (SRB1) [19].

5. Conclusion

- Our study concludes that, in nephrotic syndrome, there is generalized hyper - lipidemia (except HDL) and hypo - albuminemia. We observed high values of total cholesterol, LDL cholesterol, VLDL cholesterol, and triglycerides levels at recruitment compared to those on follow up.
- In our study, 74% of children went into remission over 12 week follow - up. The mean serum values of Triglycerides (213±39.65 mg/dL; p= 0.003) and Low density lipoprotein (213.38+35.594 mg/dL. and p= 0.009) were significantly high in relapse compared to remission.
- In the present study, there is generalized hyper - lipidemia in relapse cases even after steroid therapy, which may lead to the risk of atherosclerosis and the progression for chronic renal failure, which calls for modalities to reduce the lipoprotein levels in the management of the nephrotic syndrome.
- Time taken for normalization of values for Total cholesterol was 3 months in 74% of children, Triglycerides 3 months in 74% of children, LDL 3 months in 70%, VLDL 3 months in 90%, Albumin 3 months in 80% of children.

6. Limitations of the study

1) Baseline values were not known before recruitment.
2) The steroid was a confounding factor, and the amount of steroid takenwas not knownRelapses, although less in number, altered the values and should beexcluded in future studies.
3) Larger groups will be required in further studies.
4) Follow up period is less compared to the disease course.

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Conflicts of interest: There are no conflicts of interest.

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