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Original Research Article

STUDY OF LIPID PROFILE AND THYROID FUNCTION ABNORMALITY IN CHILDREN OF NEPHROTIC SYNDROME

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ABSTRACT

Background: To study the correlation between lipid and thyroid Profile with different types of nephrotic syndrome in children between 1 to12yrs. And also study the association between serum albumin with lipid profile and TSH.

Materials and Methods: It was a cross sectional study. Study was conducted at Department of paediatrics, GEMS Medical College & Hospital Srikakulam. All cases of nephritic syndrome which includes1episode, relapse, SDNS, SRNS and remission between age group of 1 to 12yrs. 40 cases of nephritic syndrome between1to12yrs.Which include all type of nephrotic syndrome.

Results: Most common age group of presentation is 6 to 10yrs 24cases (60%), followed by 1 to 5yrs 12 cases (30%), 11 to 12yrs 4 cases (10%). Mean age of presentation is 6.9 yrs. Males (63%) are affected more than females (37%) but no significant gender difference of all parameters. There is increased serum cholesterol (mean= 344.30mg/dl), LDL (mean=234.650mg/dl)), VLDL (mean=61.625mg/dl), Triglycerides (mean304.025mg/dl) and normal or borderline HDL (mean 46.07mg/dl). Serum cholesterol compared to first episode elevated in relapse cases. Serum cholesterol in SRNS cases shows statistically significant elevation compared to other types. LDL values compared to first episode were elevated in relapse cases which was found out to be statistically insignificant. LDL values in SRNS cases shows statistically significant elevation compared to first episodes and SDNS cases. Serum T3, T4, TSH were found to be within normal limits. But TSH values compared to remission were significantly elevated in first episode.

Conclusions: There is a negative relation between serum albumin and cholesterol and the correlation is statistically insignificant (p=0.35) while the negative relation between albumin and TSH is statistically significant (p=0.003).

Keywords: Nephrotic syndrome, TSH, Albumin, Cholesterol, SRNS, SDNS.

INTRODUCTION

Nephrotic syndrome is characterized by massive proteinuria, (>40mg/m2/hr (or)>100mg/m2/day (or) >3.5gm/day (or) spot protein creatinine ratio of>2), will lead to hypoproteinemia (serum albumin <2.5gm/dl), generalized edema and hyperlipidemia (serum cholesterol >200mg/dl).[1] 1-3 per100000 children less than 16yrs affected with nephrotic syndrome. Most of them affected with primary or idiopathic type. Minimal change disease is the most common idiopathic type. One of the characteristic feature of nephrotic syndrome is 80% of them respond to corticosteroid therapy.

In nephrotic syndrome there will be elevated serum lipids and cholesterol level. During nephrosis there will be more loss of protein in urine this will lead to hypoalbuminemia. In addition to low serum albumin, more production of lipoproteins with impaired lipoprotein lipase activity will increase the lipoprotein level. Lipids are mainly transported by lipoproteins, so in nephrotic syndrome becoz of more lipoproteins there will high serum cholesterol, LDL cholesterol, VLDL cholesterol and Triglycerides.[2]

Thyroid hormones T3 and T4 binds with thyroid binding globulin ,pre albumin and albumin in circulation.[3] During nephrosis due to loss of albumin ,thyroid binding globulin with T4 and other proteins in urine there will be decrease in serum level of thyroid hormones and stimulation of TSH production.[4] Afroz S et al in 2011 told that even though urinary losses of thyroid hormones, T3 and T4 level were normal with compensatory rise in TSH level.[5] so during proteinuria phase there will be mild or subclinical hypothyroidism. Because it is a treatable condition in all cases of nephrotic syndrome always investigate for hypothyroidism.

Many studies were done in the past in nephrotic syndrome to evaluate lipid profile and thyroid function test both in active disease and in remission. Inactive disease that is in proteinuria phase there is hypercholesterolemia and mild (or) subclinical hypothyroidism. During remission after completion of 6 weeks of steroids there will be normalisation of serum cholesterol andt hyroid function.so if the serum cholesterol level was high even during remission more risk for relapses. Serum albumin shows inverse relation with lipid profile and TSH. So more severe the hypoalbuminemia more will be serum cholesterol and TSH.

In our study lipid profile and thyroid function test was done in all cases of nephrotic syndrome during the study period of 9months.which includes first episode, relapses, steroid dependent nephrotic syndrome (SDNS), steroid resistant nephrotic syndrome (SRNS) and in remission. This study was done to determine the various parameters of lipid and thyroid profile and its correlation with different types of nephrotic syndrome and to look for association between serum albumin with lipid profile and TSH.

Aim of the Study

To study the correlation between lipid and thyroid Profile with different types of nephrotic syndrome in children between 1 to12yrs. And also study the association between serumalbumin with lipid profile and TSH.

Objectives

1. To study the correlation between lipid profile with different types of nephrotic syndrome.
2. To study the correlation between thyroid profile with different type of nephrotic syndrome.
3. To study the association between serum albumin with lipid profile and TSH.

MATERIAL AND METHODS

Study Centre

Study was conducted at Department of paediatrics, GEMS Medical College & Hospital Srikakulam.

Study Group: All cases of nephritic syndrome which includes1episode, relapse, SDNS, SRNS and remission between age group of 1 to 12yrs.

Study Design: Cross sectional study

Study Duration: 9 months from December2022to August2023

Sample size: 40 cases of nephritic syndrome between1to12yrs.Which include all type of nephrotic syndrome.

Collaborating Department: Department of Biochemistry, GEMS Medical College & Hospital, Srikakulam.

Inclusion Criteria

1. All cases of nephritic syndrome between1to12yrs.
2. New and old cases which include relapses, SDNS, SRNS and on remission.

Exclusion Criteria

1. Children with family history of hyperlipidemia
2. Children with previous history of thyroid dysfunction
3. Children with other causes of hypoproteinemia like liver disease and malnutrition.
4. Age less than1yr and more than12yr

ETHICAL APPROVAL AND INFORMED CONSENT

Hospital ethics committee approved the study protocol. Informed consent was obtained from the parents of the study subjects after explaining to them in detail the nature of the study.

Methodology

Pre structured profoma was used to record the information from the individual. After getting the consent from the parents clinical data was collected and entered in the profoma, which include age, sex, presenting complaints, drug history and type of nephrotic syndrome (1 episode/relapse/SDNS/SRNS/remission).

After history taking and clinical examination, blood samples were collected from the patients for lipid profile and thyroid function. Enzymatic method used for measurement of serum cholesterol and VLDL, enzymatic calorimetric method used for measurement of LDL and triglycerides, phosphotungstate method for HDL and photometric methodused for measuring serum albumin. T3, T4 and TSH level measured by ELIZA (Enzyme Linked Immunosorbent Assay).

Statistical Analysis

The data collected from patients were entered in Microsoftexcel sheet and analysed. For continuous variables mean and standard deviation were calculated. To compare the statistically significant association between the means of the two group student t test was used. Categorical variables were expressed as percentages or proportions. For categorical variable chi square test was used. P value of < .05considered as statistically significant.

RESULTS

Among the 40 cases between 1 to 12 yrs. included in our study19 cases were first episode (47.5%),11 cases were relapses (27.5%) which includes both frequent and infrequent relapses, 3 cases were steroid dependent nephrotic syndrome (SDNS 7.5%),3 cases were steroid resistant nephrotic syndrome (SRNS

7.5%) and 4 of them were included at the time of remission (10%).

In our study cases are diagnosed and categorized in to different types and blood samples were collected within 48 hrs of admission in our hospital and in 1 episode cases before starting steroids. Among 4 remission cases sample taken after one month of daily steroids and 3 consecutive early morning samples negative for albumin.

Among 40 cases of nephrotics syndrome 32 children presented with facial puffiness (80%), 26 children presented with decrease during output (65%) an 22 cases with abdominal distention (45%).In our study most common presenting complaint is facial puffiness.

Distribution of various parameters

In the 40 cases included in our study mean seruma albumin was low (mean 2.212gm %), mean total cholesterol (mean=344.300mg/dl) mean triglycerides (mean=304.025mg/dl) mean LDL (mean=234.650mg/dl) and mean VLDL (mean=61.625mg/dl) were elevated. But mean HDL (mean=46.07 mg/dl) within normal limit. Thyroid profile mean T3 (mean=0.923ng/ml) mean T4 (mean 6.105 microg/dl) and mean TSH (mean = 4.2925 iu/ml) all were normal. [Table 1]

During relapse mean albumin (mean=1.96gm %) level less than that of first episode (mean=2.08gm %) and SRNS (mean2.03gm %) but the mean difference is statistically insignificant. (p value >0.05)

In SRNS mean albumin level (mean=2.03gm %) lower than that of SDNS (mean=2.23 mg%) and1episode (mean=2.08gm%). But the difference statistically insignificant. In remission albumin level (mean=3.65 gm%) was statistically significant from all other types (p value less than<0.05). [Table 3]

In our study compared to 1 episode (mean=348.63mg/dl) mean cholesterol level was elevated in relapse cases (mean363.00mg/dl) but the difference is statistically insignificant (p value>0.05). Mean cholesterol level in SDNS (mean=290mg/dl) is less than that of1episode and relapse cases, but again statistically insignificant (P value >0.05). [Table 4]

Mean Serum cholesterol level in SRNS (mean543mg/dl) compared to all other types very much elevated.

Mean difference between cholesterol values of SRNS with 1episode (md=194.37) and the P value 0.012. (<0.05 Significant) With relapse cases the mean difference (md=180.00) and p value was 0.037. (<0.05 significant) Mean difference between cholesterol value of SRNS with SDNS (md=253) and P value 0.013 (<0.05 significant).

In steroid resistant nephrotic syndrome (SRNS) serum cholesterol level significantly elevated compared to other types, and the rise in cholesterol statistically significant compared to other types of nephrotic syndrome. [Table 5]

Mean Triglycerides level in 1 episode (mean=329.95mg/dl) higher than relapse (mean=290.64mg/dl) and SDNS (mean=229.33mg/dl) cases. In SRNS cases TG level (mean=500.57mg/dl) highly elevated compared to1. [Table 6]

Mean serum LDL level in relapse cases (mean=257.64mg/dl) higher than 1 episode, (mean=233.58mg/dl) and SDNS (mean=205.00mg/dl) cases but statistically insignificant (p value >0.05). In SRNS cases mean serum LDL (mean=372.67mg/dl) highly elevated compared to other types but statistically significant when compared to SDNS (P value 0.048) and 1 episode cases (p value 0.023). [Table 7]

In our study mean serum VLDL level in 1 episode (mean=66mg/dl) higher than relapse (mean 60.27mg/dl) and SDNS (mean=49.00mg/dl) cases but statistically insignificant (P value >0.05).

In SRNS cases VLDL level (mean= 100.33mg/dl) higher than other types but insignificant statistically. Compared to remission (mean=25mg/dl) cases VLDL in SRNS cases statistically significantly elevated. (pvalue0.016). [Table 8]

Mean serum HDL in 1 episode (mean=49.05mg/dl) higher than relapse (mean 45.55mg/dl) and SDNS (mean 36.00mg/dl) cases. Mean HDL in SRNS (mean42.33mg/dl) cases lower than 1 episode and relapse cases. [Table 9]

Serum T3 level was within normal limit in all of the 40 cases included in our study. Mean serum T3 level in 1 episode (mean= 0.89ng/ml), relapse (mean =0.93ng/ml) cases, SDNS (mean= 0.87ng/ml) cases, SRNS cases (mean=0.83ng/ml) and in remission cases (mean 1.15ng/ml). [Table 10]

Mean serum T4 in 1 episode (mean=5.73 microgr/dl) less than that of relapse (mean = 6.71microgr/dl) cases and higher than SDNS(mean=5.33microgr/dl) cases. Mean T4 in SRNS (mean=6.87microgr/dl) cases. Compared to all other types shows statistically insignificant elevation. (P value .0.05). [Table 11]

Mean serum TSH level in 1 episode (mean=4.90 iu/ml) higher than that of relapse (mean4.12 iu/ml) and SDNS (mean=3.77 iu/ml) cases but statistically insignificant. Mean serum TSH level in SRNS cases (mean=5.00 iu/ml) elevated when compared to other types of nephritic syndrome, but statistically insignificant (P value>0.05). Compared to remission casesTSH level in 1 episode significantly elevated. (P value 0.018). [Table 12]

Table shows negative relation between serum albumin and cholesterol and the correlation is statistically insignificant (p=0.35) while the negative relation between albumin and TSH is statistically significant (p=0.003). [Table 13]

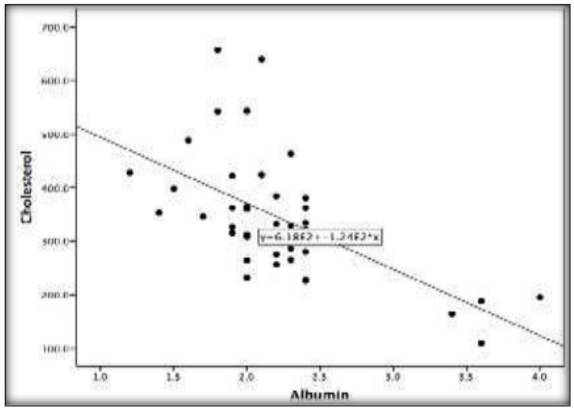

Figure 1: Scatter plot showing relationship between cholesterol and albumin

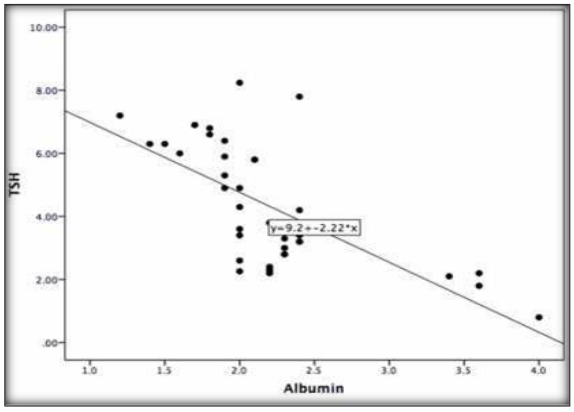

Figure 2: Scatter plot showing correlation between TSH and albumin

Table 1: Frequency of cases

DIAGNOSIS	FREQUENCY	PERCENT
FIRSTEPISODE	19	47.5%
RELAPSE	11	27.5%
SDNS	3	7.5%
SRNS	3	7.5%
REMISSION	4	10%
TOTAL	40	100%

Gender variation of all parameters

Table 2: Gender variation of all parameters. No significant gender variation of all parameters. p value >0.05 insignificant

	Sex	N	Mean	Std. Deviation	Std. Error Mean	Student's t est p value
Age	Male Female	25 15	6.960 6.800	2.4406 2.9809	.4881 .7697	0.85
Protein	Male Female	25 15	4.476 4.847	.7287 .7680	.1457 .1983	0.13
Albumin	Male Female	25 15	2.136 2.340	.5936 .5207	.1187 .1344	0.27
Cholesterol	Male Female	25 15	349.920 334.933	103.4694 141.2209	20.6939 36.4631	0.70
TG	Male Female	25 15	312.000 290.733	154.4531 176.6637	30.8906 45.6144	0.69
LDL	Male Female	25 15	238.800 227.733	77.4871 107.2257	15.4974 27.6856	0.70
HDL	Male Female	25 15	47.760 48.800	12.5807 16.3016	2.5161 4.2091	0.82
VLDL	Male Female	25 15	63.560 58.400	30.4632 35.3024	6.0926 9.1150	0.62
T3	Male Female	25 15	.888 .980	.2635 .3986	.0527 .1029	0.38
T4	Male Female	25 15	5.708 6.767	1.5384 2.3151	.3077 .5977	0.09
TSH	Male Female	25 15	4.3384 4.2160	1.83808 2.02692	.36762 .52335	0.84

Table 3: Mean albumin level in different types of nephritic syndrome

SERUMALBUMIN	MEAN	SD
FIRSTEPISODE	2.08	0.33
RELAPSE	1.96	0.29
SDNS	2.23	0.29
SRNS	2.03	0.21
REMISSION	3.65	0.25

Table 4: Mean cholesterol level in different type of nephritic syndrome

SERUMCHOLESTEROL	MEAN	SD
FIRSTEPISODE	348.63	83.88
RELAPSE	363.00	83.35
SDNS	290.00	67.56
SRNS	543.00	182.93
REMISSION	164.00	39.00

Table 5: Compare the cholesterol level of SRNS with other types

SRNS	Diagnosis	MD	PVA
	episode1	194.37	0.012
	Relapse	180.00	0.037
	SDNS	253.00	0.013
	Remission	379.00	0.000

Table 6: Mean TRIGLYCERIDES level in all type of cases

TRIGLYCERIDES	MEAN	SD
FIRST EPISODE	329.95	171.93
RELAPSE	290.64	98.63
SDNS	229.33	57.07
SRNS	500.67	227.01
REMISSION	126.25	17.02

Table 7: Mean LDL level in all cases

LDL	MEAN	SD
FIRSTEPISODE	233.58	65.51
RELAPSE	257.64	68.72
SDNS	205.00	54.56
SRNS	372.67	120.70
REMISSION	92.25	33.14

Table 8: Mean VLDL level in all type of nephritic syndrome

VLDL	MEAN	SD
FIRSTEPISODE	66.00	34.31
RELAPSE	60.27	19.37
SDNS	49.00	8.89
SRNS	100.33	45.35
REMISSION	25.00	3.37

Table 9: Mean HDL in all type of nephritic syndrome

HDL	MEAN	SD
FIRSTEPISODE	49.05	12.18
RELAPSE	45.55	8.84
SDNS	36.00	6.0
SRNS	42.33	29.05
REMISSION	43.75	9.60

Table 10: Mean T3 Level in all type of cases

T3	MEAN	SD
FIRSTEPISODE	0.89	0.29
RELAPSE	0.93	0.35
SDNS	0.87	0.15
SRNS	0.83	0.32
REMISSION	1.15	0.49

Table 11: Mean Serum T4 level in all type of cases

T4	MEAN	SD
FIRSTEPISODE	5.73	1.66
RELAPSE	6.71	2.21
SDNS	5.33	0.23
SRNS	6.87	2.47
REMISSION	6.25	2.68

Table 12: Mean TSH level in all type of cases

TSH	MEAN	SD
FIRSTEPISODE	4.90	1.82
RELAPSE	4.12	1.71
SDNS	3.77	0.98
SRNS	5.00	2.31
REMISSION	1.73	0.64

Table 13

Albumin level		N	Mean	Std. Deviation	Anovatest, pvalue
	<1.5	3	393.0	37.7	0.35
	1.6-2.0	15	389.4	118.3	
	2.1-2.5	18	338.6	98.9	

Cholesterol	Total	36	364.3	105.4	
	<1.5	3	6.6	0.5	0.003
	1.6-2.0	15	5.2	1.7	
	2.1-2.5	18	3.7	1.4	
TSH	Total	36	4.5	1.7	

DISCUSSION

Age of onset

In our study among 40 children between1 to 12yrs most commonage group of presentation is 6 to 10yrs (24/40) followed by 1 to 5yrs (12/40). Mean age of presentation is 6.9 yrs. In a study done by Indumati et al1among 20 cases of nephrotic syndrome12 cases were between1 to4yrs, 5cases werebetween5to 9yrs and mean age of presentation was 5.85yrs.

Gender variation

In our study among the 40 cases 27 cases were male (68%) and13 caseswere female (32%). Study done by imran gatto et al6 among 208 Cases 62.5% were males (130) and 37.5% were females (78).

Common Presentation

Among 40 cases of nephrotic syndrome 32 children presented with facial Puffiness (80 %), 26 children presented with decreased urine output (65%) and 22 cases with abdominal distention (45%). Vidhi sahni et al7 in their study among 35 children of 1 to 8yrs showed that most common presentation is facial puffiness (80%) followed by decreased urine output (62.85%) and by abdominal distention (31.42%).

Lipid profile

In the 40 cases included in our study mean total cholesterol (mean=344.300mg/dl), mean triglycerides (mean=304.025mg/dl), mean LDL (mean=234.650mg/dl) and mean VLDL (mean=61.625mg/dl) were elevated but mean HDL(mean=46.07mg/dl) within normal limit. Dynase et al8 done a study on serum lipids in nephrotic syndrome in 30 cases and 10 children were taken as control. They showed that there was high cholesterol, LDL, VLDL and triglycerides and the HDL level was normal. According to their study serum cholesterol in relapse cases were significantly higher than first episode. In steroid resistant cases serum cholesterol level highly elevated than steroid responsive cases. They also told the rise in serum cholesterol less when compared to western studies. They noticed positive relation between serum cholesterol and LDL and negative relation between albumin and cholesterol. Arije et al in their study showed that serum cholesterol level continuously elevated in frequent relapse cases. In our study serum cholesterol in relapse cases higher than 1 episode but the value is insignificant. In steroid resistant casesserum cholesterol significantly elevated compared to other types. LDL level compared to first episode and steroid dependent nephrotic syndrome significantly elevated in steroid resistant nephrotic syndrome. Tsukhara et al showed that children with frequently relapsing nephrotic syndrome had high level of serum cholesterol even during remission. They also showed that negative correlation between albumin with LDL and VLDL. In our study negative correlation between serum albumin and serum cholesterol but the association is statistically insignificant (P value 0.30).

Indumati et al 1 in their study showed negative correlation between albumin and cholesterol. But the correlation is insignificant (P> 0.01). They also showed an inverse correlation between albumin and VLDL. Heymann et al told thatno correlation between hyperlipidemia and hypoalbuminemia and the amount of hyperlipidemia is dueto the amount of kidney tissue which was nephrotic. Falaschi F et a ltold that patients with nephrotic range proteinuria had a significantly higher carotid artery intimal thickness compared to those without nephrotic syndrome.

THYROIDPROFILE

In our study among 40 case serum T3, T4 and TSH all within normal imit. But TSH value in first episode significantly higher than remission. Vidhi sahnietal7 in their study on hypothyroidism in nephrotic syndrome showed that T3 and T4 values normal both during active disease and in remission, but TSH values were higher in active disease. During remission TSH become normal and producing a state of Sub clinical hypothyroidism in proteiuria stage that didn't need treatment of thyroxine. They also explained the negative correlation between albumin and TSH. Jasashree choudhury et al in their study compared thyroid profile of 30 controls with 30 children with nephrotic syndrome. Thyroid profiles in control were in normal range. The T4 and T3 levels in in nephritic syndrome were low and TSH was high. Hypothyroidism was more common in children less than 6yrs. U. Sawant et al in their study showed that Nephritic syndrome patient have an more risk of subclinical hypothyroidism. Thyroid profile becomes normal when the non-thyroid illness is resolved. Giles et al told that abnormalities in thyroid function were seen in patients with proteinuria stage, Specifically, TSH levels were higher in patients with active disease than with controls when there was proteiuria and hypoalbuminemia. In our study negative correlation between serum albumin and TSH and that is statistically significant.

CONCLUSION

There is a negative relation between serum albumin and cholesterol and the correlation is statistically insignificant (p=0.35) while the negative relation between albumin and TSH is statistically significant (p=0.003).

Limitations

1. Our study was conducted with 40 cases of nephrotic syndrome.so we were unable to make definite recommendations due to the small sample size.
2. Our study was conducted in those children admitted as in patient in our hospital (tertiary care referral hospital), hence it will not reflect the data from entire community.
3. In our study no controls were used.
4. We were unable to measure 24 hr urinary T3, T4, TSH and urinary thyroid binding globulin.

Recommendations

In nephrotic syndrome relapse cases lipid profile (Cholesterol, LDL, VLDL, Triglycerides) persistently elevated and predispose to development of atherosclerosis, hence serum cholesterol level should be monitored in relapse cases.

In steroid resistant nephrotic syndrome (SRNS), cholesterol level very much elevated compared to other types and they require treatment with lipid lowering agents.

In our study thyroid profile within normal limit, hence no need of routine thyroid screening in a case of nephrotic syndrome.

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