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Original Research Article

Comparison of clinical and lab profile between steroid sensitive and steroid resistant nephrotic syndrome at onset of disease and evaluating predictors for developing steroid resistance in nephrotic syndrome

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ABSTRACT

Background: Nephrotic syndrome is a notable chronic disease in children. The objective of this study was to compare the clinical and lab profile between steroid sensitive nephrotic syndrome and steroid resistant nephrotic syndrome at the onset of disease. Certain parameters were tested if they could be significate predictors of developing steroid resistance at the onset of first episode of nephrotic syndrome.
Methods: Retrospective observation study done children 1-12 years diagnosed with nephrotic syndrome in Sri Ramachandra Medical College and Hospital, Department of Paediatrics, Chennai. Sample size 150. Period of study Jan 2013- Dec 2015. Variables considered were age at onset, sex, parental consanguinity with essential lab parameters done at the onset of nephrotic syndrome proteinuria, pyuria, microscopic hematuria, urine protein creatinine ratio, serum creatinine, serum triglycerides and serum albumin. Children less than 1 year of age, cases with secondary causes of nephrotic syndrome and steroid dependant nephrotic syndrome, children with incomplete records were not included in this study. 150 cases who fulfilled the study criteria were included in this study.
Results: 75 cases of steroid sensitive nephrotic syndrome (SSNS) were compared with an equal number of steroid resistant nephrotic syndrome (SRNS). 85 children had onset of disease before 3 years of age and majority had 3+ proteinuria and males predominated in both the groups. The overall consanguinity rates were higher among SRNS group. Triglyceride level >300 mg/dl predominated in SRNS group along with a higher severity of hypoalbuminemia when compared to SSNS group. None of the parameters tested were significant predictors of developing SRNS subsequently.
Conclusions: Comparing steroid sensitive with steroid resistance nephrotic syndrome, no lab parameter could identify the risk of a child developing steroid resistance subsequently. This could be a field of interest in future studies that could predict the development of steroid resistance at the onset of first episode of nephrotic syndrome itself.

Keywords: Nephrotic syndrome, Steroid sensitive nephrotic syndrome, Steroid resistant nephrotic syndrome

INTRODUCTION

Nephrotic syndrome is characterized by massive proteinuria, hypoalbuminemia (serum albumin <2.5 g/dl), hyperlipidemia (serum cholesterol >200 mg/dl) and edema. It affects 1-3 per 1,00,000 children <16 years of age.[1] They are classified as steroid sensitive or resistant based on their response to steroids after 4 weeks of therapy. About 80% of children with nephrotic syndrome show remission of proteinuria following treatment with oral steroids and are classified as steroid sensitive. 10-20% do not show remission after 4 weeks and are classified as steroid resistant nephrotic syndrome.[2]

SRNS children represent a heterogeneous group with resistance to immunosuppressive drugs with substantial morbidity both from the disease coursed and from the side effects of prolonged treatment.

METHODS

A retrospective observation study among children with primary nephrotic syndrome between 1-12 years of age was done. Children less than 1 year of age, cases with secondary causes of nephrotic syndrome and steroid dependant nephrotic syndrome, children with incomplete records were not included in this study. 150 cases who fulfilled the study criteria were included in this study.

In this study 75 cases were studied each in SSNS and SRNS after obtaining consent. Details regarding their clinical and lab parameters at the onset of disease were procured from patient's records. Parameters considered were age at onset, sex, parental consanguinity with essential lab parameters done at the onset of nephrotic syndrome - proteinuria, pyuria, microscopic hematuria, urine protein creatinine ratio, serum creatinine, serum triglycerides and serum albumin.

Statistical analysis

Data was entered in MS Excel and was analysed using SPSS version 20. Categorical variables such as gender, presence of pyuria, hematuria, proteinuria at onset, protein-creatinine ratio at onset, serum creatinine at onset, serum albumin at onset were represented as proportions.

To test the association between steroid sensitive and resistant status with the exposure variables and other clinical parameters, Pearson's chi square test was used. All the analysis were carried out at a significance level of 5%. Bivariate analysis was done to determine the predictors of steroid resistance nephrotic syndrome.

RESULTS

In a total of 85 children, the onset of disease was before 3 years of age (p value 0.061) (Table 1). Males predominated in both the groups- 58.7% in SSNS and 73.3% in SRNS.

Table 1: Age at onset (p value 0.061).

AGE	SSNS	SRNS	Total
1-3 years	46 (61.3%)	39 (52.0%)	85 (56.7%)
4-6 years	14 (18.7%)	26 (34.7%)	40 (26.7%)
7-9 years	12 (16.0%)	10 (13.3%)	22 (14.7%)
10-12 years	3 (4%)	0 (0%)	3 (2%)
Total	75 (100%)	75 (100%)	150 (100%)

In a total of 85 children, onset of the disease was before the age of 3 years. (p value 0.061)

Among 21.4% of SSNS had consanguineous parents (either second or third degree) while it was 45.4% in SRNS group.

In both the groups, majority had 3+ proteinuria (p value 0.170) (Table 2). Spot urine protein:creatinine in the range of 5.1-10 predominated in SRNS group (Table 3).

Table 2: Proteinuria at onset (p value 0.170).

Proteinuria	SSNS	SRNS	Total
3+	54 (72%)	60 (80%)	114 (76%)
4+	21 (28%)	15 (20%)	36 (24%)
Total	75 (100%)	75 (100%)	150(100%)

In both the groups, majority had 3+ proteinuria. (p value 0.170)

Table 3: Protein: Creatinine ratio at onset (p value 0.036).

Protein: Creatinine	SSNS	SRNS	Total
< 2	1 (1.3%)	4 (5.3%)	5 (3.3%)
2.1-5	39 (52%)	35 (46.7%)	74 (49.3%)
5.1-10	9 (12%)	20 (26.7%)	29 (19.3%)
> 10.1	26 (34.7%)	16 (21.3%)	42 (28%)
Total	75 (100%)	75 (100%)	150 (100%)

PCR range of 5.1-10 predominates more in SRNS group. (p value 0.036)

In this study 4% of children in SRNS group had serum creatinine level of more than 1.5 at onset of illness (Table 4).

Table 4: Serum creatinine at the onset.

Creatinine (mg/dl)	SSNS	SRNS	Total
<0.5 mg/dl	3 (4%)	14 (18.7%)	17 (11.3%)
0.6-1 mg/dl	48 (64%)	45 (60%)	93 (62%)
1.1-1.5 mg/dl	24 (32%)	13 (17.3%)	37 (24.7%)
>1.5 mg/dl	0 (0%)	3 (4%)	3 (2%)
Total	75 (100%)	75 (100%)	150(100%)

4% children in SRNS group had serum creatinine level of more than 1.5 at onset of illness. (p value 0.004)

Table 5: Serum triglyceride at onset.

S. Triglyceride (mg/dl)	SSNS	SRNS	Total
151-200 mg/dl	12 (16%)	0	12
201-300 mg/dl	14 (18.7%)	20 (13.3%)	24
301-400 mg/dl	37 (49.3%)	29 (52%)	76
401-500 mg/dl	12 (16%)	24 (32%)	36
501-600 mg/dl	0	2 (2.6%)	2
	75	75	150

Triglyceride range more than 300mg/dl predominated in SRNS group**.** (P value 0.00)

Triglyceride range more than 300 mg/dl predominated in SRNS group at onset of disease (Table 5). The severity of hypoalbuminemia was higher at onset of disease in SRNS group (Table 6). The incidence of pyuria and microscopic hematuria was more among the SRNS group (Tables 7 and 8).

Table 6: Serum albumin at onset.

Albumin (g/dl)	SSNS	SRNS	Total
<1 g/dl	2 (2.7%)	4 (5.3%)	6 (4%)
1.1-1.4 g/dl	15 (20%)	27 (36%)	42 (28%)
1.5-1.9 g/dl	23 (30.7%)	31 (41.3%)	54 (36%)
2-2.4 g/dl	35 (46.7%)	13 (17.3%)	48 (32%)
Total	75 (100%)	75 (100%)	150 (100%)

Severity of hypoalbuminemia was more in SRNS group. (P value 0.002).

Table 7: Pyuria at onset.

PYURIA	SSNS	SRNS	Total
Yes	8 (10.7%)	14 (18.7%)	22 (14.7%)
No	67 (89.3%)	61 (81.3%)	128 (85.3%)
Total	75 (100%)	75 (100%)	150 (100%)

Pyuria noted more in SRNS group. p value 0.124

Table 8: Microscopic hematuria at onset.

Hematuria	SSNS	SRNS	Total
Yes	4 (5.3%)	11 (14.7%)	15 (10%)
No	71(94.7%)	64 (85.3%)	135 (90%)
Total	75 (100%)	75 (100%)	150 (100%)

Microscopic hematuria at onset predominant in SRNS (p value 0.050).

Table 9: Bivariate analysis showing predictors of steroid resistance (n=150).

		Presence of steroid resistance Yes n (%)	Presence of steroid resistance No n (%)	Unadjusted OR	Adjusted OR	p value
Hematuria	Yes (n=15)	11 (73.3)	4 (26.7)	3.05	1.8	0.438
	No (n=135)	64 (47.4)	71 (52.6)	1	1	
S. Albumin	<3 (n=6)	2 (33.3)	4 (66.6)	0.14	0.78	0.052
	3.1-4 (n=42)	15 (35.7)	27 (64.3)	0.215	0.107	0.011
	4.1-5 (n=55)	24 (43.6)	31 (56.4)	0.211	0.190	0.30
	5.1-6 (n=29)	20 (69)	9 (31.4)	0.63	0.671	0.63
	>6 (n=18)	14 (77.8)	4 (22.2)	1	1	
S. Creatinine	<0.5 (n=17)	14 (82.4)	3 (17.6)	7	5.87	0.33
	0.6-1.0 (n=93)	45 (48.4)	48 (51.6)	1.4	0.98	0.96
	>1.1 (n=40)	16 (43.2)	24 (57.8)	1	1	0.998
Triglycerides	<200 (n=46)	32 (69.5)	14 (30.4)	1.05	1.01	
	201-300 (n=66)	29 (43.9)	37 (56.1)	0.3	0.61	0.414
	301-600 (n=38)	26 (68.4)	12 (31.6)	1	1	0.031
Protein creatinine ratio	<2 (n=5)	4 (80)	1 (20)	6.5	3.4	0.99
	2.1-5 (n= 74)	35 (47.3)	39 (52.7)	1.45	1.28	0.63
	5.1-10 (n= 29)	20 (69)	9 (31)	3.6	8.5	0.001
	>10 (n= 42)	16 (38.1)	26 (61.9)	1	1	

(Dependant variable = Presence of steroid resistance)

Binary logistic regression model was tested to see if hematuria, creatinine, protein creatinine ratio, serum albumin and serum triglyceride at onset of disease with steroid resistance as dependant variable was a risk factor for SRNS. None of them was found to have an increased risk (Table 9). None of the factors studied were a significant predictor for SRNS.

DISCUSSION

The mean age at onset of disease was 4.1 years in SSNS group and 3.8 years in SRNS. This was similar to a study done by McKinney PA et al where the peak incidence of nephrotic syndrome was between 1-4 years of age.[3]

Consanguinity rate was higher in SRNS group similar to a study done by Al Salloum AA et al.[4] Spot urine protein creatinine ratio was in the higher range in SRNS group, with significant p value, similar to a study done by Sahana et al.[5]

It is known that hypertriglyceridemia predisposes to future atherosclerosis and chronic renal sufficiency.[6] Triglyceride level more than 300mg/dl was higher in SRNS group at onset of disease, which is statistically

significant. Raised blood levels of lipids may persist in children with SRNS and potentially contribute to cardiovascular morbidity and progression of glomerulosclerosis.[7] The other significant findings in this study were the severity of hypoalbuminemia and microscopic hematuria which were noted to be higher in SRNS group, similar to other studies.[8] Presence of pyuria at onset of disease was not significant when compared between the two groups.[9]

None of the studied variables were able to predict the possibility of steroid resistance at the onset of first episode of nephrotic syndrome.

CONCLUSION

Comparing steroid sensitive with steroid resistance nephrotic syndrome, no lab parameter could identify the risk of a child developing steroid resistance subsequently. This could be a field of interest in future studies that could predict the development of steroid resistance at the onset of first episode of nephrotic syndrome itself.

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