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A Clinical Study on Nephrotic Syndrome in Children

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Abstract **Original Research Article**

Nephrotic syndrome is one of the most common glomerular disorders of childhood characterized by proteinuria that is severe enough to cause hypoalbuminemia and edema. A prospective observational study was done at Government General Hospital Kakinada over a period of 18 months to evaluate the clinical, biochemichal profile and outcome of nephrotic syndrome in children less than 14 years of age. Out of 36 children enrolled in the study anasarca is seen in all the cases with a mean albumin of 2.06 ± 0.3 mg/ dl, mean cholesterol is 342.5±101mg/dl and anaemia in 28 children (77%).35 cases (97%) are steroid sensitive and 1(3%) case is steroid resistant. Out of 35 steroid sensitive cases 2 cases turned out to be steroid dependent on followup. Nephrotic syndrome is a chronic disease with good prognosis. However most of the steroid sensitive cases during follow up become steroid dependent and are at risk of developing steroid toxicity .Availability of steroid sparing drugs greatly reduced the side effects associated with long-term usage of steroids. However good multicenter randomized control trials with large number of cases, followed up till adolescent age group are required to evaluate the therapeutic efficacy and safety profile of these agents.

Keywords: Nephrotic syndrome, clinical profile, biochemical profile, steroid responsiveness.

INTRODUCTION

Nephrotic syndrome is one of the most common glomerular disorders of childhood. The International Study of Kidney Disease in Children (ISKDC) defined nephrotic syndrome as massive proteinuria (greater than 40mg/m^2/hr, or 1000mg/m^2/24 hr) leading to hypoalbuminemia (less than 2.5g/dl), edema and hyperlipidemia. The urine protein creatinine ratio more than 2 also correlates well with nephrotic range proteinuria [1]. It is primarily a paediatric disorder and is seen among school-aged children and adolescence. Children with nephrotic syndrome have a variable disease course. Upto 1/3rd cases have 1 attack and following a course of treatment with corticosteroids, maintain remission. 10-20% experience relapses several months after stopping the treatment and after 3-4 episodes of relapse maintain remission following a standard course of corticosteroid therapy [3]. Remaining 40-50% patients experience frequent relapses either shortly after stopping the treatment or when the dose of corticosteroid is decreased (steroid dependent). This study intends to evaluate clinical, biochemical profile and outcome of nephrotic syndrome patients.

PATIENTS AND METHODOLOGY

A prospective observational study was conducted to ascertain clinical, biochemical profile and outcome of nephrotic syndrome patients. Children under 14 years admitted in the Department of Paediatrics, Government General Hospital, Kakinada, who met the ISKDC criteria of Nephrotic Syndrome i.e. nephrotic range proteinuria (urinary spot protein creatinine ratio>2), hypoalbuminemia (serum albumin<2.5 g/dl), hyperlipidemia (serum cholesterol > 200 mg/dl) and edema were included in the study. After taking informed consent and fulfilling inclusion criteria a total of 36 children were included in the study. The study was done over a period of 18 months from December 2016 to May 2017 after taking Ethics committee approval.

RESULTS

Out of 36 cases of Nephrotic Syndrome 19 were male and 17 were female with male to female ratio of 1.1: 1, showing slight male preponderance. Number of cases seen in 1-5 years age group are 15, 6-10 year age group are 17 and 4 cases are seen in >10 years age group. Initial episode is seen in 20 cases and relapse is

seen in 16 cases. The demographic details are shown in table 1.

Table-1: Demographic profile

S.NO	DEMOGRAPHIC FEATURE	NUMBER
1	Male	19
	Female	17
2	1-5 Years	15
	6-10 years	17
	>10 years	4
3	Initial episode	20
	Relapse	16

All the 36 children presented with facial puffiness and anasarca. 29 patients (80%) presented with decreased urine output whereas genital edema was present in 17 cases (47%). Ascites was present in 22 (61%) cases and pleural effusions in 13 (36%) cases. Respiratory distress was present at admission in 3 cases. Clinical profile of cases was represented in table 2.

Table-2: Clinical profile

Clinical feature	Number of cases	Percent of cases
Facial puffiness	36	100
Anasarca	36	100
Decreased urine output	29	80
Genital edema	17	47
Ascites	22	61
Pleural effusion	13	36
Respiratory distress	3	8.3

On laboratory evaluation, 22 cases (61.1 %) had anemia (Hb < 10 gm/dl). Among these, 12 were male children and 10 were female children. Mean Hb was 9.63 (±1.4) gm/dl. Mean ESR was 13.5 (7.14) mm/1st hr. On biochemical evaluation, blood urea was in the range of 18 to 55 mg/dl, with mean of 29.4 mg/dl. Serum creatinine ranged from 0.2 to 1.8 mg/dl, with mean value being 0.76mg/dl. Mean Serum albumin in the study was 2.06 ± 0.3 gm/dl. Serum cholesterol ranged from 250 to 682 with a mean value of 342.5±101 mg/dl.

Table-3: Laboratory data

Parameter	**Range**	**Mean ±SD**
Haemoglobin	6 -13gm/dl	9.63 ±1.4
ESR	5-35 mm/1st hr	13.5±7.14
Blood urea	18-55mg/dl	29.4±7.39
Serum creatinine	0.2 – 1.8mg/dl	0.76±0.33
Serum albumin	1.5-2.4gm/dl	2.06±0.3
Serum cholesterol	250-682mg/dl	342.5±101

On Urine analysis, the colour of the urine was cloudy in 16 (44.4%) cases and there was no case of gross hematuria. On urine microscopy hematuria (RBC>5/HPF) was noted in 2 cases and pyuria (pus cells /HPF > 7) in 3 cases. Urine culture was positive in 2 cases; E.coli was isolated in one case and Klebsiella in the other. In both the cases, treatment with steroid was started after treating the urinary tract infection with antibiotic [4, 5]. Urine protein done by dipstick method was 4+ in 16 (44.4%) cases, 3+ in 17 (47.2%) cases and 2+ in 3 (8.3%) cases. Early morning urine spot protein creatinine ratio was in the range of 2.1 to 14.48 with a mean of 3.96 ±2.

In the present study infection is the most common complication, noted in 6 (16.6%) cases. Diarrhoea was the most common infection, noted in 4 cases followed by Urinary tract infection in 2 cases. One child developed sagittal sinus thrombosis and one child developed acute renal failure (ARF) and he was referred to higher centre. After initiation of treatment with prednisolone, hypertension was the most common complication noted in 4 (11%) cases, growth failure in 2 (5.5%) cases and posterior sub capsular cataract was observed in one case which was a longstanding case of nephrotic syndrome with frequent relapses.

Table-4: Complications of nephrotic syndrome inclundig adverse effets of steroids

Complication	Number of cases
Infections	6(16.6%)
Acute renal failure	1(2.7%)
Thrombosis	1(2.7 %)
Hypertension	4(11%)
Growth failure	2(5.5%)
Cataract	1(2.7%)

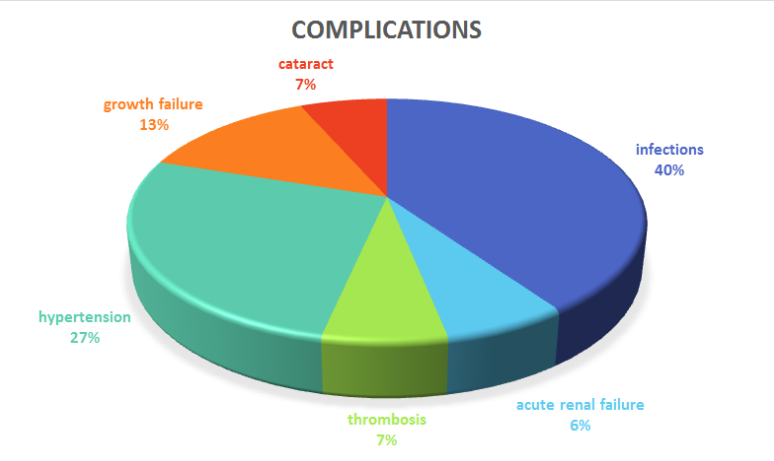


Fig-1: Pie chart showing complications of nephrotic syndrome (n=15)

Among the 36 nephrotic syndrome children in the study, 35 (97%) of the cases were steroid responsive and one child was steroid resistant i.e. failure to achieve remission even after 8weeks of steroid therapy and he was started on oral cyclophosphamide. Of the 35 steroid responsive cases, 2 were steroid dependent on follow. One was started on levamisole in view of developing steroid toxicity – hypertension and growth failure. The other case was on long term alternate day prednisolone therapy with minimal dose of 0.5mg/kg.

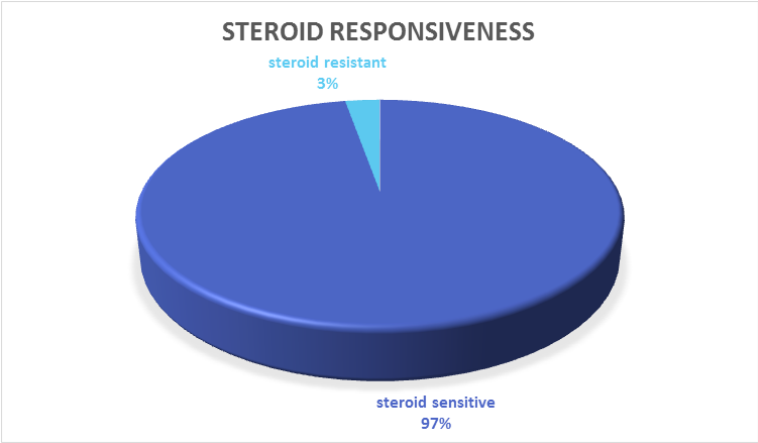


Fig-2: Steroid responsiveness in nephrotic syndrome

DISCUSSION

In the present study, the age distribution ranged from 15 months to 13 years. The mean age at presentation was 6.3 ± 3 years which correlated with other studies. In a study conducted in India by Kumar *et al.* [6], the mean age at onset was 7.9 ± 5.1 years. In a study conducted by Mubarack *et al*. [8] in Pakistan, the mean age at presentation was 9.79 ± 4.59 years. In a Study conducted in Iran by A. safaei *et al*. [11], the mean age at onset was 4.87 ± 3.24 years. In other studies conducted in New Zealand William Wong *et al*. [7] and Saudi Arabia by Kari JA *et al*. [2] the mean age at onset was 5.4 ± 3.9 and 4.3 ± 3.1 years respectively.

In the present study, all children presented with facial puffiness and anasarca (100%). This was similar to observations made by Chowdhary *et al*. [12]. Genital edema was seen in 17(47%) cases, 8 male and 9 female cases. Whereas in a study conducted by Safaei *et al*. [14] it was seen in 54.5 % cases. Decreased urine output was seen in 29 (80%) cases in our study, whereas it was seen in 53% cases in a study conducted by Sahana K.S *et al*. [9].

In the present study of a total of 36 children with nephrotic syndrome, 20 children presented as the first episode whereas 16 children presented as relapse. Most of the children presenting as first episode were in the age group of 1-5 years (11) i.e.,55%, followed by 6-10 years (7) 35% and 2 children were in > 10 year age group making 10%. Among the relapses, the first episode occurred mostly in the age group of 1-5 yrs. (11 cases) i.e., 68.8% followed by 6-10 yr. age group (5 cases) i.e., 31.2%.

In the present study precipitating infection was found in 12 cases while in the remaining cases no precipitating factor is found. Among infections upper respiratory tract infections are most common, seen in 6

children, diarrhoea in 4 children and Urinary tract infection in 2 children with E.coli and Klebsiella being isolated in these 2 cases and they were treated with antibiotics before starting steroid.

In the present study of 36 children, 28 (77.7%) children were found to be anaemic, 25 of them have microcytic hypochromic picture and 3 have normocytic normochromic picture. Iron deficiency anaemia can occur in nephrotic syndrome because of loss of transferrin in the urine. In a study done by Anochie *et al*. [10], nearly half of the patients had anaemia. ESR ranged from 5 to 35 mm/1st hr with a mean of 13.5 ± 7.14mm / 1st hr. Blood urea in the present study ranged from 18 to 55 mg/dl with a mean of 29.4 ± 7.39 mg/dl. Serum creatinine ranged from 0.2 to 1.8 mg/dl, with a mean of 0.76 ± 0.33 mg/dl. In our study one child who presented with relapse, landed in AKI and had a serum creatinine of 1.8 mg/dl due to usage of diuretics prior to the admission. Serum albumin ranged from 1.5 to 2.4 gm/dl, with a mean of 2.06 ±0.3gm/dl. Similar observations were made by Hiraoka *et al*. [13]. Serum cholesterol in the study ranged from 250 to 682 mg/dl with a mean of 342.5 ± 101gm/dl.

Urine spot protein creatinine ratio was used as the measure of proteinuria as 24 hr urine collection was troublesome in children below 5 years of age. So we have chosen early morning urine spot protein creatinine ratio to demonstrate nephrotic range proteinuria. In our study the urine spot protein creatinine ratio ranged from 2.1 to 14.8 with a mean of 3.96 ± 2.55. Similar results were obtained in a study conducted by Sahana K.S[9], where the mean urine protein to creatinine ratio was 4.79. Out of 36 children in the study, ultra-sonogram abdomen showed ascites in 24 cases (66.6%) – 19 of them had mild effusion and 5 had moderate effusion. Chest X ray showed mild pleural effusion in 11 cases and moderate effusion in 2 cases.

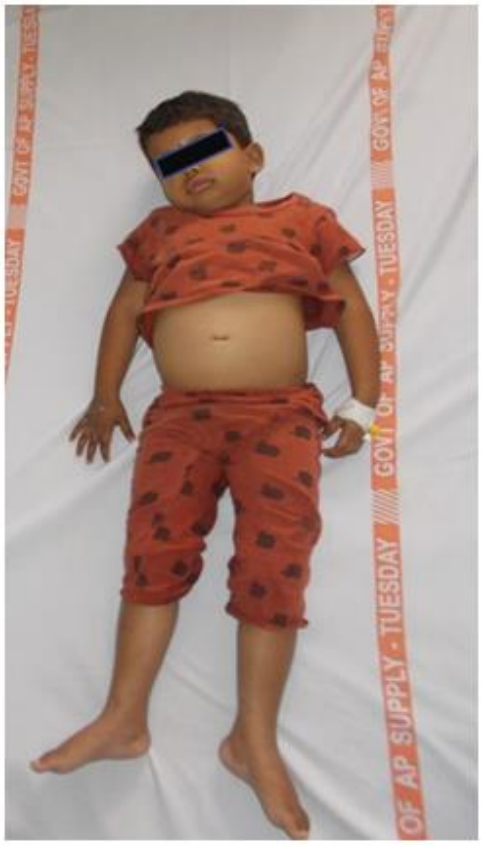
In the present study of 36 children with nephrotic syndrome, 35 children were steroid responsive (97%), one child (3%) was a steroid resistant case who was on oral Cyclophosphamide prior to admission in our hospital. The child had undergone renal biopsy prior to admission in our hospital and it showed a MCNS. In a study conducted in India by Sahana *et al*. [9] also reported a high response to steroid (97.6%) In various studies, the steroid responsive rates ranged from 67% to 87.5%. Steroid responsiveness is the most important prognostic indicator in nephrotic syndrome. Of the 35 steroid responsive cases 2, cases were found to be steroid dependent.

Of the 36 children who were followed up for 6 months after admission, 31(86%) children were found to have infrequent relapse. Most were in the age group of 6-10 years (15 cases) followed by 1-5 years (12 cases) and 4 cases in the > 10 years group. 5 (14%) children were found to have frequent relapses in our study. Of the 5 children, 3 were in the age group of < 5 years, 1 each in 6-10 year and > 10 year age group.

In the present study, infections were the most common complication, occurring in 6 (16.6%) cases, with diarrhoea being the most common infection, seen in 4 cases followed by UTI in 2 cases. In a study conducted by Sahana *et al*. [9] too, infections were the most common complications seen in 31% cases, though UTI was the most common infection in that study followed by pneumonia, tuberculosis and peritonitis. One child developed Acute Renal Failure in our study and he was referred to a paediatric nephrologist. One child presented with ataxia during follow up and on neuroimaging cerebral sinus venous thrombosis was found. None of the children in our study had hypertension at the time of admission. However after initiation of treatment with prednisolone, hypertension developed in 4 children and hypertension was controlled with ACE inhibitor. Posterior sub capsular cataract was noted in one case of longstanding steroid dependent nephrotic syndrome and the child was operated for cataract. Growth failure was noted in 2 cases on follow up.

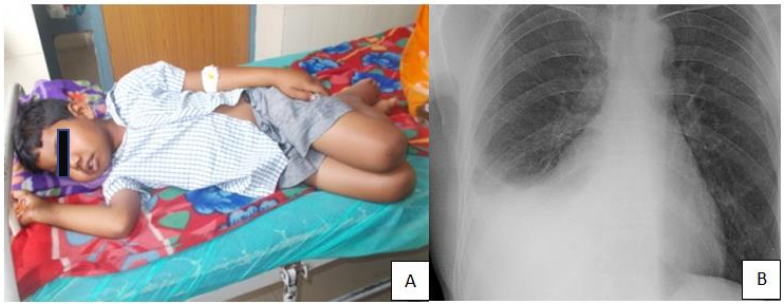
CONCLUSION

Nephrotic syndrome in children is a chronic disease with good prognosis as many of them are steroid sensitive and go into complete remission in the second decade. However most of the steroid sensitive cases during follow up, suffer from multiple relapses and some of them become steroid dependent and are at high risk of developing steroid toxicity. Availability of steroid sparing drugs like levamisole, mycophenolate mofetil, cyclophosphamide etc. greatly reduced the side effects associated with long term usage of steroids. However good multicentre randomised control trials with large number of cases, followed up till adolescent age group are required to evaluate the therapeutic efficacy and safety profile of these agents so as to select the most suitable drug to improve the long term outcome in children with steroid dependent and steroid resistant nephrotic syndrome.



Facial pufffiness, abdominal distension in a 3yr female child presenting with nephrotic syndrome

Cushingoid facies, short stature in a 13yr old female child with steroid dependent nephrotic syndrome



A showing facial oedema in 7yr male child with nephrotic syndrome chest x-ray of the same child showing right sided pleural effusion in figure b

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