

## Original Article

# Clinical and Biochemical Profile of Nephrotic Syndrome in Children in A Tertiary Care Hospital

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## ABSTRACT

**Introduction:** Nephrotic syndrome is a common renal disease worldwide and an important chronic renal disease in children. **Objective:** This prospective study is undertaken to assess clinical presentation, associated complications, investigative profile and therapeutic response in children with nephrotic syndrome. **Methods and Material:** Prospective observational study at pediatric department of our tertiary care hospital. 95 children who were diagnosed to have nephrotic syndrome were included in the study. Cases were noted down into the prestructured proforma with respect to history, examination and investigations. Statistical analysis was done by standard descriptive statistics including Chi-square test and calculating the p value. **Results:** All patients presented with puffiness of face and swelling of limbs and genital edema in 34.7% & ascites was present in 84.2% of cases, pleural effusion in 17% of cases and HTN in 10.5% of cases. Infections were

seen in 33% of cases with UTI being the commonest infection noted (29%). On investigation all patients had hypoalbuminemia in the range of 1.1-2.3 gm./dl and hypercholesterolemia 202-379mg/dl. Renal function test was normal in all the patients. Microscopic hematuria noted in 9.5 % of cases. Urine protein was 3+ in all cases. Mean urine total protein value was 3.77gm/24 hours and mean protein creatinine was 4.10. Majority of cases (97%) were responders to steroid therapy. **Conclusion:** In our study clinical and laboratory data were in concordance with typical nephrotic syndrome in children. Pattern of nephrotic syndrome and response to treatment did not differ significantly from other studies.

**Key Words:** Nephrotic syndrome, Children, Edema, infections

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## INTRODUCTION

Nephrotic syndrome is a common renal disease worldwide and an important chronic renal disease in children. Its incidence is reported to be 2 -3 /100000 children in western countries, 1 while as its incidence is slightly higher (2-7/100000) in children with South Asian origin and its prevalence is 12-16/100000 children.<sup>1, 2</sup> According to Edelmann,<sup>1</sup> NS is neither a single disease nor even a heterogeneous group of disease. Rather it is a clinical state characterized by heavy proteinuria and hypoalbuminemia, often associated with edema, hypercholesterolemia and hyperlipidemia. Most children with nephrotic syndrome have a form of primary or idiopathic nephrotic syndrome and the most common glomerular lesion is minimal change disease. The idiopathic nephrotic syndrome most commonly appears between the ages of 2-6 years of age, more common in boys and it is steroid sensitive in majority of cases[95%].<sup>3</sup> The cause of idiopathic nephrotic syndrome is unknown but evidence suggests that primary T cell disorder leading to glomerular podocyte dysfunction.<sup>4</sup> The clinical presentation of nephrotic syndrome vary widely from mild edema to severe cases presenting with complications important being life threatening infections and thromboembolic episodes. Nephrotic syndrome with significant glomerular lesion can have hypertension, renal insufficiency, and gross haematuria. Overall incidence of MCNS has been generally stable over past 3 decades. However, incidence of FSGS seems to be increasing.<sup>5</sup> Secondary nephrotic syndrome due to systemic causes include SLE, HSP, Amyloidosis, DM, HIV, Parvovirus B19, and Hepatitis B AND C virus infections.

There is lack of studies on clinical profile of nephrotic syndrome in Indian children in recent past. Though the incidence of nephrotic syndrome is not changed but due to increased availability of medical services and scattered distribution of

patient's pediatricians are getting to see a smaller number of cases compared to past. So, we decided to do this study in order to assess clinical presentation, associated complications, investigative profile and therapeutic response in children with nephrotic syndrome.

## METHODS AND MATERIAL

This study was a prospective observational study conducted at Pediatric inpatient department at Sher-E-Bangla Medical College Hospital, Barisal, Bangladesh, from July 2020 to August 2021. Children suffering from Nephrotic syndrome in whom steroid therapy was not yet started were included for the study. Both the patients with first attack and relapse were included in the study. Diagnosis of nephrotic syndrome was based on the following criteria – massive proteinuria >40 mg/m<sup>2</sup>/hr. or protein creatinine ratio >2, hypoalbuminemia <2.5 gm/dl, generalized edema and hypercholesterolemia >200 mg/dl. Nephrotic syndrome secondary to systemic causes were excluded from the study.

Cases were noted down into the prestructured proforma with respect to history, examination and investigations. Following investigations were done in all suspected cases of nephrotic syndrome. Complete blood count including peripheral smear and ESR, blood urea, serum creatinine serum cholesterol, serum albumin was done in all the patients. Urine was examined for the presence of gross haematuria or cloudy appearance followed by microscopic examination to look for pus cells and RBC, and urine culture. Urine protein was measured by sulfosalicylic acid test, protein creatinine ratio and 24 hours urine protein measured using Eshbach's albuminometer. Chest X-ray and Mantoux test were done to rule out tuberculosis. Blood pressure, weight, intake and output chart, abdominal girth, urine for proteinuria were done daily on all patients. Patients were started treatment with steroids according to standard

protocol,<sup>6</sup> along with fluid and salt restriction and their response was noted. Statistical analysis was done by standard descriptive statistics using the Statistical Package for the Social Sciences (SPSS) version 17.

## RESULTS

In the present study children presented between the ages of 2-15 years with mean age at presentation being 6.3 years. In the present study, 69.47% of the cases belonged to 6-12 years age group followed by 1-5 years age group, which accounted for 31% of the nephrotic syndrome

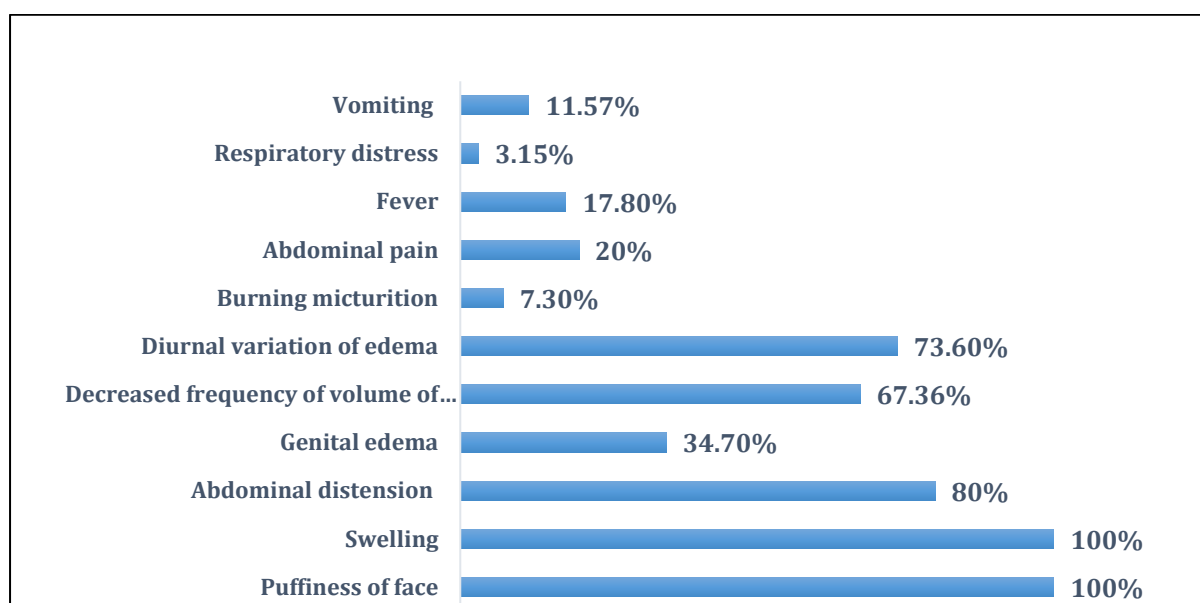
patients. 45% of the cases were male while as 55% of cases were female with male to female ratio of 1:1.2 suggesting female preponderance. Table 1 shows age and sex distribution of cases. 33 % of cases presented for the first time (first attack) where as 67% of patients had one or more relapse at the time of presentation but statistically not significant. ( $\chi^2=3.596$ ,  $p < 0.058$ ). Majority of cases i.e., 70% of cases presented to the hospital within 10 days of onset of symptoms where as 10% of cases had duration of symptoms for more than 20 days before coming to hospital.

**Table 1: Age and sex (n=95) Distribution of cases**

Age	Male No.	Male %	Female No.	Female %	Total No.	Total %
0-1	-	-	-	-	-	-
1-5	13	13.6	11	11.57	24	25.26
6-12	27	28.4	39	41.0	66	69.47
>12	3	3.15	2	2.1	5	5.2
<b>total</b>	<b>43</b>		<b>52</b>		<b>95</b>	

All patients presented with puffiness of face and swelling of limbs with diurnal variation noted in 73.6% of cases. 80% patients presented with abdominal distension while as 31% of cases complained of genital swelling. History of decreased frequency and volume of

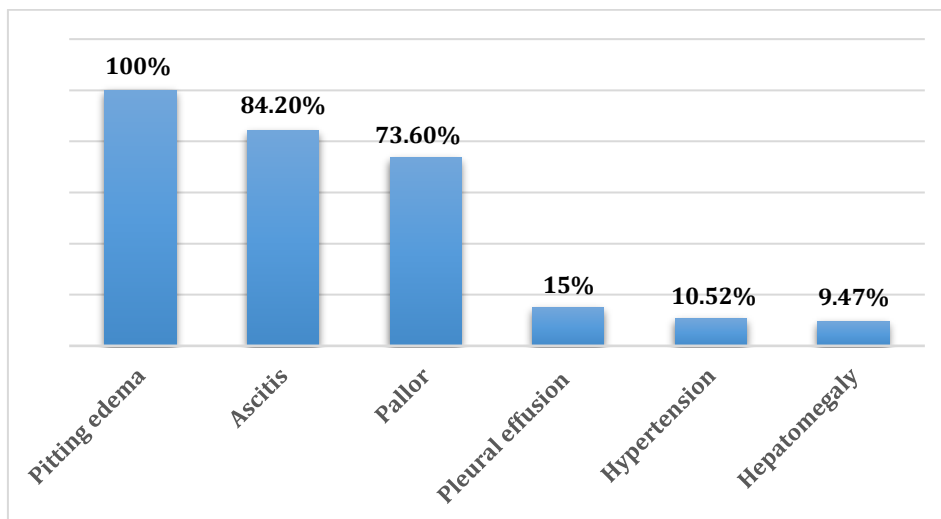
micturition was obtained in 67.36% while as burning micturition was noted in 7.30% of cases. Other symptoms include abdominal distension, fever, vomiting and respiratory distress. Figure 1 shows presenting symptoms and their frequency.



**Fig. 1: Graphical representation of presenting symptoms in Nephrotic syndrome.**

On examination bilateral pitting pedal edema with facial puffiness was present in 100 % of cases. Ascites was present in 63% of cases, pleural effusion in 17% of cases while as hepatomegaly was noted in

9.47% of cases. Hypertension was notes in 10.52 % of cases prior to initiation of corticosteroid therapy. Pallor was noted in 42% of cases. Figure 2 shows signs on examination and their frequency.



**Fig 2: Graphical representation of signs in nephrotic syndrome.**

On investigation 73.6% of cases had anemia with peripheral smear showing normocytic hypochromic in 48 cases and microcytic hypochromic in 15 cases. Total leukocyte range was between 6000-13,300 with mean leukocyte count of  $7780/\text{mm}^3$ . ESR was elevated in all cases with mean ESR of 70mm at first hour. On biochemical investigation blood urea was between the range of 13-42 mg/dl with mean value of 23 mg/dl. Serum creatinine

was in the range of 0.3-1.4mg/dl with mean value of 0.65mg/dl. Serum albumin was between 1.1-2.3mg/dl with mean value of 1.7 mg/dl indicative of hypoalbuminemia. Serum cholesterol range was in between 202-379 mg/dl with mean level of 291mg/dl suggestive of hypercholesterolemia. Hypoalbuminemia and hypercholesterolemia was present in all cases. Table 2 shows investigative profile in nephrotic syndrome.

**Table 2- Investigative profile of Nephrotic syndrome**

Parameter	Range	Mean $\pm$ SD
Haemoglobin	8.3-12.7 gm./dl	10.5gm/dl $\pm$ 1.42
Total count of WBC	6000-13,300 cells/ $\text{mm}^3$	7780 $\pm$ 1499
ESR	19-136mm at first hour.	70 $\pm$ 19
Blood urea	13-42mg/dl	23 $\pm$ 7.11
Serum creatinine	0.3-1.4mg/dl	0.65 $\pm$ 0.24
Serum albumin	1.1-2.3gm/dl	1.7 $\pm$ 0.37
Serum cholesterol	202-379 mg/dl	291 $\pm$ 63.59

On urine examination color of the urine was cloudy in 71% of cases and there was

no case of gross haematuria. Specific gravity of urine was between 1020-1060.

On urine microscopy Haematuria was noted in 9 cases (9.5%) and pyuria noted in 12 cases (25%). Urine culture was positive in 20% of cases with E Coli (70%) being the commonest organism isolated followed by klebsiella (21.6%) and proteus (5.2%). Urine protein was 3+ in all cases by sulfosalicylic acid method.

Urine total protein in a timed 24 hours sample was in the range of 0.6-6.5 gm/24 hour and mean value was 3.77gm/24 hours. Protein creatinine ratio in a spot sample of urine was in the range of 2.8-8.3 and mean value was 4.10. Table 3 shows analysis of urinary parameters.

**Table 3 - Analysis of urinary parameters.**

Cloudy appearance	68 (71%)
Hematuria	9 (9.5%)
Pyuria	27 (28.42%)
Urine culture positive	20 (21%)
E coli positive	14 (70%)

Infections were the most common complications [33%] noted though one patient presented with severe respiratory distress due to massive ascites. UTI was the commonest infection noted (in 21% of cases) and it is statistically significant ( $\chi^2=11.255$ ,  $p<0.001$ ) followed by pneumonia, tuberculosis and peritonitis (one case each)

Majority of cases (96%) were responders to steroid therapy and it is statistically significant ( $p<0.001$ ). One was non – responder to steroid therapy even after four weeks and labelled him as steroid resistant and patient was referred to Nephrologists. In 9 cases steroids were not started as they underwent spontaneous remission.

## DISCUSSION

This study was conducted on 95 children who were diagnosed to have nephrotic syndrome in our institution. In the present study the age distribution of cases ranged from 2 years to 15 years. The mean age at presentation was 6.3 years. Similar observations were made by Chahar OP et al,<sup>7</sup> and Shastri NG et al.<sup>8</sup>. Even though commonly nephrotic syndrome is seen in pre-school children in our study the mean age was 6.3 years as majority of cases (67%) were relapses. Younger the age of

onset of nephrotic syndrome more likely is the chance of MCNS<sup>9</sup>. In the present study (n=95) male: female ratio was noted to be 1:1.2 Similar observations were made by Siegal NJ et al.<sup>10</sup> Among the frequent relapses, two patients had features of steroid toxicity namely posterior capsular cataract in one case and HTN, osteoporosis in the other case.

In the present study the duration of symptom at the time of presentation ranged from 3 to 45 days. Majority of cases i.e., 70% presented to the hospital within 10 days of onset of symptoms, whereas 10 % cases had duration of symptoms for more than 20 days prior to hospital. Among the patients who presented late, there were no complications noted except for one case, which had associated tuberculosis. Present study showed face and limbs as the commonest site to be involved i.e., in 100 % similar to observation made by Chowdhary et al.<sup>11</sup> Edema involving genital area was least it in 34.7 % of cases where as in a study done by Safaei et al,<sup>12</sup> it was found to be 54.5%. three patients presented with respiratory distress due to massive edema (pleural effusion and massive ascites). 67.36% of cases presented with history of decreased frequency and volume of micturition. Only

7.3% cases had burning micturition and all of them had UTI. Other symptoms noted by various studies include anorexia, lethargy, abdominal pain and diarrhoea.<sup>11, 12</sup>

In the present study, HTN was noted in 10 cases (10.52%) prior to initiation of steroid therapy. As there were no other associated features like haematuria or renal insufficiency to suggest significant glomerular lesion, these children were not investigated further and they responded to steroid therapy. Gabban et al. prospectively examined a cohort of 71 children 1–18 years old: 33 (46.5%) with steroid sensitive NS, 28 (39.4%) with steroid dependent NS, and 10 (14.1%) with steroid-resistant NS. HTN was present at diagnosis in 5 patients (7%) with steroid sensitive NS, 9 patients (12.6%) with steroid resistant NS and 14 patients (19.7%) with steroid dependent NS. Family history of HTN was reported in 4 cases (5.6%). In over 7 months of follow-up, the overall prevalence of HTN increased to 39.4%.<sup>13</sup> According to Nelson, hypertension can be present in about 10% of MCNS while as nephrotic syndrome due to significant glomerular lesion, the incidence of HTN varies from 20-35%.<sup>3</sup>

On examination pitting type of edema was noticed in all patients in the present study. Generalized edema with ascites was present in 74% of cases which is similar to study done Safaei et al.<sup>12</sup> Other uncommon sign noted was hepatomegaly present in 9.47% of cases.

Present study (N=95) showed UTI, peritonitis, tuberculosis, pneumonia to be present in 29%, 2%, 2 % and 2 % of cases respectively. In contrast to our study UTI was present only in 8.1% of cases in a study done by Ajayan et al.<sup>14</sup> but observed a higher incidence of pneumonia (35%). Gorensek Mj et al.<sup>15</sup>. (N=214) in a 20-year retrospective study observed 17.3% cases of peritonitis. Smaller percentage observed in our study could be attributed to small number of sample size and short duration

of study whereas Gorensek et al,<sup>15</sup> studied for a period of 20 years.

In the present study 73.6 % of cases had anaemia and both normocytic and microcytic pictures were seen. Iron deficiency anaemia in nephrotic syndrome is attributed to loss of transferrin in the urine. In a study done by Anochie et al nearly half of the patients had anaemia.<sup>16</sup> Feinstein and his group showed a prevalence of 59% in their study population.<sup>17</sup>

Renal function was normal in all the patients. Serum albumin ranged from 1.1 gm to 2.3 gm/dl with the mean level of 1.7 gm/dl. Similar observations made Hiaoka et al.<sup>18</sup> The range of serum cholesterol in the present study was 202-379 mg/dl and the mean serum cholesterol was noted to be 291 mg/dl. Similar observations were made by Appeal GB et al.<sup>19</sup>

On microscopic examination in the present study 9.5% of cases showed presence of haematuria. Similar observations were made by Siegal NJ et al.<sup>10</sup> Among 9 of these cases with microscopic haematuria, three cases had UTI while rest of the two cases responded to steroids and haematuria subsided. Siegal NJ et al have discussed the cause of haematuria and observed that microscopic haematuria may be either asymptomatic or accompany UTI whereas macroscopic haematuria in patients of nephrotic syndrome should be expected only in cases with UTI, renal vein thrombosis and other secondary causes of nephrotic syndrome associated with significant glomerular lesions.

In a study done by Ali AM et al 10 patients (out of 231) had gross haematuria and on biopsy FGCS was found in 6 and mesangial proliferative and membranoproliferative in 2 each.<sup>20</sup> In previous literatures, transient microscopic hematuria has been described in 10–30% of children with minimal-change NS<sup>21,22</sup>

In the present study urine total protein in timed 24 hour sample the range observed was 0.6-6.5 gm/24 hour with mean value of 3.77gm / 24 hour. Iyer Rs et al,<sup>23</sup> found

the range of timed 24 hours urine protein to be 1.6-8.6gm/24 hour and a mean value of 4.6/24 hour was observed. In the present study (n = 95) the range of urine protein/creatinine value observed was 2.8-8.3 with a mean of UP/UC 4.10. In the various studies,<sup>7, 8, 20, 24</sup> done previously range of UP/UC ratio in nephrotic syndrome was 1.2-9.8 but the mean value is more than 2 in all the studies.

In the present study 2.1% cases (2 case) was non-responder to steroid therapy while as in a study by KIM JS et al,<sup>25</sup> it was found to be about 15 % may be because they have included patients upto 18 years of age. They have also found that steroid resistance is more in American and African children. As we have noted that 97.6% of cases were responders to steroid therapy similar observations were made by Madani et al,<sup>5</sup> and they have also noted that 96% of children with MCNS were responders to steroid therapy though in our study histopathological picture was not available. Steroid responsiveness is of greater prognostic use than renal histology.<sup>4</sup> There was no mortality in our case series

## CONCLUSION

In our study clinical and laboratory data were in concordance with typical nephrotic syndrome in children. Pattern of nephrotic syndrome and response to treatment did not differ significantly from other studies.

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