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ORIGINAL ARTICLE

URINARY TRACT INFECTION IN CHILDREN WITH NEPHROTIC SYNDROME: A PROSPECTIVE OPEN LABELED STUDY

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ABSTRACT: BACKGROUND: Nephrotic syndrome is an important chronic disorder in children in which prevalence of urinary tract infection (UTI) is high. UTI may also be responsible for steroid resistance and relapse. UTI is an important but often undiagnosed condition in children with nephrotic syndrome. Hence the present study is being conducted. **AIMS AND OBJECTIVES:** The study is conducted to determine the clinical features of nephrotic syndrome and to evaluate the incidence, etiological agents, clinical features and the antibiotic sensitivity pattern of Urinary Tract Infections in children with Nephrotic Syndrome. **MATERIAL & METHODS**: The study was a Prospective hospital based study done by Stratified random sampling conducted on all the paediatric patients with a diagnosis of nephrotic syndrome attending the OPD and admitted to Paediatric hospital. Fifty children with diagnosis of Nephrotic Syndrome were studied. The specimen for urine culture was obtained carefully to prevent contamination by periurethral flora. A clean-catch midstream urine specimen was used. Contamination by periurethral and prepucial organisms was minimized by washing the genitalia. The specimen was directly collected in a sterile container. Prompt plating of the urine specimen, within one hour of collection was ensured. Identification of the organism to species level was done and antibiotic sensitivity pattern was also studied. **RESULTS:** Among the fifty children studied, boys were affected more than girls by Nephrotic syndrome with a ratio of 1.5:1. The mean age was 4.75 years. Urinary Tract Infection was detected in seventeen children (34%). The present study was statistically significant with $p<0.001$. The commonest Micro-organism isolated was Escherichia coli, followed by Staphylococcus aureus. Most of the Micro-organisms were sensitive to cephalosporins. **CONCLUSION:** Urinary Tract Infection is a significant infection detected in cases of Nephrotic Syndrome affecting one third of the cases. Early detection and prompt treatment with appropriate antibiotics will play a major role in preventing the morbidity and mortality as well as it avoids the relapse and facilitates early remission of Nephrotic Syndrome. High index of suspicion, early institution of appropriate antibiotics and aggressive management of infections can attenuate morbidity and mortality.

KEYWORDS: Nephrotic Syndrome; Albuminuria; Urinary Tract Infection; Micro-Organisms; Antibiotic sensitivity.

INTRODUCTION: Nephrotic syndrome is a common renal disease all over the world and it is also an important chronic disorder in children. Its incidence is reported to be 3/100, 000 children per year.[1]

Nephrotic syndrome is a manifestation of glomerular disease characterized by nephrotic range proteinuria and the triad of clinical findings associated with large urinary losses of protein: hypoalbuminemia, edema and hyperlipidemia.

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Infection is the major complication of nephrotic syndrome. Children in relapse will have increased susceptibility to bacterial infection because of urinary losses of immunoglobulins and properdin factor B, defective cell mediated immunity, immunosuppressive therapy, malnutrition and edema/ ascites acting as a potential "culture medium".[2]

UTI result in significant morbidity and may also be responsible for a poor response to steroid therapy or induce relapse in a child who has already attained remission, besides being the commonest cause of mortality. UTI is an important but often undiagnosed in children with nephrotic syndrome.[3] Hence the present study is being conducted.

METHODOLOGY:

Source of Data: All pediatric patients with a diagnosis of nephrotic syndrome attending the OPD and admitted to Paediatric hospital.

Sample Size: A sample size of 50 children with nephrotic syndrome admitted in the Department of Paediatrics and attending the OPD of Paediatrics.

Sampling Method: Stratified random sampling.

Type of the Study: Prospective hospital based study.

Inclusion Criteria: All patients with the age group below 12 years, attending Paediatrics OPD and admitted in Paediatrics Department with the diagnosis of Nephrotic Syndrome according to ISKDC classification.

Exclusion Criteria:

1. Patients aged more than 12 years.
2. Nephrotic syndrome patients already on antibiotics.
3. Children with gross urogenital anomalies.

Method of Study: The proposed study is a prospective and descriptive study. A total of 50 children of pediatric age group (up to 12 years) are included in the present study. Details were entered in a pre-designed proforma which has detailed history of edema, ascites, burning micturition and fever. Then a detailed anthropometry, head to toe examination and systemic examination is done.

All children were subjected to International Study of Kidney Diseases in Children (ISKDC) classification for diagnosis of nephrotic syndrome. Then blood urea, serum creatinine and renal ultrasound were done in all patients

The specimen for urine culture was obtained carefully to prevent contamination by periurethral flora. A clean-catch midstream urine specimen is used. Contamination by periurethral and prepucial organisms were minimized by washing the genitalia.

Antiseptic washes and forced prepucial retraction are not advised. The specimen was directly collected in a sterile container. Prompt plating of the urine specimen, within one hour of collection was done.

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OBSERVATIONS:

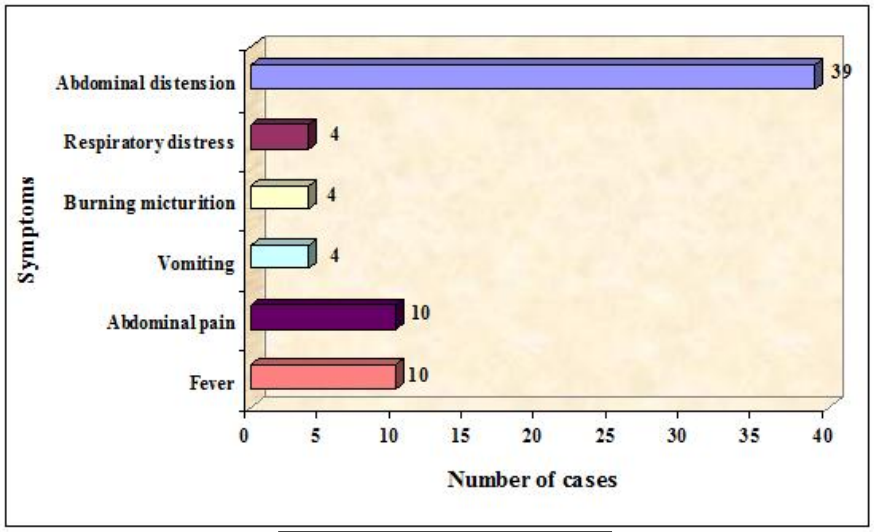

Fig. 1: Symptomology

In the present study, 4% of the cases belonged to <2 years age group, 84% belonged to 2-6 years age group, followed by 12% belonging to 6-12 years age group with male preponderance, 60% of cases were male while 30% of cases were female. 58% of patients presented for the first time, about 24% of patients were frequent relapsers and 18% were infrequent relapsers.

All patients presented with puffiness of face and swelling of limbs. The least common pattern was genital edema which was seen in only 16% of cases. History of diurnal variation of edema at the time of admission was available in 88% of cases. The symptomology at presentation was Abdominal distension in 78% of cases, Abdominal pain and Fever in 20%, whereas Respiratory distress, Burning micturition and Vomiting were seen in 4% of the cases as shown in Figure 1.

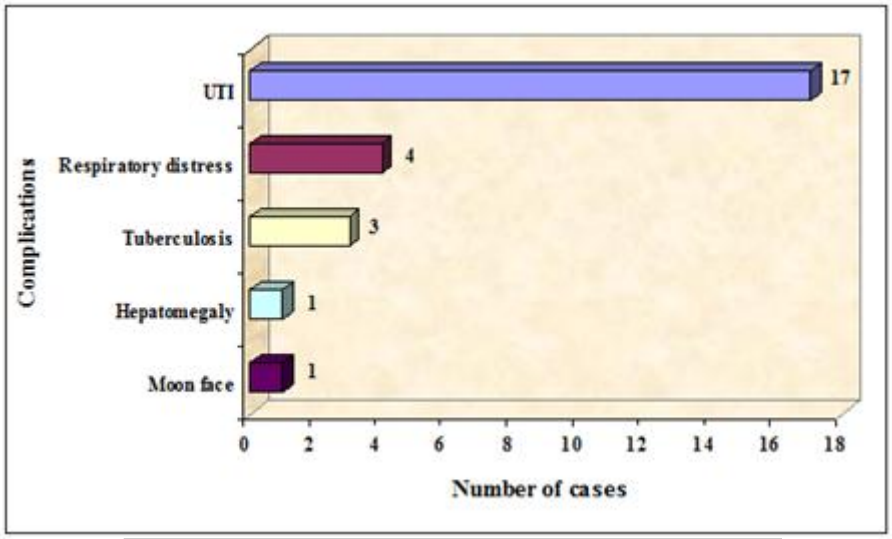

Fig. 2: Associated complications/infections

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A history of decreased frequency and volume of micturition was obtained in 80% of the cases and history of burning micturition was seen in only 8% of cases. The following complications were observed in the present study. Respiratory distress in 4 cases (one had pneumonia, one was a known case of HRAD and two cases had distress due to massive edema), tuberculosis in 3 cases, hepatomegaly in one case. Moon facies as a complication of steroid therapy was observed in one case as shown in Figure 2.

Parameter	Mean	S.D	S.E
Total leukocyte count	11855 cells/mm^3	5313 cells/mm^3	751 cells/mm^3
ESR	28 mm at 1st hour	24.5 mm at 1st hour	3.45 mm at 1st hour
Blood urea	32.1 mg/dl	13.61 mg/dl	1.95 mg/dl
Serum creatinine	0.77 mg/dl	0.16 mg/dl	0.22 mg/dl
Serum albumin	2.2 gm/dl	0.41 gm/dl	0.05 gm/dl
Serum cholesterol	324 mg/dl	71.2 mg/dl	8.9 mg/dl
Urine total protein	3.9 gm/24 hour	1.8 gm/24 hour	7.9 gm/24 hour
Urine Protein/ Creatinine Ratio	3.8 mg/mg	2.2 mg/mg	7.8 mg/mg

Table 1: Baseline Investigative Parameters

UTI was present in 17 cases. Majority of cases (76%) were responders to steroid therapy and it is statistically significant ($p < 0.001$). Twelve patients were non-responder to steroid therapy of which 4 were Steroid Dependent (SDNS), 3 were Steroid Resistant (SRNS) and 5 were Frequent Relapse Nephrotic Syndrome (FRNS) cases.

Among the SRNS cases 2 were evaluated by Nephrologist by doing renal biopsy and diagnosed to have Membrano Proliferative Glomerulo Nephritis (MPGN), while the other did not undergo evaluation. Analysis of baseline investigative parameters is shown in Table 1.

Urine culture	Number of cases	Percentage
Growth	17	34
No growth	33	66
Total	50	100

Table 2: Urine culture and sensitivity (n=50)

The present study of Urinary Tract Infection in children with Nephrotic Syndrome has revealed positive growth and isolation of bacterial organisms in 17 cases. No growth was observed in 33 cases. As shown in Table 2.

Age group (years)	Sex		Total	
	Male	Female	No.	%
<2	00	00	00	00
2-6	10	05	15	88
6-12	01	01	02	12
Total	**11**	**06**	**17**	**100**

Table 3: Age and sex distribution of UTI

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UTI was observed in 17 cases among them 11 cases were males and only 6 cases were females. The age group affected to the maximum extent was from 2-6 years contributing 88% out of 17cases, as shown in Table 3.

Micro-Organisms	Number of cases	Percentage
Escherichia coli	6	12
Staphylococcus aureus	5	10
Klebsiella	2	4
Proteus	1	2
Citrobacter	1	2
Acenetobacter	1	2
Enterobacter	1	2

Table 4: Spectrum of Bacteria (n=50)

In this study, among the 34% of the cases of urinary tract infection, 12% were caused by Escherichia coli, 10% were caused by Staphylococcus aureus, 4% were caused by Klebsiella whereas 2% cases of each was caused by Proteus, Citrobacter, Acenetobacter and Enterobacter species, as shown in Table 4.

DISCUSSION: In the present study is conducted among 50 children with nephrotic syndrome, the age distribution of cases ranged from 2 years to 11 years. The mean age in the present study was 4.7 years. Male**:** female ratio was noted to be 1.5**:**1. Similar observations were made by Adeleke S[4] Senguttuvan P.[5] 58% of patients presented as first episode of Nephrotic Syndrome, 24% had infrequent relapse, 18% had frequent relapse. Among the frequent relapsers, one patient had Cushingoid features like moon facies, two patients developed hypertension. The duration of symptoms prior to the presentation ranged from 3 days to 14 days.

Among them, 44% presented within 7 days, 46% from 7-10 days and 10% of cases had duration of symptoms for more than 10 days prior to the arrival to hospital. Among the patients who presented late, two cases had pyoderma. 80% patients presented with decreased frequency and volume, whereas 20% cases had normal frequency and volume. Appearance of the urine was normal in 70%, cloudy in 14% and red in 16% of the cases.

Burning micturition was observed in 8% of cases presented with history of decreased frequency and volume of micturition. Abdominal distension was observed in 78% cases. Four patients presented with respiratory distress, two had massive edema (pleural effusion and massive ascitis), one had pneumonia and one was a known case of hyper reactive airway disease, a total of 8% of the cases. Vomiting was observed in 8% of the cases.

Abdominal pain was present in 20% of the cases. Fever was present in 20% of the cases. Pyoderma was observed in 2 cases. it is observed that history of similar illness in the past in 34% of the patients of which 20% cases had 1st episode of Nephrotic syndrome in the past. History of contact with TB was present in 2 cases. Hyper tension was noted in 3 cases (6%) prior to initiation of steroid therapy but all of them responded well.

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Similar observations were made by Malla T et al[6], Nasir Uddin et al[7] and Ibadin MO.[8] Pitting type of edema was noticed in all the patients in the present study. Massive edema with ascitis was present in 60% of cases and mild edema in 40% of the cases. Periorbital and lower limb edema was seen in all cases. Abdominal wall edema was observed in 22% of the cases and genital edema in 16%.

This study (N=50) observed Urinary tract infections in 34% of the cases, Tuberculosis was seen in 6% of the cases. Hepatomegaly was found in one case and 8% of the cases presented with Respiratory distress. Similar observations were made by Gulati S et al., 1995[9], Sarker MN et al., 2005[10]. In the present study 76% of the cases were steroid responders and 24% of the cases were non-responder to steroid therapy. Similar observations was made by Kim JS et al., 2005.[11]

Kim JS et al. have evaluated the children aged from 1-18 years and have found that steroid resistance is more likely in African, American children and in children with older age of onset (11.5 years). Baseline parameters were within normal range.

Studies of various Authors	case No.	E COLI) Escherichia coli	Staphylococcus aureus	Klebsiella	Proteus	Citrobacter	Acenetobacter	Enterobacter	Others
Present Study	**50**	**06**	**05**	**02**	**01**	**01**	**01**	**01**	**00**
Gulati S et al., 1995	154	18	01	03	02	00	00	00	06
Adeleke SI, 2006	42	00	19	05	00	00	00	00	04
Senguttuvan P, 1998	199	73	00	52	00	00	00	00	25
Odedoyin OT, 2004	32	03	06	03	00	00	00	00	00
Emilla Maria, 1998	92	04	00	02	00	00	00	01	02
Ibadin MO, 1995	58	06	16	00	00	00	00	00	04

Table 5: Comparison of micro-organisms isolated with other studies

Pyuria (pus cells >10 per high power field (HPF) on random urine sample)was observed in 48% (24) of cases and absence of pyuria (pus cells <10 per HPF on random urine sample) was observed in 52% (26) of the cases. Similar observations were made by Odedoyin OT, 2010[12]. 12% of cases showed presence of haematuria in our study.

Similar observations were made by Siegal NJ et al., 1972[13]. Among six of these cases with microscopic haematuria, four 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 have observed that microscopic haematuria may be either asymptomatic or accompany UTI.

Urine total protein in a timed 24 hour sample the range observed was 1.8-7.9 gms/24 hour with a mean value of 3.9 gm/24 hour as against a mean of 4.6gm/24hr by Iyer RS et al.1991[14]. Urinary Tract Infection was noted in 34% of cases in the present study.

12% were caused by Escherichia coli, 10% were caused by Staphylococcus aureus, 4% were caused by Klebsiella whereas 2% of each was caused by Proteus, Citrobacter, Acenetobacter and Enterobacter species. Similar observations were made by the following studies as in Table 5.

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CONCLUSION: Urinary Tract Infection is a significant infection detected in cases of Nephrotic Syndrome affecting one third of the cases. Early detection and prompt treatment with appropriate antibiotics will play a major role in preventing the morbidity and mortality. Further, it avoids the relapse and facilitates early remission of Nephrotic Syndrome.

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