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Original Article

Urinary tract infection at presentation of nephrotic syndrome: A clinical evaluation

B Sreenivasa[1], C L Srinivasa Murthy[1], K Raghavendra[1], S P Basavanthappa[1], Rajath Pejaver[1], Hareesh Vardhan Jadala[1], Somarouthu Rajashekar[2]

From Departments of [1]Pediatrics, [2]Preventive and Social Medicine, Basaveshwara Medical College Hospital, Chitradurga, Karnataka, India

Correspondence to: Dr. C L Srinivasa Murthy, Department of Pediatrics, Basaveshwara Medical College Hospital and Research Centre, Chitradurga - 577 501, Karnataka, India. Phone: +91-9590385655, E-mail: clsrinivasamurthy@gmail.com

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Abstract

Aims: The aim was to study the incidence, etiology, clinical features and the antibiotic sensitivity pattern of urinary tract infections (UTI) in children at presentation of nephrotic syndrome (NS) (first or recurrent episodes before starting immunosuppressive therapy). **Methods:** This was a prospective hospital-based study carried out in Basaveshwara hospital, Chitradurga. Fifty children with a diagnosis of NS were studied from June 2010 to October 2014. The cases with recurrence of NS or those with the first episode of NS were evaluated before placing on immunosuppressive therapy. A clean-catch midstream urine specimen was collected from all children to avoid contamination. For younger children, where collection of urine was difficult in the manner described above, suprapubic aspiration was done. Prompt plating of the urine specimen, within 1-h of a collection, was ensured. Identification of the organism and antibiotic sensitivity patterns was determined. **Results:** Among the fifty children studied, boys were affected more than the girls with a ratio of 1.5:1. The mean age was 4.75 years. Pyuria was noted in 64% of the patients. The most common organism isolated was *Escherichia coli* in 10 cases, followed by *Klebsiella pneumoniae* in 4 cases. About 75% of the organisms were sensitive to third-generation cephalosporins. **Conclusions:** UTI is a common infection accompanying NS. A high index of suspicion and early institution of appropriate antibiotics will help in attenuating morbidity and mortality.

Key words: *Escherichia coli, Nephrotic syndrome, Pyuria, Urinary tract infections*

In India, idiopathic nephrotic syndrome (NS), congenital renal anomalies, systemic renal diseases and urinary tract infections (UTI) are of similar prevalence and pattern to those reported from Europe and the United States [1]. NS is characterized by edema, low serum albumin, hyperlipidemia and proteinuria. The course of NS is often complicated by frequent relapse, steroid resistance, thrombosis and infections [2]. The common infections seen in NS are pneumonia, UTI, bacteremia, septicemia, peritonitis, and cellulitis [3]. UTI is often underdiagnosed in NS and may also be responsible for poor response to steroid therapy. Some studies have shown that UTI is the most common infectious complication of NS [4,5]. However, other studies suggested that the incidence of UTI is low in the first episode and high following relapses of NS [6-9]. Hence, we planned this prospective hospital-based study to determine the number of culture-positive UTI and to determine the type of organism and their sensitivity patterns.

METHODS

This prospective hospital-based study was conducted in the department of pediatrics of Basaveshwara Medical College Hospital, Chitradurga between June 2010 and October 2014. All patients below the age of 12 years with clinical and laboratory evidence of NS, who were not on steroids or other immunosuppressive therapy at the time of presentation to hospital were enrolled in the study. The following children were excluded from the study: (1) Children more than 12 years of age; (2) patients already on steroids, immunosuppressives and antibiotics and (3) children with gross urogenital anomalies. Ethical clearance was sought from institutional ethical committee. Informed written consent and where applicable assent was taken from parents and patients for participation in the study.

A clean-catch midstream specimen was used to minimize the contamination by periurethral flora. Contamination was minimized by washing the genitalia with soap and water. Antiseptic washes and forced retraction of the prepuce were not advised. For younger children, where collection was difficult in the manner described above, suprapubic aspiration was done. The urine specimen was promptly plated within 1-h of a collection. If the delay was anticipated, the sample was stored in a refrigerator at 4°C for up to 12-24 h. Cultures of specimens

collected from urine bags were not used in our study. In the case of suspected contamination or in equivocal results, urine culture was repeated. Urine samples were collected before the first dose of antibiotic was given.

UTI was considered as the growth of one microorganism with colony count of $>10^5$ per ml. First episode NS was defined as a child presenting for the first time with nephrotic range proteinuria (3+ or 4+ urine albumin), hypoalbuminemia (serum albumin <2.5 g/dl), hyperlipidemia (serum cholesterol >200 mg/dl), and edema. Remission of NS was characterized by urine albumin nil or trace (or proteinuria <4 mg/m^2/h) for three consecutive early morning specimens. Relapse of NS was characterized by urine albumin 3+ or 4+ (or proteinuria >40 mg/m^2/h) for three consecutive early morning specimens, having been in remission previously.

Antibiotics treatment with ceftriaxone was started in symptomatic cases with abnormal urine microscopy, which was later changed according to sensitivity pattern and continued for 10-14 days. Data was analyzed using means, frequencies, and percentages.

RESULTS

We collected data from 50 NS patients; out of these, 35 (70%) cases presented as first episode and 15 (30%) came with relapse. Table 1 shows the baseline characteristics of the study cohort. Fever was present in 09 (18%) cases, dysuria was observed in 04 (8%), and abdominal pain was present in 5 (10%) patients, while none of the patient had gross hematuria. All children had blood pressure in the normal range. No costovertebral angle tenderness was present in any of the children studied.

All patients underwent urine microscopy, culture, and sensitivity. The results of urine routine analysis are shown in Table 2. The mean specific gravity was 1.028 (1.010-1.060) and mean urinary pH was 6.8 (5.8-7.8). Pyuria with more than 10 pus cells was seen in 31 (64%) of patients. Sensitivity and specificity of pyuria (> 10 pus cells/HPF) for diagnosing UTI in NS was 95% and 56.7% respectively (Table 1). No child had red blood cell casts on urine microscopy.

Urine culture for bacterial organisms was positive in 20 (40%) cases (Table 3). *Escherichia coli* was the most common organism isolated in 10 (50%) cases followed by *Klebsiella pneumoniae* species cultured in 4 (8%) of cases. Their antibiotic sensitivity pattern is shown in Table 4. About 75% of organisms were sensitive to ceftriaxone followed by gentamicin in 70% of an organism. In our study, cefuroxime sensitivity was present in only 5% of organisms.

DISCUSSION

UTI is seen in 1/10 girls and 1/30 boys by the age of 16 years in the general population [10]. NS represents an immunocompromised state, predisposing patients to various infectious complications including UTI [2,5,11]. Pyuria was one of the common findings in our study seen in 64% of the study patients. However, a mere presence of pus cells does not signify the presence of UTI [10]. Properly collected urine culture sample is considered as the standard reference method for the diagnosis of UTI [10].

UTI was noted in 40% of cases in the present study; a relatively high incidence of UTI when compared to other studies. Various studies have reported varied incidence of UTI ranging from 13.8% by Gulati et al. to 21% incidence by McVicar et al. to as high as 66.7% in a study conducted by Adeleke et al. [4-6,9,12,13]. Relative high incidence of UTI seen in our study may be secondary to difference in race, nutritional and immune status of the participants [14].

The commonest organism isolated in our study was *E. coli* followed by *K. pneumoniae*; while *Citrobacter* and *Enterobacter*

Table 1: Characteristics of nephrotic syndrome in children with and without UTI

Characteristics	Nephrotic syndrome cases without UTI (n=30) (%)	NS with UTI (n=20) (%)	Total number of cases (n=50) (%)
Age			
<2 years	3 (10)	0 (0)	3 (6)
2-6 years	23 (76.7)	14 (70)	37 (74)
>6 years	4 (13.4)	6 (30)	10 (20)
Sex			
Males	18 (60)	12 (60)	30 (60)
Females	12 (40)	8 (40)	20 (40)
First episode NS	21 (70)	14 (70)	35 (70)
Relapsed NS	9 (30)	6 (30)	15 (30)
Pyuria			
>10 pus cells/HPF	13 (43.3)	19 (95)	32 (64)
<10 pus cells/HPF	17 (56.7)	1 (05)	18 (36)

UTI: Urinary tract infection, NS: Nephrotic syndrome

Table 2: Urine microscopy findings of patients with nephrotic syndrome

Urine microscopy	Number (%)
Appearance	
Normal and clear	35 (70)
Cloudy	12 (24)
Straw colored	3 (06)
WBC casts	14 (28)
Epithelial cells	25 (50)
Microscopic hematuria	10 (20)
Pyuria (cells/HPF)	
Less than 10 cells	18 (36)
More than or equal to 10 cells	32 (64)

WBC: White blood cell

Table 3: Spectrum of bacteria in urine cultures

Organisms	Number of cases (n=20)	Percentage
E. coli	10	20
K. pneumoniae	4	8
S. aureus	3	6
P. mirabilis	1	2
Citrobacter	1	2
Enterobacter	1	2

E. coli: Escherichia coli, K. pneumonia: Klebsiella pneumonia, S. aureus: Staphylococcus aureus, P. mirabilis: Proteus mirabilis

Table 4: Antibiotic sensitivity pattern of the organisms isolated in the present study

Micro organisms	Antibiotic sensitivity
E. coli	Cefotaxime, Ceftriaxone, Ciprofloxacin, Gentamicin, Norfloxacin, Ofloxacin
K. pneumoniae	Gentamicin, Ciprofloxacin, Ceftriaxone
S. aureus	Linezolid, Vancomycin, Ciprofloxacin
P. mirabilis	Cefuroxime, Amikacin, Azithromycin
Citrobacter	Cefotaxime, Ciprofloxacin, Norfloxacin
Enterobacter	Amikacin, Ceftriaxone

E. coli: Escherichia coli, K. pneumonia: Klebsiella pneumonia, S. aureus: Staphylococcus aureus, P. mirabilis: Proteus mirabilis

were isolated occasionally. In comparison to the study conducted by Gulati et al., [4] where non-*E. coli* organisms accounted for only 39% of the culture isolates, our study had shown relatively high incidence of non-*E. coli* in up to 50% of the cases. In another study, conducted by Adeleke et al., urine infection by *Staphylococcus* was most common followed by *Klebisiella* [6]. A study conducted in China had shown enterococcus as the most common organism followed by *E. coli* [7].

The majority of the organisms in our study were sensitive to third-generation cephalosporins and aminoglycosides, whereas staphylococci were sensitive to vancomycin and ciprofloxacillin. These results were similar to the study conducted by Adeleke et al. and by Song et al. [6,7]. UTI, if left untreated, can cause long term complications such as reflux nephropathy, hypertension, and chronic renal failure [15]. The high incidence of UTI obtained in the present study and its long-term implications warrants early and aggressive treatment [15]. It can be advocated that routine urine cultures should be carried out on patients with NS, especially in cases with relapse and early and aggressive therapy with appropriate antibiotics should be used to attenuate morbidity and mortality.

The major limitation of our study was that we could not evaluate the underlying cause of UTI; therefore, whether it was related to immunosuppression induced by the disease per se or any other factors is not clear and needs more investigation. Second, we did not evaluate the congenital anomalies as the cause of UTI. It was necessary to do ultrasonography and in special cases voiding cystourethrogram to rule out these congenital anomalies. Further studies are needed in cases of NS with UTI to define the role of urological anomalies in these cases.

CONCLUSION

UTI is a common complication detected in cases of NS in children. Although, *E. coli i*s the common organism isolated in children with NS and UTI, non-*E. coli* is present in half the cases and therefore urine cultures and sensitivity patterns with appropriate adjustment of antibiotic choices are necessary.

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