

## The Prevalence of Urinary Tract Infection in Childhood Nephrotic Syndrome

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### Summary

**Ibadin MO. The Prevalence of Urinary Tract Infection in Childhood Nephrotic Syndrome.** *Nigerian Journal of Paediatrics* 1997; 24:40. A retrospective analysis of hospital records of 89.2 percent of 65 paediatric patients with nephrotic syndrome (NS) admitted into the University of Benin Teaching Hospital (UBTH), between January 1992 and December 1996 was undertaken for the prevalence of urinary tract infection (UTI), causative organisms, pattern of *in-vitro* antibiotic sensitivity and the effect on patients' management. Urinary tract infection prevalence of 44.8 percent in this small series was high compared with that of 0.04 percent for the general population. Similarly, the 42.1 percent of males in the present study was in contrast to 0.04 percent, as seen in the general population. Presence of UTI did not influence the response to steroid therapy ( $p>0.05$ ), duration of hospitalization ( $p>0.05$ ) and the incidence of relapse ( $p>0.05$ ). UTI was caused predominantly by *Staphylococcus aureus* in 54.3 percent and untyped coliform organisms in 31.4 percent of the cases. There was high *in-vitro* resistance of these organisms to nalidixic acid, ampicillin and nitrofurantoin, but sensitivity to gentamicin, streptomycin, ceftazidime and cefuroxime. In view of the long term morbidity associated with UTI, it is recommended that UTI be sought for, in patients with NS and treated promptly and appropriately. In communities with inadequate or lack of laboratory facilities for bacteriological studies and sensitivity patterns, empirical use of any of gentamicin, streptomycin, ceftazidime and cefuroxime may be justified.

### Introduction

URINARY tract infection (UTI), a leading cause of childhood morbidity and mortality, is one of the commonest renal diseases in childhood.<sup>1-3</sup> The prevalence of UTI varies from 4.0 percent in the neonatal period to 0.4 percent in the school and pre-school-age children.<sup>4</sup> Among patients with nephrotic syndrome (NS), another common childhood renal disorder, the prevalence of UTI is high.<sup>5</sup> Gulati *et al*<sup>5</sup> have reported a prevalence of 13.7 percent, while 21.0 percent was reported by McVicar *et al*.<sup>6</sup> The increased prevalence of UTI in patients with NS is variously ascribed to immunoglobulin loss in the urine,<sup>7</sup> defective T-cell function, presence of ascites and relative malnutrition.<sup>7</sup>

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<sup>8</sup> UTI has also been reported to adversely influence the response of patients with nephrotic syndrome to corticosteroids.<sup>9</sup> Mc Vicar *et al*,<sup>6</sup> however, did not find any relationship between UTI and response to steroid therapy. UTI has also been shown to have no role in the incidence of relapses<sup>6</sup> in nephrotic syndrome.

The above cited studies were carried out mainly on caucasian populations, but there are important differences in the epidemiology and histopathology between the NS in caucasians and those in Africans.<sup>10 11</sup> Unlike in the caucasians, there is a high incidence of secondary NS in Africans caused mainly by quartan malaria nephropathy.<sup>10 11</sup> Since the prevalence of UTI among patients with secondary NS is unknown, the present study was undertaken to evaluate the prevalence of UTI, its aetiological agents, *in-vitro* antibiotic sensitivity

pattern to the organisms and the outcome in patients with NS. The influence of UTI on the course of NS during corticosteroid treatment and relapses was also studied.

### Patients and Methods

A retrospective analysis of case notes of all the patients with nephrotic syndrome (NS) admitted to the paediatric wards, University of Benin Teaching Hospital (UBTH) between January 1992 and December 1996 was undertaken. Age, sex, results of urinalysis on admission, results of urine culture, response to corticosteroid therapy and duration of treatment, *in-vitro* antibiotic sensitivity pattern of isolated organisms and the duration of follow-up were also recorded. Urine specimens from children with NS were routinely obtained by the clean-catch method following careful preparation of the urethral orifices and were collected into sterile plastic-capped containers and promptly transported to the laboratory. The specimens were either processed immediately, or stored at 4°C until processed within 12 hours of collection. Specimens were incubated on sheep-blood agar and eosin methylene blue agar, using the quantitative loop method. The plates were examined at 24 and 48 hours. A yield of multiple organisms was considered as contaminant. Pus cell count of over five per high power field was considered suggestive of UTI. In all cases however, UTI was later confirmed by the demonstration of significant bacteriuria.

Such suspected cases of UTI were routinely placed on nalidixic acid or nitrofurantoin or gentamicin, pending culture reports, while treatment continued for seven to 10 days with the same antibiotic unless otherwise indicated. Patients with NS were routinely offered a four-to-six weeks course of corticosteroid therapy. Non-responders were treated with cyclophosphamide and low-dose steroid, unless there was contraindication, or development of adverse reactions. The chi squared test with Yates correction and Student's 't' test respectively, were used for statistical analysis.

### Results

In the present small series, 58(89.2 percent) of

the 65 patients with NS were analysed as records were incomplete in seven (10.8 percent) others. The 58 patients consisted of 38 (65.5 percent) males and 20 (34.5 percent) females (a male to female ratio of 1.9:1). The mean age and SEM for males was  $8.3 \pm 0.6$  years compared with  $8.0 \pm 0.9$  years for females (age range, two to 15 years). Thirty six (62.1 percent) of the 58 patients were aged seven years and above. The age and sex distribution of the patients is as shown in Table I.

Table I

Age Groups and Sex Distribution in 58 Patients with Nephrotic Syndrome

Group (years)	Sex		Total No of Cases	Percent of Total
	Male	Female		
1 - 3	2	4	6	10.4
4 - 6	12	4	16	27.6
7 - 9	12	4	16	27.6
10 - 12	5	5	10	17.2
13 - 15	7	3	10	17.2
Total	38(65.5)	20(34.5)	58	100.0

Figures in parentheses represent percentages.

There were 35 episodes of UTI in 26 (44.8 percent) of 58 patients with NS. Sixteen (42.1 percent) of 38 males in comparison with 10 (50.0 percent) of 20 females had UTI. Eight (30.8 percent) of the 26 patients had more than one episode of UTI. *Staphylococcus aureus* in 19 instances (54.3 percent) and untyped coliform organisms in 11 (31.4 percent) were the commonest causative organisms of the UTI. Other causative organisms included *Klebsiella* species on three occasions (8.6 percent) and *Pseudomonas* species in two instances (5.7 percent). The *in-vitro* sensitivity patterns of isolated organisms to various antibiotics is as shown in Table II. All the *Staphylococcus aureus* organisms and the untyped coliform organisms were 100 percent sensitive to ciproxin, cefotaxime and amikacin. However, *in-vitro* sensitivity of the same organisms to commonly used antibiotics, including ampicillin, cotrimoxazole and nalidixic acid was 33.3 percent or less. Gentamicin and streptomycin offered 100 percent coverage for the untyped coliform organisms.

Table II

***In-vitro Sensitivity Patterns of Bacterial Isolates to Antibiotics***

Antibiotics	Isolates of	Percent	Isolates of	Percent	Isolates of	Percent	Isolates of	Percent
	<i>Staph. aureus</i>	sensitivity	coliforms	sensitivity	<i>Klebs. spp</i>	sensitivity	<i>Pseudo. spp.</i>	sensitivity
Nalidixic Acid	16	25.0	8	25.0	-	-	1	0.0
Nitrofurantoin	12	83.3	6	33.3	2	0.0	-	-
Tetracycline	17	0.0	11	0.0	2	0.0	2	0.0
Ampicillin	10	20.0	10	33.3	3	0.0	-	-
Sultamicillin	3	100.0	3	100.0	-	-	1	100.0
Cloxacillin	2	0.0	-	-	-	-	-	-
Cotrimoxazole	12	33.3	2	0.0	-	-	-	-
Erythromycin	3	0.0	-	-	1	0.0	1	0.0
Gentamicin	12	66.6	10	100.0	1	100.0	2	100.0
Ciproxin	3	100.0	4	100.0	1	100.0	-	-
Cefotaxime	4	100.0	5	100.0	-	-	-	-
Ceftriaxone	6	66.0	4	100.0	-	-	-	-
Amikacin	4	100.0	-	-	1	100.0	2	100.0
Streptomycin	14	42.8	3	100.0	-	-	-	-
Ceftazidime	8	75.0	2	100.0	-	-	1	100.0

*Staph aureus* = *Staphylococcus aureus*

*Klebs. spp* = *Klebsiella* species

*Pseudo spp.* = *Pseudomonas* species.

Table III

***Relationship between Steroid Responsiveness, Sex, Occurrence of Relapse, and Presence of UTI***

	Positive Urine Culture	Negative Urine Culture	P value
Males	16	22	>0.05
Females	10	10	
Steroid resistant	14	14	>0.5
Steroid responsive	12	18	
Relapsers*	10	8	>0.5
Non-relapsers	2	10	

\* 28 cases were steroid-resistant and were therefore, not evaluated for relapse

The mean and SEM duration of treatment for patients with NS and UTI ( $37.5 \pm 2.7$  days) was not significantly different from that of patients without

associated UTI ( $32.9 \pm 1.5$  days) ( $t=0.88$ ;  $p>0.05$ ). Mean periods and SEM of treatment and follow-up of the 58 patients were  $35.2 \pm 1.5$  days and  $7.4 \pm 1.2$  months, respectively. Twenty eight (48.3 percent) of the 58 patients with NS were steroid-resistant, while 30 (54.9 percent) were steroid-responsive after the first course of steroid therapy lasting 28 days. Of the 30 steroid-responsive patients, 14 (46.7 percent) relapsed within the first six months of follow-up. Two patients (3.5 percent) died of septicaemia and suspected thromboembolic phenomena during hospitalization. Analysis of the relationship between steroid responsiveness, sex, occurrence of relapses and the presence or absence of UTI (Table III) showed that the presence of UTI did not affect steroid responsiveness to treatment ( $X^2 = 0.25$ ;  $p>0.05$ ), or relapses ( $X^2 = 3.06$ ;  $p>0.05$ ).

**Discussion**

In the present study, 44.8 percent of the 58 patients with NS had UTI, a high prevalence of UTI among patients with NS that had also been reported by other workers.<sup>5,6</sup> While Gulati *et al*<sup>5</sup> reported 13.8 percent, McVicar *et al*<sup>6</sup> reported a prevalence of 21.0 percent in comparison to the 44.8 percent in our series. The differences in the types of NS

seen in our local population as compared to those in caucasians may account for the varying prevalence rates of UTI in patients with NS, as it is possible that impaired immunity associated with NS is more marked in patients with secondary NS. Over 62 percent of our patients were aged seven years and above which makes them unlikely to have primary NS.<sup>12</sup>

Unlike in the general population where post-neonatal UTI is relatively rare in males,<sup>9</sup> sex did not influence the development of UTI. Our patients were not radiologically assessed for urological anomalies, but it is possible that the immune compromise associated with NS is not sex discriminatory, which could explain the increased prevalence of UTI in males.

Unlike in an earlier report<sup>9</sup> where the presence of UTI was noted to influence negatively, the course of NS and relapse, the presence of UTI in our study did not affect response or relapse. Our finding is in consonance with that of McVicar *et al*<sup>6</sup> who reported no relationship between UTI and the course of NS.

*Staphylococcus aureus* was the commonest organism comprising 54.3 percent of the isolates followed by coliform organisms (31.4 percent). The present findings are in contrast to those of Tsau *et al*<sup>13</sup> who reported Gram-negative bacilli as the predominant cause of infections, including UTI, in patients with NS. Indiscriminate use and misuse of antibiotics known to cause selective repression of sensitive strains of bacteria and emergence of resistant ones, could account for the regional differences in the aetiological bacterial agents reported. Although the sensitivities of *Staphylococcus aureus* and untyped coliform organisms to ceftazidime, cefotaxime, ceftriaxone and ciproxin were close to 100 percent, their sensitivities to commonly used antibiotics such as nalidixic acid and ampicillin were low. Gentamicin and streptomycin offered 100 percent coverage for coliform organisms, but much lower rates for *Staphylococcus aureus*. The increasing trend to resistance by common bacteria to routinely used antibiotics have been noted by other workers in the country.<sup>14 15</sup> The common practice of self medication, use of fake and substandard drugs and drug abuse could explain this trend.

Prompt treatment of any associated UTI in our patients could have masked the probable effect of the disease on the course of NS. Nevertheless, the high prevalence of UTI as obtained in the present

study and its known long-term complications warrant its aggressive management. Where laboratory facilities are available, routine urine cultures should be carried out on patients with NS, otherwise, the empirical use of gentamicin or streptomycin or other appropriate antibiotics in such patients should be seriously considered.

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