

Prevalence of Urinary Tract Infection in Nephrotic Syndrome

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ABSTRACT

Objective: To assess the prevalence of urinary tract infection in nephrotic syndrome.

Design: A descriptive study.

Place and Duration of study: Department of Pediatric Medicine, Combined Military Hospital, Lahore, Pakistan. January 2003 to December 2009.

Patients and Methods: During the study, all children with nephrotic syndrome, irrespective of the stage of their disease, were evaluated for the presence of UTI with a 12 month follow up period. The ages ranged between 1-14 years.

Results: Out of the included 70 cases, between 1-14 years of age, 47 (67.1%) were boys and 23 (32.8%) girls in a ratio of 2.04:1. Twenty one patients were newly diagnosed and the remaining 49 children were known cases of nephrotic syndrome. Pyuria was seen in 22 (31.4%) cases, Covert bacteriuria in 32 (45.7%) and culture positive UTI in 18 (25.7%). Of the 18 culture positive cases, 13 (72.2%) cases had primarily presented with a relapse, being treated with various immunosuppressive agents. *Escherichia coli* was the commonest pathogen grown in 38.8% of the culture positive cases.

Conclusion: UTI may be a significant co-existing infection in children suffering from NS. It is usually difficult to diagnose but needs early recognition and treatment.

Key Words: Urinary Tract Infection. Nephrotic Syndrome.

INTRODUCTION

Nephrotic Syndrome (NS) is the commonest and leading glomerular disease in children [1]. The disease has a well-recognized and increased susceptibility to infections, usually attributed to defective T-cell function in addition to the loss of immunoglobulins, properdin and decreased factor B concentration as a result of heavy nephrotic range proteinuria. Antibody formation may be inhibited by the soluble immune response suppressor (SIRS) factor. Defective complement system, abnormal lymphocyte function, low zinc levels, functional hyposplenism and relative malnutrition may also be amongst the important predisposing factors [2, 3, 4, 5, 18, 19]. The prevalence of urinary tract infection (UTI) in NS patients has been widely reported in the international literature, but presently very little is found on this subject in the local data [6, 7, 8]. In nephrotic syndrome, the urinary tract is quite frequently affected by occult and symptomatic bacterial infections. Moorani (2003), Gulati et al and McVicar et al have reported UTI prevalence rates of 12.1%, 23.2%, and 21% in their respective series [8, 9, 10]. The symptoms of UTI in children are often non-specific and atypical. About 50% of

the patients may not complain of any urinary symptoms such as foul smelling or turbid urine, dysuria and systemic symptoms like fever, suprapubic or flank pains, increased frequency etc. This is particularly true during treatment of NS as the general symptoms and signs of infection are often masked because of the iatrogenic immunosuppression and the diagnosis may be delayed or uncertain due to difficulties in obtaining reliable urine sample in children and culture facilities [11, 20]. There is a clinical significance related to the presence of UTI in NS in terms of poor response to corticosteroid therapy and a possible tendency to relapse frequently [12]. The present study was designed with an objective to assess the prevalence of UTI in our NS patients.

PATIENTS AND METHODS

This descriptive study was conducted in the Department of Pediatric Medicine, Combined Military Hospital, Lahore, between January 2003 and December 2009. With an informed parental consent, the study sample included all children between 1-14 years of age with a diagnosis of NS. Exclusion Criteria: 1. Children with co-morbid conditions like acute or chronic renal

failure. 2. Associated anomalies/abnormalities or stones of urinary system. 3. Antibiotic treatment in preceding 2 weeks.

Besides the standard clinical and laboratory work-up, monitoring and treatment of the disease in all cases, first morning mid-stream urine samples were collected by clean catch method in sterile universal bottles, irrespective of the presence or absence of urinary symptoms such as smelly turbid urine or dysuria. In 7 patients, bag specimens had to be collected under sterile precautions on account of poor parental co-operation. The urine specimens were sent to the hospital laboratory for routine examination (naked eye, biochemical & microscopy) and culture. Laboratory diagnosis was established by the presence of significant pyuria, bacteriuria and 10^4 - 10^5 colony forming units (CFUs)/ml in urine culture. Multiple micro-organisms grown in culture were considered as most likely contaminants. All the patients were followed up for a period of 12 months with the help of urine routine examination and culture every 4-8 weeks. Due to a descriptive study design, inferential statistics were not applicable while data calculations were analyzed by using the latest SSP version.

Operational definitions:

Nephrotic Syndrome: Generalized edema, Proteinuria >2 grams/day, Hypoalbuminemia <2.5 grams/dl, Hypercholesterolemia >200 mg/dl.

Relapse: albuminuria 3+ or 4+ by dipstick or >40 mg/m²/h in three consecutive morning specimens, having been in remission previously.

Dysuria: burning sensation or pain on micturition.

Pyuria: 10 or more neutrophils per high power field of freshly voided, centrifuged urine.

Covert Bacteriuria: 10 or more bacteria per high power field or a count of 10^4 - 10^5 CFUs/ml of freshly voided, centrifuged urine.

Positive Urine Culture: Growth of a single identifiable organism after 24 hours of incubation.

RESULTS

Amongst the 70 children who met inclusion criteria of the study, there were 47 (67.1%) boys and 23 (32.8%) girls in a male to female ratio of 2.04:1. Twenty one were newly diagnosed cases whereas 49 were known NS patients. Of the 49 known cases, 33 were steroid sensitive, 10 were steroid dependent and 7 patients were steroid resistant. Their ages ranged between 1-14 years with a mean age of 5.2 years (± 0.5 SD). Mean age for boys was 7.3 years (± 0.2 SD) and for girls 6.9

years (± 0.8 SD) [Table: 1]. Pyuria was found in 22 (31.4%) and 32 (45.7%) patients had covert bacteriuria mostly with Coliform organisms. Out of the 70 children, urine culture positive UTI was confirmed in 18 (25.7%) cases comprising 7 (38.8%) boys and 11 (61.1%) girls. All of them had significant covert bacteriuria. Comprising the 18 urine culture positive UTI cases, 5 (27.8%) were newly diagnosed NS patients while the remaining 13 (72.2%) were previously known cases. The later had primarily presented with a relapse and were being treated with steroids and/or 2nd line immunosuppressive agents such as cyclosporine-A or cyclophosphamide for different durations. The identifiable bacterial isolates in urine culture positive cases were Escherichia coli in 7 (38.8%), Proteus mirabilis in 3 (16.7%), Klebsiella species in 6 (33.3%) and Staphylococcus aureus in 2 (11.1%) cases [Table: 2].

Table 1: Distribution of age (n=70)

Mean age	5.2 years (± 0.5 SD)
Mean age boys (n=47)	7.3 years (± 0.2 SD)
Mean age girls (n=23)	6.9 years (± 0.8 SD)
Male/Female ratio (47:23)	2.04:1

Table 2: Culture +ve UTI and bacterial isolates (n=18)

Culture positive UTI	Boys 7 (38.8%)	Girls 11 (61.1%)	Total 18 (100%)
Escherichia coli	4 (28.5%)	3 (16.7%)	7 (38.8%)
Proteus	1 (05.6%)	2 (11.1%)	3 (16.7%)
Klebsiella	2 (11.1%)	4 (28.5%)	6 (33.3%)
Staphylococcus aureus	2 (11.1%)	2 (11.1%)	

DISCUSSION

Children suffering from NS are more prone to acquire a variety of serious systemic infections as compared to the general pediatric population. The International Study of Kidney Disease in Children (ISKDC) and other authors have reported Infection as the commonest cause of death in such patients. UTI may either be acquired by a hematogenous spread or as an ascending infection from the lower urinary tract [1, 11]. The relatively immunocompromised state associated with NS seems to be a strong predisposing factor for

increased incidence of UTI. Various factors that may be responsible for the increased susceptibility have already been accounted for [13, 18, 19, 20]. The present study shows an incidence of culture positive UTI in 25.7% of the included 70 patients. A number of comparable studies are available in the literature. Two studies from Africa by Adeleke (2009) Ibadin (1997) have reported an unusually high prevalence of UTI in 66.7% and 44.8% of their patients probably explained on account of a higher incidence of secondary NS due to quartan malarial nephropathy amongst the children in the tropics [6, 14]. Whereas another African study by Adedoyin (2010) reported a statistically very low prevalence in only 3% cases apparently due to an extremely small study sample [15]. Treatment induced immunosuppression in known NS patients has been related with an overall increased incidence of UTI. In the present study, we report a rather low incidence of UTI in 27.8% in the newly diagnosed NS cases whereas all the remaining cases with UTI (72.2%) were in a relapse being managed with high dose steroids or 2nd line immunosuppressive drugs such as cyclosporine-A or cyclophosphamide. Data from other studies on this subject also suggests somewhat similar prevalence figures of 12.5-44.8% [6, 7, 8, 9]. Moorani (2003) reported a relatively low incidence of NS related UTI (12.16%) as compared to the corresponding figures of 25.7% in our study [8]. UTI in general pediatric population is usually caused by Coliform bacteria, Klebsiella spp, Proteus mirabilis and Pseudomonas aeruginosa. Senguttuvan (2004) found 22.4% boys and 24.1% girls having UTI as the commonest infection followed by peritonitis in their series of NS patients. Escherichia coli was the commonest bacterial organism (36.6%) found in urine cultures [16]. These findings correspond well with our results showing the same organism in 38.3% cases. But another Indian study by Gulati et al (1995) reported an exceptionally high incidence of Escherichia coli growth in 60% of the urine cultures [9]. Staphylococcus aureus has been reported as the predominant UTI related pathogen in 67.9% and 54.3% cases in the two African studies respectively [6, 14] whereas Tsai et al (1991) have found Gram negative bacilli as the leading organisms in NS associated UTI [17]. On the other hand, Staphylococcus aureus was the least common pathogen identified in only 2 (11.1%) female children in our series [Table 2].

CONCLUSION

Contrary to the usual perception, UTI is not that uncommon in NS. Therefore, with the policy of keeping a high index of suspicion, we recommend periodic urine cultures be undertaken particularly in those patients who present with a relapse and are on immunosuppressive therapy, especially in girls.

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