

The risk of urinary tract infection in children with nephrotic syndrome

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Abstract

Background Urinary tract infections (UTI) may affect any part of the urinary system: the kidneys, ureters, bladder, or urethra. Nephrotic syndrome (NS) is the most common glomerular disorder in childhood, comprising a group of symptoms that include proteinuria, hypoalbuminemia, hypercholesterolemia, and edema. The prevalence of UTI in NS patients is high, around 25-66.7%. The increased prevalence of UTI in NS is due to immunoglobulin loss, defective T cell function, the presence of ascites, and relative malnutrition.

Objective To study the risk of UTI in children with NS.

Methods We performed a retrospective study of NS and UTI patients from January 2004 to December 2013 in the Division of Nephrology at Prof. Dr. R.D. Kandou Hospital, Manado. Data was collected from medical records. Diagnosis of UTI was made based on urine culture results. Diagnosis of NS was made based on the group of symptoms mentioned above. Analysis was done using Chi-square test with SPSS version 22 software.

Results Of 74 NS patients, 34 (46%) had UTIs. During the same study period, 117 patients had UTIs. NS was more common in boys (64.9%), while NS with UTI was more common in girls (67.6%). The most common organisms causing UTI in NS patients were *Escherichia coli* and *Citrobacter diversus* (23% each). Imipenem and amikacin were most commonly used antibiotics to which the bacteria were sensitive. Increased risk of UTI was significant in children with NS (OR 1.8; P=0.03).

Conclusion Children with NS are at significantly increased risk of UTIs. [Paediatr Indones. 2016;56:238-41. doi: 10.14238/pi56.4.2016.238-41].

Keywords: urinary tract infection, nephrotic syndrome, children

A urinary tract infection (UTI) is an infection in any part of the urinary system: the kidneys, ureters, bladder, or urethra.¹ A diagnosis of UTI is made if urine culture results from midstream urine reveal bacterial colonization >100,000 colonies/mL urine of a single bacterial type, or >10,000 colonies/mL urine, but accompanied by specific clinical UTI manifestations.² Nephrotic syndrome (NS) is the most common glomerular disorder in childhood, which include massive proteinuria (> 40 mg/m²/hour), hypoalbuminemia (< 2.5 g/dL), hypercholesterolemia (>200 mg/dL), and edema.^{3,4}

The prevalence of UTI in NS patients is high, due to immunoglobulin loss, defective T-cell function, the presence of ascites, and relative malnutrition.⁵ A study in Pakistan reported that UTI was the second most common infection in NS patients (25.2%), after bronchopneumonia (46.6%).⁶ Another previous study found the prevalence of UTI in NS patients in Yogyakarta to be 25%.⁷ The objective of this study was to study the risk of UTI in children with NS.

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Methods

We performed a retrospective study. The inclusion criteria were all children (aged 1-18 years) hospitalized at the Division of Nephrology in Prof. Dr. R.D. Kandou Hospital from January 2004 to December 2013 with complete medical records. Diagnoses of NS in this study were made for patients with massive proteinuria (> 40 mg/m²/hour), hypoalbuminemia (< 2.5 g/dL), hypercholesterolemia (>200 mg/dL), and edema. Concurrently, we identified patients with UTI. Diagnoses of UTI were made in patients with urine culture results (from mid-stream urine collection) revealing bacterial colonization >100,000 colonies/mL urine of one bacterial type. The exclusion criteria were comorbid renal disease such as acute glomerulonephritis, or chronic disease which causes immunocompromised conditions, such as severe malnutrition, pulmonary tuberculosis, or cancer. Subjects were taken retrospectively from medical records, from January 2004 to December 2013. Collected data included identity, urine culture results, and antibiotic sensitivity test results. Further analysis was done using Chi-square test with SPSS version 22 software. Results with P values < 0.05 were considered to be statistically significant.

This study was approved by the Ethics Committee Sam Ratulangi University Medical School, Manado.

Results

During the study period, there were 74 NS patients and 117 UTI patients (Table 1). Thirty-four children (46%) had both NS and UTI. The 74 NS patients comprised 48 (64.9%) males and 26 (35.1%) females (Table 2). Among the NS patients, UTI was more common in females (67.6%) compared to males (32.4%).

The most common organisms causing UTI in NS patients were *Escherichia coli* and *Citrobacter diversus* (23% each), followed by *Staphylococcus aureus*, *Proteus reigeri*, *Proteus mirabilis* (12% each), as well as *Enterobacter aerogenes* and *Staphylococcus epidermidis* (9% each). Antibiotic sensitivity tests revealed that the most common antibiotics to which bacteria were sensitive were imipenem and amikacin, followed by chloramphenicol, ciprofloxacin, meropenem, ofloxacin, and levofloxacin. The remaining cultures were sensitive to norfloxacin, fosfomycin, aztreonam, ceftazolin, cefepime, ceftriaxone, ceftacide, ertapenem, gentamicin, piperacilin/taxobactam, trimetoprim, linezolid, cefotaxime, nalidixid acid, and nitrofurantoin.

Chi-square analysis revealed a significantly increased risk of UTI in children with NS ($\chi^2=4.9$; OR 1.8; P=0.03).

Table 1. Number of UTI and NS patients

	UTI		Total
	Positive	Negative	
NS positive	34	40	74
NS negative	83	176	259
Total	117	216	333

Table 2. NS patients distribution based on age and gender

Age in years	Gender		Total, n (%) (N=74)
	Males, n (%) (n=48)	Females, n (n=26)	
0-3	8 (16.7)	5	13 (17.6)
3-6	12 (25)	6	18 (24.3)
6-9	10 (20.8)	6	16 (21.6)
9-12	12 (25)	8	20 (27)
12-15	6 (12.5)	1	7 (9.5)

Discussion

Urinary tract infections are common in children, as the second most common cause of morbidity in children, after respiratory tract infections. The prevalence ranges from 3-5% in females and is around 1% in males.¹ Nephrotic syndrome (NS) is a chronic disease often found in children, with an incidence of 2-4 cases per 100,000 children under 16 years of age each year.³ From this study, we found 117 UTI patients and 74 NS patients among children hospitalized in the Nephrology Division, Department of Child Health, Prof. DR. R. D. Kandou Hospital, Manado from January 2004 to December 2013.

Nephrotic syndrome can occur at any age, but it predominantly occurs in children aged 2-6 years, with a male: female ratio of 3:2.³ In our study, we found the most common age to be 9-12 years and gender predominance to be male, with a male: female ratio of approximately 2:1.

Infection easily occurs in NS patients as a result of the leakage of IgG and complement B and D factors in urine. Immunosuppressive agents also increase the risk of infection.³ Urinary tract infection, in particular, is common in NS patients. Besides the loss of immunoglobulin via urine, UTI may result from T cell dysfunction, ascites, and relative malnutrition in NS patients.⁵ In addition to UTI, other infections commonly found in NS are peritonitis, pneumonia, cellulitis, and fungal infection.³

In this study, UTI occurred in 34 of 74 NS patients (46%). Arcana *et al.*⁸ and Adeleke *et al.*⁵ reported UTIs in 42% and 66.7%, of NS patients, respectively. However, Moorani *et al.*⁶ and Ritonga⁷ found only 25%. Just as overall prevalence of UTI occurred more frequently in females, UTI in NS patients in our study occurred more frequently in females (67.6%, or 23/34 children) than in males.

Urinary tract infection is caused by bacteria, viruses, or fungi. The most common etiology of UTI, both symptomatic and asymptomatic, including in neonates, is *Escherichia coli*.¹ Subandiyah found that *Escherichia coli* was the etiologic agent in 48.9% of UTIs in both outpatient and hospitalized children in Saiful Anwar Hospital, Malang.⁹ Similarly, the most common causes of UTI were *Escherichia coli* and *Citrobacter diversus* (23% each, or 8/34 children) in our study. However, Adeleke *et al.* found *Staphylococcus aureus*

to be the most common cause of UTI in NS patients (67.9%).⁵ This difference may be due to location, which may lead to variations in bacterial trends.

Escherichia coli is part of the colon's normal flora. It can cause UTIs, but not all types of *Escherichia coli* have the ability to colonize the urinary tract. Only the uropathogenic type of *Escherichia coli* can invade anatomically normal urinary tracts.^{9,10}

The goal of UTI treatment in children is to eradicate the cause, eliminate clinical manifestations, and prevent kidney failure, as early as possible.¹¹⁻¹³ Most UTIs are caused by bacteria, hence the need for antibiotic treatment. Bacterial trends in populations easily change, which in turn change the antibiotic sensitivity trends at different times and places. Ideally, empiric antibiotic for UTI treatment is based on antibiotic sensitivity trends in the specific health centers.^{1,6} The problem, however, is that sensitivity testing can not always be done, and antibiotic treatment should be started immediately, while waiting for urine culture results. Antibiotics are generally given for 7-10 days, but by 48 hours clinical improvement usually has occurred and urine cultures performed after this time are sterile.¹¹⁻¹³

Subandiyah found that as the most common UTI cause, *E. coli* was sensitive to the antibiotics nitrofurantoin, nalidixic acid, cefotaxime, and amoxicillin-clavulanic acid.⁹ In our study, the cultured bacteria were most sensitive to the antibiotics amikacin and imipenem.

We found an increased risk of UTI in children with NS (OR 1.8; P=0.03). In contrast, Adeyodin *et al.* found a low prevalence of UTI in NS,¹⁴ but they did not analyze for a correlation between NS and UTI. A prospective, analytical study is recommended to confirm these results.

Conflict of Interest

None declared.

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