

## Prevalence of Urinary Tract Infection in Nephrotic Syndrome at Zagazig University Children Hospital

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### ABSTRACT

**Background:** Nephrotic syndrome (NS) is the most common chronic glomerular diseases in children. Nephrotic syndrome increases a child's susceptibility to infection. Urinary tract infection (UTI) is the second most common bacterial disease in children after upper respiratory tract infection.

**Aim of this work:** To find out the prevalence of UTI (either community acquired or hospital acquired) in NS children and to uncover the bacterial spectrum and their sensitivity pattern for selecting the empirical antibiotic therapy till the results of culture are awaited.

**Subjects and methods:** This study was descriptive cross sectional. 33 nephrotic syndrome cases were included in study. All patients were subjected to full history taking, complete clinical examination and investigations as urine analysis and urine culture. **Results:** The percentage of community acquired urinary tract infection (CA-UTI) was 57.6 % and hospital acquired urinary tract infection (HA-UTI) was 42.4 %. E. coli is the commonest organism causing UTI followed by klebsiella and proteus mirabilis. The isolated organisms showed resistance to many oral and parenteral antibiotics. Amikacin gentamycin may be the first option of empiric therapy while waiting for culture reports. **Conclusion:** Children with nephrotic syndrome are frequently predisposed to UTI and in most cases it is asymptomatic often undiagnosed. Identifying bacterial causes and their susceptibility pattern of UTI will help in selecting the empirical antibiotic therapy till the results of culture are awaited. Although dipstick and microscopic urinalysis can support the diagnosis of UTI, growth of a single type of bacteria on urine culture is the gold standard.

**Key words:** Urinary Tract Infection- Nephrotic Syndrome- Prevalence.

### INTRODUCTION

Nephrotic syndrome is most prevalent in children with chronic glomerular diseases. In children the incidence of this syndrome is 2-7 cases per 100.0000 <sup>(1)</sup>. Most (90 per cent) cases of nephrotic syndrome are idiopathic. The other 10 % have a secondary idiopathic nephrotic syndrome to glomerular or systemic diseases <sup>(2)</sup>. Nephrotic syndrome patients suffer from various complications such as infection, effusion, hypovolemia, hyperlipidemia and hypercoagulability <sup>(3)</sup>. When children suffering from nephrotic syndrome reach the pediatric ward in the hospital, it is essential to examine them first in order to avoid possible complications or immediate discovery of infections and to initiate appropriate therapy <sup>(4)</sup>.

Nephrotic syndrome makes the child more susceptible to infection. Urinary tract infection is the 2nd most common bacterial disease in children following infection of the upper respiratory tract and is the most prevalent bacterial infection that affects humans throughout their lives <sup>(5)</sup>.

Symptoms of the urinary tract infection differ in age and the younger the child the much more non-specific these symptoms are <sup>(6)</sup>.

The aim of this work was to find out the prevalence of UTI (either community acquired or hospital acquired) in NS children and to uncover the bacterial spectrum and their sensitivity pattern for selecting the empirical antibiotic therapy till the results of culture are awaited.

### SUBJECTS AND METHODS

#### Technical design:

**Study design:** A descriptive cross-sectional study, carried out at a Pediatric Nephrology Unit of Children Hospital and Medical Microbiology and Immunology Department, Faculty of Medicine, Zagazig University. It was carried out over a period of twelve months from February 2018 to January 2019.

**Subjects:** Thirty-three nephrotic syndrome cases were included in study. This study was designed to assess the prevalence of urinary tract infections (either community acquired or hospital acquired) and bacterial spectrum and their sensitivity pattern in children with nephrotic syndrome either newly diagnosed (1st attack) or relapsed cases of nephrotic syndrome attending at children hospital.



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**Ethical approval:**

The study was approved by the Ethics Board of Zagazig University and an informed written consent was taken from each participant in the study.

**Case definition:**

■ HA-UTI is a urinary tract infected patient that was not manifested or incubated at the time of admission. Infection may appear even after discharge (7).

■ CA-UTI has been defined as any urinary tract infection that tends to occur in the community, or as the second most commonly diagnosed infection in the community in less than 48 hours of hospital admission (7).

**Inclusion criteria:** Children from 6 months up to 15 years, both male and female children and cases of nephrotic syndrome either newly diagnosed or relapsed were included.

**Exclusion criteria:** Children less than 6 months, above 15 years, who were already on antibiotics either oral or parenteral in the last 48 hours or with urogenital malformations.

**Methods:**

**All patients were subjected to the following:**

A- Full history taking with special focus on the presence of urological manifestations (dysuria, loin pain, frequency, supra-pubic pain, change of the color of urine, offensive smell of urine, enuresis), treatment with certain drugs for long period and past history of renal diseases or family history of renal diseases.

B-Complete clinical examination with special focus on weight, edema and abdominal examination (for renal mass or fullness of renal angles).

C- Investigations:

1- Urine analysis: Urine samples from children were obtained then complete urine analysis was done on this urine specimens by microscopic urine examination and dipstick analysis.

2- Urine cultures were done.

The pattern of antibiotic susceptibility was done by the method of diffusion of the disks.

- Detection of most prevalent multi drug resistant (MDR) pathogen: MDR was defined as non-susceptibility to at least one agent in three or more antimicrobial categories. (8)

**Administrative considerations:** Written informed consent was obtained from all participants or their parents and the study was approved by the Research Ethical Committee of Faculty of Medicine, Zagazig University (Institutional Research Board IRB). The work was carried out in accordance with World Medical Association's Code of Ethics (Helsinki Declaration) for human involvement studies.

**Data management and Statistical analysis:**

The data were coded, entered and processed on computer using statistical package for social science (SPSS) version 18. The results were presented then interpreted in tabular and diagrammatic forms. Mean, as descriptive figures; standard deviation, frequency, range and percentage are used.

**RESULTS**

**Table (1):** Frequency of UTI of the study population

Types of UTI	UTI patients (n=33)	
	N	%
Community Acquired	19	57.6%
H. Acquired	14	42.4%

Table (1) showed that the percentage of CA-UTI was 57.6 % and HA-UTI was 42.4 %.

**Table (2):** Comparison between CA- UTI and HA- UTI regarding organism

Organism	CA- UTI (n=19)		HA- UTI (n=14)	
	N	%	N	%
E. coli	6	31.6%	8	57.1%
Klebsiella pneumonia	4	21.1%	2	14.3%
Proteus mirabilis	4	21.1%	2	14.3%
Staph aureus	4	21.1%	1	14.3%
Enterococcus faecalis	1	5.3%	1	7.1%

Table (2) showed that the highest percentage among the organisms was E. coli (57.1 % & 31.6 %) in HA-UTI and CA- UTI respectively. Klebsiella and Proteus were higher in CA-UTI than HA-UTI (21.1 % & 14.3 % respectively). The least percentage was Staph and Enterococcus faecalis.

**Table (3):** Multidrug resistant (MDR) distribution according to UTI types

MDR	UTI patients (n=33)	
	CA- UTI	HA-UTI
	15 (78.9%)	6 (42.9%)

Table (3) demonstrated that antibiotic susceptibility showed that 21 cases (63.6 %) were of MDR type divided into 15 cases (78.9 %) of community origin and 6 cases (42.9 %) of hospital acquired origin.

**Table (4):** Antibiotic susceptibility pattern of Gram-negative bacteria from CA-UTI

Gram-negative bacilli										
Antibiotics		Escherichia coli (n=6)			Klebsiella (n=4)			Proteus (n=4)		
		I	R	S	I	R	S	I	R	S
Ampicillin	No.	0	6	0	0	4	0	0	4	0
	%	00.0%	100 %	00.0%	0.0%	100.0%	0.0%	0.0%	100.0%	0.0%
Ciprofloxacin	No.	1	0	5	2	1	1	1	1	2
	%	16.7%	0.0%	83.3%	50.0%	25.0%	25.0%	25.0%	25.0%	50.0%
Gentamycin	No.	1	0	5	3	0	1	2	0	2
	%	16.7%	0.0%	83.3%	75.0%	0.0%	25.0%	50.0%	0.0%	50.0%
Amikacine	No.	3	0	3	1	0	3	2	0	2
	%	50.0%	0.0%	50.0%	25.0%	0.0%	75.0%	50.0%	0.0%	50.0%
Nitrofurantoin	No.	5	1	0	0	3	1	0	4	0
	%	83.3%	16.7%	0.0%	0.0%	75.0%	25.0%	0.0%	100.0%	0.0%
Sulfamethoxazole	No.	3	1	2	0	4	0	0	4	0
	%	50.0%	16.7%	33.3%	0.0%	100.0%	0.0%	0.0%	100.0%	0.0%
Ceftazidime	No.	3	3	0	2	1	1	2	2	0
	%	50.0%	50.0%	0.0%	50.0%	25.0%	25.0%	50.0%	50.0%	0.0%
Amoxicillin	No.	0	6	0	0	4	0	0	4	0
	%	0.0%	100.0%	0.0%	0.0%	100.0%	0.0%	0.0%	100.0%	0.0%
Ceftriaxone	No.	2	2	2	2	1	1	2	0	2
	%	33.3%	33.3%	33.3%	50.0%	25.0%	25.0%	50.0%	0.0%	50.0%
Cefepime	No.	3	3	0	0	4	0	1	0	3
	%	50.0%	50.0%	0.0%	0.0%	100.0%	0.0%	25.0%	0.0%	75.0%
Cefoxitine	No.	1	5	0	1	3	0	0	4	0
	%	16.7%	83.3%	0.0%	25.0%	75.0%	0.0%	0.0%	100.0%	0.0%
Cefazoline	No.	1	5	0	1	3	0	0	4	0
	%	16.7%	83.3%	0.0%	25.0%	75.0%	0.0%	0.0%	100.0%	0.0%
Meronem	No.	1	2	3	0	2	2	0	4	0
	%	16.7%	33.3%	50.0%	0.0%	50.0%	50.0%	0.0%	100.0%	0.0%

Table (4) showed the antibiotic susceptibility pattern of Gram-negative bacteria from CA-UTI.

**Table (5):** Antibiotic susceptibility pattern of Gram-negative bacteria from HA-UTI

<b>Gram-negative bacilli</b>										
<b>Antibiotics</b>		<b>Escherichia coli (n=8)</b>			<b>Klebsiella (n=2)</b>			<b>Proteus (n=2)</b>		
		<b>I</b>	<b>R</b>	<b>S</b>	<b>I</b>	<b>R</b>	<b>S</b>	<b>I</b>	<b>R</b>	<b>S</b>
<b>Ampicillin</b>	No.	0	8	0	0	2	0	0	2	0
	%	0.0%	100.0%	0.0%	0.0%	100.0%	0.0%	0.0%	100.0%	0.0%
<b>Ciprofloxacin</b>	No.	4	0	4	2	0	0	0	1	1
	%	50.0%	0.0%	50.0%	100.0%	0.0%	0.0%	0.0%	50.0%	50.0%
<b>Gentamycin</b>	No.	2	0	6	1	0	1	1	0	1
	%	25.0%	0.0%	75.0%	50.0%	0.0%	50.0%	50.0%	0.0%	50.0%
<b>Amikacine</b>	No.	4	0	4	0	0	2	1	0	1
	%	50.0%	0.0%	50.0%	0.0%	0.0%	100.0%	50.0%	0.0%	50.0%
<b>Nitrofurantoin</b>	No.	5	0	3	1	1	0	0	2	0
	%	62.5%	0.0%	37.5%	50.0%	50.0%	0.0%	0.0%	100.0%	0.0%
<b>Sulfamethoxazole</b>	No.	5	1	2	0	2	0	0	2	0
	%	62.5%	12.5%	25.0%	0.0%	100.0%	0.0%	0.0%	100.0%	0.0%
<b>Ceftazidime</b>	No.	2	6	0	0	0	2	0	2	0
	%	25.0%	75.0%	0.0%	0.0%	0.0%	100.0%	0.0%	100.0%	0.0%
<b>Amoxicillin</b>	No.	0	8	0	0	2	0	0	2	0
	%	0.0%	100.0%	0.0%	0.0%	100.0%	0.0%	0.0%	100.0%	0.0%
<b>Ceftriaxone</b>	No.	3	3	2	1	1	0	1	0	1
	%	37.5%	37.5%	25.0%	50.0%	50.0%	0.0%	50.0%	0.0%	50.0%
<b>Cefepime</b>	No.	1	6	1	0	2	0	2	0	0
	%	12.5%	75.0%	12.5%	0.0%	100.0%	0.0%	100.0%	0.0%	0.0%
<b>Cefoxitine</b>	No.	2	6	0	0	2	0	0	2	0
	%	25.0%	75.0%	0.0%	0.0%	100.0%	0.0%	0.0%	100.0%	0.0%
<b>Cefazoline</b>	No.	0	8	0	0	2	0	0	2	0
	%	0.0%	100.0%	0.0%	0.0%	100.0%	0.0%	0.0%	100.0%	0.0%
<b>Meropenem</b>	No.	0	5	3	1	1	0	0	2	0
	%	0.0%	62.5%	37.5%	50.0%	50.0%	0.0%	0.0%	100.0%	0.0%

Table (5) showed the antibiotic susceptibility pattern of Gram-negative bacteria from HA-UTI.

**Table (6):** Antibiotic susceptibility pattern of Gram- positive bacteria from CA-UTI

Antibiotics		Gram-positive cocci					
		Enterococcus (n=1)			Staph (n=4)		
		I	R	S	I	R	S
Ampicillin	No.	0	1	0	1	1	2
	%	0.0%	100.0%	0.0%	25.0%	25.0%	50.0%
Ciprofloxacin	No.	0	1	0	0	4	0
	%	0.0%	100.0%	0.0%	0.0%	100.0%	0.0%
Gentamycin	No.	0	1	0	0	4	0
	%	0.0%	100.0%	0.0%	0.0%	100.0%	0.0%
Nitrofurantoin	No.	0	0	1	1	1	2
	%	0.0%	0.0%	100.0%	25.0%	25.0%	50.0%
Sulfamethoxazole	No.	1	0	0	0	3	1
	%	100.0%	0.0%	0.0%	0.0%	75.0%	25.0%
Cefoxitine	No.	0	1	0	0	4	0
	%	0.0%	100.0%	0.0%	0.0%	100.0%	0.0%
Vancomycin	No.	0	1	0	1	2	1
	%	0.0%	100.0%	0.0%	25.0%	50.0%	25.0%
Erythromycin	No.	0	1	0	2	0	2
	%	0.0%	100.0%	0.0%	50.0%	0.0%	50.0%
Clindamycin	No.	0	1	0	0	4	0
	%	0.0%	100.0%	0.0%	0.0%	100.0%	0.0%
Linezolid	No.	1	0	0	0	3	1
	%	100.0%	0.0%	0.0%	0.0%	75.0%	25.0%
Rifampicin	No.	0	1	0	0	2	2
	%	0.0%	100.0%	0.0%	0.0%	50.0%	50.0%
Amoxicilline-Clavulenic acid	No.	0	1	0	1	1	2
	%	0.0%	100.0%	0.0%	25.0%	25.0%	50.0%

Table (6) showed the antibiotic susceptibility pattern of Gram-positive bacteria from CA-UTI.

**Table (7):** Antibiotic susceptibility pattern of Gram- positive e bacteria from HA-UTI

Antibiotics		Gram-positive cocci					
		Enterococcus (n=1)			Staph (n=1)		
		I	R	S	I	R	S
Ampicillin	No.	0	1	0	0	1	0
	%	0.0%	100.0%	0.0%	0.0%	100.0%	0.0%
Ciprofloxacin	No.	0	1	0	0	1	0
	%	0.0%	100.0%	0.0%	0.0%	100.0%	0.0%
Gentamycin	No.	0	1	0	0	1	0
	%	0.0%	100.0%	0.0%	0.0%	100.0%	0.0%
Nitrofurantoin	No.	0	1	0	1	0	0
	%	0.0%	100.0%	0.0%	100.0%	0.0%	0.0%
Sulfamethoxazole	No.	0	1	0	0	1	0
	%	0.0%	100.0%	0.0%	0.0%	100.0%	0.0%
Cefoxitine	No.	0	1	0	0	1	0
	%	0.0%	100.0%	0.0%	0.0%	100.0%	0.0%
Vancomycin	No.	0	1	0	0	0	1
	%	0.0%	100.0%	0.0%	0.0%	0.0%	100.0%
Erythromycin	No.	0	1	0	1	0	0
	%	0.0%	100.0%	0.0%	100.0%	0.0%	0.0%
Clindamycin	No.	0	1	0	0	0	1
	%	0.0%	100.0%	0.0%	0.0%	0.0%	100.0%
Linezolid	No.	0	1	0	0	0	1
	%	0.0%	100.0%	0.0%	0.0%	0.0%	100.0%
Rifampicin	No.	0	1	0	0	1	0
	%	0.0%	100.0%	0.0%	0.0%	100.0%	0.0%
Amoxicilline-Clavulenic acid	No.	0	1	0	0	1	0
	%	0.0%	100.0%	0.0%	0.0%	100.0%	0.0%

Table (7) showed the antibiotic susceptibility pattern of Gram-positive bacteria from HA-UTI.

## DISCUSSION

Nephrotic syndrome is a common renal disorder in pediatric population, which predisposes to various systemic infections. Immunosuppression may mask the typical clinical presentation of infections in NS and proper management might be delayed. Understanding the pattern of infections is important in the appropriate management of these children and to institute preventive measures<sup>(9)</sup>. Of all infections, urinary tract infection is of special interest because most of the urinary tract infection in nephrotic syndrome are asymptomatic and can be easily missed if active search is not made. Besides, in general the younger the child the less localized the signs and symptoms of urinary tract infection are<sup>(10)</sup>.

The present study was conducted to find out the prevalence of UTI (either community acquired or hospital acquired) in NS children and to uncover the bacterial spectrum and their sensitivity pattern for selecting the empirical antibiotic therapy till the results of culture are awaited.

Infections of the urinary tract remain commonly diagnosed in outpatients and hospitalized patients. Our study showed that the most common organisms causing CA-UTI in NS patients were *Escherichia coli* (31.6 %), followed by *Proteus mirabilis* as well as *Klebsiella pneumoniae* and *Staphylococcus aureus* (21.1 % each). The least common organisms in the study causing CA-UTI in NS was *Enterococcus faecalis* (5.3 %). These results agree with **Nimri et al.**<sup>(11)</sup> who published that CA-UTI is generally caused by *Escherichia coli* and other members of the family Enterobacteriaceae.

The current study found that the most common organisms causing HA-UTI in NS patients were *Escherichia coli* (57.1 %), followed by *Proteus mirabilis* as well as *Klebsiella pneumoniae* (14.3 % each), while the least common organisms in the study causing HA-UTI in NS were *Enterococcus faecalis* and *Staphylococcus aureus*. Finally, the most common organisms causing both CA-UTI and HA-UTI in NS patients were *Escherichia coli* but more in HA-UTI, followed by *Proteus mirabilis* as well as *Klebsiella pneumoniae* but more in CA-UTI. Our results are supported by **Edlin et al.**<sup>(12)</sup> and **Paschke et al.**<sup>(13)</sup>.

Current study showed that multidrug resistant to CA-UTI was in 15 cases (78.9 %) and to HA-UTI was in 6 cases (42.9 %). Our results worried about and reflected that the overuse of antibiotics had increased

extensively these days and this intense expansion in use of antibiotics had significantly intensified the antibiotic resistance. As with any infection treatment, the function of antibiotics is very crucial in UTI. The resistant forms have greater frequency variation with regard to localities and age groups. In many researches the organisms that cause UTI have shown multidrug resistance. In addition, **Ronald**<sup>(14)</sup> found that pathogens traditionally related to UTI change many of their characteristics, especially due to antimicrobial resistance.

Antibiotic sensitivity tests revealed that the most common antibiotics to which *Escherichia coli* were sensitive were gentamycin (78.6 %) followed by ciprofloxacin (64.3 %) followed by amikacin (50 %) then meropenem (42.6 %). The remaining cultures were sensitive to ceftriaxone (35.7 %), sulfamethoxazole (28.6 %), nitrofurantoin (21.4 %) and cefepime (7.1 %). **Mazzalli**<sup>(15)</sup> reported that *E coli* was sensitive to cotrimoxazole (80 %), ciprofloxacin (91.3 %), nitrofurantoin (98.2 %).

Current study showed that the most common antibiotics to which *Escherichia coli* were resistant were amoxicillin, ampicillin, cefazolin, ceftazidime, cefepime, ceftazidime, meropenem, ceftriaxone, sulfamethoxazole and nitrofurantoin by different percent. **Arredondo and Amabile**<sup>(16)</sup> found more than 70 % of *E coli* were resistant to AMP and 32.6 % to ciprofloxacin. However, another study showed that *E coli* were resistant to amoxicillin-clavulanic acid in 68.6 % - 86 % of cases<sup>(17)</sup>.

Susceptibility pattern of *Klebsiella* isolated from cultures to antibiotics were amikacin (83.3 %), ceftazidime (50 %), followed by gentamycin and meropenem (33.3 %). The most common antibiotics to which *Klebsiella* were resistant were amoxicillin, ampicillin, cefepime, cefazolin, ceftazidime. Our results agree with **Anandkumar et al.**<sup>(18)</sup> who found that *Klebsiella* was sensitive to amikacin, azithromycin, ceftazidime, amoxicillin-clavulanic acid in 100 % of cases, to ceftriaxone, ciprofloxacin and nitrofurantoin in 75 % of cases, then to cotrimoxazole and gentamycin in 50 % of children. *Klebsiella* species showed 75.3 % resistance to 3 or more drugs but this disagrees with **Anandkumar et al.**<sup>(18)</sup> for sensitivity to amoxicillin.

The most sensitive antibiotics to *Staph aureus* were amoxicillin-clavulanate, ampicillin, erythromycin, vancomycin, rifampicin, nitrofurantoin and linezolid. The most resistant



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antibiotic to Staph aureus were cefoxitin, ciprofloxacin and gentamycin. However, **Dash et al.** (19) found that the sensitivity of Staphylococcus aureus organism to ceftriaxone, amikacin, piperacillin-tazobactam and vancomycin was very promising out of which vancomycin showed 100% coverage. Their sensitivities to commonly used antibiotics such as cefixime and ampicillin were low.

Finally, there is an increasing trend of resistance by common bacteria to routine antibiotics. This had been noted in the region and thus the scientific management of UTI needs a continuous updating depending on the antimicrobial sensitivity of the area's or country's key uropathogens.

### CONCLUSION

Identifying the bacterial causes of UTI and their susceptibility pattern will help in selecting the empirical antibiotic therapy till the results of culture are awaited. E. coli is the commonest organism causing UTI followed by klebsiella and proteus mirabilis in children in our study. The isolated organisms showed great resistance to parenteral and oral antibiotics. Amikacin gentamycin may be the first option of empiric therapy while waiting for culture reports. Ceftazidime and ciprofloxacin could be a reserve. Although dipstick and microscopic urinalysis can support the diagnosis of UTI, growth of a single type of bacteria on urine culture is the gold standard.

### RECOMMENDATIONS

It should be asked for urine analysis and culture for any nephrotic syndrome patients either symptomatic or asymptomatic to avoid prolonged hospital stay or relapse thereby to prevent long term renal damage. Constant updating for antimicrobial susceptibility of the main uropathogens of the area should be done. Antibiotic stewardship program is highly encouraged to prevent the hazardous consequences of antibiotic resistance.

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