International Journal of Drug Research and Technology

Available online at http://www.ijdrt.com

Research Article

MICROBIOLOGICAL PROFILE OF URINARY TRACT INFECTION IN PEDIATRIC AGE, EGYPTIAN TWO CENTERS EXPERIENCE

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ABSTRACT

Background: Urinary tract infection (UTI) is the most common nosocomial infection among hospitalized patients. Area specific monitoring studies aimed to gain knowledge about the type of pathogen responsible for UTIs and their resistance patterns may help the clinician to choose the correct empirical treatment. We aimed to study the type of urinary pathogens isolated from hospitalized patients with 1st episode UTI in our locality and its antibiotic susceptibility pattern.

Patient and method: Urine samples were collected from 320 clinically suspected cases of urinary tract infection from inpatient wards and outpatient clinic of Pediatric Nephrology unit of Pediatric Departments of Tanta University Hospital and Aswan University Hospital during the period from June 2016 to June 2017. The samples were tested microbiologically by standard procedures. Antibiotic susceptibility of the isolated pathogens was tested for commonly-used antibiotics by disc diffusion method according to hospital policy.

Results: Significant bacteruria was present in 75% of the samples, 16.25% were sterile and 8.75% showed insignificant bacteruria. The most common pathogen were *E. coli* (55%), *Klebsiella* spp. (26.6%) and *Proteus mirabilis* (14.2%). The mean susceptibility was high for *Amikacin* (85%), Ceftriaxone (82%), Cefotaxime (80%), Nitrofurantoin (80%), and *Nalidixic acid* (78%) but low for Ampicillin (21%), Cephalaxin (30%), and *Sulphamethoxazol + Trimethoprim* (37%).

Conclusion: The antibiotics commonly used in UTIs like *trimethoprim / sulphamethoxazole*, *ampicillin* and *cephalexin* does not seem to be appropriate for the empirical treatment of community-acquired UTIs because of their very high rate of resistance., regular monitoring is required to establish reliable information about resistance pattern of urinary pathogens for optimal empirical therapy of patients with UTIs.

Keywords: Microbiological, Urinary Tract Infection, Pediatric.

INTRODUCTION

Urinary tract infections (UTIs) are the most common nosocomial infection among hospitalized patients (Nicolle, 2001). It occurs in 3-5% of girls and 1% of boys. In girls, the first UTI usually occurs by the age of 5 y, with peaks during infancy and toilet training. After the first UTI, 60–80% of girls will develop a second UTI within 18 months. In boys, most UTIs occur during the first year of life (Jack, 2007). In infancy, non-specific manifestations such as fever, vomiting and abdominal pain, can make the diagnosis of UTI challenging. In infancy and young children, fever without localization is frequently the admitting diagnosis (Charisse, *et al*., 2008). Recurrent UTIs are common and can lead to irreversible damage of the kidneys, resulting in renal hypertension, renal scarring and chronic renal failure (Jahnukainen, *et al.*, 2005). It is universally accepted that UTI can be only ascertain on the basis of microscopy and microbial culture. In almost all cases, treatment must be initiated before the final bacteriological results are available. Therefore, studies to increase our knowledge about the type of pathogens responsible for UTIs and their susceptibility patterns to antibiotic drugs are very important to help clinician to choose the correct empirical

treatment. We aimed to study the type of urinary pathogens isolated from hospitalized patients with first episode UTI in our locality and its antibiotic susceptibility pattern.

MATERIALS AND METHODS

Design of the study and setting

The present cross-sectional study was conducted after approval from the research ethical committees of the Faculty of Medicines of Tanta University and Aswan University and informed oral or written parental consents on 320 pediatric patients selected from the inpatient ward and outpatient clinic of Pediatric Nephrology Units of Tanta University Hospital and Aswan University Hospital from June 2016 to June 2017. Inclusion criteria included all clinically suspected pediatric patients for 1st episode of UTI. Exclusion criteria included previous history of UTI, known congenital anomalies of the kidney and urinary tract especially on current prophylactic treatment with antibiotics**.**

All patients were subjected to full history taking, thorough clinical examination especially anthropometric measurements (weight and height**),** vital signs**,** and laboratory investigations including complete urine analysis.

Urine samples were collected by one of three methods included med-stream clean catch method, suprapubic bladder aspiration or urethral catheterization according to the age and compliance of patients and their families. All samples were processed using standard microbiological procedure. Samples were processed on blood agar and MacConkey medium by standard loop method and incubated at 37^{o}c overnight. Single organism growth of ≥ 100,000 colony forming units/ml was considered as significant bacteruria. The organisms were identified by routine methods from samples showing significant bacteruria. Antibiotic susceptibility of the isolated pathogens was tested for commonly used antibiotics by standard disc diffusion technique on Muller-Hinton agar as recommended by Bauer, *et al*., (1996). After 24 h at 37°C, the zone of inhibition was measured. Antibiotic discs were obtained from Oxoid and Himedia. The results were interpreted according to National Committee for Clinical Laboratory Standards, 2000.

RESULTS

There were 320 urine samples collected,162 (67.5%) samples collected by midstream clean catch method, 38 (15.8%) samples obtained by suprapubic bladder aspiration and 40 (16.7%) samples collected by in and out catheter.

Out of the 320 samples processed, 240 (75%) showed significant bacteruria, 52 (16.25%) were sterile and 28 (8.75%) showed insignificant bacteruria.

Age and sex distribution of the culture positive urine samples was shown in Table 1. From a total of 240 samples, 56 (23.3%) urine samples were from infants below 2 years, 108 (45%) were from children aged 2–6 years and 78 (31.7%) were from those between 6–12 years.

Table 1: Age and sex distribution of the patients with culture Positive urine samples.

Age (in years)	***Male***	***Female***	***Total***	***P value***
0–2 years	34 (14,2%)	22 (9.2%)	56 (23.4%)	P<0.05
2–6 years	24 (10 %)	84 (35%)	108 (45%)	
6–12 years	14 (5.8%)	62 (25.8)	76 (31.6 %)	
Total	72 (30%)	168 (70%)	240 (100%)	

Regarding sex distribution, there was statistically significant difference. UTIs were more common in females above age of two years than in males .On other side UTIs were more common in males below age of two years than in females (P<0.05).

The organisms grown on the culture of all 240 samples with significant bacteriuria were as follow, *E. coli* 132 (55%), *Klebsiella* spp. 64 (26.6%), *Proteus mirabilis* 34 (14.2%) and *Enterococcus faecalis* 10 (4.2%) (Table 2).

Significant bacteruria was present in midstream clean catch samples in 162 out of 240 samples (67.5%). This percent was lower in suprapubic bladder aspiration and urethral catheter collected samples (15.8 % and 16.7 %, respectively)

The antibiogram of isolated pathogens shown in Table 3 and Figure 1. The highest susceptibility for all isolated pathogens was for Amikacin (85%), Ceftriaxone (82%), Cefotaxime (80%), Nitrofurantoin (80%) and Nalidixic Acid (78%) susceptibility was low for Ampicillin (21%), Cephalexin (30%), and Sulphamethoxazol + Trimethoprim (37%).

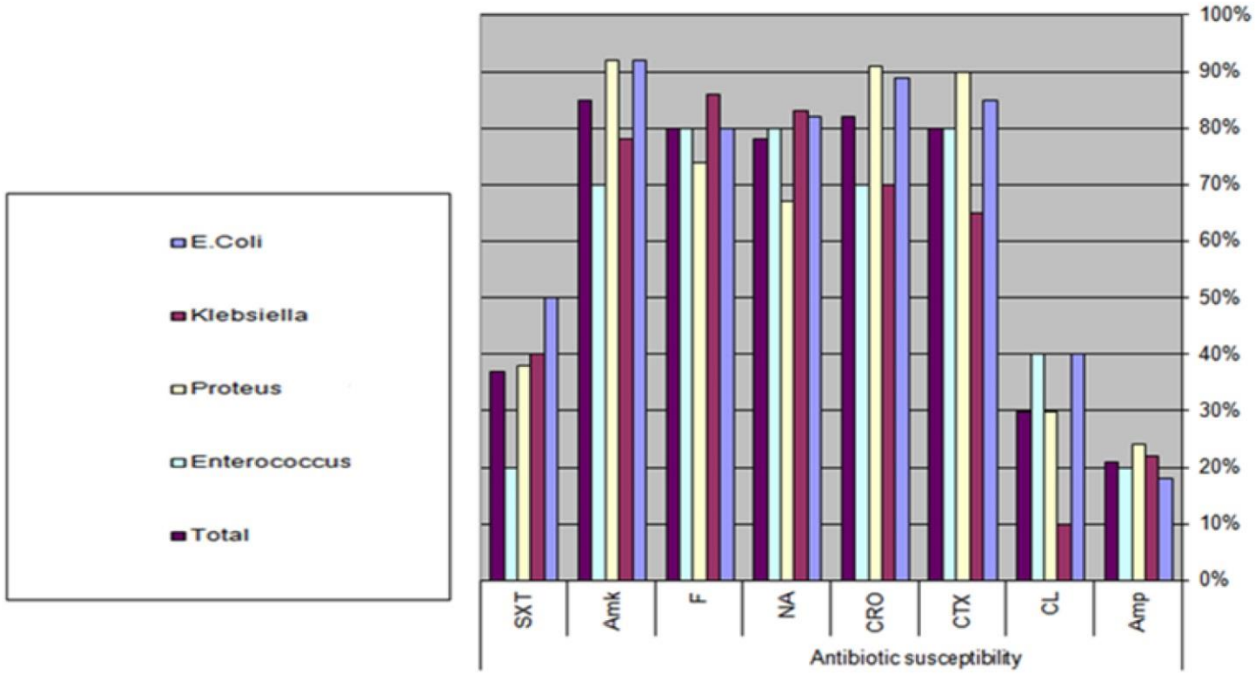
Table 2: Distribution of isolated bacteria according to method of collection of urine samples.

Organism	Clean catch mid stream	Suprapubic Bladder aspiration	Urithral Catheter	Total
E. Coli No (%)	80 (33.3%)	26 (10.8%)	26 (10.8%)	132 (55%)
Klebsiella No (%)	50 (20.8%)	6 (2.5%)	8 (3.3%)	64 (26.7%)
Proteus No (%)	24 (10%)	6 (2.5%)	4 (1.7%)	34 (14.2%)
Enterococcus No (%)	8 (3.3%)	0 (0%)	2 (0.83%)	10 (4.2%)
Total No (%)	162 (67.5%)	38 (15.8%)	40 (16,7%)	240 (100%)

Table 3: Results of couture and sensitivity of urine samples of the studied patients.

Organism Isolated (no= 240)	***Antibiotic susceptibility***							
	Amp	**CL**	**CTX**	**CRO**	**NA**	**F**	**Amk**	**SXT**
E. Coli 66 (55%)	18%	40%	85%	89%	82%	80%	92%	50%
Klebsiella 32(26.6 %)	22%	10%	65%	70%	83%	86%	78%	40%
Proteus 17(14.2%)	24%	30%	90%	91%	67%	74%	92%	38%
Enterococus 5(4.2%)	20%	40%	80%	70%	80%	80%	70%	20%
Total	21%	30%	80%	82%	78%	80%	85%	37%

Amp: Ampicillin; CL: Cephalexin; CTX: Cefotaxime; CRO: Ceftriaxon; NA: Nalidixic Acid; F: Nitrofurantoin; Amk: Amikacin; SXT: Sulphamethoxsol+Trimethopri



Amp: Ampicillin; CL: Cephalexin; CTX: Cefotaxime; CRO: Ceftriaxon; NA: Nalidixic Acid; F: Nitrofurantoin; Amk: Amikacin; SXT: Sulphamethoxsol+Trimethopri

Figure 1: The antibiogram of isolated pathogens.

E. coli was most sensitive to Amikacin (92%), followed by Ceftriaxone (88%), Cefotaxime (85%), Nitrofurantoin (82%), and Nalidixic Acid (81%).

Klebsiella spp. was most susceptible to Nitrofurantoin (86%), Nalidixic acid (83%), and Amikacin (81%). *Proteus mirabilis* was most sensitive to Amikacin (92%), Ceftriaxone (91%), and Cefotaxime (90%). *Enterococcus faecalis* was most sensitive to Nalidixic Acid (100%), Nitrofurantoin (80%), and Cefotaxime (80%) but less susceptibility was observed for Sulphamethoxazol + Trimethoprim (20%), Ampicillin (20%), and Cephalexin (40%).

DISCUSSION

Diagnosis of UTI is a good example of the need for close cooperation between the clinician and the microbiologist. Studies have established that a normal urinalysis does not rule out UTI in children. The presence of significant bacteruria in 75% of samples indicates the significance of microbiological culture to clinch the diagnosis of UTI.

In the present study, significant bacteruria was present in 67.5% of samples collected by midstream method, which is greater than the results of samples collected by suprapubic aspiration and catheterization (15.8% and 16.7% respectively). In circumcised males, mid-stream urine is highly recommended as a reliable non-invasive procedure for diagnosis of UTI (Prais, *et al*., 2003). Furthermore, the American Academy of Pediatrics recognizes that the low rate of UTI in this population (0.2–0.4%) does not justify the routine use of an invasive, potentially traumatic diagnostic procedure (Amir, *et al*., 1993).

Insignificant bacteruria or sterile samples were found in 25% of patients this may be explained by prior antibiotic treatment before submitting the urine sample, and other clinical conditions that may mimic UTI .

The demographic data of our patients shows that females are more affected than males (number=168 and 72, respectively) but males are affected by first episode UTI at significantly younger age than females. The relatively high percent (70%) of female patients in our study can be explained by the older median age of the patients, in a younger sample, the relative rate of males would probably be higher.

The Enterobacteriacae group, namely, *E. coli* (55%), *Klebsiella* spp. (26.6%), and *Proteus mirabilis* (14.2%), were the most common pathogens isolated. The isolation rates of urinary pathogens are consistent with reports of the recently- published studies from different countries (Sharifian, *et al*., 2006; Keah, 2007; Zhanel, *et al*., 2005 and Andrade, *et al*., 2006). Enterobacteriacae have several factors responsible for their attachment to the uroepithelium. These gram–negative aerobic bacteria colonize the urogenital mucosa with adhesin, pili, fimbria, and P1-blood group phenotype receptors (Lomberg, *et al*., 1983).

This study shows high bacterial resistance of uropathogens to common antibiotics namely ampicillin, cephalaxin and sulphamehoxasol - trimethoprim (SMX/TMP) in children with first episode UTI. Most cases of UTI are treated empirically, especially in developing countries, where patients often cannot afford to consult a physician or have a laboratory analysis made. The WHO guidelines indicate SMX/TMP and ampicilin as first choice for treatment of UTI in children in developing countries (Lomberg, *et al.,* 1983). Our study recommend against this advice. The low susceptibility to these drugs could be due to widespread use of these antibiotics in the community for treating other common infections as otitis media and pharyngitis (Currie, *et al.*, 2003).

According to Iranian study (Kashef, *et al.,* 2010), *E. coli* isolates were highly resistant to ampicillin (88%) and resistance rates to ampicillin have been reported in other countries which was 88% in India (Gupta, *et al.,* 2007), 80% in Taiwan (Lau, *et al*., 2004) and 47.8% to 64.6% in Turkey (Kurutepe, *et al.,* 2005).

Ampicillin is rapidly excreted and the duration of significant drug concentration in the urine is short. This may predispose to increased bacterial resistance when used to treat UTI. In addition, ampicillin is relatively ineffective in clearing *E. coli* from intestinal and vaginal mucosa, which may predispose to recurrence of UTIs (Daikos, *et al.,* 1987).

Nitrofurantoin and nalidixic acid are still maintaining good activity against *E. coli* (82% and 81% respectively) and *Klebsiella* spp. (86% and 83% respectively). However, they are not widely used due to their rapid excretion in urine and so they fail to achieve therapeutic concentrations in blood (Committee on Quality Improvement, 1999). Because of this pharmacokinetic profile, Nitrofurantoin and nalidixic acid are commonly used for prophylaxis and not recommended to treat febrile infants with UTI.

Aminoglycosides and 3rd generation cephalosporins are considered safe in treatment of UTI in children. *E. coli* was most sensitive to Amikacin (92%), followed by Ceftriaxone (88%),

Cefotaxime (85%). Intravenous therapy should be considered in children who have failed oral therapy and continue to be febrile. These results are consistent with other recommendation for empirical therapy of UTIs. Haller *et al.*, concluded that ampicillin and an aminoglycoside were appropriate empirical treatments for UTIs in hospitalized children in University Hospital of Feilburg (Germany). While Hoberman *et al.*, 1999, recommended cefixime as a 1st line empirical antibiotic for outpatient therapy of community acquired UTIs.

CONCLUSIONS

The antibiotics commonly used in UTIs like trimethoprim/sulphamethoxazole, ampicillin and cephalexin does not seem to be appropriate for the empirical treatment of community-acquired UTIs because of its very high rate of resistance. Since the present study was a cross- sectional study, regular monitoring is required to establish reliable information about resistance pattern of urinary pathogens for optimal empirical therapy of patients with UTIs.

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Cite This Article: El-Gamasy, MA; Mehrez, MM; Fakhreldin, AR and Alenany, AE (2017), "Microbiological Profile of Urinary Tract Infection in Pediatric age, Egyptian two centers experience." ***International Journal of Drug Research and Technology*** Vol. 7 (5), 223-233.

INTERNATIONAL JOURNAL OF DRUG RESEARCH AND TECHNOLOGY