Antibiotic sensitivity pattern of common community-acquired uropathogens in children in a Saudi tertiary care hospital

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Urinary tract infection (UTI) is one of common community-acquired as well as healthcare-associated infection in childhood. Previous reports have shown a decrease in the sensitivity pattern of uropathogens to commonly described antibiotics with considerable geographic variations attributed to different local antibiotics usage.[1] Sensitivity pattern of community-acquired uropathogens in Saudi children is underreported. Only one study has reported sensitivity pattern in children.[2] However, that study did not differentiate between community-acquired UTI (CA-UTI) and healthcare-associated UTI.[2] Therefore, we aimed to assess sensitivity pattern of community-acquired uropathogens in Saudi children in King Abdulaziz Hospital (KAH), Al-Ahsa area, Kingdom of Saudi Arabia (KSA). This will help in the selection of appropriate empirical antibiotics for CA-UTI in our population, which is crucial in decreasing UTI-associated morbidity, including renal scaring with subsequent hypertension, renal failure, and impaired growth.

The KAH is the second largest tertiary hospital in the Al-Ahsa area, and was commissioned in late 2002 to provide health care for Saudi National Guard employees and their dependents. It is accredited by the Joint Commission of International Accreditation and has a 35-bed pediatrics ward. Al-Ahsa is an oil- and gas-producing area located approximately 60 km inland from the Arabian Gulf in the eastern province of KSA. It has an area of 534,000 km^2 with a population of more than 908,000 (year 2005 estimate).

This is a retrospective study including all urine samples that were sent from non-hospitalized children to the bacteriology laboratory of KAH from January 2003 to April 2009. All CA-UTI and their uropathogens susceptibility pattern for children aged 14 years or less were reviewed and data were extracted relating to UTI from the medical records of these children. Children who had healthcare-associated UTI, recurrent UTI defined as 2 proven episodes within 6 months, neurogenic bladder, vesicostomy, and who are on intermittent catheterization were excluded. All possible contaminated urine samples were excluded including those who grew *Candida*, *Staphylococcus species*, or group B *Streptococcus*.

Urine samples were processed on blood agar and MacConkey medium with a standard loop, and were incubated at 35ºC overnight. Significant growth was considered when the colony count is ≥10,000 colony forming uniy (CFU)/ml of midstream urine and bag sample ≥1000 CFU/ml of catheter specimen. Identification of Gram-negative bacteria was performed by standard biochemical methods and confirmed by API 20E (BioMerieux Inc., Hazelwood, MO, USA). Antibiotics susceptibility testing was performed by Kirby-Bauer methods, confirmed, if required, by testing minimum inhibitory concentration using E. strip test. Interpretation followed the Clinical and Laboratory Standards Institute (CLSI) M100 guidelines that are updated every year. Extended-spectrum beta-lactamase (ESBL) activity was detected by using E test ESBL cefotaxime/cefotaxime+clavulanic acid strip and ceftazidime/ceftazidime+clavulanic acid strip. For a given uropathogen and a given antibiotic, antibiotics sensitivity as proportion rounded to the nearest whole number (the number of sensitive organisms/ the total number of tested organisms) with its 95% confidence interval (95% CI) was calculated. Quantitative variables that were not normally distributed were presented as medians with their interquartile range (IQR). Chi square and Fisher exact test were used when appropriate. A 2-sided p-value<0.05 was considered statistically significant. All statistical analysis was performed by using Epi Info (CDC statistical software version 3.5.3).

A total of 258 community-acquired uropathogens were isolated in 249 children; 62 in boys and 187 in girls. Age (months) at presentation of CA-UTI in boys was significantly earlier than in girls (6; IQR: 2-15 versus 45; IQR: 10-83, p<0.001). Methods of urine collection in 70% of CA-UTIs were not documented in patients' medical records, however, the remaining was by urine bag (17%), catheterization (8%), and midstream clean catch (5%). Overall, *Escherichia coli (E. coli)* was the most frequent identified community-acquired uropathogens followed by *Klebsiella* and *Pseudomonas species* (**Table 1**). The *E. coli* and *Klebsiella species* constituted 64% (95% CI: 51-75) in boys versus 85% (95% CI: 79-90) of uropathogens in girls (p<0.001). **Table 1** depicts the sensitivity pattern of community-acquired uropathogens to commonly used antibiotics.

Table 1 - Sensitivity pattern of 258 community-acquired uropathogens to commonly used antibiotics.

Antibiotics	*E. coli*	*Klebsiella*	*Pseudomonas*	*Citrobacter*	*Enterobacter*	*Enterococcus*	*Proteus*	*Acinetobacter*
				n (%)				
	175 (68.0)	**32 (12.4)**	**16 (6)**	**8 (3.1)**	**6 (2.3)**	**11 (4.0)**	**8 (3.1)**	**2 (1.0)**
Ampicillin	48 (27.4)	0	NT	0	0	10 (90.9)	6 (75.0)	0
Cefuroxime	166 (94.8)	28 (87.5)	NT	5 (62.5)	5 (83.3)	NT	8 (100)	0
Nitrofurantoin	168 (96.0)	23 (71.8)	NT	8 (100)	3 (50.0)	10 (90.9)	0	0
Co-trimoxazole	77 (44.0)	24 (75.0)	NT	6 (75.0)	6 (100)	NT	5 (63.0)	1 (50.0)
Cefotaxime	166 (94.8)	29 (90.6)	NT	6 (75.0)	5 (83.3)	NT	8 (100)	0
Ceftazidime	166 (94.8)	29 (90.6)	16 (100)	6 (75.0)	5 (83.3)	NT	8 (100)	1 (50.0)
Cefatriaxone	166 (94.8)	29 (90.6)	NT	6 (75.0)	5 (83.3)	NT	8 (100)	0
Gentamicin	159 (90.8)	29 (90.6)	15 (93.7)	8 (100)	6 (100)	NT	8 (100)	1 (50.0)
Amikacin	102 (98.0)*	19 (95.0)‡	10 (90.9)§	5 (100)£	3 (100)¶	0	5 (100)**	0
Tazocin	163 (93.1)	28 (87.5)	16 (100)	8 (100)	6 (100)	NT	8 (100)	1 (50.0)
Imipenem	167 (100)†	32 (100)	16 (100)	8 (100)	6 (100)	NT	8 (100)	2 (100)

Data is presented as number (%), NT - not tested, *reported for 104 uropathogen, †reported for167, ‡reported for 20, §reported for 11, £reported for 5, ¶reported for 3, **reported for 5.

The overall sensitivity is lowest to ampicillin followed by co-trimoxazole, cefuroxime, and nitrofurantoin were the most active oral agents against the common uropathogens. Extended spectrum beta-lactamase producing organisms (ESBL) was observed in 10 (4%) isolates *(E. coli* - 7, *Klebsiella* - 3). Five of the ESBL isolates were from children less than one year old. There was a trend of more ESBL isolates in the 2007-2009 than 2003-2006 period (8/124 versus 2/136; p=0.05). All ESBL isolates were sensitive to imipenem, 7 to amikacin, 3 to gentamicin, and 4 to ciprofloxacin.

Our findings showed that sensitivity pattern of these uropathogens are better for cefuroxime, nitrofurantoin, cefotaxime, and gentamicin than both ampicillin and co-trimoxazole. Our findings are similar to the studies from United Arab Emirates (UAE) and Turkey that showed gram negative organisms have good sensitivity to the third generation cephalosporins making them a reasonable choice as intravenous empirical treatment for CA-UTI.[3,4] These 2 studies have shown a low sensitivity rate to second generation cephalosporin by *E. coli* and other gram negative uropathogens which is in disagreement with our study.[3,4] We observed a good sensitivity by *E. coli* and other negative uropathogens that maintained in the 2 study period. This difference might be related to frequent use of second generation cephalosporins as empirical treatment in their countries. Similar to previous studies, we found that nitrofurantoin had a steady excellent sensitivity against *E. coli* and slightly lower sensitivity against *Klebsiella*.[3] However, we should be cautious on using nitrofurantoin as empirical treatment in our population. Nitrofurantoin has a low sensitivity against *Klebsiella* and a low tissue concentration, besides that, it causes hemolysis in glucose-6-phosphate dehydrogenase deficiency, which is very common in our population.[5]

Sensitivity to ampicillin and cotrimoxazole is decreasing progressively over the years worldwide as these antibiotics are frequently used for treatment and prophylaxis of UTI.[1] Our study partially concurs with this as the low sensitivity rate of *E. coli* to ampicillin was steady during the 2 study period. Unfortunately, we could not draw a firm conclusion regarding sensitivity pattern of ESBL as there were only 10 isolates. Our study has few limitations in addition to inherited limitation of its methodology, and retrospective chart review. We had a small number of uropathogens, and no data on the method of urine collection in 70% of UTIs, however, we excluded all possible contaminated urine samples.

In conclusion, empirical antibiotic selection should be based on knowledge of the local susceptibility pattern of the uropathogens. In our experience, sensitivity pattern of common uropathogens was highest to cefuroxime, nitrofurantoin, cefotaxime and gentamicin.

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