ETIOLOGY AND ANTIBACTERIAL RESISTANCE OF BACTERIAL URINARY TRACT INFECTIONS IN CHILDREN'S MEDICAL CENTER, TEHRAN, IRAN

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Abstract- Urinary tract infection (UTI) is a common bacterial illness in children. Knowledge of the antimicrobial resistance patterns of common uropathogens in children according to local epidemiology is essential for providing clinically appropriate, cost effective therapy for UTI. The aim of this study was to determine the distribution of urinary tract infections in a referral hospital, Children's Medical Center, and determination of *in vitro* susceptibility of these organisms to antimicrobial agents. Of the 1231 bacterial isolates the most frequent isolates were *Escherichia coli* (38.66%), *Klebsiella* spp. (22.25%), Coagulase-negative staphylococci (10.1%), *Pseudomonas* spp. (8.7%), enterococci (8.28%), *Enterobacter* spp. (4.1%), *staphylococcus aureus* (3.24%), and *proteus mirabilis* (2.9%). Among *Enterobacteriaceae*, 79.80% of *E. coli* were amikacin-sensitive. Of Gram-positive cocci, 66.66% of *staphylococcus aureus* were vancomycin-sensitive. Our data show the original distribution of uropathogens from UTIs in children referred to Children's Medical Center in Tehran and the emergence of multidrug resistant strains.

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Key words: Urinary tract infection, antibiotic resistance, children, Iran

INTRODUCTION

Urinary tract infection (UTI) is a common bacterial illness in children (1, 2). UTI is defined as the present of bacteria in urine along with symptoms of infection. These occur in as many as five percentages of girls and 1 to 2 percent of boys (3). The incidence of UTI in infants ranges from approximately 0.1 to 1.0 percent in all newborn infants to as high as 10 percent in low-birth-weight infants (4). Urine is the single most frequently received specimen in routine microbiology laboratories, with many thousands of urinary antimicrobial sensitivity results being issued each day (5). Current guidelines "best guess" antibiotic should be started in all cases of suspected UTI after an appropriate urine specimen is obtained (6).

Knowledge of the antimicrobial resistance patterns of common uropathogens in children according to local epidemiology is essential for providing clinically appropriate, cost effective therapy for UTI (7-9). Early diagnosis and prompt antimicrobial treatment are required to minimize renal scarring and progressive kidney damage (10).

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The aim of this study was to determine the distribution of uropathogens isolated from children's referred to a referral hospital, Children's Medical Center, in Tehran, as well as to evaluate their *in vitro* susceptibility to antimicrobial agents so that the optimal empirical antibiotic therapy in these patients could be determined.

MATERIALS AND METHODS

The study was performed over one year period from March 2003 to March 2004. A total number of 13339 urine samples from children suspected to UTI that referred to Children's Medical Center was sent to laboratory of microbiology in order to perform analysis.

Isolation of uropathogens was performed by a surface streak procedure of CLED agar (bio Merieux, France). Samples with one bacterial isolate, with more than 10^4 CFU/ml and with significant leukocyturia (more than 4-5 leucocytes/field), were used in this study.

Gram-negative isolates were identified by conventional biochemical tests as well as API 10S (bioMerieux). Organisms with typical morphology which were lactose- and indole- positive as well as urease-negative were accepted as *Escherichia coli*. Gram positive isolates were subcultured on blood agar and depending on colonial morphology, additional tests were performed. Enterococci were identified by growth in bile- aesculin broth as well as by API STEREP (bioMerieux). Staphylococci were checked for clamping factor producing by Staphaurex (bioMerieux®). Streptococci identified by slide agglutination test (Streptex–Murex®) by API STEREP (bioMerieux®).

The sensitivity of urine isolates to 21 antimicrobials commonly used in the community and hospitals was determined. Susceptibility was tested to ampicillin, trimethoprim-sulfamethoxazole, cephalothin, gentamycin, amikacin, nitrofurantoin, nalidixic acid, kanamycin, ceftriaxone, ceftizoxime, ceftazidime, cefixime, tobramycin, carbenicillin, clindamycin, cefazolin, cephalexin, erythromycin, penicillin, vancomycin and cloxacillin.

Disk diffusion tests were performed with antibiotic containing disks (BBL Microbiology Systems, Cockeysville, USA). Results were interpreted according to criteria recommended by the National Committee for Clinical Laboratory Standards (11). Antibiotic tested were available in microbiology laboratory of Children's Medical Center in Tehran. The inhibition zone diameter was record on i2® software and classified according to the criteria of the SFM (1). Quality control was performed using strains from the American Type Culture collection: *E. coli* (ATCC 25922), *Pseudomonas aeruginosa* (ATCC 27853), *Staphylococcus aureus* (ATCC 25923), and *Enterococcus faecalis* (ATCC 29212).

RESULTS

From a total of 1231 isolates, 955 (77.57%) were Gram-negative and 276 (22.43%) were Gram-positive. The most frequent Gram negative isolates were *E. coli* (38.66 %), fallowed by *Klebsiella* spp. (22.25), *Pseudomonas* spp. (8.1%), *Enterobacter* spp. (4.1%) and *Proteus mirabilis* (2.9%). The most frequent Gram positive isolates were Coagulase-negative staphylococci (10.1%), enterococci (8.28%) and *S. aureus* (3.24%). Antibiotic resistance in the most common Gram-negative and-positive isolates is shown in Tables 1 and 2.

DISCUSSION

UTIs are the most common nosocomial infections, with similar pattern of infection reported in many other countries. They are often associated with significant mortality and morbidity. Typically, urinary tract infections extend the average stay in hospital by an average 2.4 days, with an associated additional cost of at least $500 to $700 (12). Understand of etiology and antimicrobials susceptibility of major bacteria that cause urinary tract infections in Iranian patients provide essential information regarding the selection of antibiotic therapy for these infected children.

In this study, an evaluation was performed on species distribution and susceptibility of uropathogens isolated from children suspected UTI referred to Children's Medical Center in Tehran. Our data was restricted to patient who can

Table 1. Resistance of leading Gram negative bacterial isolates*

	AMP	STX	CEF	GEN	AMK	NIT	NAL	KAN	CRO	ZOX	CAZ	CFM	TOB	CAR
E. coli	89.3	70.7	66.2	25.05	30.9	44	44.2	69.9	18.35	25.55	22.25	23.5	26.65	18.55
Klebsiella spp	72.5	65.2	91.7	58.4	55.9	92.4	58.5	94.6	59.5	53	58.2	58.4	55.9	44.1
Pseudomonas spp	97.4	96.6	100	44.2	30.5	100	97.9	97	76.5	87.9	49.8	92.6	55	41.9
Enterobacter spp	72	44	76	34	14	58	58	78	34	30	40	40	28	16
Proteus mirabilis	82.6	75	65	39.4	17.7	87.9	67.7	63.3	14.7	14.7	24.6	16.9	20.2	13.9
Citrobacter spp	83.3	83.3	83.3	33.3	33.3	33.3	83.3	83.3	17.6	16.6	41.6	41.6	41.6	16.6
Acinetobacter spp	25	100	100	100	100	100	100	100	100	100	100	100	100	100
Salmonella typhi	0	0	100	0	0	100	100	100	0	0	0	0	0	0
Hafnia	100	100	0	0	0	100	100	100	0	0	0	0	0	0
M. morganii	100	100	100	0	0	100	100	100	0	100	0	100	0	0

Abbreviations: AMP, ampicillin; STX, trimethoprim-sulfamethoxazole; CEF, cephalothin; GEN, gentamicin; AMK, amikacin; NIT, nitrofurantoin; AL, nalidixic acid; KAN, kanamycin; CRO, ceftriaxone; ZOX, ceftizoxime; CAZ, ceftazidime; CFM, cefixime; TOB, tobramycin; CAR, carbenicillin.
*Data are given as percent.

afford medical analysis, and so this study may not reflect the true prevalence of UTI among children in Tehran as most children are initially treated empirically for their UTI. Some of the recorded cases are likely to be recurrent infections or infected already failing one more curses of therapy.

Nevertheless our data show the antibiotic resistance pattern present among organisms isolated of children in Tehran. Uropathogens have shown a slow but steady increase in resistant to several antibiotics over the last decade. This study revealed that *Enterobacteriaceae*, especially *E. coli*, were the predominant bacterial pathogens detected in UTI. Similar frequencies of *E. coli* isolates have been obtained in studies performed in Israel, Kuwait, India, Nigeria, Britain and two USA studies (10, 12-16).

E. coli showed high resistance to ampicillin (89.3%), but was sensitive to ceftriaxone (81.65%) and carbenicillin (89.45%). Most of *E. coli* isolates in this study were resistance to oral antibiotics that commonly used in general practice. For example the rate of resistance to ampicillin, trimethoprim–sulfamethoxazole and nitrofurantoin among *E. coli* isolates were 89.3%, 70.7% and 44%, respectively. This finding is similar to other reports (13, 16, 17). *E. coli* was sensitive to cephalosporins such as cefixime and ceftazidime. These data are similar to those obtained in other countries indicating that *E. coli* is still susceptible to many cephalosporins' agents (13). Isolates of *P. aeruginosa*, in our study found exclusively in nosocomial infections, presented a worrying pattern of resistance. These isolates were shown very high resistance to most antimicrobial agents. The rate of resistance

Table 2. Resistance of leading Gram positive bacterial isolates*

Isolate	AMP	STX	CEF	GEN	AMK	NIT	NAL	CLI	CFZ	LEX	ERY	PEN	VAN	OXA
CoNS	9.7	93.8	65.1	58.1	30	35.7	72.1	37.2	72.87	75.97	76.7	99.33	33.8	93
Enterococci	75	92	90	90	90	37	96	87	94	93	89	2	46	100
S. aureus	82.5	77.5	72.5	67.5	50	37.5	100	35	20	77.5	72.5	97.5	42.5	90
G. D. streptococci	75	75	75	50	100	0	100	25	100	100	100	100	0	100
Pneumococci	0	100	100	76.7	100	0	100	33.3	0	0	0	0	0	33.3
S. Viridans	50	100	50	100	100	0	100	100	100	100	50	100	0	100
S. .saprophyticus	0	0	100	100	100	0	100	100	100	100	100	100	100	100

Abbreviations: AMP, ampicillin; STX, trimethoprim-sulfamethoxazole; CEF, cephalothin; GEN, gentamicin; AMK, amikacin; NIT, nitrofurantoin; NAL, nalidixic acid; CLI, clindamycin; CFZ, cefazolin; LEX, cephalexin; ERY, erythromycin; PEN, penicillin; VAN, vancomycin; OXA, oxacillin; CoNS, coagulase negative staphylococci; G. D. streptococci; group D streptococci.
* Data are given as percent.

to both cephalothin and nitrofurantoin among these isolates were 100%. Only amikacin had good activity (65% of isolates were sensitive). A high cephalosporin's resistant strains were found as compared with recent publication on nosocomial isolates recovered from various clinical specimens (18). Our data shown that, *Enterobacter* isolates were highly resistant to kanamycin and cephalothin (78.7% and 76%, respectively), but very sensitive to amikacin and carbenicillin (96% and 94%, respectively).

In this study, resistance to nitrofurantoin and ampicillin among *P. mirabilis* isolates was high (87.9% and 72%, respectively). Among antibiotic used in this investigation, *P. mirabilis* isolates were very sensitive to carbenicillin (86.7%), amikacin (82.3%) and ceftriaxone (85.8%). *Klebsiella* species were shown high resistant to kanamycin (94.6%) and cephalothin (91.7%). However the resistant rate to carbenicillin among *Klebsiella* isolates was very low (4.9%). The resistance rate to cephalosporins among *Klebsiella* isolates was moderate (53-59.5%). Among Gram positive isolates, *staphylococcus epidermidis* were shown high resistant to penicillin (99.33%), but very sensitive to ampicillin (91.3%).

Enterococci isolates was resistant to nalidixic acid and cefazolin in 96% and 94% of the isolates, respectively, but were sensitive to penicillin and vancomycin in 98% and 55% of the isolates, respectively. These finding about resistance of enterococci to vancomycin was similar to previous reports (19). Also resistance rate to penicillin among *S. aureus* isolates was very high (97.5%), but resistance to clindamycin (35%) and vancomycin (46%) was moderate.

The results of this survey endorse the importance of enterobacteriaceae as cause of UTI in children of Tehran, Iran. Furthermore, high antimicrobial resistance rates in *P. aeruginosa* and *Klebsiella* species have profoundly affected the choices of therapeutic agents. The massive use of antibiotics in the pediatric population is probably a risk factor for increased resistance of uropathogens in our study. Moreover we considered only the fully susceptible specimens as sensitive; all intermediate ones were classified as resistant, leading to lower susceptibility rates. Susceptibility to antibiotics is changing in general and increase in antibiotic resistance has been shown all around the world. The main reason for this trend is the increase in antibiotic consumption, because increased usage of antibiotic may affect the rate of UTI caused by resistant bacteria in that population (20). Degree of antibiotic resistance of uropathogens in Children's Medical Center of Tehran is worrying. Global trends of increase and dissemination of resistant strains of uropathogens have shown the necessity of keeping up the monitoring of antibiotic resistance.

In conclusion, based on the data from patients with UTI, we would like to emphasis that prevalence of pathogens isolated from these patients and antimicrobial susceptibility patterns among these pathogens is different in Iran. We are found, antibiotic resistance among these isolates on the rise in Iran. We recommended continuous monitoring of changes in bacterial isolates and antimicrobial resistances among pathogens isolated from UTI in Iranian pediatric children for local intervention efforts in Iran.

Conflict of interests

The authors declare that they have no competing interests.

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