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Etiology Agents and Drug Resistance Pattern of Urinary Tract Infections in Children under 12 Years Old Hospitalized in an Iranian 1000-bed Tertiary Care Hospital

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Epidemiology and resistance patterns of bacterial pathogens in pediatric urinary tract infections (UTIs) show large inter-regional variability, and rates of bacterial resistance are changing due to different antibiotic treatment policy. The aim of this study was to determine the etiology and antibiotic resistance pattern UTI in an Iranian hospital. All children with culture proven UTI from April 2010 to March 2011 were included in our study. Urine culture was deemed positive with a pure growth >10^5CFU/ML (single organism).Identification of all isolates were performed by convectional bacteriology methods .Susceptibility testing was performed by disk diffusion methods as recommended by Clinical laboratory standard institutes. (CLSI) During our study in total 60951 urine specimen were cultured in our laboratory. Of 60951 urine cultures, 2676 (4.3%) were obtained from children under 12 years old. A total of 322 positive urine cultures were yielded. *E.coli* with 137 (42.54%) isolates was the predominant organisms. The second common organism was *K.pneumoniae* with 72(22.36) isolates .Among gram- positive organisms entrococci with 38 (11.80) isolate was the predominant organisms. .*E. coli* was found to be most sensitive to amikacin, nitrofurantoin ,ofloxacin ,ciprofloxacin and least sensitive to most commonly used drugs like ampicillin ,cefazoline , nalidixic acid, Co-trimoxazole .Drug resistance among *K.pneumoniae* isolates were prevalent in comparison *E.coli* isolates. Vancomycin resistance among enterococci isolates was 7.4% .Nitrfuantoin was the second most effective antibiotic against entrococci isolates. Resistance rate of entrococci to tereacyclin ampicillin, nofloxacin was 70.37%, 48.14 and 33.33% respectively.

Key words: UTI, Children, Drug Resistance.

The presence of significant quantity of microorganism in the urine along with or without signs and symptoms of infection is defines as urinary tract infection[1]. Urinary Tract infections (UTIs) have been considered an important risk for the developing of progressive renal disease and long term complications [2, 3].

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UTIs is one of the most prevalent infections among children.[4,5,6] At least 8% of girls and 2% of boys will have a UTIs in childhood, and between 30% and 40% will have another episode within two years.[7]. Early diagnosis and treatment of UTIs in children is a crucial key factor for prevention of risk of hypertension and renal failure[8]. Increasing antibiotic resistance among urinary tract isolates in recent because of wide and misused of antimicrobial agents has been resulted an emergence of increased drug resistance among UTI

etiological agents[9]. It is estimated that more than 80% of bacteria isolated from urine samples are resistant to routinely used antibiotics such as Co-trimoxazole and emerging of ESBLs producing organisms such as *E.coli* and *Klebsiella* spp is the most common therapeutic problem[4,9-12] .

Unfortunately, little has been published on the range and antimicrobial susceptibilities of urinary tract pathogens in children in Iran. In a retrospective study we defined organisms isolated from the urinary tracts infections of children in an Iran referral none teaching 1000-bed tertiary care hospital in Tehran. We also determined antimicrobial resistance profile of all isolates. We hope that this information will encourage other units to examine their data and develop local recommendations for empiric treatment of UTI in children.

METERIALS AND METHODS

During the period, between April 2010 to March 2011 urine specimens of children clinically suspected to have UTI who were admitted to Milad Hospital were sent to Microbiology laboratory for culture and susceptibility testing. Milad hospital is a 1000 bed -tertiary care hospital affiliated by social security organization in Tehran, Iran. Urine specimen was collected from a total of children ages between 0-12 years old. Urine specimens of hospitalized patients were subject of our study. All specimens were collected by conventional methods. In toilet trained pediatrics, a midstream urine specimen was collected. In infants the application of an adhesive, sealed sterile collecting bag after disinfecting of the skin of the genital area was used for obtaining urine specimen. Each specimen was inoculated with a 0.01 ml platinum loop onto Blood agar and EMB agar plates. The plates were incubated at 35ºC for 18 to 24 hours. A positive culture defined as the growth of $\geq 10^5$ CFU /ml of a single uropathogene[13]. Pyuria and hematuria were defined as the presence of more than five leukocytes or erythrocyte per high power (HPF) in centrifuged urine respectively.

The methods used for identification and characterization bacteria included colony morphology, Gram stain, and conventional biochemical tests as described previously[14].

Antimicrobial susceptibility testing was performed on all isolates using disk diffusion method as recommended by CLSI[15]. For susceptibility testing we used commercially available disks (ROSCO Denmark). The test disks used included: ampicillin(10 mcg), Co-trimoxazole (1.25/23.75 mcg), ceftriaxone (30 mcg), Cefazolin (30 mcg), cephalothin (30 mcg), ceftazidime (30mcg),amikacin (30 mcg), tobramycin((10mcg), Vancomycin (30 mcg) ,Penicillin (10units) ,norfloxacin (10 mcg), chloramphenicol (30 mcg),gentamicin (10 mcg), tobramycin (10 mcg), nitrofurantoin (300 mcg), nalidixic acid (30 mcg), amikacin (30 mcg), ofloxacin (5 mcg), ciprofloxacin (5mcg) and tetracycline((30 mcg)

RESULTS

A total of 60951 urine specimens were collected from patients hospitalized in Milad Hospital of the 60951 specimens 2676(4.3%) obtained from children under 12 years old with suspicion of UTI. The age and sex distribution of the children from whom the urine specimen were collected is shown in table-1, Majority of the patients were in the age group of under 8 years old, Relatively more specimens were collected from

Table 1. Age and sex distribution of children with UTIs

AgeGroup	Sex					
	Female		Male		Total	
(yr)	n	%	n	%	n	%
<1	43	21.71	19	15.32	62	19.25
1-4	72	36.36	47	30.90	119	36.95
4-8	47	23.73	36	29.03	83	25.77
8-12	36	18.18	22	17.74	58	18.01
Total	198	61.49	124	38.51	322	100

Table 2. Antibiotic resistance of *E.coli* and *K.pneumoniae* isolated from urine

Antibiotics Organism	Ampicillin	Carbenicillin	Cefazolin	Cefalotin	*Ceftizoxime*	*Ceftriaxone*	Ceftazidime
E. coli	66.42	51.09	62.77	62.77	45.98	50.36	49.63
K. pneumoniae	73.61	54.16	65.27	66.66	52.77	55.55	58.33

Gentamycin	Amikacin	*Tobrom-ycin*	*Ciprofel-oxacin*	*Nitrofu-rantoin*	Oflo-xacin	*Nalidixic* acid	*Co-trimo xazole*	Tetra-cyclin
31.38	6.56	30.65	26.27	9.48	26.27	56.93	53.28	56.93
43.05	31.94	45.83	2.77	48.61	2.77	11.11	31.94	26.38

Table 3. Antibiotic Ressitabce of *E. faecalis* isolated from Urine

Antibiotics Organism	*Nitrofurantoin*	Vancomycine	Norfeloxacine	Penicilline	Ampicillin	Rifampicin	Tetracyclin
E. fecalis	11.11	7.4	48.14	92.59	33.33	70.37	70.37

female children compared with male. The types of organisms isolated are shown in Fig. 1. *Escherichia coli* was isolated in 137 (42.54%) cases and was the predominant organism.This organism was found to be most sensitive to amikacin (92.7%), nitrofurantoin (89.05), ciprofloxacin (73.72%), ofloxacin (73.72), tobramycin (68 .61%) respectively. Resistance to commonly used antibiotics such as ampicillin, Co-trimoxzole and the third generation of cephalosporins such ceftizoxime, ceftriaxone and ceftazidime was prevalent. *K.pneumoniease* was the second leading cause of UTI with 72 isolates. Drug resistance among *K.pneumoniae* isolates were prevalent in comparison *E.coli* isolates. Resistance rate of this organism to routinely used antibiotics for treatment of UTI such as ampicillin and nitrofurantoin was 73.51 and 48.61% respectively. More than 50% of isolates were resistant to third generation of cephalosporins. The most effective antibiotics against *K.pneumoniae* were nalidix acid, ciprofloxacin, and amikacin respectively.

Among gram-positive cocci Enterococci following by S.aureus with 38 and 15 isolates respectively, were the predominant organisms. Resistance rate of Enreococci spp to vancomycin was 7.4% and the majority resistant species was *E. faceuim*. Nitrofurantoin was the second effective antibiotic against Entrococci spp. Resistance to

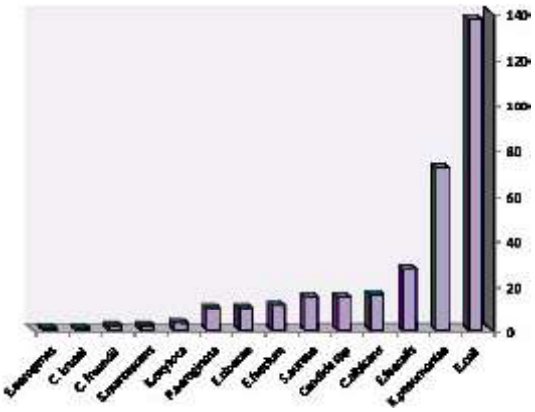

Fig.1.

other antibiotics such as norfloxacin, and tetracycline was 48.14% and 70.37 % respectively.

DISCUSSION

Urinary tract infections are one of the most common infectious diseases in both community and hospital. Nearly 10% of people experiences a UTI during their life and UTIs are the first nosocomial infection[16, 17]. Nosocomial infections are important in terms of their potential for high mortality and morbidity[18].

The prevalence UTIs varies with the sex and age. The prevalence of UTI in girls is higher

than boy. In our study the majority positive growth were from children in the age group less than eight years old. Our finding agrees with other studies which has been carried out previously in Iran and other countries such as Nepal[23,24]

In recent years wide used of antibiotics has been resulted an increased of antibiotics resistance among etiological agents of UTI. It is estimated that more than 80%urine isolates are resistant to commonly used antibiotics used for treatment of UTI.[19-20]

Many studies have been shown that the members of the Enterobacteriaceae including *E. coli* and *Klebsiella* spp. are the most frequently etiological agents of UTI worldwide [17,21]. In our study *E.coli* was the most prevalent organism isolate and accounted 137 (42.54) of all positive specimens. This finding was not in agreement with otter studies in children from other counties. In a study by Rai eta al in Nepal *E.coli* accounted for 93.3 % isolates which is very higher than our finding [24]. A lower rate of infection with *E coli* was previously observed in children with urinary malformations, hospital-acquired infections, a history of UTIs, or receiving prophylactic antibiotics In another pediatric study, *E coli* was more common in girls than in boys, and younger patients were less likely than older patients to be infected with *E.coli* Klebsiella spp with isolates accounted the second most common agent for UTI[6, 23-24].

Our study has shown a high rate of resistance to third- generation cephalosporins in children admitted to the hospital and more than 50% of isolates were resistant to third generation of cephalosporins. In our previous study we also observed a high rate of ESBLs producing *E.coli* and *K.pneumoniae* which are isolated from uine specimen. Resistance rate of *E.coli* and *K.pneumpniae* to third generation of chalosprins in our study is agreement with finding other investigators such as Khotaii *et al*.However other studies have been showed a high rate of sensitivity among isolates of E.coli and K.pneumoniae to third generation of cephalosporins[1]. In our study resistance rate of *E.coli* to commonly used antibiotics for treatment of UTIs such as ampicillin ,Ciprofloxacin, nitrofurantion nalidixic acid and Co-trimoxazole was 66.42%,26.27%9.48%56.93 and 53.28% respectively.These figs for *K.pneumoniae* were 73.61%, 2.77%, 48.62%, 11.11% and 26.38% respectively. Our study showed that resistance rate of *E.coli* to commonly used antibiotics in comparison with *K.pneumoniae* was higher. In spite of susceptibility of *E.coli* and *K.pneumoniae* to fluoroqinolones such as ciprofloxacin and ofloxacin, using of these antibiotics in children has some limitation. Nitrofuantion is one of the widely used antibiotics for treatment of UTIs.In present study resistance rate of *E,coli* and *K.pneumoniae* to this antibiotics was 9.48% and 48.61% respectively. The resistance rate Enteeococci as third agents of UTI against antibiotics such as ampicillin, norfloxacin and tetracycline was 33.33% 48.14% and 70/.37% respectively. Nitofunation was also the second most effective antibiotic against Entrococci isolates which is resemble with our previous findings. [25] .Our study reveled that there is an increasing trends of drug resistance among uropathogenic organisms isolated from children in our hospital .This finding is also true in other centres[4] . The main reason for this trend is the increase in antibiotic usage for treatment and prophylaxis because increased usage of antibiotic may increase the chance of the

UTI caused by resistant bacteria in children[26,27]. The rate of antibiotic resistance in uropathogens in our hospital has shown the necessity of keeping up the monitoring of antibiotic resistance pattern periodically.

CONCLUSSION

In occlusion findings of our study revealed a high incidence of bacterial resistance to antibiotics such as ampicillin, third generation of cephalosporins and Co-trimaxzole in urinary tract infections among children admitted to our hospital. Our results suggest the physicians to be cautious about treatment with antibiotics. Regular monitoring is necessary to obtain reliable data regarding resistance pattern of among etiological agents of UTI for optimal empirical therapy of childrens with UTIs. We also suggest that empirical antibiotic therapy should be based on the data of local prevalence of organisms involved in UTI and drug susceptibility testing results rather than on universal guidelines. In other hand rational antibiotic use as well as adoption of strict national antibiotic policy is nesseccary to regulate the prescription, sale and use of antibiotics.

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