Original Article

HIGH RESISTANCE IN UROPATHOGENS ISOLATED FROM CHILDREN AT PAKISTANI HOSPITAL

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ABSTRACT:

Urinary tract infection is one of the most important clinical infections in the world. Due to empirical therapy, antibiotic resistance pattern has been altered in the causative microbes of urinary tract infection in childhood. The objective of this study was to find out causative agents of urinary tract infection in children and their antimicrobial profile. A total of 1370 urine samples were collected and identified by standard microbiological techniques. Antimicrobial susceptibility of isolates was performed according to CLSI 2012 guidelines. Significant bacterial count was found in 8.32% children. Most common isolated pathogens were *Escherichia coli* (60.5%) and *Klebsiella pneumoniae* (26.3%). Pathogens were resistant to cefixime (83%), ceftriaxone (81%) and amoxicillin-clavulanic acid (69%). *Acinetobacter baumannii* were found most resistant. Meropenem, amikacin and piperacillin-tazobactam were most effective. It is concluded that multidrug resistant organisms causing UTI in children in our locality. It is suggested that local surveillance studies should be done continuously to screen antimicrobial resistance.

KEY WORDS: Urinary tract infections, antimicrobial resistance, children.

INTRODUCTION:

Urinary tract infection (UTI) is one of the most commonly encountered diseases in clinical practice. Bacterial infections of the urinary tract are flagship, infecting a worldwide population of 150 million annually[1]. UTI is the second most common infectious disease in toddlers and infants[2,3]. It causes considerable morbidity and mortality, during first two years of life, especially in children with weakened immune system and those who are hospitalized[4-6]. The reported incidence of UTI is 7% among girls and 2% among boys during the first 6 years of life[7]. Reports show a huge variability of infection rates, among children of different ethnic origins, ranging from 3.3% in USA to 37.5% in Pakistan[8,9].

Commensals of the perineum are major contributors of childhood UTIs[9]. Gram negative rods (GNR) are predominant agents of urinary tract infections. Various reports showed infectivity rates of 80-85% with gram negative rods while Gram positive cocci were found to be responsible for 15-20% of UTIs[10]. Among GNR *Escherichia coli* is responsible for 75% to 95% of UTIs followed by *Klebsiella pneumoniae*[11,12]. Rapid recovery from complaints and prevention of related complications such as urosepsis, urolithiasis, renal abscess and permanent renal parenchymal damage are the main objects of childhood UTI management[13]. UTI may lead to transient renal damage in 40% and permanent renal scarring in 5% of patients[14]. Children having UTI are usually given empirical antibiotic therapy Thus, a parallel correlation between the overuse of antimicrobials and emergence of increasingly resistant bacteria seems natural[15]. The UTI recurrence rate is 12% in children[16].

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Uropathogens among pediatric patients are becoming resistant to commonly used antibiotics such as fluoroquinolones and third generation cephalosporins[17]. These conditions make the treatment more challenging and even can lead to death. Detection and resistance of UTI causing pathogens in clinical set ups which is essential and helpful in improving the efficacy of empirical treatment. Therefore, we designed this study to determine the frequency and resistant pattern of uropathogen in a tertiary care hospital, Lahore.

METHODOLOGY:

Study population

This observational study was carried out at Fatima Memorial Hospital Lahore, Pakistan. A total of 1370 urine samples of children were collected during a period of six months from December 2012 to May 2013. Sterile containers were used to collect urine specimen from children by which technique.

Isolation and identification of pathogen

All the specimens were inoculated on CLED agar using standard aseptic inoculation technique and incubated aerobically at 37^{0}C for 24 hours. Initial identification was carried out on the basis of morphology and cultural characteristics and standard microbiological techniques. Among gram positive organisms the *Streptococcus spp.* were identified down to specie level by Lancefield grouping (Latex agglutination). Whereas, gram-negative isolates were identified by API 20E and 20NE (BioMerieux France).

Antimicrobial susceptibility testing

Antimicrobial susceptibility of isolates was performed by Kirby Bauer disc diffusion method, according to Clinical Laboratory Standards Institute (CLSI) 2012 guidelines. Drugs used for testing were amoxicillin-clavulanic acid (20/10µg), amikacin (30µg), ciprofloxacin (5µg), fosfomycin (200µg), ceftriaxone (30µg), cefixime (5µg), aztreonam (30µg), meropenem (10µg) and piperacillin-tazobactam (100/10 µg).

RESULTS:

In current study, significant bacteriuria was found in 114 (8.32%) patients out of 1370. Children of both genders were infected almost equally. Most of the infected children were in <5 years old age group (71.2%) and the lowest were in the 9-12 years old age group (12.3%). In positive culture samples, majority were gram negative rods (91.22%) while remaining were gram positive cocci (8.78%). *Escherichia coli* (60.5%) was found to be the commonest organism followed by *Klebsiella pneumoniae* (26.3%), *Pseudomonas aeruginosa* (2.6%) and *Acinetobacter baumannii* (1.8%) Table1. Among Gram positive cocci, Group D *Streptococcus* (8.8%) were the only isolated organisms.

Antimicrobial susceptibility results showed that the majority of the isolates were resistant to cefixime (83%), ceftriaxone (81%) and augmentin (69%) (Figure 1). *Acinetobacter baumannii* were found to be the most resistant organisms as these isolates showed complete resistance to all the tested antibiotics; amikacin, ciprofloxacin, ceftriaxone, meropenem and piperacillin-tazobactam. *Escherichia coli* and *Klebsiella pneumoniae* were mostly resistant to cefixime (86%), clavulanic acid and ceftriaxone (73.3%), aztreonam 54% and ciprofloxacin 46% (Table 2). Most effective antibiotics were meropenem, amikacin and piperacillin-tazobactam.

Table 1. Frequency of organisms isolated from urine samples

Organism (n=114)	Frequency	(%)
Escherichia coli	69	60.5%
Klebsiella pneumoniae	30	26.3%
Pseud omonas aeruginosa	03	2.6%
Acinetobacter baumannii	02	1.8%
Streptococcus group D	10	8.8%

Table 2. Antimicrobial profile of isolated organisms

Organisms	Amoxicillin - clavulanic acid (20/10ug)	Amikacin (30ug)	Ciprofloxacin (5ug)	cin (200ug)	Ceftriaxone (30ug)	Cefixime (5ug)	Aztreonam (30ug)	meropenem (10ug)	Pipperacillin-Tazobactam (100/10 ug)
Escherichia coli (n= 69)	(63.8%)	(7.3%)	(46.4%)	(1.4%)	(71%)	(78.3%)	(53.6%)	(0%)	(1.4%)
***Klebsiella pneumoniae* (n=30)**	(73.3%)	(16.7%)	(46.7%)	(6.7%)	(73.3%)	(86.7%)	(50%)	(0%)	(6.7%)
Pseudomonas aeruginosae (n=3)	NT	(0%)	(33.3%)	NT	NT	NT	NT	(0%)	(0%)
Acinetobacter baumannii (n=2)	NT	(100%)	NT	NT	(100%)	NT	NT	(100%)	(100%)
Streptococcus group D (n=10)	NT	NT	(70%)	(40%)	NT	NT	NT	NT	NT

NT= Not tested

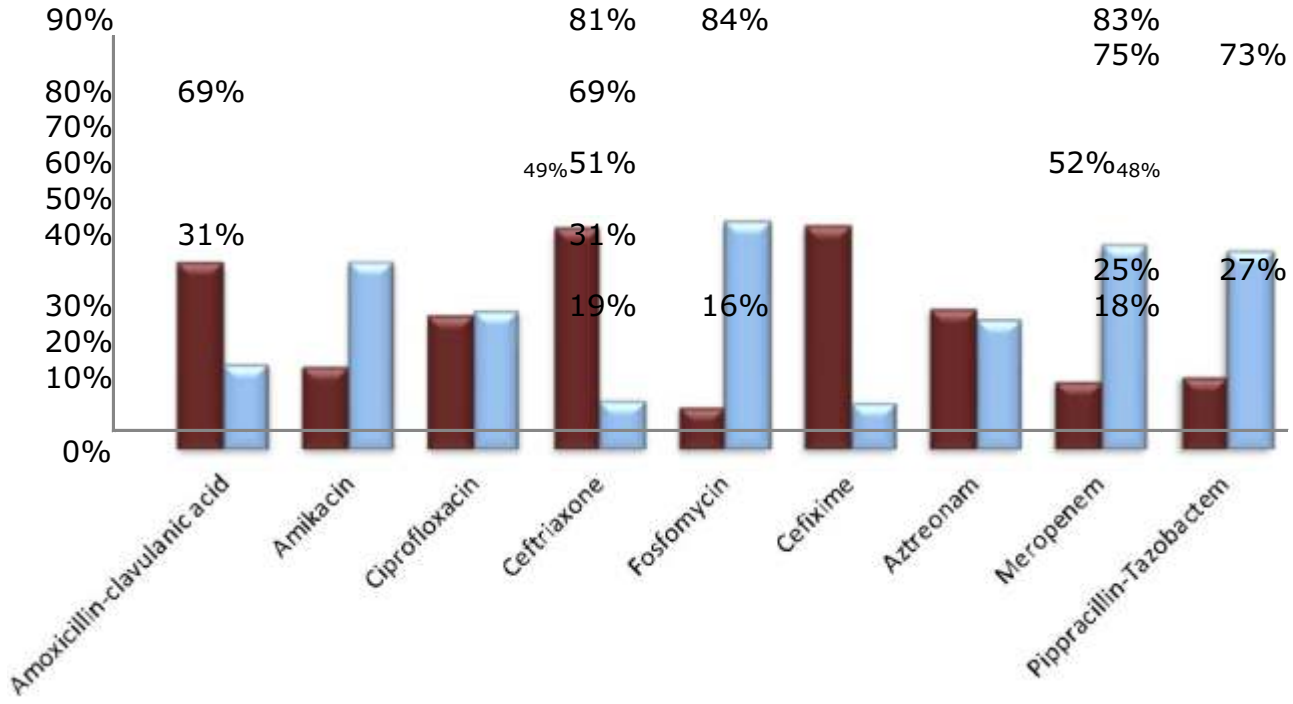

Figure 1. Overall susceptibility pattern of organisms isolated

DISCUSSION:

UTI is among one of the most common problems in children. Its prevalence varies with age and sex of children. It has been reported in one percent of boys and three to five percent of girls[18,13]. In the present study, we observed that incidence of UTI was same among males (49.9%) and females (50.9%). Study conducted in Turkey has also reported almost similar results i.e. 47.2% and 52.8% in males and females respectively[18]. Most of the infected children were in age group of less than 5 years which is in accordance with studies conducted in Nepal (32.34%), Iran 77% and Nepal (65%)[17, 19,20].

Among the total samples, only 8.32% samples were positive for bacterial growth which in accordance with studies done by Mansour et al (8.7%) and Banazadehi et al (8.49%)[21,22]. In this study, 91.7% gram negative rods of 8.32% positive samples were isolated which are almost similar with previous studies conducted in Iran (90.3%), Turkey (89%), and Australia (96%)[23, 24,25]. Due to close proximity of rectum with urinary tract, poor personal hygiene contributes to a high percentage of Enterobacteriaceae infections in UTI patients[26,27].

In the present study, *E. coli* (60.5%) was the commonest isolated pathogen among children with UTI which is in accordance with results of other studies done in Pakistan, Iran and Nigeria [28,29,30]. Various other studies also documented that *E. coli* is the predominant pathogen in UTI patients[31,28]. However, in contrast to this study, two studies in Pakistan also documented that *Klebsiella pneumoniae* is the most common pathogen among UTI infected children [27,32]. Other UTI isolates in this study were *Klebsiella pneumoniae* (26.3%), *Streptococcus group D* (8.8%), *Pseudomonas aeruginosa* (2.6%) and *Acinetobacter baumannii* (1.8%) which are different from various other studies[33,2]. Difference in isolated organisms might be due to difference in geographical distribution of the pathogens[34].

Antibiotic susceptibility pattern of the pathogens isolated is shown in table 2. And almost similar results have been reported by Pakistani and Indian studies in which almost 70% *Klebsiella pneumoniae* and *E. coli* were resistant to commonly available antibiotics[34].

Acinetobacter baumannii were found to be the most resistant organisms as these isolates showed (100%) resistance to all the tested antibiotics. Study from Pakistan reported 50% resistant isolates of *Acinetobacter baumannii* which is in contrary to the present study. This indicated that resistance in *Acinetobacter baumannii* is snowballing day by day in our setup.

High resistance in pathogens is associated with incongruous infection control practices. Major contributing factors are contaminated intravenous catheters, poor hospital sterilization and disinfection practices and colonized hands of health care staff[34]. Another important factor is the absurd use of pragmatic remedy which is not according to WHO criteria[35].

Finally, it is the need of the hour to conduct large longitudinal nationwide studies to determine incidence, demographic features, potential etiology, and antibiotic resistance. This will help in constructing appropriate recommendations for the treatment and prophylaxis of children with UTI in local set-ups.

However, there are also limitations in our study due to limited resources and limited research facilites. We did not perform phenotypic testing nor genotypic testing of bacterial enzymes and any other phenomenum which induce resistance.

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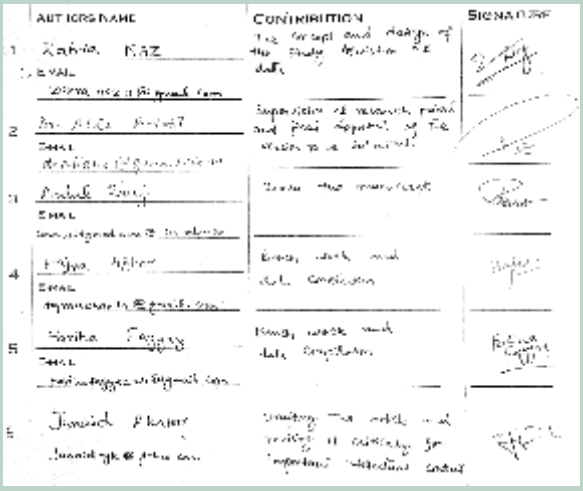

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After Revision

When you have to depart from this world and have to meet death (eventually), then why wish delay (why feel nervous about death).

Hazrat Ali (Karmulha Wajhay)