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Research article

PREVALENCE OF MULTIDRUG RESISTANT PATHOGENS IN CHILDREN WITH URINARY TRACT INFECTION: A RETROSPECTIVE ANALYSIS

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ABSTRACT

Urinary tract infection (UTI) is one of the commonest medical problems in children. It can distress the child and may cause kidney damage. Prompt diagnosis and effective treatment can prevent complications in the child. But treatment of UTI in children has now become a challenge due to the emergence of multidrug resistant bacteria. **Aims & Objectives:** To know the bacteriological profile and susceptibility pattern of urinary tract infections in children and to know the prevalence of multidrug resistant uropathogens. **Materials & Methods:** A retrospective analysis was done on all paediatric urine samples for a period of one year. A total of 1581 samples were included in the study. Antimicrobial susceptibility testing was done on samples showing significant growth by Kirby-Bauer disc diffusion method. Statistical analysis: Prevalence and pattern were analyzed using proportions and percentages. **Results:** *E.coli* was the most predominant organism (56%) causing UTI in children followed by *Klebsiella sp* (17%). Fifty three percent of gram negative organisms isolated from children were found to be multidrug resistant. Majority of *E. coli* isolates were found to be highly resistant to Ampicillin (91%) and Cotrimoxazole (82%) and highly sensitive to Imipenem (99%) and Amikacin (93%). **Conclusion:** Paediatric UTI was common in children less than 5 years of age. Gram negative bacteria (*E. coli and Klebsiella sp)* were more common than gram positive bacteria. Our study revealed that multidrug resistance was higher in *E.coli.*

Keywords: Children, Urinary tract infection, Multidrug resistance, *E.coli*

INTRODUCTION

Urinary tract infections are common among paediatric age group and are important cause of morbidity. UTI may vary by gender and age. Many occasions it may be difficult to make a diagnosis of UTI in children as the presenting symptoms like fever and chills are usually nonspecific. An early urine culture and sensitivity can guide to a proper diagnosis and treatment. Although several microorganisms are responsible for UTI, *E.coli, Klebsiella sp* and *Proteus sp* are the most common cause of urinary tract infection in children[1].Treatment is often started empirically based on the local prevalence of organisms and susceptibility pattern. Presently this situation is challenging to the treating paediatricians as multidrug resistant organisms are on the rise among children.[2] Multidrug resistance is defined as resistance to two or more different structural classes of antimicrobial agents[3]. Multidrug resistance has become a universal phenomenon across organisms and may complicate the therapeutic management of infections. Antibiotic resistance can cause serious disease and is an important public health problem.

Drug resistance has been a common occurrence in infections among adults and elderly, but now it is frequently seen in children as well. Overuse and use of incomplete course of antibiotics as well as empirical antibiotic therapy have been the major contributing factor in the development of multidrug resistant bacteria[4]. To reduce the rate of resistance it is pertinent to initiate antibiotic therapy after microbiological confirmation. In a study conducted by Mohammed et al[5] in Delhi, *E.coli* was the predominant pathogen causing UTI and resistance against different generation of cephalosporin was found to be 60–80 % in paediatric patients. There are various studies on the prevalence of drug resistance in adults with urinary tract infections[6, 7], but there are very few studies on children. Hence this study was taken up in our hospital to know the bacteriological profile and susceptibility pattern of organisms causing UTI among children and also to know the prevalence of multidrug resistant uropathogens.

MATERIALS AND METHODS

This is a retrospective descriptive study undertaken to analyze the data collected during the period of one year from January 2013 to December 2013 in the department of Microbiology at a tertiary care hospital. Institutional ethical clearance has been obtained. The data analysed included all midstream urine samples received from children (<14y) of age from paediatric ward with provisional diagnosis mentioned as UTI in the laboratory requisition forms. Children having fever with obvious foci of infection like Respiratory tract infections were excluded from the study. A total of 1581 samples were included. Direct gram staining was done on uncentrifuged urine samples and culture was done on CLED (Cystine Lactose Electrolyte Deficient) agar by semiquantitaive technique[8]. Samples showing $>10^5$ col/ml were taken as significant. Organisms were identified by standard microbiological procedures[8]. Antimicrobial sensitivity testing was done by Kirby – Bauer disc diffusion method as per CLSI guidelines[9]. *E. coli* ATCC 25922, and *P. aeruginosa* ATCC 27853 were used as controls. Ampicillin (10µg), co-trimoxazole (1.25/23.75 µg), cefuroxime (30 µg), norfloxacin (10 µg), nitrofurantoin (300 µg), and amikacin (30 µg) were used as I line agents. If three or more agents are found to be resistant then, ceftriaxone (30 µg), cefepime (30 µg), piperacillin - tazobactam (100/10 µg), imipenem (10 µg) and meropenem (10 µg) were used as II line agents. All antibiotic discs were from Himedia Laboratories, Mumbai. The isolates were reported as Susceptible (S), Intermediate (I) and Resistant) as per CLSI guidelines[9.]

RESULTS

A total of 1581 samples were included in the study, out of which 229 samples (14%) showed significant growth. Out of 229 samples 206 were gram negative bacilli (90%) and 23 were gram positive cocci (10%). Among these 229 cases, males (52%) were marginally affected more than females (48%). UTI was predominantly seen in the age group between 0-5years. The age wise distribution of the prevalence of UTI is shown in table 1.

Table 1: Age wise distribution of isolates

S.no	Age	Isolates (%)
1.	1-5 yrs	131 (57%)
2.	5 – 10 yrs	63 (27%)
3.	Above 10 but below 14 years	35 (15%)

Among gram negative bacteria, *E.coli* was the predominant isolate (56%) followed by *klebsiella sp* (17%) and *Proteus sp* (6%). The isolation of various pathogens is depicted in table 2. Among gram positive cocci, *Enterococcus faecalis* was the predominant isolate (98%). The majority of isolates of *E.coli* was found to be highly resistant to ampicillin (91%) followed by co-trimoxazole (82%). It was also found to be resistant to norfloxacin (68%), ceftriaxone (76%) and meropenem (77%). *Klebsiella sp* was found to be most resistant to ceftriaxone (70%) and meropenem (50%). All gram negative bacteria in general were found to be highly sensitive to nitrofurantoin, amikacin, imipenem and piperacillin – tazobactam.

Non fermenting gram negative bacteria was highly resistant to nitrofurantoin (90%), while it was sensitive to all other agents (table 3). *Enterococcus faecalis* which was the predominant isolate among gram positive cocci was highly resistant to norfloxacin (80%) but sensitive to other agents (Table 4). Among 206 isolates of gram negative bacilli, 123 isolates (53%) were found to be resistant

to 3 or more drugs and hence considered to be multidrug resistant.

Multidrug resistance was not found among gram positive organisms. Among gram negative organisms MDR was more prevalent in *E. coli* (75%) followed by *Klebsiella sp* (28%).

Table showing percentage (%) of gram negative and gram positive isolates with multidrug resistant organisms.

Table 2: Pattern of isolates

Organisms	Isolates (%)	MDR isolates (%)
GNB (Gram negative bacilli)		
E.coli	116 (56%)	88 (42%)
Klebsiella sp	35 (17%)	10 (5%)
Citrobacter sp	9 (4%)	7 (3%)
Enterobacter sp	8 (4%)	5 (2%)
Non fermenting GNB	22 (11%)	5 (2%)
Proteus sp	16 (7%)	8 (4%)
Total	**206 (90%)**	**123 (53%)**
GPC (Gram positive Cocci)		
Enterococcus faecalis	23 (10%)	0

Table 3: Number (%) of Gram negative bacteria resistant to antimicrobial agents

Antibiotic	*E. coli* n=116 (%)	*Klebsiella sp* n= 35	*Proteus sp* n = 16	Nonfermenting GNB (n=22)
AMP	105/116 (90%)	35/35 (100%)	11/16 (70%)	6/22 (28%)
CoT	95/116 (82%)	26/35 (74%)	11/16 (70%)	2/18 (12%)
CXM	81/106 (76%)	21/32 (66%)	6/12 (50%)	4/18 (23%)
NX	72/106 (68%)	11/33 (33%)	2/12 (17%)	3/18 (17%)
NT	13/113 (12%)	10/34 (29.4%)	11/15 (73%)	2/19 (11%)
CTR	85/113 (75%)	22/35 (63%)	1/16 (7%)	7/19 (39%)
AMK	7/114 (6%)	6/35 (17%)	2/15 (13%)	2/18 (12%)
CPM	59/92 (64%)	15/31 (50%)	8/15 (53%)	2/18 (12%)
PIT	12/106 (11%)	3/35 (9%)	2/15 (13%)	1/18 (5%)
IM	1/106 (1%)	2/33 (6%)	1/15 (6%)	1/18 (5%)
MR	70/106 (66%)	12/30 (40%)	4/14 (28%)	3/18 (17%)

Amp = ampicillin, CoT = Cotrimoxazole, Cxm= cefuroxime, Nx = norfloxacin, Nt = Nitrofurantoin, Ctr = ceftriaxone, Amk = amikacin, Cpm = cefepime, PIT = piperacillin – tazobactam, Im = imipenem, MR = meropenem

Table 4: Number of isolates (%) of *Enterococcus faecalis* resistant to antimicrobial agents

Organism	Amp	Gen	Nx	Nt		L
Enterococcus sp	6/21 (33%)	7/21 (39%)	16/21 (80%)	3/21 (15%)		0 (0

Gen = gentamicin, LZ = linezolid,

DISCUSSION

The appropriate choice of empiric antibiotic for a child with UTI requires adequate knowledge of the prevalence of organisms and resistance pattern. The emergence of multidrug resistant organisms is a cause of concern worldwide. This study describes the resistance profile of uropathogens and the prevalence of multidrug organisms among children. In this study, we isolated 229 (14%) uropathogens out of 1581 samples from children. In a similar study conducted by shreshta et al[10], 60 uropathogens (16%) were obtained from 372 samples. UTI is a common problem in children, but the prevalence varies with age and sex of children[11.] Our study showed a marginally higher positivity of UTI among males (52%) compared to females (48%). A similar result was seen in a study conducted by Patel P et al[12]. The majority of infections was seen in children under the age of 5 years (57%) which could be attributed to ineffective toilet training in this age group and the chance of ascending infection from the urethra which can lead to complications like recurrent infections and pyelonephritis[13].

Gram negative bacteria were the predominant cause of UTI when compared to gram positive bacteria[3]. Our study revealed *E.coli* as the predominant organism (56%) causing UTI among children. There are several studies showing *E.coli* as the significant pathogen causing UTI[12,14]. *Klebsiella sp* was the second most predominant organism followed by nonfermenting gram negative bacilli and *proteus sp* in our study.

With regard to sensitivity pattern, *E.coli* was found to be sensitive only to higher antibiotics like imipenem (99%) piperacillin tazobactam (89%) and amikacin (94%) while front line antibiotics like ampicillin and cotrimoxazole which are often used by paediatricians to treat UTI showed a high resistance (90% and 82% respectively). In a similar study conducted by Patel

P[12], *E.coli* was found to be highly sensitive to gentamicin, amikacin and piperacillin -tazobactam . Our study showed nitrofurantoin having lesser resistance to gram negative bacilli when compared to ampicillin and cotrimoxazole which was observed in other studies also[10, 15,16]. As *E. coli* resistant to trimethoprim - sulphamethoxazole and Fluoro quinolones has become more common, nitrofurantoin has become an important oral agent in the treatment of uncomplicated urinary tract infection[17].

With increasing resistance to ampicillin and co trimoxazole[1,2], physicians started using quinolones and cephalosporins as first line agents. But unfortunately due to excessive use of these agents resistance is fast emerging in these agents too[18].A study conducted by NK Ganguly et al[19] showed that one of the main reasons for antibiotic resistance seems to be increased use of antibiotics. They have documented that between 2005 and 2009 the unit of antibiotics sold increased by about 40 percent and particularly sale of cephalosporins strikingly increased by about 60 percent. Even in our study norfloxacin showed 68% resistance and ceftriaxone, a III generation cephalosporins showed 75% resistance. The present study revealed that all gram negative bacteria had a high sensitivity to nitrofurantoin, amikacin and imipenem which is concurrent to other studies conducted in other parts of India as well[15]. *Enterococcus faecalis* a gram positive bacteria, in contrast to gram negative bacteria was found to be sensitive to all antibiotics except to norfloxacin.

In the present study prevalence of multidrug resistant organisms among gram negative bacilli was about 53%, which means 123 organisms out of 206 were resistant to two or more different structural classes of antibiotics. Among 123 MDR isolates, maximum isolates (75%) were *E.coli*. Similar studies conducted elsewhere also showed that maximum MDR isolates were seen in *E.coli* [10,19,20]. Since *E.coli* is the major causative organism causing UTI across age group, various drugs are being used in hospitals empirically for treating *E.coli* which leads to drug resistance

CONCLUSION

The present study reveals that *E. coli* was the most common organism isolated and constituted 42% of all isolates from children with UTI. *E.coli* was found to be highly sensitive to amikacin (94%), imipenem(99%), nitrofurantoin(88%) and piperacillin-tazobactam(89%) and was highly resistant to ampicillin (90%) and cotrimoxazole (82%). Paediatricians can hence defer using ampicillin and cotrimoxazole as first line agents and rather prefer nitrofurantoin and amikacin to treat UTI in children. The only disadvantage being amikacin has to be administered only intravenously. Ceftriaxone used commonly to treat children admitted with UTI, henceforth may have to be used only after obtaining the sensitivity report as there is emerging resistance (75%) to this drug as seen in the present study. Our study showed that the prevalence rate of multidrug resistant isolates was 53% among gram negative bacilli. As susceptibility pattern is changing around the globe, a regular monitoring of antibiotic resistance pattern is required to ensure proper therapy for children with urinary tract infections.

Limitation of study: Although our sample size is large, the number of cases analyzed with significant growth is less which is a limitation of our study.

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Conflict of Interest: Nil

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