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ORIGINAL ARTICLE

Patterns of antibiotics sensitivity in culture positive cases of urinary tract infections in children.

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ABSTRACT… Objective: To determine the effective narrow spectrum antibiotics for treatment of UTI in children in order to control the rapidly increasing antibiotic resistance to broad spectrum antibiotics. **Study Design:** Prospective Clinical study. **Setting:** Department of Pediatric, Akbar Niazi Teaching Hospital, Bhara Kahu-Pakistan. **Period:** January 2021 to December 2021. **Material & Methods:** 361 children with clinical suspicion of UTI were enrolled in the study.. Antimicrobial sensitivity test was applied on Samples on which bacterial growth was identified using Clinical Laboratory Standards Institute (CLSI) guidelines. The data was analyzed using SPSS version 25. **Results:** Total 361 patients were enrolled in the study according to inclusion criteria, out of which, 30 (8.3%) were infants (<1 years old), 178 (49.3%) were aged 1 to 5 years and 153 (42.4%) were aged from 5 to 12 years of age. Out of 361 patients, 125 (34.6%) patients were males and 236 (65.4%) were females. Out of 124 patients, whose urine culture was positive, most common pathogen was E. coli that was observed in 92 (25.5%) cases, followed by Klebsialla in 9 (2.5%) and enterococcus in 9 (2.5%) patients, Pseudomonas in 5 (1.4%), Proteus in 4 (1.1%), Mirabilis in 4 (1.1%), Acinobacter in 2 (0.6%), and enterobacter in 2 (0.6%) cases. Spectrum of sensitivity of 17 drugs was studied. The most sensitive drug was Imipenem, (29.9%), followed by Nitrofurantoin, Fosfomycin (25.8%), Amikacin (24.1%), Piperacilin / Tazobactam (22.7%). **Conclusion:** Thus E. coli was the most common pathogen and the most sensitive drug was Imipenem, followed by Nitrofurantoin, Fosfomycin, Amikacin, and Piperacilin / Tazobactam.

Key words: Urinary Tract Infection, Antibiotic Sensitivity, Uropathogens, Narrow Spectrum Antibiotics.

INTRODUCTION

Urinary tract infection (UTI) is a common and potentially serious bacterial infection in children[1], and one of the major reasons for parents bringing their children to hospitals, both outpatient and emergency.[2,3] Accurate and timely diagnosis and treatment are critical for avoiding long-term morbidity and sequelae e.g. hypertension, proteinuria, and chronic kidney disease. Children's UTI management and diagnosis differ from that of adults and necessitate special consideration.[1] According to the American Academy of Pediatrics' UTI clinical practice guidelines, febrile children between the ages of 2 months and 24 months should have a higher degree of chances to suffer from UTI. The frequency of this infection is high in both genders male and female during first year of life.[2,4,5] Whereas, few studies showed estimated percentage of UTI in male and female that at least 1 percent male and 3 percent of female experience UTI once before 11 years of age. In particular among girls, 30–50% of these patients will experience another episode within three months to 24 months.[6]

The level of evidence and grade of advice regarding pediatric UTI in Asia are as follows. It is helpful to classify children with UTI according to the sites of infection, the number of episodes, the severity, or the presence of complicating factors to determine whether or not they are at risk of renal damage.[7] The most significant and, in some cases, the only symptom of pediatric UTI is unexplained fever, especially in young children. The age of the patient has a significant impact on the wide range of UTI symptoms and signs.

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In young infants, fever may be the only symptom present, and it is recognized as a significant indicator of renal parenchymal involvement. About 5% of children 2 to 24 months old who have a fever with no obvious cause have a UTI.[8] For protection against long-term effects, early UTI treatment with a potent antibiotic is crucial. Delaying treatment increases the possibility of kidney scarring.[9] Renal scarring is less likely if acute pyelonephritis is treated with a suitable antibiotic within 48 hours of the onset of a fever and recurrent UTI is avoided. Since common antibiotic-resistant pathogens are on the rise, it is important to discourage their[1] indiscriminate use in UTI cases that are questionable.[10]

Antimicrobial therapy is therefore started empirically in nearly all cases of UTI in children before the outcome of a urine culture is known. Due to various antibiotic treatments, the sensitivity of bacterial uropathogens to antibiotics exhibits significant geographic and historical variability. So choosing the right antibiotic for empirical treatment requires knowledge of the sensitivity pattern of common uropathogens as reported by regional epidemiological studies.[11]

We don't have any latest evidence based guidelines for empirical treatment of UTI in children in Pakistan. This study was done to determine the patterns of antibiotic sensitivity of common uropathogens in children in order to recommend the most effective narrow spectrum antibiotics for treatment of UTI in children so that we can control the rapidly increasing antibiotic resistance to broad spectrum antibiotics.

MATERIAL & METHODS

The study design is prospective clinical study with intention-to-treat. This study was carried out on children of both genders from 2 months to 12 years with clinical suspicion of UTI with fever or fever without focus as per inclusion criteria and Patients with structural anomalies of urinary tract were excluded from the study as mentioned in (exclusion criteria). Sample size of 361 with Non- probability consecutive sampling as sample technique were collected from Pediatric Department of Akbar Niazi Teaching Hospital, Bhara Kahu-Pakistan from Jan 2021 to Dec 2021. After approval from hospital ethics committee for this study (23/MDC/IRB-2019), patients fulfilling inclusion criteria were enrolled in study. Data was recorded by on duty doctors on specially designed Performa after informed consent of caretakers of patients. Empirical treatment was started in all patients. Urine samples (5ml) were collected via midstream for > 1 year, catheter aspirated/collecting bag for 2 months to 1 year). Samples were sent to microbiology laboratory with in 1 hour of collection. Urine microscopy, culture and bacterial identification was done by using standard microbiological guidelines. For performing urine culture sample was first inoculated on CLED agar using 1 micron wire loop. Then it was incubated for 24 to 48 hours at 37 º C. Antimicrobial sensitivity test was applied on Samples on which bacterial growth was identified for next 24 hours using Muller Hinton agar using Clinical Laboratory Standards Institute (CLSI) guidelines for UTI. OPD patients were followed after 3 days along with urine culture report. IPD patients were reviewed on daily basis. Treatment was modified after reports of urine culture. The data was analyzed using SPSS version 25.

RESULTS

Total 361 patients were enrolled in the study according to inclusion criteria, out of which, 30 (8.3%) were infants (<1 years old), 178 (49.3%) were aged 1 to 5 years and 153 (42.4%) were aged from 5 to 12 years of age. Out of 361 patients, 125 (34.6%) patients were males and 236 (65.4%) were females. Out of 361 patients, 301 (83.4%) patients presented with fever without focus, 39 (10.8%) patients presented with fever along with specific symptoms of urinary tract infection while 21 (5.8%) patients presented with fever and nonspecific symptoms of urinary tract infection. About 124 (34.3%) patients showed growth of different organisms on their urine culture reports while 237 (65.7%) patients had no growth on urine culture as shown in Table-I.

Out of 124 patients, whose urine culture was positive, most common pathogen was E. coli that was observed in 92 (25.5%) cases, followed by Klebsialla in 9 (2.5%) and enterococcus in 9 (2.5%)

patients, Pseudomonas in 5 (1.4%), Proteus in 4 (1.1%), Mirabilis in 4 (1.1%), Acinobacter in 2 (0.6%), and enterobacter in 2 (0.6%) cases as shown in Table-II.

	F (%), mean ± SD
n	361
Age <1year	30 (8.3%)
1 to 5 years	178 (49.3%)
5 to 12 years	153 (42.4%)
Gender	
Male	125 (34.6%)
Female	236 (65.4%)
Clinical features	
Fever without focus	301 (83.4%)
Fever with specific symptoms	39 (10.8%)
Fever with non-specific symptoms	21 (5.8%)
Urine culture	
Positive	124 (34.3%)
Negative	237 (65.7%)

Table-I. Basic features of patients enrolled

Pathogen	F (%)
E. coli	92 (25.5%)
Klebsialla	9 (2.5%)
Enterococcus	9 (2.5%)
Pseudomonas	5 (1.4%)
Proteus	4 (1.1%)
Mirabillis	4 (1.1%)
Acinobacter	2 (0.6%)
Enterobacter	2 (0.6%)
None	238 (65.9%)

Table-II. Pathogen detected

Spectrum of sensitivity of 17 drugs was studied. The most sensitive drug was Imipenem, (29.9%), followed by Nitrofurantoin, Fosfomycin (25.8%), Amikacin (24.1%), Piperacilin / Tazobactam (22.7%), while others were less sensitive including Amoxicillin, Augmentin, Ampicillin, Ceftriaxone, Cefixime, Cefotaxime, Cefuroxime, Gentamicin, Cotrimoxazole, Minocycline, Ciprofloxacin, and Levofloxacin as shown in Table-III.

Antibiotic	Sensitive	Resistant	Intermediate	No Growth
Ampicillin	7 (1.9%)	112 (31.0%)	0 (0%)	242 (67.0%)
Amoxicillin	6 (1.7%)	111 (30.7%)	2 (0.6%)	242 (67.0%)
Augmentin	10 (2.8%)	105 (29.1%)	4 (1.1%)	242 (67.0%)
Ceftriaxone	18 (5.0%)	101 (28.0%)	0 (0%)	242 (67.0%)
Cefixim	16 (4.4%)	103 (28.5%)	0 (0%)	242 (67.0%)
Ciprofloxacin	48 (13.3%)	71 (19.7%)	0 (0%)	242 (67.0%)
Amikacin	87 (24.1%)	27 (7.5%)	5 (1.4%)	242 (67.0%)
Gentamycin	68 (18.8%)	46 (12.7%)	5 (1.4%)	242 (67.0%)
Levofloxacin	44 (12.2%)	73 (20.2%)	2 (0.6%)	242 (67.0%)
Imepenem	108 (29.9%)	11 (3.0%)	0 (0%)	242 (67.0%)
Piperacillin-Tazobactum	82 (22.7%)	32 (8.9%)	5 (1.4%)	242 (67.0%)
Fosfomycin	93 (25.8%)	22 (6.1%)	2 (0.6%)	242 (67.0%)
Nitrofurantoin	93 (25.8%)	16 (4.4%)	10 (2.8%)	242 (67.0%)
Cefuroxime	4 (1.1%)	115 (31.9%)	0 (0%)	242 (67.0%)
Minocycline	16 (4.4%)	97 (26.9%)	6 (1.7%)	242 (67.0%)
Cotrimaxazole	5 (1.4%)	114 (31.6%)	0 (0%)	242 (67.0%)
Cefotixime	9 (2.5%)	102 (28.3%)	62 (17.2%)	188 (52.1%)

Table-III. Antibiotic sensitivity pattern

DISCUSSION

Urinary tract infection is the most prevalent illness in both; community and hospital settings all around the world. There are few effective treatments available due to the constantly growing resistance against the antibiotics of uropathogens. Therefore, the current knowledge about the uropathogens and their antibiotic susceptibilities is crucial for the proper management of urinary tract infections.[12]

Young infants and neonates with febrile UTI are more likely than older children to have bacteremia or sepsis, so they need to be carefully assessed and treated.[13]

Infants with UTIs may experience a variety of vague symptoms. In newborns and young infants, possible symptoms include fever, sepsis, lethargy, protracted jaundice, hematuria, poor feeding, vomiting, diarrhoea, irritability, failure to thrive, cloudy or odorous urine, and crying when passing urine. Older kids are better able to describe specific symptoms like vomiting, suprapubic discomfort, abdominal or flank pain, frequency, urgency, and urinary incontinence that has just started. The presence of particular urinary symptoms in older children can serve as a threshold for additional testing.[14-16]

Although each individual symptom and sign was useful in the diagnosis of UTI, a critical review found that neither one nor any combination of them was sufficient to identify children with UTI.[17]

In our study, we observed that E. coli that was the most common pathogen (25.5%) and the most sensitive drug was Imipenem, (29.9%), followed by Nitrofurantoin, Fosfomycin (25.8%), Amikacin (24.1%), and Piperacilin / Tazobactam (22.7%).

The studies done in adult population in Punjab in 2006 to 2007 and Kohat in 2015 to see antimicrobial sensitivity showed that most E. coli strains were resistant to all the common antibiotics used by doctors including ciprofloxacin, co-trimoxazole, nitrofurantoin, nalidixic acid, ceftazidime, cefotaxime and ampicillin which is very alarming situation.[18,19]

Our study differs from this study done in adult population in a way that E. coli strains were sensitive to above mentioned drugs. Very few such studies are done so far in pediatric population in Pakistan and neighboring countries.[20]

Joya et al., conducted a similar study and found that the most common pathogen was “E. coli (63.9%), followed by Enterococcus (11.1%), Serratia species (10.8%), Staphylococcus species (8.2%), Klebsiella (2.9%), Proteus species (1.8%), and Pseudomonas aeruginosa (1.2%).”

Ampicillin was 92.6%, amoxicillin was 82.9%, & erythromycin was 82.1% resistive for above stated bacterial invasions. Moreover, “ceftriaxone, ceftazidime, cefixime, and sulfamethoxazole” also showed >70% resistance rates. But the pristinamycin as well as ticarcillin were found to be 100% sensitive to these uropathogens.[21] While in our study imipenem was the most sensitive drug.

Miron et al., also found that in about 80% infants, E.coli was the most common causative organism that was isolated from urine samples, while Proteus mirabilis (9.8%) and Klebsiella spp. (6.4%) were found in few cases. The “ampicillin, amoxicillin / clavulanate, cefuroxime, ceftriaxone, & trimethoprim / sulfamethoxazole” were found to be highly resistive for these pathogens when detected in pediatric group.[22] Recent data reported from Cluj found slightly lower resistance rates of E. coli to ampicillin (56.5%), cefuroxime (12.5%) or trimethoprim / sulfamethoxazole (24.7%).[23] In comparison, if we look at recent reports on the adult UTI population in Romania, the situation is even more alarming: in a multicenter study, E. coli resistance rates were 96.9% to ampicillin, 70.9% to trimethoprim / sulfamethoxazole and 58.5% to amoxicillin / clavulanate.[24]

Shrestha et al., found lower rate of E. coli, although it was most common pathogen in the whole group. In 52% cases, E. coli was detected. Later on, Enterococcus faecalis was detected in 22% cases, Klebsiella pneumoniae in 7% samples and Staphylococcus aureus in 7% samples. About 32% cases had multidrug resistant isolates, and 5% were extensively drug resistant. E. coli was highly resistant to “Ampicillin (87%), Ceftriaxone (62%) and Ofloxacin (62%).[25] Our study did not reported staphylococus aureus in any positive urine culture.

At the same time, the pattern of resistance of E. coli to 3rd generation cephalosporins (19.1% - ceftazidime, 13.0% - ceftriaxone in our study) raises concern about the potential production of extended-spectrum β-lactamases (ESBL). The study from Cluj reported lower resistance rates (10.5% for ceftazidime, 3.4% for ceftriaxone),[23] but there are national data that identified higher values.[26] The prevalence of ESBL-positive E. coli

in Europe has increased greatly in recent years compared to the 2000s and is a real threat to antibiotic therapy. Therefore, regular monitoring of E. coli resistance and determination of the ESBL phenotype are important to take appropriate action.[27]

CONCLUSION

According to samples obtained and tested, E. coli was the most common pathogen and the most sensitive drug was Imipenem, followed by Nitrofurantoin, Fosfomycin, Amikacin, and Piperacilin / Tazobactam. Now keeping in mind the trend of pathogen and antibiotic susceptibility, we will implement most effective narrow spectrum antibiotics for treatment of UTI in children in order to control the rapidly increasing antibiotic resistance to broad spectrum antibiotics.

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4	Sohail Aslam	Study concept, Literature review, Discussion, Proof reading.	
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