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Original Article

The Sensitivity Pattern of Uropathogens towards Oral Antibiotics among Children with Urinary Tract Infection

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Abstract:

Background: Urinary tract infection (UTI) is common in paediatric age group. Because of extensive and injudicious use of oral antibiotics, uropathogens show increasing resistance to these drugs. The objective of the study was to identify the susceptibility pattern of uropathogens towards oral antibiotics among children suffering from UTI who were admitted to the paediatric ward at Jalalabad Ragib-Rabeya Medical College Hospital, Sylhet.

Materials and methods: This cross-sectional study was carried out among 100 children aged 2 months to 12 years, who had a confirmed diagnosis of UTI based on urine culture reports and was admitted to the paediatric department of Jalalabad Ragib-Rabeya Medical College Hospital, Sylhet. The study period was 1st January 2018 to 31st December 2019.

Results: The mean age of the patients was 46.48±38.58 months. Males were 34% and females were 66% and the male-female ratio was 1:1.9. The common presenting complaints of UTI cases were fever (67%), dysuria or crying during micturition (53%), abdominal pain (42%), an increased frequency of micturition (30%), and nausea and vomiting (26%). The most common isolated organism was *E. coli* (61%), followed by *Klebsiella* species (31%). Nitrofurantoin was the drug that the isolated organisms were most sensitive to, followed by levofloxacin and ciprofloxacin. The isolated organisms were highly resistant to cephalexin, amoxicillin, cephradine, cefaclor, cefixime, azithromycin, and co-trimoxazole.

Conclusion: Uropathogens are mostly sensitive to nitrofurantoin, levofloxacin, and ciprofloxacin. These drugs may be used to empirically treat UTI in children, if necessary. Judicial antibiotic use should be practised to prevent the development of antibiotic resistance.

Key words: Urinary tract infection, Sensitivity, Oral antibiotic, Children.

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Introduction:

One of the most prevalent and serious bacterial illnesses in paediatric population is a urinary tract infection (UTI). In boys, the prevalence of UTI is 1%, whereas in girls, it ranges from 1-3%. The majority of UTIs in males develop in the first year of life. Usually at the age of five, girls experience their first UTI, which peaks during infancy and toilet training. In the first year of life, the ratio of males to females ranges from 2.8 to 5.4:1. The ratio changes to 1:10 after infancy[1].

In newborns, infants, and young children, fever is the most frequent symptom of UTI. However, in older children, particular urinary symptoms including dysuria, frequency, and urgency are more common[2]. Dysuria may be accompanied by enuresis and foul smelling urine. Some newborns and infants may experience generalised symptoms such jaundice, feeding difficulties, irritability, and weight loss[1].

UTIs are challenging to diagnose, especially in young children, because they don't present with classical symptoms of UTI like older children and adolescents, and in most cases, they typically only exhibit fever as a symptom of a UTI. Pyelonephritis, which can cause renal

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scarring and subsequent chronic renal failure, is more prevalent in febrile young infants with UTIs. To prevent long-term morbidity and death in children, early UTI diagnosis and treatment with the proper antibiotics are crucial[3,4,5].

The leading cause of UTIs in children is gastrointestinal bacteria. According to several researches, *Escherichia coli* cause 41-87% of all paediatric urinary tract infections. The other responsible microorganisms include *Klebsiella, Proteus, Enterobacter, Pseudomonas, Acinatobacter, Staphylococcus aureus,* and *Enterococci*[4,5,6,7].

In recent years, uropathogens have developed increasingly resistance patterns to widely used antibiotics in developing countries like Bangladesh. Overuse, abuse, and unrestricted use of antibiotics may be significant factors. Furthermore, due to a lack of resources and financial constrain, culture is not always possible. The selection of an antibiotic for the initial treatment of a childhood UTI is also not well established in these countries[3,4].

Particularly in underdeveloped nations, where antibiotics are arbitrarily administered by medical professionals as well as obtained directly from pharmacies without a prescription, the pattern of antimicrobial sensitivity and resistance changes regularly. Therefore, regular assessment of the sensitivity pattern is necessary for judicious and effective antibiotic use[8].

Because the sensitivity pattern of uropathogens in children has not been thoroughly investigated nationwide, antimicrobial sensitivity levels in various parts of the nation are unknown. Oral antibiotics are extensively used to treat childhood UTIs in outpatient departments throughout the country. In most cases, antibiotics are used without knowing the sensitivity pattern of the organisms. Therefore, the study's objective was to identify the uropathogens' susceptibility to oral antibiotics among children suffering from UTI who were admitted to the paediatric ward at Jalalabad Ragib-Rabeya Medical College Hospital, Sylhet, Bangladesh.

Methodology:

This cross-sectional study was carried out among children aged 2 months to 12 years, who admitted in the paediatric department of Jalalabad Ragib-Rabeya Medical College Hospital, Sylhet, Bangladesh, between the periods of 1st January 2018 to 31st December 2019. Consent was taken from the parents or caregivers before enrolling them in the study. A total of 245 children presented with signs and symptoms of UTI or other nonspecific symptoms like fever, vomiting and abdominal pain, were primarily selected for the study by consecutive sampling methods. After primary selection, detailed history was taken, and clinical examinations were done and urine samples were collected. Urine samples were collected from young children by using sterile plastic bags or wide-mouthed containers. For individuals who were critically ill, catheterization was advised. Clean catch and midstream urine samples were collected from older children and adolescents. Urine samples thus collected were sent for bacteriological culture and antibiotics sensitivity pattern in the pathology department of the hospital. Culture positive UTI was considered if a single organism was grown in culture media at a concentration of 10^5 colony-forming units per ml of urine. Finally, 100 culture positive cases were enrolled for the analysis. Patients with negative urine culture reports and those who refuse to enrol in the study were excluded. Data regarding sociodemographic characteristics and clinical profile were collected from parents or caregivers, and isolated organisms and sensitivity pattern of antibiotics were collected from laboratory reports. A semi-structured questionnaire was used to gather data. The data were then analysed using SPSS version 21. The quantitative data were presented as mean and standard deviation, and the qualitative data were presented as frequency and percentage. A Chi-squared test was performed and a p-value of <0.05 was considered as statistically significant.

Results:

Among 100 culture positive UTI patients, males were 34% and females were 66%. The male-female ratio was 1:1.9. The mean age of the patients was 46.48±38.58 months. In the age groups of patients under one year old and 1-<5 years old, there were nearly equal numbers of positive instances in both male and female patients, which was statistically non-significant. However, in patients 5-14 years old, females had

a greater incidence than males, and that was statistically significant (p=0.03) (Table-I).

The majority of the patients presented with complaints of fever (67%), followed by dysuria or crying during micturition (53%), abdominal pain (42%), an increase in frequency of micturition (30%), and nausea and vomiting (26%) (Figure-1).

The most common isolated organism was *E. coli* (61%), followed by *Klebsiella* (31%), *Pseudomonas* (4%), *Enterococcus* (2%), *Proteus* (1%) and *Staphylococcus aureus* (1%) (Figure-2).*E. coli, Klebsiella and Pseudomonas* were the pathogens commonly isolated in the age group 1-<5 years and *Proteus* and *Staphylococcus aureus* were two other organisms isolated only in this age group (Table-II). *E. coli* was isolated from 65.2% of the girls and 53% of the boys (Table-III).

Isolated organisms were highly sensitive to nitrofurantoin (77%), followed by levofloxacin (54%) and ciprofloxacin (48%), and highly resistant to cephalexin (94%), amoxicillin (88%), cephradine (87%), cefaclor (84%), cefixime (76%), azithromycin (69%) and co-trimoxazole (67%) (Figure-3).

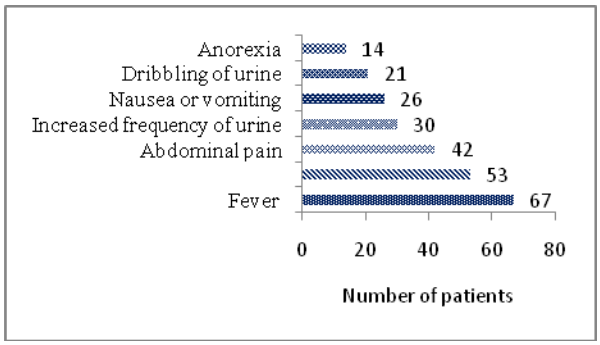

Figure-1: Presenting complaints of the patients (*Multiple responses)

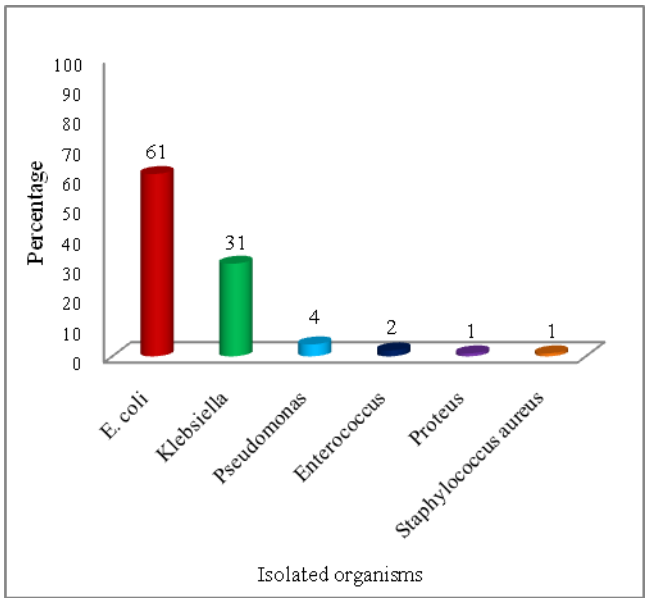

Figure-2: Organisms isolated in urine culture, N=100

Table-I: Age and gender distribution of the patients, N=100

Age	Gender		Total N(%)	p-value
	Male n (%)	Female n(%)		
2m- <1yr	8 (47.1)	9 (52.9)	17 (100)	0.03
1- <5yr	20 (41.7)	28 (58.3)	48 (100)	
5-14 yr	6 (23.3)	29 (76.7)	35 (100)	

Table-II: Distribution of uropathogens according to age, N=100

Age	Uropathogens, n (%)						Total, N (%)
	E. coli	Klebsiella	Pseudomonas	Enterococcus	Proteus	Staphylococcus aureus	
2months-<1year	12 (12%)	4 (4%)	0 (0%)	0 (%)	0	1	17 (17%)
1-<5 year	27 (27%)	15 (15%)	3 (3%)	2 (2%)	1	0	48 (48%)
5-14 year	22 (22%)	12 (12%)	1 (1%)	0 (0%)	0	0	35 (35%)
Total	61 (61%)	31 (31%)	4 (4%)	2 (2%)	1 (1%)	1 (1%)	100 (100%)

Table-III: Distribution of uropathogens according to gender, N=100

Gender	Uropathogens, n (%)						Total, N (%)
	E. coli	Klebsiella	Pseudomonas	Enterococcus	Proteus	Staphylococcus aureus	
Male	18 (53%)	11 (32.4%)	1 (2.9%)	2 (5.9%)	1 (2.9%)	1 (2.9%)	34 (100%)
Female	43 (65.2%)	20 (30.3%)	3 (4.5%)	0	0	0	66 (100%)

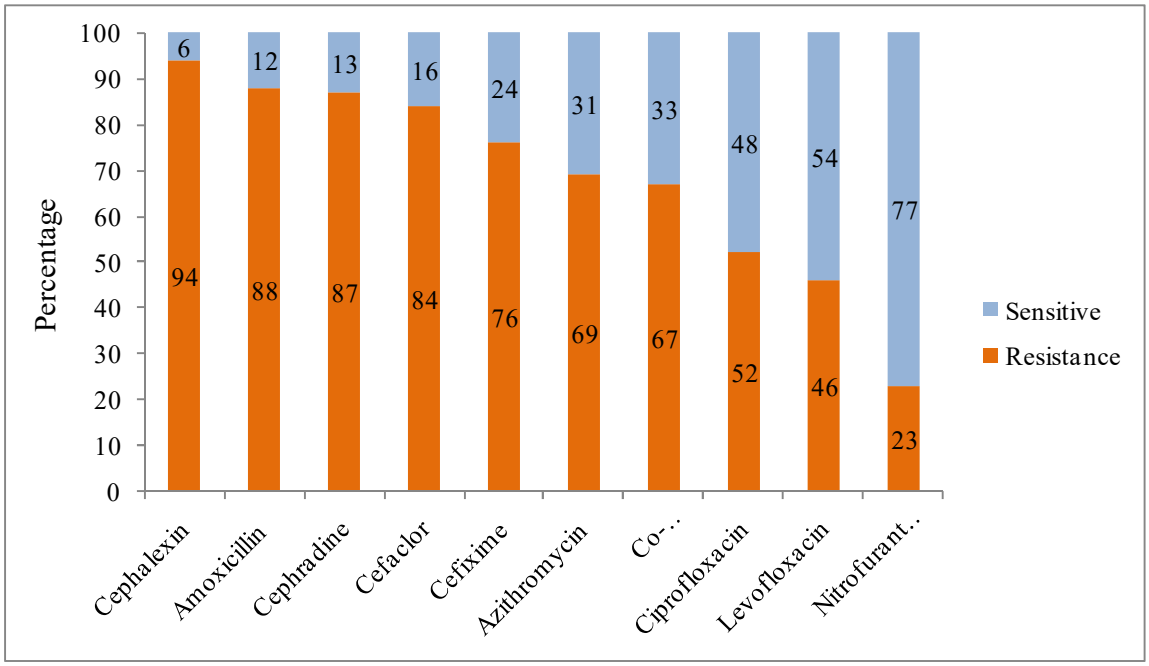

Figure-3: Susceptibility pattern of antibiotics to isolated organisms

Discussion:

A common infectious condition in children is a urinary tract infection, which, if left untreated, can cause irreversible kidney damage. In this cross-sectional study, a total of 100 children were included who had signs and symptoms of UTI or other nonspecific symptoms like fever, vomiting, and abdominal pain and whose urine cultures were positive. Among them female were 66% and male were 34%. Male to female ratio was 1:1.9. Numerous studies have revealed that UTIs affect female children more frequently than male[9,10,11]. This might be due to short female urethra and near proximity of the female urethra to the anus. Because of this, enteric pathogens easily colonise the perineum, conveniently access the urinary system, and infect females. There were nearly equal numbers of positive occurrences of UTI cases in both male and female patients in the age groups of children under the age of one year old and 1 to 5 years old; however, in patients aged 5 to 14, girls had a significantly higher frequency than boys (p=0.03). UTI was significantly higher (p<0.001) in female childrenin the age group above 2 years, according to a study by Yilmaz et al.[12], which supports our finding.

The most of the literature describes fever as the common presenting symptom of UTI in younger children. Specific UTI symptoms like dysuria, urgency, and frequency are typically present in older children and adolescents[9,13,14]. Consistent with other studies, the majority of cases in our study had fever. Other symptoms included

dysuria or crying during micturition, abdominal pain, increased frequency of micturition, and nausea and vomiting. In contrast to our study, Gul et al.[8] discovered that dysuria was the most prevalent symptom, accounting for 64.15% of patients followed by flank pain 46.22%, and fever 41.51%. The age differences among the patients may be the cause of these discrepancies.

In the present study, the most common organisms isolated were *Escherichia coli,* followed by *Klebsiella*. Numerous studies have found that *E. coli* and *Klebsiella* are the two most frequent causes of paediatric UTIs[9,10,15]. However, Lalhmangaihzuali et al.[5] showed that the most prevalent uropathogens were *E. coli* followed by *Entercoccus spp*. in a research in Mizoram, India, and that *E. coli* followed by *Proteus* in another study by Shrestha et al.[16] in Nepal, which is different from our finding. This disparity could be owed to differences in geographic regions, the nature of the study samples, and sociodemographic variations.

In children with urinary tract infections, the findings of the current study point to a high incidence of microbial resistance to commonly used oral antibiotics, including amoxicillin, first-, second-, and third-generation cephalosporins (Cephradine, cefalexin, cefaclor, and cefixime), co-trimoxazole, and azithromycin. The most sensitive antibiotic, however, was discovered to be nitrofurantoin, which was then followed by levofloxacin and ciprofloxacin. Studies by Patwardhan et al.[4] in India and Lehrasab et al.[17] in Pakistan, respectively, reported that the rates of amoxicillin resistance were 40.5% and 31.9%, which was much lower than our study. However, both studies discovered lower levels of resistance to nitrofurantoin, levofloxacin and ciprofloxacin, which is similar to our study. A different experiment by Islam et al.[10] in Dhaka, Bangladesh, found greater resistance to cephradine and co-trimoxazole and decreased resistance to nitrofurantoin, which is consistent with our findings. However, they also found less than 50% resistance to azithromycin, which was 69% in our study. A significant level of resistance of microorganisms to cotrimoxazole (98%), amoxycillin (85%), cefixime (87%) and azithromycin (77%) was also discovered in an investigation by Nazme et al[6]. These findings validate our results. In another study, Sadia et al.[9] observed that *E. coli* and *Klebsiella* had high resistance to cephalexin (81.8% and 87.5%), amoxicillin (72.7% and 87.5%), and co-trimoxazole (78.8% and 87.5%). Additionally, they discovered reduced resistance to cefixime (57.6% and 25%) and nitrofurantoin (9.1% and 0%), but increased resistance to levofloxacin (57.5% and 100%) and ciprofloxacin (51.5% and 75%) in both species.

The majority of Bangladeshi studies revealed higher resistance to commonly used oral antibiotics like amoxicillin, cotrimoxazole, azithromycin, and 1st, 2nd, and 3rd generation oral cephalosporins, even though antibiotic sensitivity patterns in various studies in other countries show varying results[5,6,9,10,17]. This has serious therapeutic implications for patient care because numerous conventional antibiotics, which are still widely available and inexpensive, are no longer effective. Inappropriate antibiotic use may delay effective treatment and raise the chance of renal scarring and chronic renal failure in later life. As a result, the current study contributes to the development of a regional recommendation for the use of oral antibiotics in the treatment of paediatric urinary tract infections.

Conclusion:

This study offers insightful information on the distribution of antimicrobial resistance. We recommend nitrofurantoin, levofloxacin, and ciprofloxacin as empirical oral antibiotics for the treatment of urinary tract infections in Bangladeshi children, particularly in the Sylhet region, while the culture report is pending or urine culture could not be performed due to a lack of resources or financial issues. To determine the true resistance pattern of uropathogens in Sylhet and to create regional guidelines, additional large-scale multicenter research should be carried out.

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