DOI: https://doi.org/10.53350/pjmhs2023171824

ORIGINAL ARTICLE

Bactericidal Effect of Antibiotics against Bacteria Causing Urinary Tract Infection among Children

FATIMA IQBAL[1], FARIHA NASREEN[2], SIDRA IQBAL[3], IRUM NAZ[4], ATTIYA ELAHI[5], FAISAL REHMAN[6]
[1]*Consultant Pediatrician, Wapda Hospital Rawalpindi, Pakistan*
[2]*Consultant Pathologist, Wapda Hospital Rawalpindi, Pakistan*
[3]*Non-Trainee ST3 Registrar, Emergency Medicine, Royal Berkshire Hospital, England*
[4]*Assistant Professor Pediatrics, Naseer Teaching Hospital, Peshawar, Pakistan*
[5]*Consultant Radiologist, Wapda Hospital Rawalpindi, Pakistan*
[6]*Lab Technologist, Wapda Hospital Rawalpindi, Pakistan*
Correspondence to: Fatima Iqbal, Email: ftsiddiqui@hotmail.com

ABSTRACT

Background: Urinary Tract Infection (UTI) is one of the most common infections in children. Use of antibiotics according to updated sensitivity pattern is critical.
Aim: To determine major bacteria causing UTI with drug sensitivity pattern to find best empirical therapy.
Study design: Descriptive cross-sectional study.
Methodology: This study was conducted at WAPDA hospital Rawalpindi from June 2022 to November 2022. A total of 71 urine culture positive children aged between 1 to 14 years were enrolled. The main variables for the study included age and sex of patient, isolated bacteria and the sensitivity pattern against different drugs. The data was analyzed using SPSS version 23.0. The variables are presented in the form of standard deviation and frequency of percentages.
Results: The average age of enrolled children was 5.9 (SD ± 3.6) years. The common bacteria leading to UTI were E. coli 43 (60.6%) followed by Klebsiella 11 (15.5%) and Enterococcus 5 (7%). The most common organism isolated was E. coli. The most effective drugs against E. coli are Meropenem (97.2%), Fosfomycin (90.2%), and Amikacin (89.7%). The resistance pattern is Co-trimoxazole (86%), Amoxicillin/clavulanic acid (69.8%) and Cefixime (70.7%).
Conclusion: The most common isolate was E. coli. The sensitivity of nitrofurantoin, Fosfomycin and Amikacin to the pathogens' causing UTI is high and can be used empirically. Other commonly used antibiotics are mostly resistant, therefore regular studies in every region are necessary to update the protocols for treatment of UTI.
Keywords: Urinary tract infection, E. coli, Amikacin, Urine culture and sensitivity

INTRODUCTION

Urinary tract infection (UTI) is a commonly occurring bacterial infection during early years of life. It is caused by inflammation of urinary system [1-3]. The prevalence of afebrile UTI during infancy is 8% and febrile infants is 7% with a male to female ratio of 2.8:5.4. After first year, there is a female predominance, with a male to female ratio of 1:10 [4]. The short urethra and gram-negative bacteria of vagina are the main cause of predominance in girls [5, 6].

The diagnosis of UTI is based on signs and symptoms and urine examination. But the gold standard for the diagnosis is Urine culture [7, 8]. When a single bacterial colony count is more than 105 (CFU/ml) on clean catch and /or > 50,000 CFU/ml in transurethral specimen then it is called significant bacteriuria [9, 10].

The clinical features of UTI are different at different ages [11, 12]. Ninety-one percent of children present with fever in UTI [13]. Fever, jaundice, poor feeding, and lethargy are the most frequently present symptoms during neonatal age. Older children present with painful and frequent micturition and urgency, with suprapubic tenderness present on examination [11, 14].

The urine of healthy children is mostly uninfected. To maintain the sterile nature of urinary system it is necessary that children should fully empty their bladder every time they void [15].

During toilet training most of the time children withhold their urine causing UTI [5]. The main factor which causes UTI is bacteria. First it gathers around urethra, and then move to involve whole urinary system [15, 16]. Infection of urinary tract only once can cause long term complications, but repeated infection can be much more dangerous [17, 18].

If children having UTI are not treated properly with antibiotics it can lead to recurrence. Recurrence is defined as having UTI (cystitis) for three times or more [19]. The National Institute for Health and Clinical Excellence has recommended a 7 to 10 days of antibiotic therapy to treat UTI [1, 20]. It can prevent chronic UTI which can cause pyelonephritis, hypertension, and End stage renal disease [21]. Uncomplicated UTI is treated with oral antibiotics and intravenous are used empirically when there is complicated UTI till urine culture and sensitivity report comes [13, 22].

The resistance to antibiotics is a globally accepted challenge which medical world is facing. UTIs are the most common infections facing antibiotic resistance. Many children are getting antibiotics for several diseases such as ear infection, abdominal pain, upper respiratory tract infections and so on without proper prescription so frequently that it causes partially treated urinary infections and resistance [23]. Now another issue is resistance to two or more than two classes of antibiotics, which is called multidrug resistance [5]. There is a risk of antibiotic resistance to ten million lives by 2050 [24]. The American and Canadian society of Urology has advised that the choice of antibiotics should selected locally according to sensitivity pattern of locally done studies [1].

Pakistan is a developing country and there is a judicious use of antibiotics for different infections including UTI. If antibiotics are not used properly then it will cause resistance. Furthermore, improperly treated UTI can cause damage to urinary system causing reflux, pyelonephritis, and chronic kidney disease. Therefore, proper diagnosis and selection of antibiotics is necessary. For these studies should be conducted frequently and, in each area, to evaluate the pathogen and its sensitivity. these studies can give us a clue to start antibiotics empirically. Therefore, to make an antibiotic protocol for UTI according to sensitivity pattern we have done this study in our unit.

METHODOLOGY

A cross-sectional study was conducted at Wapda Hospital Rawalpindi from June 2022 to November 2022. A total of 176 children from 1 year to 14 years presented to the hospital with symptoms and signs of UTI, such as fever, suprapubic pain and burning micturition. Out of the observed children 71 were culture positive. Those 71 culture positive children were enrolled.

All children who took antibiotics in 72 hours were excluded. Patients having cerebral palsy, chronic kidney disease and any other urological problem were excluded.

Clean catch urine, under aseptic measures was collected. The samples were transferred immediately to the laboratory for urine analysis and urine culture and sensitivity. Cultures were done directly on CLED agar medium for 48 hours. Urine culture was

considered positive when colony count was more than 100,000 CFU/ml of a single organism. Sensitivities were checked for Amikacin, Amoxycillin, Nitrofurantoin and others. Data were stored and analyzed using IBM SPSS version 23.0, mean with standard deviation was reported for age of patients, counts with percentages were reported on gender and microorganisms. Descriptive analysis was also performed on sensitivity patterns of antibiotics for each studied microorganism.

RESULTS

A total of 176 children visited OPD in WAPDA Hospital Rawalpindi with symptoms of UTI during our study. A total of 71 patients were culture positive and were enrolled for the study. Their mean age was 5.9 (SD ± 3.6) years. Their age, gender and micro-organism status are presented in table 1.

Table 1: Baseline Characteristics of Studied Patients (n = 71)

Variables		n	%
Gender	Male	11	15.5
	Female	60	84.5
Age	Mean ± SD	5.9	± 3.6
Microorganisms	Proteus	2	2.8
	E. coli	43	60.6
	Klebsiella	11	15.5
	Enterococcus	5	7.0
	Pseudomonas aeruginosa	4	5.6
	Enterobacter cloacae	4	5.6
	Staphylococcus saprophyticus	2	2.8

There were 11 (15.5%) males and 60 (84.5%) females. Out of 71 children 62 (87.3%) had gram negative organisms and 7(9.8%) had gram positive organisms. Common bacteria leading to UTI were E. coli 43 (60.6%) followed by Klebsiella 11 (15.5%) and Enterococcus 5 (7%).

The drug sensitivity and resistance pattern for bacteria are shown in table 2. The most effective drugs against E. coli are Meropenem (97.2%), Fosfomycin(90.2%),and Amikacin(89.7%). The resistance pattern is Co-trimoxazole (86%), Amoxicillin/clavulanic acid (69.8%) and Cefixime(70.7%). The sensitivity pattern of Klebsiella (second most common) is Amikacin (100%), Meropenem (100%), Fosfomycin (72.7%). The drugs mostly resistant are Co-trimoxazole (81.8% and Cefixime (80%). Enterococcus is sensitive to Nitrofurantoin (100%), Vancomycin (100%) and Fosfomycin (60%) whereas resistance pattern is Co-trimoxazole (100%) and ciprofloxacin (80%). High sensitivity for pseudomonas was found against Amikacin (100%), Ciprofloxacin (100%) and Meropenem (100%) whereas resistance against Co-trimoxazole (100%) and Fosfomycin (75%) was high. The Enterobacter cloacae was 100% sensitive against Amikacin, Ciprofloxacin, Co- trimoxazole and Meropenem whereas 100% resistance was shown against Cefixime. The Proteus was 100% sensitive against Ciprofloxacin and Meropenem whereas it was 100% resistant to Co-trimoxazole. The Staphylococcus saprophyticus was highly(100%) sensitive against Amikacin, Vancomycin, Ciprofloxacin and Ceftriaxone. 100% resistance was found against Cefixime.

Table 2: Drug sensitivity pattern of micro-organisms

Drugs	Micro-organisms							
		Gram negative organisms					Gram positive organisms	
		Proteus n = 2	E. coli n = 43	Klebsiella n = 11	Pseudomonas Aeruginosa n = 4	Enterobacter cloacae n = 4	Enterococcus n = 5	Staphylococcus saprophyticus n = 2
Amoxicillin	S	50	18.4	0	N. T (Not tested)	25	40	50
	R	50	81.6	100	N. T	75	60	50
Amoxicillin/Clavulanic acid	S	50	30.2	36.4	N. T	25	60	100
	R	50	69.8	63.6	N. T	75	40	0
Cefixime	S	50	29.3	20	N. T	0	N. T	0
	R	50	70.7	80	N. T	100	N. T	100
Ceftriaxone	S	50	38.1	45.5	N. T	75	N. T	100
	R	50	61.9	54.5	N. T	25	N. T	0
Ciprofloxacin	S	100	44,2	54.5	100	100	20	100
	R	0	53.5	45.5	0	0	80	0
Co-Trimoxazole	S	0	14	18.2	0	75	0	50
	R	100	86	81.8	100	25	100	50
Fosfomycin	S	50	90.2	72.7	25	50	60	50
	R	50	7.3	18.2	75	50	40	50
Meropenem	S	100	97.2	100	100	100	60	50
	R	0	2.8	0	0	0	40	50
Nitrofurantoin	S	0	81	70	0	50	100	100
	R	100	16.7	30	100	50	0	0
Amikacin	S	100	89.7	100	100	100	N. T	100
	R	0	10.3	0	0	0	N. T	0
Vancomycin	S	N. T	N. T	N. T	N. T	N. T	100	100
	R	N. T	N. T	N. T	N. T	N. T	0	0

Table-3 reports the organisms with respect to age group, results showed for the samples age range between 1 – 3 years 52.6% were E. coli, 31.6% were Klebsiella, 5.3% were Pseudomonas aeruginosa, 5.3% were Enterobacter colane and 5.3% were Staphylococcus saprophyticus cases, for the age range between 4 – 7 years there were 3.2% were Proteus, 61.3% were E. coli, 9.7% were Klebsiella, 6.5% were Enterococcus, 6.5% were Pseudomonas aeruginosa, 9.7% were Enterobacter cloacae and 3.2% were Staphylococcus saprophyticus cases, whereas for age more than 7-years old samples there were 4.8% cases of Proteus, 66.7% cases of E.coli, 9.5% cases of Klebsiella, 14.3% cases of Enterococcus and 4.8% cases of Pseudomonas aeruginosa. P-value greater than 0.05 showed insignificant difference in the proportion of samples with respect to age group for each organism using Chi Square test.

Table 3: Organisms with respect to age group

Organism	Age Group						p-value
	1 - 3 years (n=19)		4 - 7 years (n=31)		>7 years (n=21)		
	N	%	n	%	n	%	
Proteus	-	-	1	3.2	1	4.8	0.99
E. coli	10	52.6	19	61.3	14	66.7	0.24
Klebsiella	6	31.6	3	9.7	2	9.5	0.30
Enterococcus	-	-	2	6.5	3	14.3	0.65
Pseudomonas aeruginosa	1	5.3	2	6.5	1	4.8	0.77
Enterobacter cloacae	1	5.3	3	9.7	-	-	0.31
Staphylococcus saprophyticus	1	5.3	1	3.2	-	-	0.11

DISCUSSION

UTIs is the second most common bacterial infection in children. The adult UTI is mostly benign whereas in children it can lead to end stage renal disease if not properly treated [5]. The treatment of UTI is started empirically with antibiotics before the culture results are available. UTIs are resistant to many drugs and empiric treatment are failing frequently which is causing problem universally [23]. Therefore, studies are needed more frequently to know the common pathogen with its sensitivity according to local area [1]. In our study, there were 11 (15.5%) males and 60 (84.5%) females. Female predominance is mostly because of its short urethra [5]. Mostly UTIs are caused by gram negative bacteria such as E.coli , klebsiella , proteus, Enterobacter and Pseudomonas. Gram positive bacteria also cause UTI such as staphylococcus saprophyticus, Group B Streptococcus and Enterococcus. In our study out of total 71 patients 62 (87.3%) were gram negative and 7 (9.8%) were gram positive. E. coli was the most common bacteria (60.6%) followed by Klebsiella (15.5%). Enterococcus was (7%), Pseudomonas and Enterobacter were (5.6%). Proteus and Staphylococcus were (2.8%). Y. Belete and N. Mumtaz et al., also found E. coli as the most common organism. In our study E. coli was highly sensitive to Meropenem(97.2%), Fosfomycin(90.2%) and amikacin(89.7%).Other gram negative and positive organisms were also highly sensitive to amikacin whereas gram positive organisms were partially sensitive to meropenem and Fosfomycin. G. Madhu and S. K. Ghosh also found amikacin as the sensitive drug against bacteria causing UTI whereas Ponvelil et al., [25] found only 33.3% sensitivity to Amikacin.

The sensitivity pattern of drugs is changing and due to rational use of the antibiotics the uropathogens are becoming resistant to multiple drugs. Therefore, frequent studies are needed to update the protocol for the treatment of UTI and to avoid resistance. This will help us to improve health of our children.

CONCLUSION

The most common isolate was E. coli. Commonly used oral antibiotics such as amoxicillin, cefixime are mostly resistant. Amikacin which is highly sensitive and cost effective can be used empirically as a parental drug. Fosfomycin is also sensitive and mostly not in use is a good option for oral use.

Other commonly used antibiotics are mostly resistant, therefore, regular studies in every region are necessary to update the protocols for treatment of UTI.

Conflict of Interest: The authors declare no conflict of interest.

Funding: There was no funding from any source:

Ethical Approval: Approval was taken from the ethical review board, Wapda Hospital Rawalpindi.

REFERENCES

1 R. Ara, S. M. Nasrullah, Z. Tasnim, S. Afrin, K. Saif-Ur-Rahman, and M. D. H. Hawlader, "Effective antimicrobial therapies of urinary tract infection among children in low-income and middle-income countries: protocol for a systematic review and meta-analysis," BMJ open, vol. 12, p. e060568, 2022.

2 K. Tullus and N. Shaikh, "Urinary tract infections in children," The Lancet, vol. 395, pp. 1659-1668, 2020.

3 L. A't Hoen, G. Bogaert, C. Radmayr, H. S. Dogan, R. J. Nijman, J. Quaedackers, et al., "Update of the EAU/ESPU guidelines on urinary tract infections in children," Journal of pediatric urology, vol. 17, pp. 200-207, 2021.

4 W. Kohler and D. Reinger IV, "Nelson Textbook of Pediatrics, International Edition, 2-Volume Set," 2019.

5 S. Nabat-ul-Hassan, K. Farva, G. A. Bhutta, R. N. Khan, S. Zia, and U. Ali, "Microorganism causing urinary tract infection among children and their antimicrobial susceptibility patterns," Rawal Medical Journal, vol. 47, 2022.

6 A. Muhammad, S. Khan, N. Ali, M. Rehman, and I. Ali, "Prevalence and antibiotic susceptibility pattern of uropathogens in outpatients at a tertiary care hospital," New Microbes and new infections, vol. 36, p. 100716, 2020.

7 N. Mumtaz, Q. S. Humayoun, I. Liaquat, T. Mahmood, M. Hafeez, and H. Zeb, "Bacteriological Spectrum of Pediatric Urinary Tract Infection and Its Drug Sensitivity and Resistance Pattern," Journal of Rawalpindi Medical College, vol. 26, 2022.

8 C. M. Chu and J. L. Lowder, "Diagnosis and treatment of urinary tract infections across age groups," American journal of obstetrics and gynecology, vol. 219, pp. 40-51, 2018.

9 G. Madhu, C. AnjumAara, and S. Mahamud, "Prevalence and antibiotic susceptibility pattern of pathogens in children with urinary tract infection in a tertiary care hospital," Int J Contemporary Pediatrics, vol. 7, pp. 1513-8, 2020.

10 T. K. Price, T. Dune, E. E. Hilt, K. J. Thomas-White, S. Kliethermes, C. Brincat, et al., "The clinical urine culture: enhanced techniques improve detection of clinically relevant microorganisms," Journal of clinical microbiology, vol. 54, pp. 1216-1222, 2016.

11 Y. Belete, D. Asrat, Y. Woldeamanuel, G. Yihenew, and A. Gize, "Bacterial profile and antibiotic susceptibility pattern of urinary tract infection among children attending Felege Hiwot Referral Hospital, Bahir Dar, Northwest Ethiopia," Infection and drug resistance, pp. 3575-3583, 2019.

12 M. Buettcher, J. Trueck, A. Niederer-Loher, U. Heininger, P. Agyeman, S. Asner, et al., "Swiss consensus recommendations on urinary tract infections in children," European journal of pediatrics, vol. 180, pp. 663-674, 2021.

13 V. R. Rai, S. Mahar, Z. Khoso, S. H. Rabab, and R. Parveen, "Frequency of culture positive urinary tract infection in febrile children," The Professional Medical Journal, vol. 29, pp. 1540-1546, 2022.

14 A. C. Simoes e Silva and E. A. Oliveira, "Update on the approach of urinary tract infection in childhood," Jornal de pediatria, vol. 91, pp. S2-S10, 2015.

15 D. Kadigi, F. Mosha, S. Moyo, and M. Matee, "Etiology and antimicrobial susceptibility patterns of bacterial agents causing urinary tract infection in children under five years, dar es salaam," J. Biotechnol. Immunol, vol. 2, 2020.

16 U. Lawani Ebidor, A. Tolulope, and O. Deborah, "Urinary tract infection amongst pregnant women in Amassoma, Southern Nigeria," Afr J Microbiol Res, vol. 9, pp. 355-359, 2015.

17 A. Ryakitimbo, R. Philemon, F. Mazuguni, and L. Msuya, "Prevalence and antimicrobial sensitivity pattern of urinary tract infection among children with cerebral palsy, Moshi, Tanzania," Pediatric Health, Medicine and Therapeutics, pp. 59-65, 2018.

18 G. Williams and J. C. Craig, "Long-term antibiotics for preventing recurrent urinary tract infection in children," Cochrane database of systematic reviews, 2019.

19 B. Bandari, S. P. Sindgikar, S. S. Kumar, M. S. Vijaya, and R. Shankar, "Renal scarring following urinary tract infections in children," Sudanese journal of paediatrics, vol. 19, p. 25, 2019.

20 M. Okarska-Napierała, A. Wasilewska, and E. Kuchar, "Urinary tract infection in children: Diagnosis, treatment, imaging–Comparison of current guidelines," Journal of pediatric urology, vol. 13, pp. 567-573, 2017.

21 S. N. ul Hassan, K. Farva, G. A. Bhutta, S. Zia, Y. Lashari, and M. Mahmood, "Bacteria causing urinary tract infection among children and their antimicrobial susceptibility patterns," Rawal Medical Journal, vol. 46, pp. 858-858, 2021.

22 C.-I. Kang, J. Kim, D. W. Park, B.-N. Kim, U.-S. Ha, S.-J. Lee, et al., "Clinical practice guidelines for the antibiotic treatment of community-acquired urinary tract infections," Infection & chemotherapy, vol. 50, p. 67, 2018.

23 F. Noman, G. A. Zahan, F. Hasnat, and M. K. Islam, "Sensitivity and resistant pattern of commonly used drugs in uti in younger children: A Study in a Tertiary Care Level Hospital, Dhaka, Bangladesh," American Journal of Pediatrics, vol. 6, p. 146, 2020.

24 S. K. Ghosh, S. K. Saha, and M. Islam, "Etioclinical profile of urinary tract infection in children," Journal of Medial Science and Clinical Researh, vol. 8, pp. 180-184, 2020.

25 J. J. Ponvelil, H. N. Gowda, and S. Raj, "Prevalence of urinary tract infection and sensitivity pattern amongst children less than 3 years of age with fever in a tertiary care hospital in South Karnataka," Int J Basic Clin Pharmacol, vol. 9, pp. 736-778, 2020.