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Original Research Article

ANTIBIOTIC PRESCRIPTION AND ANTIMICROBIAL RESISTANCE RATES OF UROPATHOGENS IN CHILDREN WITH URINARY TRACT INFECTIONS

ADNAN M[*1], SAIFULLAH[1], KHAN MAH[1], HUSSAIN M[2], HAMAYUN F[3], KHAN G[4]

[1]*Department of Urology, Bakhtawar Amin Trust Teaching Hospital Multan, Pakistan*
[2]*Department of Urology, Sharif Medical and Dental College Lahore, Pakistan*
[3]*Department of Pediatrics Urology, The Children's Hospital & Institute of Child Health Lahore, Pakistan*
[4]*Department of Urology, Gomal Medical College Dera Ismail Khan, Pakistan*
**Correspondence author email address: adnanaslam628@yahoo.com*

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Abstract: *The current study aimed to evaluate the antibiotic treatment of UTIs and antimicrobial resistance of uropathogens in children with UTIs. A retrospective study was conducted in the Pediatrics Department of different centers from November 2021-November 2022. A total of 100 children with febrile or afebrile urinary tract infections were included in the study. UTIs were categorized as febrile and afebrile. Antibiotics were prescribed according to the UTI and pathogen identified. E.coli was the most common pathogen (80%) found in patients of both groups, while Citrobacter sp and gram-positive cocci were only found in one case each. Amikacin was mostly prescribed in both groups (54 for fUTIs and 8 for aUTIs). 60% of the E.coli isolates were resistant to ampicillin, 10% to AMC (amoxicillin and clavulanic acid), and 15% to SAM (Sulfacetamide sodium). The highest resistant rates of E.coli were observed against SXT, i.e., 25%. Based on the results, it can be concluded that there is a need for antimicrobial resistance stewardship programs to control the increasing prevalence of resistance among UTI-causing pathogens.*

Keywords: Urinary Tract Infections, Pathogens, Antimicrobial Resistance, Antibiotics.

Introduction

One of the most common infections in children and febrile infants occurs in the urinary tract without localizing symptoms (Tullus and Shaikh, 2020). UTIs are approximately 7% of children and 7.8% of infants and mostly present with fever and other signs (A't Hoen et al., 2021). Antibiotics, including cephalosporins and penicillin, are mostly prescribed for UTIs in children. Due to the prescription of common antibiotics, i.e., aminopenicillins, UTI treatment has become difficult as bacteria causing UTI has grown resistant to these multiple preventive drugs (Karam et al., 2019). Studies have shown that the most common cause of UTI, gram-negative organisms, have developed multidrug resistance worldwide (Kot, 2019). In Pakistan, little to no data regarding drug-resistant UTIs in children and infants is available. The resistance to ampicillin is found to be 51% which is significantly higher than in trimethoprim, i.e., 29% (Bryce et al., 2016; Bullens et al., 2022). It is important to evaluate antimicrobial resistance considering the increasing number of UTI cases in children. We conducted this study to evaluate the antibiotic treatment of UTIs and antimicrobial resistance of uropathogens in children with UTIs.

Methodology

A retrospective study was conducted in the Pediatrics Department of different centers from November 2021-November 2022. A total of 100 neonates (birth to 29 days), infants (29 days to younger than 2 years), and older children (2 years to younger than or equal to 5 years) with febrile or afebrile urinary tract infections were included in the study. UTI was diagnosed as febrile if patients older than 1 year had ≥38 °C fever and infants younger than that had ≥37.4 °C fever. Urine culture came out positive with ≥10 000 CFU/mL and ≥100 000 CFU/mL colonies for catheter and clean-catch specimens, respectively, and pyuria was observed. If the two signs except fever were observed, the UTI was afebrile. The guardians of the patients provided their informed consent. The Ethical board of the hospital approved the study design. The patient's demographic information, diagnostic data, medical history, antibiotic prescription, and antibiograms were noted. Kirby Bauer testing was done for antibiograms by antibiotic-impregnated disks. The results were noted as susceptible and non-susceptible (immediate and resistant). A double disk synergy test was performed

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for ESBL-producing strains. All the data were analyzed by SPSS version 20. T-test was performed to compare the results of febrile and afebrile UTIs for categorical variables.

Results

100 patient with UTI were admitted to the hospital for treatment regarding pathogen identification. More than half of the study population (73%) was female. 77 patients were previously healthy, while 10 had UT disorders. 5 patients (5%) had a recent history of hospital stay, i.e., less than 2 months before the infection, and 13 (13%) completed an antibiotic course recently. The baseline characteristics of patients are shown in Table I. E.coli was the most common pathogen (80%) found in patients of both groups, while Citrobacter sp and gram-positive cocci were only found in one case each. A total of 206 antibiotics were prescribed for these 100 children, out of which 166 were for febrile UTI patients and 40 for afebrile UTI patients. Amikacin was mostly prescribed in both groups (54 for fUTIs and 8 for aUTIs). Imipenem was only used for the treatment of one febrile UTI patient. Tables II and III present the antibiotic prescription, duration, and dosage. 60% of the E.coli isolates were resistant to ampicillin, 10% to AMC, and 15% to SAM. The highest resistant rates of E.coli were observed against SXT, i.e., 25%. Similarly, Klebsiella spp. Also showed high resistance to SXT, i.e., 27%, and AMC, i.e., 12%.

Table I: Baseline patients' characteristics and pathogen data

Patients' characteristics	All UTIs (n=100)	Febrile UTIs (n= 78)	Afebrile UTIs (n= 22)	P-Value
Age				
Less than 29 days	7 (7%)	5 (6.4%)	2 (10%)	0.06
29 years < 2 years	61 (61%)	49 (62.8%)	12 (54.5%)	
2 years to 5 years	15 (15%)	10 (12.8%)	5 (22.7%)	
5 years or older	17 (17%)	11 (14.1%)	6 (27.3%)	
Sex				
Male	22 (22%)	17 (21.8%)	5 (22.7%)	0.70
Female	73 (73%)	55 (70.5%)	18 (81.2%)	
Medical information				
Previously healthy	77 (77%)	60 (76.9%)	17 (77.3%)	0.68
UT abnormalities	10 (10%)	8 (10.3%)	2 (10%)	0.07
Other medical disorders	11 (11%)	7 (8.9%)	4 (18.2%)	0.28
Concurrent infections	5 (5%)	5 (6.4%)	0 (0%)	0.10
Bacteraemic UTI	3 (3%)	3 (3.8%)	0 (0%)	0.32
Recurrent UTI	16 (16%)	14 (17.9%)	2 (10%)	0.18
Atypical UTI	40 (40%)	32 (41%)	8 (36.4%)	0.70
Recent hospital stay	5 (5%)	3 (3.8%)	2 (10%)	>0.97
History of antibiotic use	13 (13%)	11 (14.1%)	2 (10%)	0.04
Pathogens				
E.Coli	80 (80%)	63 (80.7%)	17 (77.3%)	0.090
Klebsiella spp.	8 (8%)	6 (7.7%)	2 (10%)	
Proteus spp.	4 (4%)	3 (3.8%)	1 (4.5%)	
P. aeruginosa	4 (4%)	3 (3.8%)	1 (4.5%)	
Enterobacter spp.	2 (2%)	1 (1.3%)	1 (4.5%)	
Citrobacter spp.	1 (1%)	1 (1.3%)	0 (0%)	
Gram positive cocci	1 (1%)	1 (1.3%)	0 (0%)	

Table II: Antibiotic treatment for UTIs

Antibiotic	No of prescriptions	Age				Treatment duration (days)
		<29 days	29 days-<2 years	2 years-< 5 years	5 years or older	
Febrile UTI (n=166)						
Penicillin G	1 (0.6%)		1			-
Ampicillin	22 (13.2%)	5	12	3	2	2.8 ± 2.5

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SAM	14 (8.4%)		7	3	4	3.7 ± 1.2
AMC	25 (15.0%)	1	15	5	4	4.6 ± 1.8
TCC	1 (0.6%)	1				7
TZP	3 (1.8%)	1	2			6.8 ± 3.7
Cefaclor	1 (0.6%)		1			-
Cefprozil	1 (0.6%)		1			-
Cefoxitin	2 (1.2%)		2			3.2
Cefuroxime	10 (6.0%)		5	1	4	3.6 ± 1.4
Cefotaxime	18 (10.8%)	4	8	3	3	6.1 ± 1.8
Ceftriaxone	8 (4.8%)		4	2	2	7.7 ± 1.8
Ceftazidime	2 (1.2%)		1		1	6.1
Imipenem	1 (0.6%)				1	8
Netilmicin	1 (0.6%)		1			4
Amikacin	54 (32.5%)	5	33	6	10	3.4 ± 1.4
SXT	2 (1.2%)		2			-
Afebrile (n=40)						
Ampicillin	4 (10%)	1	2		1	3.6 ± 3.5
Amoxicillin	1 (2.5%)			1		-
SAM	2 (5%)		1	1		2.8 ± 1.1
AMC	8 (20%)	1	3	1	3	3.0 ± 1.5
TZP	1 (2.5%)		1			7.1 ± 0.2
Cefaclor	1 (2.5%)			1		-
Cefprozil	2 (5%)			1	1	1.1 ± 0.1
Cefuroxime	6 (15%)		3	2	1	2.9 ± 1.1
Cefotaxime	1 (2.5%)		1			7.1 ± 1.6
Ceftriaxone	1 (2.5%)				1	-
Ceftazidime	1 (2.5%)		1			
Netilmicin	2 (5%)		2			3.5 ± 2.5
Amikacin	8 (20%)	2	4	1	1	4.0 ± 2.1

Table III: IV Antibiotic dosage

	Antibiotic prescription	**Dose per day**	
		Mean ± S.D	**Range**
< 29 days			
Ampicillin	4	188 ± 10.3	166-210
Cefotaxime	3	140 ± 17.1	98-148
Amikacin	4	14 ± 0.9	10-15
29 days- < 2 years			
Ampicillin	10	195 ± 2.5	188-198
SAM	3	155 ± 17.3	145-197
AMC	4	87 ± 0.9	85-90
Cefuroxime	4	99 ± 44.7	17-145
Cefotaxime	7	148 ± 2.2	140-150
Ceftriaxone	3	76 ± 8.6	70-100
Amikacin	12	14 ± 1.7	12-22
2 - < 5 years			
Cefuroxime	2	105 ± 24.1	77-145
Amikacin	3	14 ± 2.5	12-20
5 years or older			
SAM	3	133 ± 14.2	110-150
Amikacin	4	13 ± 0.2	12-13

Discussion

No study has yet been conducted in Pakistan to address the antibiotic resistance of UTI-causing pathogens. This study treated children with febrile and afebrile UTIs with antibiotics like amikacin, penicillins, and third-generation cephalosporins.

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E.coli was the most common pathogen, which was highly resistant to β-lactams. The average treatment of UTI was an average 4.5 to 5 days. Since most of the population was atypical, treatment was sometimes long (Pérez et al., 2019). IV treatments followed by oral antibiotics were effective in shorter treatment courses (Sehested et al., 2021). Prescribing errors were noted in TZP in neonates due to the absence of recommended dosage (Chardavoyne and Kasmire, 2020). Our study's resistance rates comply with other studies (De Lorenzis et al., 2020). The resistance of E.coli to ampicillin and SXT was 60% and 25% in our study, respectively, similar to 53.4% and 30.2% in another study (Bryce et al., 2016). The high rates in our study may be due to a small sample size. The resistance rate to AMC was 10% which is similar to 16.5% in a UK study (Bryce et al., 2018), 33% in a Turkish study (Yilmaz et al., 2016), and 25% in a Korean study (Seo et al., 2017). However, the ESBL-positive UTIs in our study (1%) were significantly lower than other UTI studies in children, and the high prevalence of these UTIs globally (Amin et al., 2020; Kayastha et al., 2020). Our study has some limitations. We had a small sample size and limited study period due to which resistance rates between febrile and afebrile UTIs was not compared accurately.

Conclusion

There is a need for antimicrobial resistance stewardship programmes to control the increasing prevalence of resistance among UTI-causing pathogens.

Conflict of interest

The authors declared absence of conflict of interest.

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