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Antibiotic resistance in pediatric urinary tract infections: a single-center experience

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ABSTRACT

Aims: The development of antibiotic resistance in urinary tract infections (UTIs) has become a major public health concern due to its association with treatment failure. This study aimed to investigate the distribution of uropathogens causing UTIs in children in the Black Sea region, to evaluate antibiotic resistance patterns over time, to identify risk factors influencing resistance development, and to provide guidance for the selection of appropriate empirical antibiotics.

Methods: This retrospective study included 1,252 pediatric patients aged 1 month to 18 years who were diagnosed with UTIs at the Pediatric Outpatient Clinic of Kastamonu Training and Research Hospital between 2021 and 2023. Uropathogens were categorized by age, sex, and year of isolation, and their antibiotic resistance was compared across these groups. Extended-spectrum beta-lactamase (ESBL) positivity was also analyzed.

Results: The most frequently isolated uropathogen was *Escherichia coli (E. coli)* (78%), with the highest resistance rates observed against ampicillin (61.5%) and amoxicillin-clavulanate (42.1%). Statistically significant differences in resistance were found between age groups and across different years. The ESBL positivity rate was 10.9%, predominantly associated with *E. coli* and older age groups.

Conclusion: This study provides valuable insights into the regional antibiotic resistance profile, serving as a guide for empirical treatment selection. Regional resistance data should be considered before initiating therapy, and treatment should be promptly revised based on culture results. Public awareness and training programs on rational antibiotic use are strongly recommended.

Keywords: Pediatric urinary tract infection, antibiotic resistance, ESBL, empirical antibiotic therapy

INTRODUCTION

Urinary tract infections (UTIs) are among the most common bacterial infections in childhood, and their clinical manifestations may vary depending on age, sex, and underlying anatomical or functional abnormalities. These infections are of particular importance in the early years of life due to their potential to cause renal parenchymal damage, underscoring the need for early diagnosis and appropriate treatment.[1] Pediatric urinary tract infections are a frequently encountered and significant clinical condition in early childhood, and should be managed with care due to the variability of symptoms and their potential to cause long-term renal complications.[2] The diagnosis of UTI is established based on clinical suspicion and confirmed by urinalysis and urine culture. The distinction between lower and upper urinary tract infections is crucial for determining prognosis and guiding treatment. Therefore, the clinical course of the infection, laboratory parameters, and microbiological data should be evaluated together.[3,4]

In the pediatric population, the most commonly identified uropathogens are gram-negative bacilli. *Escherichia coli* (*E. coli*) is responsible for the majority of UTIs, followed by *Klebsiella pneumoniae* (*K. pneumoniae*), *Proteus mirabilis* (*P. mirabilis*), and *Pseudomonas aeruginosa* (*P. aeruginosa*). Less frequently, gram-positive organisms such as *Enterococcus* spp. and *Staphylococcus aureus* can also cause UTIs.[5]

In recent years, inappropriate and excessive use of antibiotics has led to the development of antimicrobial resistance. The increasing prevalence of extended-spectrum beta-lactamase (ESBL)-producing uropathogens has reduced the success rate of empirical therapy and become a significant public health concern. Furthermore, it is well recognized that antibiotic resistance patterns may vary by region.[6,7] Therefore, this study aimed to investigate the distribution of uropathogens and their antibiotic resistance patterns over a three-year period in our region, in order to provide evidence-based guidance for the selection of appropriate empirical antibiotic therapy. We

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hypothesize that antibiotic resistance patterns in pediatric urinary tract infections significantly vary according to patient age, sex, and year, and that these variations can guide more effective empirical treatment strategies.

METHODS

This study was approved by the Ethics Committee of Kastamonu University Faculty of Medicine (Approval Date: 01.11.2023, Decision No: 2023-KAEK-137). All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki.

This retrospective study included data from 1,458 pediatric patients aged between 1 month and 18 years who were diagnosed with urinary tract infection (UTI) at the Pediatric Outpatient Clinic of Kastamonu Training and Research Hospital between 2021 and 2023. For patients under the age of three, urine samples were collected via transurethral bladder catheterization; for those over three years, midstream clean-catch urine samples were accepted.

Isolation of uropathogens was performed using the surface streaking method with calibrated loops on both blood agar and MacConkey agar (Oxoid Ltd., Basingstoke, Hampshire, UK) for semi-quantitative assessment. Cultures were incubated aerobically at 37°C for 24 hours. Cultures with no growth at 24 hours were incubated for an additional 48 hours. A culture was considered positive for UTI if a single organism grew at a concentration $\geq 10^5$ CFU/Ml. Bacterial identification was conducted using a range of biochemical tests, including indole production, citrate utilization, oxidase activity, hydrogen sulfide production, lysine decarboxylase activity, lactose fermentation, urease activity, gas production, catalase and coagulase activities, mannitol fermentation, and novobiocin sensitivity.[8]

Antibiotic susceptibility testing was performed on Mueller-Hinton and blood agar using the disk diffusion method, following the Clinical and Laboratory Standards Institute (CLSI) guidelines.[9] The antibiotic discs tested included: nitrofurantoin, fosfomycin, piperacillin-tazobactam, meropenem, imipenem, cefoperazone/sulbactam, nalidixic acid, ampicillin, trimethoprim, ceftriaxone, amikacin, aztreonam, ciprofloxacin, co-amoxiclav, clotrimazole, cefuroxime, chloramphenicol, ceftazidime, gentamicin, levofloxacin, gatifloxacin, cefixime, ticarcillin-clavulanate, ertapenem, cefpirome, colistin, polymyxin B, tobramycin, minocycline, cefepime, ofloxacin, norfloxacin, tigecycline, cefobid (cefoperazone), cefotaxime, sulfonamides, doxycycline, and maxipime.

Urine cultures with growth of three or more different uropathogens were considered contaminated and excluded from the study. After exclusions, 1,252 patients were included in the final analysis. The following variables were recorded: patient age, sex, type of uropathogen isolated, presence of ESBL-positive organisms, and antibiotic resistance patterns. Patients were categorized into three age groups: <12 months, 13-59 months, and ≥60 months. The years of sample collection were recorded as 2021, 2022, and 2023. Uropathogens were grouped into six categories: *E. coli*, *Enterococcus* spp., *P. mirabilis*, *K. pneumoniae*, *P. aeruginosa*, and others. The data obtained were analyzed using the SPSS version 26.0 statistical software package. Descriptive statistics were presented as mean±standard deviation for continuous variables and as frequencies and percentages (n, %) for categorical variables. Associations between categorical variables were evaluated using the Chi-square test (Pearson's and Fisher's exact tests where appropriate). A p-value of <0.05 was considered statistically significant.

RESULTS

A total of 1,252 pediatric patients aged 1 month to 18 years, who were diagnosed with urinary tract infection at Kastamonu Training and Research Hospital between 2021 and 2023, were included in the study. Of these patients, 883 (70.5%) were female and 369 (29.5%) were male. The mean age was 61.2±54.21 months. Age distribution showed that 279 (22.3%) were aged 1-12 months, 429 (34.3%) were 13-59 months, and 544 (43.5%) were ≥60 months. The number of patients with ESBL-positive isolates was 136 (10.9%).

When evaluated by sex, *E. coli* (78%) and *K. pneumoniae* (55.3%) were significantly more frequent in females, whereas *P. mirabilis* (56.9%) and other bacterial species (50.8%) were more frequent in males (p<0.001). Across all age groups, *E. coli* was the most common uropathogen; its prevalence was significantly higher in the ≥60 months age group (p<0.001). *K. pneumoniae* was most frequent in the 1-12 months group (41.2%; p<0.001), while *P. mirabilis* (53.4%) and *P. aeruginosa* (58.3%) were most common in the 13–59 months group (p=0.004). In terms of year-to-year comparison, *E. coli* (p=0.04) and *P. mirabilis* (p<0.001) were most commonly isolated in 2022, while other bacterial species were more frequently isolated in 2023 (p=0.008) (**Table 1**).

Table 1. Distribution of uropathogens by gender, age groups, and years

	E. coli	p	*E. faecalis*	p	*K. pneumoniae*	p	*P. mirabilis*	p	*P. aeruginosa*	p	Diğer	p
Sex												
Female	667 (78)	<0.001	26 (65)	0.436	110 (55.3)	<0.001	25(43,1)	<0.001	24 (66.7)	0.606	31 (49.2)	<0.001
Male	188 (22)		14 (35)		89 (44.7)		33 (56.9)		12 (33.3)		32 (50.8)	
Age												
1-12 months	159 (18.6)		10 (25)		82 (41.2)		6 (10.3)		8 (22.2)		14 (22.2)	
13-59 months	285 (33.3)	<0.001	8 (20)	0.145	62 (31.2)	<0.001	31 (53.4)	0.004	21 (58.3)	0.004	21 (33.3)	0.984
≥60 months	411 (48.1)		22 (55)		55 (27.6)		21 (36.2)		7 (19.4)		28 (44.5)	
Years												
2021	54 (6.3)		0		16 (8)		12 (20.7)		3 (8.3)		9 (14.3)	
2022	502 (58.7)	0.04	22 (55)	0.122	116 (58.3)	0.842	31 (53.4)	<0.001	19 (52.8)	0.868	25 (39.7)	0.008
2023	299 (35)		18 (45)		67 (33.7)		15 (25.9)		14 (38.9)		29 (46)	

E. coli: Escherichia coli, E. faecalis: Enterococcus faecalis, K. pneumoniae: Klebsiella pneumoniae, P. mirabilis: Proteus mirabilis, P. aeruginosa: Pseudomonas aeruginosa

Overall antibiotic resistance was highest against ampicillin (61.5%), amoxicillin-clavulanate (42.1%), cefuroxime (32.1%), cefuroxime axetil (32.1%), and cefixime (29.0%) (Table 2). Resistance patterns showed significant variation across age groups and years. Ampicillin, cefepime, imipenem, and piperacillin-tazobactam showed significantly higher resistance rates in children aged ≥60 months ($p<0.05$). Conversely, fosfomycin and nitrofurantoin resistance were highest in the 13-59 months group (Table 3).

When the antibiotic resistance of uropathogens by year is examined in Table 4, it was found that the resistance rates to Aztreonam ($p<0.001$), Ceftazidime ($p=0.03$), Cefixime ($p=0.003$), Ciprofloxacin ($p<0.001$), Cefuroxime ($p=0.031$), Cefuroxime axetil ($p=0.009$), Fosfomycin ($p<0.001$), Nitrofurantoin ($p<0.001$), Gentamicin ($p<0.001$), Imipenem ($p<0.001$), Tetracycline ($p=0.023$), and Piperacillin-tazobactam ($p<0.001$) were statistically higher in 2022 compared to other years. In contrast, resistance to Ampicillin ($p=0.033$), Amoxicillin-clavulanate ($p=0.027$), and Cefepime ($p<0.001$) was statistically higher in 2023 than in other years.

Yearly comparison revealed significantly higher resistance rates in 2022 to aztreonam, ceftazidime, cefixime, ciprofloxacin, cefuroxime, fosfomycin, nitrofurantoin, gentamicin, imipenem, tetracycline, and piperacillin-tazobactam ($p<0.05$). In contrast, resistance to ampicillin, amoxicillin-clavulanate, and cefepime was significantly higher in 2023 (Table 5).

The overall ESBL positivity rate was 10.9%. ESBL-producing organisms were most commonly *E. coli* (51.5%) and *P. aeruginosa* (25%). ESBL positivity significantly increased with age ($p=0.026$). Among ESBL-positive isolates, the

Table 2. Distribution of uropathogens according to overall antibiotic resistance

Antibiotic resistance	n	%
Ampicillin	770	61.5
Amoxicillin-clavulanate	527	42.1
Amikacin	10	0.8
Aztreonam	13	1.0
Ceftazidime	303	24.2
Cefixime	363	29.0
Ciprofloxacin	185	14.8
Clindamycin	9	0.7
Ceftriaxone	282	22.5
Cefuroxime	402	32.1
Cefuroxime axetil	402	32.1
Cefazolin	13	1.0
Ertapenem	44	3.5
Cefepime	130	10.4
Fosfomycin	48	3.8
Cefoxitin	203	16.2
Nitrofurantoin	92	7.3
Gentamicin	94	7.5
Imipenem	21	1.7
Levofloxacin	13	1.0
Linezolid	3	0.2
Meropenem	14	1.1
Trimethoprim-sulfamethoxazole	323	25.8
Tetracycline	11	0.9
Teicoplanin	3	0.2
Tigecycline	2	0.2
Piperacillin-tazobactam	210	16.8
Vancomycin	3	0.2

Table 3. Antibiotic resistance of uropathogens according to age groups

Antibiotic resistance	1-12 months, n (%)	13-59 months, n (%)	≥60 months, n (%)	X^2	p
Ampicillin	191 (24.8)	267 (34.7)	312 (40.5)	10.33	0.035
Amoxicillin-clavulanate	107 (20.3)	198 (37.6)	222 (42.1)	7.479	0.279
Amikacin	10 (30.3)	8 (24.2)	15 (45.5)	4.234	0.645
Aztreonam	4 (30.8)	2 (15.4)	7 (53.8)	9.802	0.133
Ceftazidime	68 (22.4)	100 (33.0)	135 (44.6)	10.972	0.089
Cefixime	77 (21.2)	126 (34.7)	160 (44.1)	6.521	0.367
Ciprofloxacin	44 (23.8)	60 (32.4)	81 (43.8)	6.155	0.406
Clindamycin	1 (11.1)	3 (33.3)	5 (55.6)	3.167	0.530
Ceftriaxone	66 (23.4)	102 (36.2)	114 (40.4)	3.176	0.786
Cefuroxime	87 (21.6)	141 (35.1)	174 (43.3)	4.126	0.660
Cefuroxime axetil	87 (21.6)	141 (35.1)	174 (43.3)	0.229	0.994
Cefazolin	5 (38.5)	6 (46.2)	2 (15.4)	6.189	0.338
Ertapenem	6 (13.6)	20 (45.5)	18 (40.9)	3.373	0.497
Cefepime	28 (21.5)	38 (29.2)	64 (49.2)	14.643	0.023
Fosfomycin	16 (33.3)	20 (41.7)	12 (25.0)	13.040	0.042
Cefoxitin	39 (19.2)	75 (36.9)	89 (43.8)	1.958	0.924
Nitrofurantoin	15 (16.3)	45 (48.9)	32 (34.8)	11.578	0.021
Gentamicin	24 (25.5)	34 (36.2)	36 (38.3)	11.883	0.065
Imipenem	7 (33.3)	5 (23.8)	9 (42.9)	19.957	0.003
Levofloxacin	3 (23.1)	2 (15.4)	8 (61.5)	7.950	0.242
Linezolid	0	0	3 (100)	8.274	0.082
Meropenem	6 (42.9)	3 (21.4)	5 (35.7)	10.295	0.113
Trimethoprim-sulfamethoxazole	75 (23.2)	105 (32.5)	143 (44.3)	11.994	0.062
Tetracycline	3 (27.3)	2 (18.2)	6 (54.5)	2.020	0.732
Teicoplanin	0	0	3 (100)	9.246	0.055
Tigecycline	2 (100)	0	0	14.893	0.005
Piperacillin-tazobactam	40 (19)	71 (33.8)	99 (47.1)	15.361	0.018
Vancomycin	0	0	3 (100)	8.274	0.082

Table 4. Antibiotic resistance of uropathogens by years

Antibiotic resistance	2021, n (%)	2022, n (%)	2023, n (%)	X^2	p
Ampicillin	59 (7.7)	439 (57)	272 (35.3)	10.461	0.033
Amoxicillin-clavulanate	45 (8.5)	286 (54.3)	196 (37.2)	14.212	0.027
Amikacin	2 (6.1)	19 (57.6)	12 (36.4)	0.422	0.999
Aztreonam	0	8 (61.5)	5 (38.5)	23.483	0.001
Ceftazidime	16 (5.3)	166 (54.8)	121 (39.9)	13.946	0.030
Cefixime	19 (5.2)	204 (56.2)	140 (38.6)	19.588	0.003
Ciprofloxacin	16 (8.6)	110 (59.5)	59 (31.9)	37.962	<0.001
Clindamycin	0	4 (44.4)	5 (55.6)	4.377	0.357
Ceftriaxone	19 (6.7)	154 (54.6)	109 (38.7)	10.964	0.090
Cefuroxime	23 (5.7)	220 (54.7)	159 (39.6)	13.890	0.031
Cefuroxime axetil	23 (5.7)	220 (54.7)	159 (39.6)	13.470	0.009
Cefazolin	0	13 (100)	0	146.734	<0.001
Ertapenem	2 (4.5)	24 (54.5)	18 (40.9)	4.893	0.298
Cefepime	1 (0.8)	58 (44.6)	71 (54.6)	337.133	<0.001
Fosfomycin	15 (31.3)	33 (68.8)	0	312.964	<0.001
Cefoxitin	16 (7.9)	113 (55.7)	74 (36.5)	4.990	0.545
Nitrofurantoin	14 (15.2)	56 (60.9)	22 (23.9)	20.382	<0.001
Gentamicin	4 (4.3)	67 (71.3)	23 (24.5)	36.387	<0.001
Imipenem	2 (9.5)	10 (47.6)	9 (42.9)	40.805	<0.001
Levofloxacin	0	7 (53.8)	6 (46.2)	5.934	0.431
Linezolid	0	1 (33.3)	2 (66.7)	6.287	0.179
Meropenem	0	7 (50)	7 (50)	7.664	0.264
Trimethoprim-sulfamethoxazole	30 (9.3)	176 (54.5)	117 (36.2)	5.799	0.446
Tetracycline	1 (9.1)	8 (72.7)	2 (18.2)	11.291	0.023
Teicoplanin	0	1 (33.3)	2 (66.7)	6.179	0.186
Tigecycline	1 (50)	1 (50)	0	7.259	0.123
Piperacillin-tazobactam	17 (8.1)	97 (46.2)	96 (45.7)	21.779	0.001
Vancomycin	0	1 (33.3)	2 (66.7)	6.287	0.179

Table 5. Age group-based evaluation of ESBL-producing uropathogens

Antibiotic resistance	Total, n (%)	1-12 months, n (%)	13-59 months, n (%)	≥60 months, n (%)	X^2	p
Escherichia coli	70 (51.5)	7 (30.4)	29 (49.2)	34 (63.0)	13.318	0.026
Klebsiella pneumoniae	27 (19.9)	7 (30.4)	9 (15.3)	11 (20.4)		
Pseudomonas aeruginosa	34 (25.0)	7 (30.4)	20 (33.9)	7 (13.0)		
Others	5 (3.7)	2 (8.7)	1 (1.7)	2 (3.7)		

ESBL: Extended-spectrum beta-lactamase

highest resistance rates were observed for ampicillin (72.1%), amoxicillin-clavulanate (69.1%), ceftazidime (69.1%), ceftriaxone (68.4%), cefuroxime (68.4%), and cefuroxime axetil (68.4%) (**Table 6**).

DISCUSSION

As in other parts of the world, UTIs are among the most common infections in the pediatric population in the Black Sea region. Therefore, this study retrospectively evaluated resistance patterns of uropathogens in order to identify suitable empirical treatment strategies. In our study, 70.5% of the patients were female. Akgül et al.[10] reported that 72% of pediatric UTI cases were female, and Samancı et al.[11] found that UTIs were four times more common in girls than in boys. In an Israeli study involving 53,203 children, 92.6% were female.[12] Similarly, a post-pandemic study in the United States also reported a higher UTI incidence in girls.[13] The higher prevalence of urinary tract infections among girls in our study is consistent with the literature. This increased susceptibility in females has been attributed to the shorter length of the urethra and its anatomical proximity to the perianal region.[14]

In terms of age, 22.3% of the patients were aged 1-12 months, 34.3% were 13–59 months, and 43.5% were ≥60 months. Similarly, in a study conducted by Liang et al.[13], urinary tract infections were most commonly observed in children aged 2-5 years, followed by those under the age of one. Supporting these findings, Shaikh et al.[15] also reported that the highest incidence occurred between 1 and 5 years of age. However, the findings of our study contrast with the data in the literature. Several factors may account for this discrepancy. The most prominent factor is the development of hygiene behaviors in school-aged children over 5 years. During this

Table 6. Antibiotic resistance patterns of ESBL-producing uropathogens

Antibiotic resistance	n	%
Ampicillin	98	72.1
Amoxicillin-clavulanate	94	69.1
Amikacin	13	9.6
Aztreonam	10	7.4
Ceftazidime	94	69.1
Cefixime	89	65.4
Ciprofloxacin	35	25.7
Ceftriaxone	93	68.4
Cefuroxime	93	68.4
Cefuroxime axetil	93	68.4
Cefazolin	5	3.7
Ertapenem	43	31.6
Cefepime	55	40.4
Fosfomycin	14	10.3
Cefoxitin	86	63.2
Nitrofurantoin	19	14.0
Gentamicin	17	12.5
Imipenem	12	8.8
Levofloxacin	1	0.7
Meropenem	9	6.6
Trimethoprim-sulfamethoxazole	48	35.3
Tetracycline	1	0.7
Tigecycline	1	0.7
Piperacillin-tazobactam	69	50.7

ESBL: Extended-spectrum beta-lactamase

period, the use of shared toilets, inadequate hand hygiene, and reduced fluid intake may contribute to an increased risk of infection. Additionally, dysfunctional voiding syndromes, daytime urinary incontinence, and habitual postponement of urination are also considered predisposing factors in this age group.[16] To reduce the incidence of urinary tract infections in this population, it would be beneficial to implement structured health education programs targeting school-aged children and their families, focusing on hygiene practices, proper voiding habits, and recognition of early signs of infection.

Regarding pathogen distribution by sex, *E. coli* (78%) and *K. pneumoniae* (55.3%) were more common in girls, whereas *P. mirabilis* (56.9%) and other bacteria (50.8%) were more prevalent in boys. These findings are in line with a recent Turkish study reporting similar distributions.[17] An Israeli study also found that although *E. coli* was the most common uropathogen in both sexes, infections with *P. mirabilis*, *E. faecalis*, and *P. aeruginosa* were more common in boys.[12] A review by the American Academy of Family Physicians highlighted that *Proteus* infections are especially prevalent in male children and those with kidney stones.[18] These findings in our study suggest that differences in uropathogens between sexes may be attributed to anatomical factors. In girls, the close proximity of the urethra to the perianal region may facilitate colonization by uropathogens such as *E. coli*. In contrast, the subpreputial space in boys is thought to provide a more favorable environment for the growth of organisms such as *P. mirabilis* and *P. aeruginosa*, leading to their increased frequency.[14,19] Another notable finding presented in Table 1 is that although *E. coli* was the most commonly isolated uropathogen in all age groups, its frequency was statistically higher in children aged ≥60 months compared to younger age groups. *Klebsiella pneumoniae* (41.2%) was most frequently observed in the 1-12-month age group, while *P. mirabilis* (53.4%) and *P. aeruginosa* (58.3%) were more common in the 13-59-month age range. Consistent with our findings, Zemer et al.[12] also reported in their study that *E. coli* was the most frequently isolated pathogen in children aged ≥3 years and that its prevalence increased with age. Another study indicated that *Proteus* spp. and *P. aeruginosa* were more frequently isolated in uncircumcised males and in patients with complicated urinary tract infections, particularly in the 2-5-year age group.[20] The consistency of our findings with the literature may be attributed to several factors: the progressive maturation of the immune system with increasing age, a decrease in the number of uncircumcised boys, and a lower incidence of congenital anomalies-leading to a relative decline in non-*E. coli* infections and consequently an increased proportion of *E. coli* isolates.[21]

In our study, the uropathogens exhibited the highest resistance to ampicillin (61.5%), amoxicillin-clavulanate (42.1%), cefuroxime (32.1%), cefuroxime axetil (32.1%), and cefixime (29%). When compared with the literature, Akgül et al.[10] reported resistance rates of 72% for ampicillin, 39% for amoxicillin-clavulanate, 31% for cefuroxime, and 28% for cefixime. Similarly, Samancı et al.[11] found ampicillin resistance to be 68%, amoxicillin-clavulanate resistance 41%, and cephalosporin resistance exceeding 30%. In the study by Zemer et al.,[12] the resistance rate to ampicillin was 69%, to amoxicillin-clavulanate 47%, and to second- and third-generation cephalosporins ranged between 20% and 35%. These findings indicate that resistance to beta-lactam antibiotics is a significant public health concern not only in Turkiye but also globally. The high resistance rates to beta-lactam antibiotics may be attributed to the long-standing, widespread, and often unnecessary use of antibiotics, as well as the increasing prevalence of ESBL-producing uropathogens. Therefore, empirical antibiotic selection should be guided by local resistance patterns and promptly revised based on urine culture results. Furthermore, structured educational programs on rational antibiotic use should be implemented, and regulatory public health policies should be enforced.

When analyzing antibiotic resistance of uropathogens by age group in our study, resistance to ampicillin, cefepime, imipenem, and piperacillin-tazobactam was significantly higher in children aged ≥60 months compared to younger age groups. Resistance to fosfomycin and nitrofurantoin was significantly higher in the 13-59-month age group, and a statistically significant association was found between age groups and resistance patterns. In a study by Duicu et al.,[22] higher antibiotic resistance-particularly to ampicillin-was reported in patients under 1 year and over 5 years of age. In another study conducted in Turkiye, the highest resistance was observed in the 1-12-month age group, with elevated resistance to ampicillin, amoxicillin-clavulanate, imipenem, and fosfomycin. Moreover, significant resistance to nitrofurantoin was found in the 13-59-month group, and to cefepime in those aged ≥60 months.[23] A review of both national and international literature reveals that each study demonstrates age-specific resistance patterns. This variability is likely attributable to the presence of region-

specific uropathogens, differences in empirical antibiotic selection based on local practices, and regional variations in socioeconomic and cultural conditions. Based on our findings, we recommend that empirical antibiotic selection should consider not only the geographic characteristics of the region but also age-specific resistance profiles.

When antibiotic resistance of uropathogens was analyzed by year in our study, resistance rates to aztreonam, ceftazidime, cefixime, ciprofloxacin, cefuroxime, cefuroxime axetil, fosfomycin, nitrofurantoin, gentamicin, imipenem, tetracycline, and piperacillin-tazobactam were found to be significantly higher in 2022 compared to other years. Conversely, resistance to ampicillin, amoxicillin-clavulanate, and cefepime was significantly higher in 2023. Although our study spans a relatively short time period, the findings clearly indicate a trend of increasing antibiotic resistance over time. This observation is supported by literature; for instance, Mahajan et al.[24] reported a significant rise in amoxicillin-clavulanate resistance over the years. In another long-term study from the Netherlands, resistance to amoxicillin-clavulanate increased by 2% annually, while resistance to cephalosporins rose by 1.1% per year.[25] A regional study conducted in Eskişehir, Turkiye, showed that ampicillin resistance among *E. coli* isolates increased from 45% to 66%, and amoxicillin-clavulanate resistance rose from 20% to 48% when comparing the periods 2010-2015 and 2016–2019.[23] These findings underscore the fact that rising antibiotic resistance has become a major public health concern. We recommend that treatment guidelines be updated frequently through new, region-specific studies to ensure the appropriate selection of empirical antibiotics and to guide clinical decision-making accordingly.

ESBL-positive uropathogens represent a major public health concern due to their high levels of antibiotic resistance. In our study, 136 (10.9%) of the included patients were found to have ESBL-positive isolates. This rate is comparable to other studies conducted in Turkiye, where Akgül et al.[10] reported a prevalence of 13.2%, and Samancı et al.[11] reported 11.9%. In international studies, Zemer et al.[12] reported an ESBL-positivity rate of 14.4%, while Mahajan et al.[24] found a rate of 10.8%. Our findings are therefore consistent with both national and international data. These results indicate a rising trend in ESBL-positivity rates in recent years, as observed in our study, which further complicates the empirical selection of antibiotics.

In our study, when evaluating the antibiotic resistance patterns of ESBL-positive uropathogens, the highest resistance rates were observed against ampicillin, amoxicillin-clavulanate, ceftazidime, ceftriaxone, cefuroxime, cefuroxime axetil, and cefoxitin. In comparison with the literature, Alameer et al.[26] reported that ESBL-positive uropathogens showed the greatest resistance to ampicillin (69.3%) and aztreonam (66.7%). In another study by Smriti et al.,[27] *E. coli* and *Klebsiella* isolates demonstrated resistance to nitrofurantoin, while remaining susceptible to fosfomycin and amikacin. The resistance spectrum in our study appears broader than in previous studies. This may be attributed not only to regional variations but also to the relatively high prevalence of ESBL-positive isolates in our geographic area.

Limitations

However, the study is limited by its single-center and retrospective design. Data on clinical outcomes, recurrent infections, imaging findings, and underlying risk factors were not evaluated. Therefore, future prospective multicenter studies that incorporate these variables are recommended to support and expand upon our findings.

CONCLUSION

This study provides insight into the distribution of pediatric urinary tract infection pathogens and their resistance patterns in a single center in the Black Sea region. Our findings emphasize that antibiotic resistance varies significantly according to age, sex, and over time. Notably, there was an upward trend in resistance to commonly used antibiotics in recent years. The overall ESBL positivity rate was 10.9%, with the highest rates observed among *E. coli* and *P. aeruginosa* isolates. These results highlight the need to consider local resistance data when initiating empirical antibiotic therapy. Treatment should be promptly revised according to culture and sensitivity results. Health professionals should be trained regularly on the principles of rational antibiotic use, and public awareness campaigns should be intensified to combat antimicrobial resistance. This study contributes to the development of regional antibiograms and provides data to guide clinicians in the selection of appropriate empirical therapy. Updated treatment guidelines and the implementation of antimicrobial stewardship programs are urgently needed to curb the rising threat of antibiotic resistance. The major strength of our study is the relatively large sample size collected over a three-year period, which allows for robust trend analysis. In addition, subgroup evaluations by age, sex, and year strengthen the validity of the findings.

ETHICAL DECLARATIONS

Ethics Committee Approval

This study was approved by the Kastamonu University Faculty of Medicine (Approval Date: 01.11.2023, Decision No: 2023-KAEK-137).

Informed Consent

As this was a retrospective study, formal written informed consent was not required and was therefore not obtained.

Peer Review Process

This manuscript was subject to external peer review.

Conflict of Interest

The authors declare no conflicts of interest related to this study.

Financial Disclosure

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Author Contributions

All authors contributed significantly to the study's conception, design, data acquisition, analysis, and interpretation. All authors reviewed and approved the final version of the manuscript.

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