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FACTORS ASSOCIATED WITH ANTIBIOTIC SENSITIVITY AND RESISTANCE IN CHILDREN WITH URINARY TRACT INFECTION

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ABSTRACT

Background: Urinary tract infections (UTIs) are among the most common bacterial infection of childhood. We aimed to investigate the factors influencing sensitivity and resistance to antibiotics in children with UTI. **Methods:** This cross-sectional study included children with culture-confirmed UTI, aged 2 months to 14 years, admitted to Bandar Abbas Children's Hospital, Bandar Abbas, Iran, 2017-2018. Disc antibiogram was used to determine antibiotic sensitivity and resistance. Erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) levels were also measured in all participants. **Results:** Of the 200 children included in this study with a mean age of 2.58 ± 2.81 years, 39 (19.5%) were male. *Escherichia coli* was more prevalent in girls by 16.5%. Gender and resistance to antibiotics were not correlated (P>0.05). Patients with constipation were significantly outnumbered by those without constipation regarding sensitivity to amikacin and nitrofurantoin (70.4% vs 89.2%, P=0.012, and 75% vs 96%, P=0.002, respectively). Sensitivity to imipenem was higher in summer (86%, P=0.007), and to nitrofurantoin in autumn (75%, P=0.008). Fewer subjects with prior antibiotic intake were sensitive to ciprofloxacin compared to those without such history (P=0.016). Sensitivity to antibiotics was neither significantly correlated with hydronephrosis or anatomical abnormalities, nor with labial adhesion, yet 100% of patients with labial adhesion were sensitive to cotrimoxazole (P=0.009). No significant relationship was observed between antibiotic resistance and ESR or CRP levels, except for significantly lower CRP in patients resistant to ceftazidime compared to those sensitive to it (P=0.027). **Conclusions:** Resistance to antibiotics was not influenced by gender, hydronephrosis, anatomical abnormalities, labial adhesion (to a great extent), ESR, and CRP (with one exception), while it was affected by the presence of constipation, prior antibiotic intake, and change in seasons.

KEYWORDS: Urinary tract infection, antibiotic resistance, children.

INTRODUCTION

Urinary tract infections (UTIs) are among the most common bacterial infection of childhood.[1] Many children are admitted to the hospital due to UTI and the majority of them receive antibiotics without knowledge of the responsible pathogen or its antibiotic resistance.[2] In fact, in children with suspected UTI, the most common approach is to empirically administer antibiotics while waiting for the results of the culture and antibiogram.[2] because timely treatment of UTI can prevent serious renal complications such as scarring, hypertension, and chronic kidney disease.[3-5]

Although viruses, fungi, and parasites can also cause UTI, important infections are often cause by bacteria. The most common urogenital pathogens in children are the bacteria from the Enterobacteriaceae family, such as *Escherichia coli* (*E. coli*) and *Klebsiella*.[3,6,7] *E. coli* is responsible for 80% of all UTIs.[2] Treatment of UTI is based on the antibiotic resistance of the responsible pathogen; however, the resistance of urogenital pathogens is increasing worldwide. Since urine culture and antibiogram take at least 48 hours, the initial empirical treatment of UTI is done according to the antibiotic sensitivity and resistance profile of the common urogenital pathogens, often based on the previous research and observations.[3] There can be geographical variations in this profile due to the common infections in each region and the antibiotics prescribed for every condition. Therefore, we aimed to investigate the factors influencing sensitivity and resistance to antibiotics in children with UTI admitted to Bandar Abbas Children's Hospital, Bandar Abbas, Iran.

METHODS

Participants and study design

This study received ethics approval from the Ethics Committee of Hormozgan University of Medical

Sciences. Written informed consent was obtained from the parents/guardians of the patients. This cross-sectional study included pediatric patients aged 2 months to 14 years admitted to Bandar Abbas Children's Hospital, Bandar Abbas, Iran, from 2018 to 2019, due to culture-confirmed UTI. Accordingly, patients with a negative urine culture were excluded from the study.

All patients with suspected UTI and having urinary symptoms, such as dysuria or discomfort during voiding, were evaluated. Urine samples were collected using one of these four methods: suprapubic aspiration (SPA), catheterization, urine bag, and mid-stream. Urine bags were used for patients <3 years. In cooperative patients, the mid-stream method was used. When sampling was not possible with the mid-stream method or if the patient was uncooperative, catheterization or SPA was performed. All urine specimens were cultured using the standard method. Urine cultures were considered positive if the colony-forming unit (CFU)/ml was $>10^4$ in the catheterization method, $>10^5$ in the mid-stream and urine bag methods, and >1000 in SPA. Disc antibiogram test (Padtan Teb Co., Iran) was used to determine antibiotic susceptibility and resistance to imipenem, ceftriaxone, amikacin, ciprofloxacin, nitrofurantoin, cotrimoxazole, ampicillin, cefotaxime, gentamycin, vancomycin, cephalexin, erythromycin, ceftazidime, and nalidixic acid. Patients with a positive urine culture were admitted to the hospital. Upon admission and before the initiation of antibiotics, random venous blood samples were collected from all the patients, in which CRP (using the COBAS INTEGRA® 400 plus analyzer and the Roche kit, Roche Diagnostics, Germany), and ESR (using the ESR reader device) were measured.

Patients' data including age, gender, constipation, the season when UTI occurred, history of antibiotic used within the past 3 months, ultrasound (US) reports of anatomic abnormalities or hydronephrosis, and labial adhesion in female patients were recorded.

Data analysis

We used the Statistical Package for the Social Sciences (SPSS) software (version 26.0, Armonk, NY: IBM Corp., USA) for data analysis. Quantitative variables were described using means and standard deviations. Qualitative variables were described using frequencies and percentages.

Based on the results of the Kolmogorov-Smirnov normality test, the Kruskal-Wallis test and the Mann-Whitney test were used to compare quantitative variables. The chi-squared test and the Fisher's exact test were used for the comparison of qualitative variables. P-values <0.05 were regarded as statistically significant.

RESULTS

Of the 200 children included in this study with a mean age of 2.58 ± 2.81 years, 39 (19.5%) were male and 161 (80.5%) were female. In general, 42 patients (21%) had constipation, 67 (33.5%) had a history of antibiotic use within the past 3 months. UTI occurred in spring in 71 (35.5%), in summer 54 (27%), in fall 50 (25%), and in winter 25 (12.5%). Anatomic abnormalities or hydronephrosis were present in 42 patients (21%). Four female patients (2.5%) had labial adhesion (Table 1).

The most common isolated pathogen from urine cultures was *E. coli* (80%), followed by Gram-negative bacilli (7%), and nonhemolytic *Streptococcus* (6%) (Table 2). A significant correlation was found between the urogenital pathogen responsible for UTI and age, gender, season of UTI occurrence, antibiotic use within the past 3 months, anatomic abnormalities or hydronephrosis in US, labial adhesion in female patients, and CRP (Table 3).

The antibiotic sensitivity and resistance profiles are demonstrated in Figure 1. The highest sensitivity of the urogenital pathogens was to imipenem (95.2%), followed by nitrofurantoin (91.4%), amikacin (85.7%), and ciprofloxacin (76.9%). The highest resistance was observed with cephalexin (93.1%). Moreover, *E. coli* was most susceptible to imipenem (95.1%), followed by nitrofurantoin (90.2%), amikacin (87.4%), and ciprofloxacin (79.8%) (Figure 2).

Antibiotic sensitivity and resistance were not correlated with gender, anatomic abnormalities or hydronephrosis in US, and ESR (Table 4). Sensitivity to amikacin and nitrofurantoin was significantly lower in patients with constipation compared to those without constipation (P=0.012 and P=0.002, respectively), while sensitivity to cotrimoxazole was significantly higher in patients with constipation (P<0.001). Sensitivity and resistance of other antibiotics was not correlated with constipation. Sensitivity to imipenem was 100% in all seasons except for summer (86%) (P=0.007). Also, the sensitivity and resistance of nitrofurantoin, cotrimoxazole, and ampicillin were correlation with the season in which UTI occurred. Resistance to ciprofloxacin was significantly higher in patients who had used antibiotics within the past 3 months compared to those with no such prior use of antibiotics (P=0.016). Sensitivity to cotrimoxazole was 100% in female patients with labial adhesion (P=0.009). CRP was significantly lower when there was resistance to ceftazidime compared to when there was sensitivity to this antibiotic (P=0.027).

Table 1: General characteristics of the study population.

Variables	Values
Age (years) mean ± SD	2.58 ± 2.81
Gender N (%)	
Male	39 (19.5)
Female	161 (80.5)
Constipation N (%)	42 (21.0)
Season of UTI occurrence N (%)	
Spring	71 (35.5)
Summer	54 (27.0)
Fall	50 (25.0)
Winter	25 (12.5)
Antibiotic use in the past 3 months N (%)	67 (33.5)
US reports N (%)	
Normal	150 (75.0)
Abnormal	42 (21.0)
Not available	8 (4.0)
Labial adhesion in female patients (n=161)	4 (2.5)
ESR (mm/h) mean ± SD	40.55 ± 31.7
CRP (mg/L) mean ± SD	33.84 ± 30.91

Abbreviations: N, number; SD, standard deviation; UTI, urinary tract infection; US, ultrasound; ESR, erythrocyte sedimentation rate; CRP, C-reactive protein.

Table 2: The responsible urogenital pathogens isolated from urine cultures.

Pathogens	N (%)
E. coli	160 (80.0)
Streptococcus	2 (1.0)
S. saprophyticus	6 (3.0)
Gram-negative bacilli	14 (7.0)
Pseudomonas	2 (1.0)
S. hemolyticus	4 (2.0)
Nonhemolytic *Streptococcus*	12 (6.0)

Abbreviations: N, number; *E. coli*, *Escherichia coli*; *S. saprophyticus*, *Streptococcus saprophyticus*; *S. hemolyticus*, *Streptococcus hemolyticus*.

Table 3: The correlation of the responsible urogenital pathogens with age, gender, constipation, season of UTI occurrence, antibiotic history, US findings, labial adhesion in females, ESR, and CRP.

Factors	*E. coli*	*Streptococcus*	*S. saprophyticus*	Gram-negative bacilli	*Pseudomonas*	*S. hemolyticus*	Nonhemolytic *Strep.*	P-value
Age (years) mean ± SD	2.75 ± 2.92	1.00 ± 0.70	2.72 ± 2.18	1.38 ± 2.19	0.18 ± 0.02	2.31 ± 2.70	2.64 ± 2.27	0.007*
Gender N (%)								
Male	26 (66.7)	2 (5.1)	0 (0.0)	7 (17.9)	0 (0.0)	4 (10.3)	0 (0.0)	0.001†
Female	134 (83.2)	0 (0.0)	6 (3.7)	7 (4.3)	2 (1.2)	8 (5.0)	4 (2.5)	
Constipation N (%)	31 (73.8)	0 (0.0)	0 (0.0)	7 (16.7)	0 (0.0)	4 (9.5)	0 (0.0)	0.058†
Season of UTI occurrence N (%)								
Spring	45 (63.4)	2 (2.8)	5 (7.0)	13 (18.3)	2 (2.8)	0 (0.0)	4 (5.6)	<0.001†
Summer	49 (90.7)	0 (0.0)	0 (0.0)	1 (1.9)	0 (0.0)	4 (7.4)	0 (0.0)	
Fall	42 (84.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	8 (16.0)	0 (0.0)	
Winter	24 (96.0)	0 (0.0)	1 (4.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	
Antibiotic use in the past 3 months N (%)	52 (77.6)	0 (0.0)	6 (9.0)	2 (3.0)	2 (3.0)	2 (3.0)	3 (4.5)	0.001†
US reports N (%)								
Normal	120 (80.0)	0 (0.0)	4 (2.7)	14 (9.3)	0 (0.0)	8 (5.3)	4 (2.7)	0.019†
Abnormal	34 (81.0)	0 (0.0)	2 (4.8)	0 (0.0)	2 (4.8)	4 (9.5)	0 (0.0)	
Labial adhesion in female patients	2 (50.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (50.0)	0 (0.0)	0.003†

(n=161)								
ESR (mm/h) mean ± SD	42.43 ± 31.80	20.00 ± 0.00	24.00 ± 20.45	35.20 ± 30.87	13.00 ± 0.00	43.00 ± 39.63	34.50 ± 28.29	0.631*
CRP (mg/L) mean ± SD	37.61 ± 30.99	7.00 ± 0.00	20.50 ± 24.57	9.00 ± 7.71	13.00 ± 0.00	19.80 ± 22.17	50.50 ± 56.00	0.019*

Abbreviations: N, number; SD, standard deviation; *E. coli*, *Escherichia coli*; *S. saprophyticus*, *Streptococcus saprophyticus*; *S. hemolyticus*, *Streptococcus hemolyticus*, *Strep.*, *Streptococcus*; UTI, urinary tract infection; US, ultrasound; ESR, erythrocyte sedimentation rate; CRP, C-reactive protein.
*Analyzed by the Kruskal-Wallis test.
†Analyzed by the Fisher's exact test.

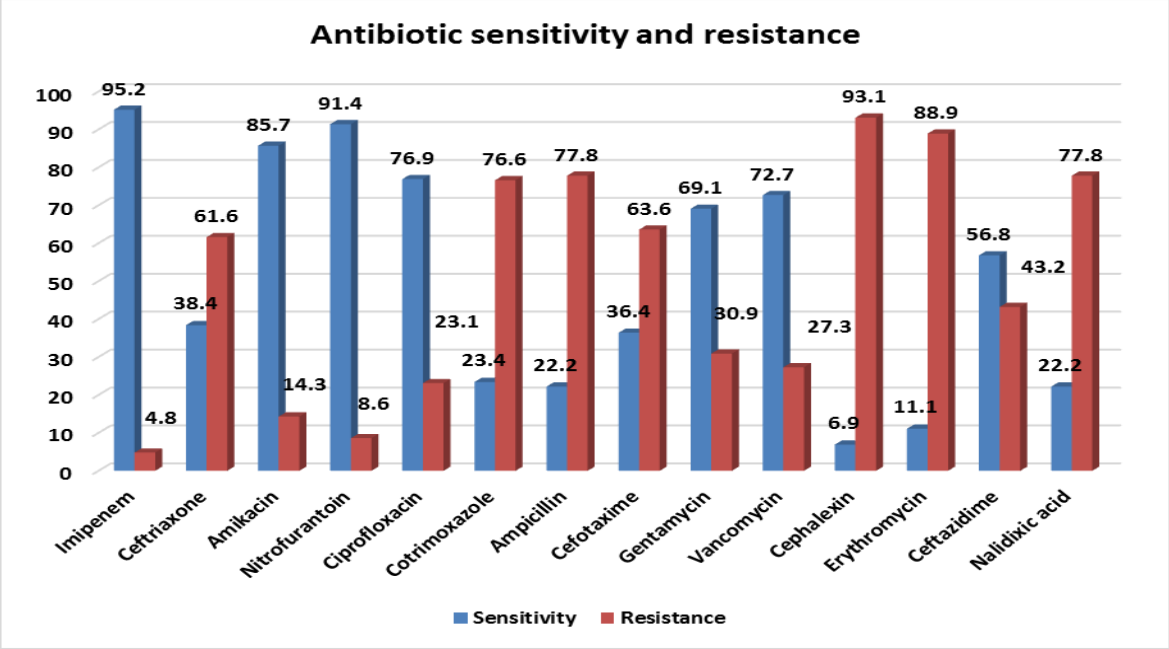

Figure 1: Antibiotic sensitivity and resistance of the responsible urogenital pathogens.

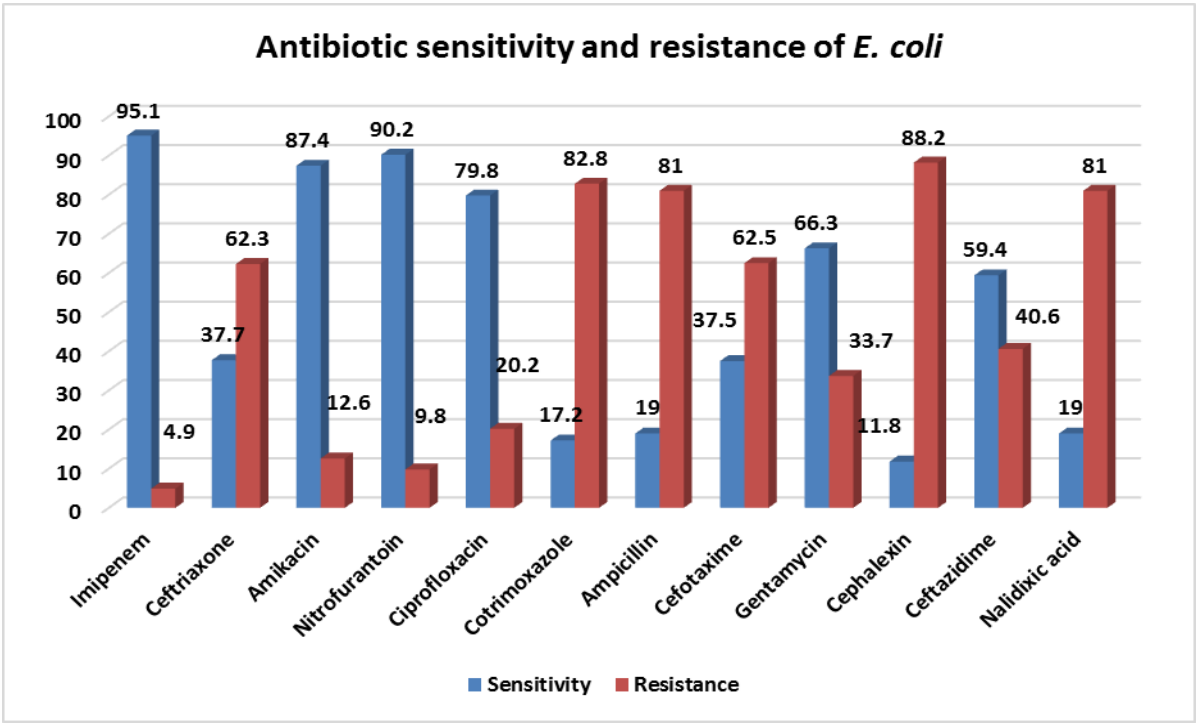

Figure 2: Antibiotic sensitivity and resistance of *E. coli*.

Table 4: The correlation between antibiotic sensitivity and resistance with different factors.

Antibiotics	Gender N (%)		Constipation N (%)		Season N (%)				Antibiotic use N (%)		US reports N (%)		Labial adhesion N (%)		ESR (mm/h)‡	CRP (mg/L)‡
	Male	Female	Yes	No	Spring	Summer	Fall	Winter	Yes	No	Normal	Abnormal	Yes	No	mean ± SD	mean ± SD
Imipenem																
Sensitivity	17 (89.5)	102 (96.2)	26 (100.0)	93 (93.9)	40 (100.0)	37 (86.0)	28 (100.0)	14 (100.0)	40 (95.2)	79 (95.2)	86 (95.6)	31 (93.9)	2 (100.0)	100 (96.2)	41.67 ± 30.92	35.72 ± 28.46
Resistance	2 (10.5)	4 (3.8)	0 (0.0)	6 (6.1)	0 (0.0)	6 (14.0)	0 (0.0)	0 (0.0)	2 (4.8)	4 (4.8)	4 (4.4)	2 (6.1)	0 (0.0)	4 (3.8)	56.33 ± 27.73	57.66 ± 41.63
P-value	0.226*		0.343†		0.007†				1.000†		0.659†		1.000†		0.163	0.230
Ceftriaxone																
Sensitivity	8 (33.3)	45 (39.5)	8 (34.8)	45 (39.1)	16 (38.1)	13 (31.0)	15 (48.4)	9 (39.1)	17 (41.5)	36 (37.1)	44 (41.1)	9 (33.3)	1 (50.0)	44 (39.3)	48.64 ± 33.42	43.00 ± 33.11
Resistance	16 (66.7)	69 (60.5)	15 (65.2)	70 (60.9)	26 (61.9)	29 (69.0)	16 (51.6)	14 (60.9)	24 (58.5)	61 (62.9)	63 (58.9)	18 (66.7)	1 (50.0)	68 (60.7)	37.02 ± 29.65	35.38 ± 30.49
P-value	0.574*		0.696*		0.513*				0.631*		0.460*		1.000†		0.064	0.209
Amikacin																
Sensitivity	26 (92.9)	100 (84.0)	19 (70.4)	107 (89.2)	39 (78.0)	37 (90.2)	28 (87.5)	22 (91.7)	36 (87.8)	90 (84.9)	95 (85.6)	27 (84.4)	1 (100.0)	99 (83.9)	46.15 ± 31.51	39.12 ± 31.42
Resistance	2 (7.1)	19 (16.0)	8 (29.6)	13 (10.8)	11 (22.0)	4 (9.8)	4 (12.5)	2 (8.3)	5 (12.2)	16 (15.1)	16 (14.4)	5 (15.6)	0 (0.0)	19 (16.1)	33.70 ± 29.39	30.42 ± 28.44
P-value	0.368*		0.012*		0.273† 38 †				0.652*		0.865*		1.000†		0.103	0.181
Nitrofurantoin																
Sensitivity	23 (92.0)	94 (91.3)	21 (75.0)	96 (96.0)	46 (97.9)	41 (91.1)	18 (75.0)	12 (100.0)	33 (89.2)	84 (92.3)	95 (94.1)	19 (82.6)	3 (100.0)	91 (91.0)	39.52 ± 30.90	35.61 ± 31.68
Resistance	2 (8.0)	9 (8.7)	7 (25.0)	4 (4.0)	1 (2.1)	4 (8.9)	6 (25.0)	0 (0.0)	4 (10.8)	7 (7.7)	6 (5.9)	4 (17.4)	0 (0.0)	9 (9.0)	25.60 ± 20.99	27.20 ± 21.87
P-value	1.000*		0.002*		0.008†				0.729*		0.088†		1.000†		0.243	0.265
Ciprofloxacin																
Sensitivity	19 (70.4)	84 (78.5)	22 (88.0)	81 (74.3)	32 (71.1)	31 (75.6)	30 (78.9)	10 (100.0)	21 (61.8)	82 (82.0)	82 (82.0)	19 (65.5)	1 (100.0)	83 (78.3)	39.78 ± 29.53	39.02 ± 30.63
Resistance	8 (29.6)	23 (21.5)	3 (12.0)	28 (25.7)	13 (28.9)	10 (24.4)	8 (21.1)	0 (0.0)	13 (38.2)	18 (18.0)	18 (18.0)	10 (34.5)	0 (0.0)	23 (21.7)	53.37 ± 37.50	37.78 ± 37.00
P-value	0.370*		0.191*		0.264†				0.016*		0.058*		1.000†		0.116	0.544
Cotrimoxazole																
Sensitivity	7 (30.4)	19 (21.6)	12 (52.2)	14 (15.9)	4 (11.4)	14 (33.3)	4 (14.3)	4 (66.7)	7 (23.3)	19 (23.5)	22 (24.4)	4 (21.1)	3 (100.0)	16 (18.8)	42.27 ± 38.60	39.09 ± 30.56
Resistance	16 (69.6)	69 (78.4)	11 (47.8)	74 (84.1)	31 (88.6)	28 (66.7)	24 (85.7)	2 (33.3)	23 (76.7)	62 (76.5)	68 (75.6)	15 (78.9)	0 (0.0)	69 (81.2)	37.72 ± 28.50	34.54 ± 30.15
P-value	0.373*		<0.001*		0.005†				0.989*		1.000†		0.009†		0.986	0.219
Ampicillin																
Sensitivity	5 (16.1)	25 (24.0)	6 (27.3)	24 (21.2)	15 (34.1)	9 (23.7)	6 (18.8)	0 (0.0)	13 (26.0)	17 (20.0)	26 (24.8)	4 (14.3)	1 (33.3)	24 (23.8)	44.42 ± 34.21	40.61 ± 37.86
Resistance	26 (83.9)	79 (76.0)	16 (72.7)	89 (78.8)	29 (65.9)	29 (76.3)	26 (81.3)	21 (100.0)	37 (74.0)	68 (80.0)	79 (75.2)	24 (85.7)	2 (66.7)	77 (76.2)	38.66 ± 31.06 90.537	29.93 ± 29.50
P-value	0.353*		0.533*		0.020†				0.418*		0.313†		0.566†		0.537	0.935
Cefotaxime																
Sensitivity	8 (29.6)	35 (38.5)	7 (28.0)	36 (38.7)	16 (36.4)	12 (30.8)	12 (46.2)	3 (33.3)	10 (32.3)	33 (37.9)	35 (38.5)	8 (34.8)	1 (100.0)	0 (0.0)	47.17 ± 38.88	40.75 ± 33.67
Resistance	19 (70.4)	56 (61.2)	18 (72.0)	57 (61.3)	28 (63.6)	27 (69.2)	14 (53.8)	6 (66.7)	21 (67.7)	54 (62.1)	56 (61.5)	15 (65.2)	34 (37.8)	56 (62.2)	39.81 ± 29.31	32.70 ± 29.02

P-value	0.402*		0.323*		0.651*				0.573*		0.745*		0.385†		0.649	0.333
Gentamycin																
Sensitivity	12 (54.5)	53 (73.6)	15 (71.4)	50 (68.5)	11 (61.1)	18 (64.3)	23 (76.7)	13 (72.2)	18 (60.0)	47 (73.4)	46 (69.7)	16 (64.0)	2 (100.0)	10 (62.5)	43.08 ± 35.93	33.84 ± 28.64
Resistance	10 (45.5)	19 (26.4)	6 (28.6)	23 (31.5)	7 (38.9)	10 (35.7)	7 (23.3)	5 (27.8)	12 (40.0)	17 (26.6)	20 (30.3)	9 (36.0)	0 (0.0)	6 (37.5)	51.40 ± 33.35	40.43 ± 32.08
P-value	0.090*		0.797*		0.630*				0.189*		0.603*		0.526†		0.364	0.611
Vancomycin																
Sensitivity	4 (100.0)	12 (66.7)	2 (50.0)	14 (77.8)	8 (80.0)	4 (100.0)	4 (50.0)	0 (0.0)	7 (77.8)	9 (69.2)	8 (80.0)	6 (60.0)			40.12 ± 37.31	24.42 ± 36.03
Resistance	0 (0.0)	6 (33.3)	2 (50.0)	4 (22.2)	2 (20.0)	0 (0.0)	4 (50.0)	0 (0.0)	2 (22.2)	4 (30.8)	2 (20.0)	4 (40.0)			51.00 ± 50.80	1.50 ± 0.00
P-value	0.541†		0.292†		0.146†				1.000†		0.628†				0.704	0.108
Cephalexin																
Sensitivity	0 (0.0)	2 (10.0)	0 (0.0)	2 (9.1)	2 (10.5)	0 (0.0)	0 (0.0)	0 (0.0)	2 (25.0)	0 (0.0)	2 (8.7)	0 (0.0)				
Resistance	9 (100.0)	18 (90.0)	7 (100.0)	20 (90.9)	17 (89.5)	0 (0.0)	6 (100.0)	4 (100.0)	6 (75.0)	21 (100.0)	21 (91.3)	4 (100.0)				
P-value	1.000†		1.000†		0.568†				0.069†		1.000†					
Erythromycin																
Sensitivity	0 (0.0)	2 (14.3)	0 (0.0)	2 (14.3)	0 (0.0)	0 (0.0)	2 (33.3)	0 (0.0)	0 (0.0)	2 (22.2)	2 (14.3)	0 (0.0)			39.00 ± 0.00	33.00 ± 0.00
Resistance	4 (100.0)	12 (85.7)	4 (100.0)	12 (85.7)	9 (100.0)	2 (100.0)	4 (66.7)	1 (100.0)	9 (100.0)	7 (77.8)	12 (85.7)	4 (100.0)			27.25 ± 19.01	28.18 ± 35.20
P-value	1.000†		1.000†		0.212†				0.471†		1.000†				0.259	0.572
Ceftazidime																
Sensitivity	10 (43.5)	57 (60.0)	13 (59.1)	54 (56.3)	19 (47.5)	17 (54.8)	17 (73.9)	14 (58.3)	19 (54.3)	48 (57.8)	50 (54.3)	17 (73.9)	1 (100.0)	56 (59.6)	45.16 ± 34.44	44.11 ± 33.95
Resistance	13 (56.5)	38 (40.0)	9 (40.9)	42 (43.8)	21 (52.5)	14 (45.2)	6 (26.1)	10 (41.7)	16 (45.7)	35 (42.2)	42 (45.7)	6 (26.1)	0 (0.0)	38 (40.4)	34.70 ± 27.41	24.66 ± 24.00
P-value	0.151*		0.808*		0.238				0.722*		0.089*		1.000†		0.216	0.027
Nalidixic acid																
Sensitivity	2 (50.0)	4 (17.4)	2 (28.6)	4 (20.0)	2 (22.2)	0 (0.0)	4 (30.8)	0 (0.0)	2 (40.0)	4 (18.2)	4 (21.1)	2 (28.6)			51.00 ± 39.25	14.00 ± 8.08
Resistance	2 (50.0)	19 (82.6)	5 (71.4)	16 (80.0)	7 (77.8)	4 (100.0)	9 (69.2)	1 (100.0)	3 (60.0)	18 (81.8)	15 (78.9)	5 (71.4)			63.52 ± 35.00	45.92 ± 28.57
P-value	0.204†		0.633†		0.577†				0.303†		1.000†				0.280	0.069

Abbreviations: N, number; SD, standard deviation; *E. coli*, *Escherichia coli*; *S. saprophyticus*, *Streptococcus saprophyticus*; *S. hemolyticus*, *Streptococcus hemolyticus*, *Strep.*, *Streptococcus*; UTI, urinary tract infection; US, ultrasound; ESR, erythrocyte sedimentation rate; CRP, C-reactive protein.

*Analyzed by the chi-squared test.

†Analyzed by the Fisher's exact test.

‡Analyzed by the Mann-Whitney test.

DISCUSSION

In the current study, *E. coli* was the most common urogenital pathogen isolated from urine cultures, which is in line with the findings of Lutter et al.[8] Lutter et al. reported *Klebsiella pneumoniae* (3%), *Pseudomonas* (2%), and *Enterococcus* (2%) as other common pathogens responsible for UTI in children, while in our study, *Pseudomonas* accounted for 1% and Gram-negative bacilli for 7 % of the responsible pathogens. Velez et al. showed that *E. coli* and *Klebsiella pneumoniae* were the most common pathogens.[9] Moreover, Marcus et al. reported *E. coli* in 60% of their cultures.[10] Tarhani et al. stated that *E. coli* accounts for 73.3% of urogenital pathogens.[11] On the other hand, Barzan et al. also found *E. coli* as the most common bacterium and *Klebsiella pneumoniae* was the second most common.[3] The results of the studies by Fesharkinia et al.[12] and Rahimzadeh et al.[13] were both comparable with our findings.

In the current study, *E. coli* was 16.5% more prevalent in female patients compared to male patients. Furthermore, *Pseudomonas* and nonhemolytic *Streptococcus* were only reported in girls, while Gram-negative bacilli were more prevalent in boys. Marcus et al. also reported that non-*E. coli* etiologies were more common among male patients.[10]

E. coli was the most common pathogen across all seasons in our study; however, during spring it had the lowest prevalence, while at this time other pathogens were more common compared to other seasons. No cases of *Streptococcus hemolyticus* were reported in spring and winter, while it was the second most common etiology during summer and fall. *E. coli* was less common in patients with constipation by 8%, while Gram-negative bacilli had a higher prevalence in this group of patients. Thus, it appears that UTI with *E. coli* is more prevalent when diarrhea is also common.

We found that antibiotic use within the past 3 months slightly decreased the rate of UTI with *E. coli*, while UTI due to *S. saprophyticus*, *Pseudomonas*, and nonhemolytic *Streptococcus* increased. This was consistent with the findings of Lutter et al.[8] They also showed a significantly lower frequency of *E. coli* UTI in patients with antibiotic prophylaxis.

In the current study, the highest level of ESR belonged to *S. hemolyticus* and *E. coli* and the lowest level to *Pseudomonas*. On the other hand, the highest level of CRP was observed with nonhemolytic *Streptococcus* and *E. coli*, while CRP was quite low with *Pseudomonas*. The reason behind this finding can be the prior use of antibiotics in the two patients whose cultures were positive for *Pseudomonas*. Antibiotic use might be responsible for low ESR and CRP in these patients.

The most important finding of our study was that all pathogens as well as *E. coli* alone were most susceptible to imipenem, nitrofurantoin, amikacin, and ciprofloxacin. Therefore, these antibiotics appear to be the best empirical treatments for children with UTI in our hospital, while waiting for the results of urine culture and antibiogram.

In the current study, resistance to ampicillin was 77.8%, to ciprofloxacin 23.1%, and to nitrofurantoin 8.6%. The corresponding figures were 53.4%, 2.1%, and 1.3%, respectively in the study by Bryce et al.[8] The lower resistance to these antibiotics in their study compared to ours can be due to temporal and geographical differences.

The major strength of the current study was that we evaluated the potential factors influencing antibiotic sensitivity and resistance in pediatric UTI. We found that Antibiotic sensitivity and resistance were not correlated with gender, anatomic abnormalities or hydronephrosis in US, and ESR. Nevertheless, constipation, prior antibiotic use, seasons when UTI occurred, labial adhesion, and CRP were correlated with the sensitivity profile of antibiotics, at least to some extent. On the other hand, the limitation of our study was its relatively small sample size, which made some comparisons impossible and limits the generalizability of our findings.

CONCLUSIONS

Resistance to antibiotics was not influenced by gender, hydronephrosis, anatomical abnormalities, labial adhesion (to a great extent), ESR, and CRP (with one exception), while it was affected by the presence of constipation, prior antibiotic intake, and change in seasons. Imipenem, nitrofurantoin, amikacin, and ciprofloxacin appear to be the best empirical treatments for children with UTI, while waiting for the results of urine culture and antibiogram.

Declarations

Ethics approval and consent to participate

The study received ethics approval from the Ethics Committee of Hormozgan University of Medical Sciences and complies with the statements of the Declaration of Helsinki. Written informed consent was obtained from the parents/guardians of the patients.

Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Competing interests

The authors declare that they have no competing interests.

Consent for publication

Not applicable.

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Author's contributions
Conceptualization and study validation: KG
Implementation and supervision: KG
Data analysis and interpretation: KG
Writing and reviewing: KG

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