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Etiology and Antibiotic Susceptibility Patterns of Urinary Tract Infections in Children in a General Hospital in Kuwait: A 5-Year Retrospective Study

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Highlights of the Study

- *E. coli* is the predominant uropathogen causing urinary tract infections in children.
- The rate of drug resistance among pediatric uropathogens is alarming.
- The prevalence of extended-spectrum beta-lactamase-producing bacteria.
- The importance of choosing empiric antibiotics for pediatric urinary tract infections based on local antibiotic resistance patterns cannot be overstated.

Keywords
Etiology · Antibiotic susceptibility · Urinary tract infection · Children · Kuwait

Abstract

Objective: The aim of this study was to determine the bacterial profile and prevalence of antibiotic resistance patterns of uropathogens, as well as to evaluate the problem with extended-spectrum β-lactamases (ESBLs)-producing isolates, causing urinary tract infections (UTIs) in children in Al-Amiri Hospital, Kuwait, over a 5-year period. ***Materials and Methods:*** Significant isolates from symptomatic pediatric patients with UTIs from January 2017 to December 2021 were identified by conventional methods and by the VITEK 2 identification card system. Antimicrobial susceptibility testing was performed by the disk diffusion method for Gram-positive organisms and an automated VITEK 2 system for Gram-negative organisms. ESBL-producing Enterobacterales were detected by the double-disk diffusion method and VITEK 2 system. ***Results:*** Significant bacteriuria was detected in 13.7% of the 9,742 urine samples. *Escherichia coli* accounted for 67.3% of these, followed by *Klebsiella pneumoniae* (8.9%), *Proteus* spp. (5.7%), and *Enterococcus* spp. (7.4%), respectively. High resistance rates were observed among the Enterobacterales against ampicillin, cephalothin, nitrofurantoin, amoxicillin/clavulanic acid, and trimethoprim-sulfamethoxazole. The prevalence of ESBL-producing *E. coli* and *K. pneumoniae* was 26% and 55%, respectively. The most sensitive among the antibiotics tested for Gram-negative organisms were meropenem, amikacin, gentamicin, and piperacillin/tazobactam, while the antibiotics tested for Gram-positive organisms were vancomycin, ampicillin, linezolid, and nitrofurantoin. ***Conclusion:*** *E. coli* remains the most common uropathogen. A high percentage of uropathogens causing UTI in children were highly resistant to the first- and second-line antibiotics for the therapy of UTI. ESBL-producing bacteria were highly prevalent in children in our hospital. Local antibiograms should be used to assist with empirical UTI treatment.

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Introduction

Urinary tract infections (UTIs) commonly cause acute illness in infants and children. Although most patients have a good prognosis, UTIs can cause significant morbidity, including renal parenchymal scarring, hypertension, poor kidney function, high blood pressure, and even chronic kidney disease [1, 2]. If treatment is delayed or inadequate, recurrent UTIs are associated with increased severity of infection and a greater likelihood of renal damage in experimental, retrospective, prospective, and small randomized studies [3, 4].

In almost all cases, treatment must be initiated before the final microbiological results are available, particularly in the outpatient setting. Data on the prevalence and antibiotic susceptibility patterns of uropathogens in children are limited, especially in Kuwait. However, there is a growing concern regarding antimicrobial resistance worldwide because several countries have experienced rising resistance rates, particularly *Escherichia coli* isolates to beta-lactam antibiotics. Approximately, 61% of *E. coli* isolates were reported to be resistant to amoxicillin or ampicillin [5].

This study was focused on the pediatric population because the choice of empiric antibiotics for pediatric UTIs is based on local bacterial profiles and resistance patterns in the pediatric population. Thus, precise knowledge of the organisms that cause UTI and their antibiotic susceptibility is essential. This is mainly because the etiology of UTI and the antibiotic susceptibility of the causative uropathogens have been changing over the past years, both in community and nosocomial infections [4]. However, information on the etiology and resistance pattern of UTI isolates in Kuwait is not up to date [6, 7]. The aim of this study was to determine the distribution of local bacterial species in UTI isolates and their antibiotic susceptibility patterns, as well as to evaluate the problem with extended-spectrum β-lactamase (ESBL)-producing isolates causing UTIs in children in Al-Amiri Hospital, Kuwait.

Material and Methods

The study was performed in the Department of Microbiology of Al-Amiri Hospital, a 400-bedded teaching hospital, including a 15-bedded surgical intensive care unit, 25-bedded medical intensive care unit, and urology, renal dialysis, and kidney transplant units. This hospital serves about 400,000 people of different nationalities and provides clinical laboratory services to 22 polyclinics. Data were based on laboratory findings. Urine cultures were collected using midstream clean-catch catheterization or suprapubic aspiration.

A total of 9,742 urine samples were collected between January 2017 and December 2021 from both inpatients and the outpatients. In Kuwait, the term "pediatric patients" refers to patients aged 12 years or younger at the time of the diagnosis or treatment. All samples were inoculated onto a set of cysteine lactose electrolyte deficient agar (Oxoid, Basingstoke, UK) and blood agar (Oxoid) plates according to standard procedures. The plates were incubated in the air at 37°C for 24 h. Urine specimens with bacterial growth of ≥100,000 colony-forming units/mL were regarded as significant bacteriuria and included in the study [8, 9].

All significant Gram-negative bacteria were identified and antibiotic susceptibility testing performed by an automated VITEK 2 machine (bioMérieux, Marcy-I'Étoile, France); a VITEK 2 GN card was used for identification and the AST-N366 card for susceptibility testing (bioMérieux). All Gram-positive bacteria were identified by standard biochemical tests and the sensitivity of the organisms was determined by the Kirby-Bauer method [10]. The results were interpreted according to the recommendations of the Clinical and Laboratory Standards Institute [11]. ESBL activity was detected by the double-disk synergy method using amoxicillin/clavulanic acid, cefotaxime, and ceftazidime disks. ESBL-producing strains were confirmed with the automated VITEK 2 system according to the manufacturer's instructions. The following strains were used for the quality control of susceptibility tests: *E. coli* A TCC 25922, *Pseudomonas aeruginosa* ATCC 27853, *Staphylococcus aureus* ATCC 25923, and *Enterococcus faecalis* ATCC929212.

Data analysis was performed with IBM SPSS statistics 25. Discrete variables were expressed as percentages. Due to the retrospective nature of this study, ethical clearance was not required as the extracted data did not include any personal information and the identity of subjects remained anonymous.

Results

Of the 9,742 urine samples processed during the study period, 1,342 (13.7%) yielded significant bacteriuria and were analyzed. As shown in Table 1, a significantly higher incidence of UTI was observed in females compared with males. Of the 1,342 samples, 1,020 (76%) were from female patients and 322 (24%) from male patients. The most infected group was infants aged between 1 day and 12 months (infants younger than 12 months), which comprised 353 (26%) of the total UTIs.

Gram-negative aerobic rods accounted for 1,174 (87.4%) of the total pathogens, and Gram-positive cocci for 165 (12.6%). The detailed analysis of the etiological agents is shown in Table 2. *E. coli* was the predominant pathogen, accounting for 903 (67.3%). The following top 5 uropathogens, after *E. coli*, were the following: *Klebsiella pneumoniae* 119 (8.9%); *Enterococcus* spp. 98 (7.4%); *Proteus* spp. 77 (5.7%); *P. aeruginosa* 32 (2.4%); and *Streptococcus agalactiae* 31 (2.3%).

Table 1. Gender and age distribution of pediatric patients with UTIs in Al-Amiri Hospital in Kuwait (percentages in parentheses)

	Age													Total
	days	months	years											
	0–28 days	1–12 months	1–2	2–3	3–4	4–5	5–6	6–7	7–8	8–9	9–10	10–11	11–12	
Female	23	96	39	68	121	107	115	98	108	72	70	55	48	1,020
Male	48	186	15	10	14	10	6	12	8	2	4	0	7	322
Total	71 (5)	282 (21)	54 (4)	78 (6)	135 (10)	117 (9)	121 (9)	110 (8)	116 (9)	74 (5)	74 (5)	55 (4)	55 (4)	1,342

Table 2. Microbial uropathogens isolated from urine samples of children with UTIs in Al-Amiri Hospital

Micro-organism	*N* (%) of micro-organisms isolated from UTI					Total
	2017	2018	2019	2020	2021	
Gram-negative						
Escherichia coli	169 (69.8)	202 (70.6)	212 (68.6)	132 (64)	188 (62.9)	903 (67.3)
Klebsiella pneumoniae	18 (7.4)	24 (8.4)	28 (9.1)	18 (8.7)	31 (10.4)	119 (8.9)
Proteus spp.	13 (5.4)	15 (5.2)	18 (5.8)	16 (7.7)	15 (5.0)	77 (5.7)
Pseudomonas aeruginosa	5 (2.1)	4 (1.4)	6 (2.0)	10 (4.8)	7 (2.3)	32 (2.4)
Citrobacter spp.	4 (1.7)	4 (1.4)	2 (0.6)	4 (1.9)	1 (0.3)	15 (1.1)
Enterobacter spp.	2 (0.8)	4 (1.4)	3 (1.0)	2 (0.9)	2 (0.6)	13 (1.0)
Morganella spp.	1 (0.4)	2 (0.7)	2 (0.6)	0 (0)	3 (1.0)	8 (0.6)
Acinetobacter spp.	1 (0.4)	0 (0)	1 (0.3)	0 (0)	5 (1.7)	7 (0.5)
Gram-positive						1,174 (87)
Enterococcus spp.	11 (4.5)	13 (4.5)	18 (5.8)	24 (11.5)	33 (11)	98 (7.4)
Streptococcus agalactiae	6 (2.5)	11 (4.0)	9 (3.0)	0 (0)	5 (1.7)	31 (2.3)
Staphylococcus aureus	5 (2.1)	4 (1.4)	5 (1.6)	0 (0)	6 (2)	20 (1.5)
Streptococcus pyogenes	4 (1.7)	2 (0.7)	3 (1.0)	0 (0)	0 (0)	9 (0.7)
Group D streptococci	2 (0.8)	1 (0.3)	2 (0.6)	0 (0)	0 (0)	5 (0.4)
Staphylococcus saprophyticus	1 (0.4)	0 (0)	0 (0)	0 (0)	0(0)	1 (0.0)
Yeast						
Candida spp.	–	–	–	1 (0.5)	3 (1)	4 (0.3)
						168 (13)
Total	242	286	309	206	299	1,342

Antimicrobial Susceptibility Patterns

To evaluate the antimicrobial susceptibility of Gram-negative bacilli that caused UTIs in children in Al-Amiri Hospital, Kuwait, over a 5-year period, we determined the susceptibilities to 13 antimicrobial agents. Susceptibility of the Gram-negative bacterial isolates, expressed as resistance rates, is shown in Table 3.

Enterobacterales

Approximately, 62% of *E. coli* isolates were resistant to ampicillin, 37% to trimethoprim-sulfamethoxazole (SXT), 17% to ciprofloxacin, 32% to cephalothin, 29% to amoxicillin-clavulanic acid, and 26% to cefotaxime. Meropenem (0.1%), amikacin (0.5%), piperacillin-tazobactam (2%), and nitrofurantoin (4%) had excellent activities against *E. coli*. Overall, *K. pneumoniae* had high resistance rates against SXT (34%), ciprofloxacin (13%), cephalothin (41%), amoxicillin-clavulanate (37%), and cefotaxime (35%). The resistance rates of *K. pneumoniae* to piperacillin-tazobactam were 10% and to amikacin 0.8%. All *K. pneumoniae* isolates were susceptible to meropenem. *Proteus* spp. resistance rates against the first-line antibiotics were the following: ampicillin (39%), SXT (36%), ciprofloxacin (10%), and cephalothin (10%). As shown in Table 3, there was an increase in the isolation rates of resistant *K. pneumoniae* isolates against amika-

Table 3. Frequency and percentage of resistant Gram-negative uropathogens isolated from children with UTIs in Al-Amiri Hospital

Bacteria	Year	Isolates, *N*	Percentage of bacteria resistant to												
			A	AUG	AMP	CF	CTX	CXM	CIP	SXT	GN	NIT	CEF	TZ	MEM
E. coli	2017	169	0	21	54	38	18	20	19	41	9	3	25	3	0
	2018	202	1	27	65	28	25	28	18	33	5	3	15	5	0
	2019	212	1	24	70	38	37	38	19	41	7	6	0	7	0
	2020	132	0	15	62	33	29	32	18	27	1.5	3	21	0	0
	2021	188	0	20	56	23	22	23	11	38	5	5	16	3	0.5
		903	0.5	29	62	32	26	28	17	37	6	4	3	2	0.1
K. pneumoniae	2017	18	0	28	100	50	33	33	17	22	17	22	0	5	0
	2018	24	4	25	100	29	29	29	4	29	8	30	0	4	0
	2019	28	0	53	100	53	50	53	25	36	11	40	0	25	0
	2020	18	0	22	100	40	11	22	0	33	0	55	11	0	0
	2021	31	0	45	100	31	42	48	13	42	6	77	22	10	0
		119	0.8	37	100	41	35	39	13	34	8	47	8	10	0
Proteus spp.	2017	13	0	–	46	8	0	8	8	38	31	100	0	0	0
	2018	15	0	–	13	7	0	7	7	20	26	100	0	0	0
	2019	18	0	–	39	11	11	11	11	22	22	100	0	5	0
	2020	16	0	–	62	6	0	12	25	75	25	100	0	0	0
	2021	16	0	–	31	15	15	15	0	23	8	100	0	0	0
		77	0	–	39	10	5	10	10	36	32	100	0	1	0
P. aeruginosa	2017	5	0	–	–	–	–	–	20	–	20	–	0	20	20
	2018	4	0	–	–	–	–	–	0	–	0	–	0	0	0
	2019	6	0	–	–	–	–	–	33	–	33	–	0	17	33
	2020	10	0	–	–	–	–	–	0	–	0	–	0	0	20
	2021	7	0	–	–	–	–	–	0	–	0	–	0	0	0
		32	0	–	–	–	–	–	9	–	9	–	0	9	13
Other Gram-negative	2017	7	0	29	100	57	28	57	–	28	0	14	0	0	0
	2018	10	0	70	90	50	30	50	–	30	0	10	0	0	0
	2019	7	0	43	86	71	43	71	29	43	0	57	0	0	0
	2020	6	33	100	33	16	–	33	33	–	0	–	0	0	0
	2021	6	0	67	83	67	–	–	–	–	0	–	0	0	0
		36	6	61	81	52	22	44	11	22	0	17	0	0	0

A, amikacin; AUG, amoxicillin/clavulanic acid; AMP, ampicillin; CF, cephalothin; CTX, cefotaxime; CXM, cefuroxime; CIP, ciprofloxacin; SXT, trimethoprim-sulfamethoxazole; GN, gentamicin; NIT, nitrofurantoin; CEF, cefepime; TZ, piperacillin/tazobactam; MEM, meropenem; – , not tested.

cin, cefotaxime, cefuroxime, SXT, and cefepime, while there was a drop in resistance to gentamicin over a 5-year period.

Non-Glucose-Fermenting Gram-Negative Bacterial Isolates

The resistance rates of *P. aeruginosa* isolates to the commonly tested antibiotics in Al-Amiri Hospital are shown in Table 3. None of *P. aeruginosa* was resistant to amikacin and cefepime, while 9% were resistant to piperacillin-tazobactam and ciprofloxacin. Thirteen percent of *P. aeruginosa* were resistant to meropenem.

Gram-Positive Bacterial Isolates.

Resistance rates of Gram-positive bacterial isolates are shown in Table 4. All the Gram-positive isolates were susceptible to vancomycin. Although all the *Enterococcus* spp. were susceptible to vancomycin and penicillin, the resistance rates to nitrofurantoin was 5%. None of the *S. agalactiae* isolates was resistant to penicillin. All the *S.*

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Table 4. Frequency and percentage of resistant Gram-positive uropathogens isolated from children with UTIs in Al-Amiri Hospital

Bacteria	Year	Isolates, *N*	Percentage of bacteria resistant to									
			AMP	CF	CC	Clox	SXT	P	Van	E	NIT	LZ
Enterococcus spp.	2017	11	0	–	–	–	–	0	0	–	0	0
	2018	13	0	–	–	–	–	0	0	–	7.6	0
	2019	18	0	–	–	–	–	0	0	–	0	0
	2020	24	0	–	–	–	–	0	0	–	2	0
	2021	32	0	–	–	–	–	6	0	–	9	0
		98	0	–	–	–	–	2	0	–	5	0
S. agalactiae	2017	6	0	–	33	–	–	0	0	17	0	0
	2018	11	0	–	45	–	–	0	0	27	0	0
	2019	9	0		22	–	–	0	0	22	0	0
	2020	0	–	–	–	–	–	–	–	–	–	–
	2021	5	6	–	40	–	–	0	0	40	0	0
		31	–	–	35	–	–	0	0	26	0	0
S. aureus	2017	5	-	20	–	20	0	100	0	0	0	0
	2018	4	-	75	–	75	0	100	0	0	0	0
	2019	5	-	60	–	60	0	100	0	0	0	0
	2020	0	–	–	–	–	–	–	–	–	–	–
	2021	6	–	33	–	33	33	66	0	33	17	0
		20	–	45	–	45	10	90	0	10	5	0
S. pyogenes	2017	4	0	–	0	–	–	0	0	0	0	0
	2018	2	0	–	0	–	–	0	0	0	0	0
	2019	3	0	–	0	–	–	0	0	0	0	0
	2020	0	–	–	–	–	–	–	–	–	–	–
	2021	0	–	–	–	–	–	–	–	–	–	–
Total		9	0	–	0	–	–	0	0	0	0	0

AMP, ampicillin; CF, cephalothin; CC, clindamycin; Clox, cloxacillin; SXT, trimethoprim-sulfamethoxazole; P, penicillin; Van, vancomycin; E, erythromycin; NIT, nitrofurantoin; LZ, linezolid; –, not tested.

aureus isolates were resistant to penicillin, but susceptible to vancomycin and erythromycin; the resistance rates of cephalexin and cloxacillin were 45% and 45%, respectively. All *Streptococcus pyogenes* were susceptible to vancomycin, penicillin, clindamycin, and erythromycin.

Prevalence of ESBL-Producing Isolates

The number of the members of the family of Enterobacterales that were positive for ESBL production by the double-disk synergy test essentially tallied with those detected by the VITEK 2 system. Approximately, 238 (27%) of the *E. coli* were ESBL producers. A relatively high proportion of *K. pneumoniae* 42 (35%) were also ESBL producers. The resistance of ESBL-producing *E. coli* and *K. pneumoniae* is shown in Table 5.

Discussion

UTI is one of the most common bacterial infections in children. The infection may affect the upper urinary tract (pyelonephritis) or the lower urinary tract (cystitis). A course of antibiotic is usually the initial treatment of acute pyelonephritis or cystitis. Empiric therapy is initiated after a urine culture has been obtained. It is essential to start empirical treatment early in young children with febrile UTI, to minimize renal scarring, hypertension, and end-stage renal disease that results from acute pyelonephritis [9]. Urine culture results are usually ready in 1–2 days. Expected resistance patterns must be considered when selecting empirical antimicrobial treatment strategies for UTI. Consequently, antibiotic policy should be formulated according to local surveillance data [12]. To the best of our knowledge, we present the first study focusing on the bacterial profile and prevalence of antibiotic resis-

Table 5. Antimicrobial susceptibility results of ESBL-producing *E. coli* and ESBL-producing *K. pneumoniae* isolates

	2017		2018		2019		2020		2021		Total, %	
	ESBL-positive isolates, %		ESBL-positive isolates, %		ESBL-positive isolates, %		ESBL-positive isolates, %		ESBL-positive isolates, %			
	E. coli *N* = 30 (18%)	*K. pneumoniae* *N* = 6 (33%)	*E. coli* *N* = 51 (25%)	*K. pneumoniae* *N* = 7 (29%)	*E. coli* *N* = 78 (37%)	*K. pneumoniae* *N* = 14 (50%)	*E. coli* *N* = 38 (29%)	*K. pneumoniae* *N* = 2 (11%)	*E. coli* *N* = 41 (22%)	*K. pneumoniae* *N* = 13 (42%)	*E. coli* *N* = 238 (26%)	*K. pneumoniae* *N* = 42 (35%)
AUG	50	35	56	29	29	9	58	O	32	23	37	28
A	100	100	98	71	95	100	100	100	100	100	98	86
GN	70	100	84	71	72	79	95	100	88	85	80	78
NIT	83	67	92	57	71	21	100	0	88	31	95	43
CIP	40	67	74	86	76	29	79	100	82	70	73	69
CEF	17	27	22	33	33	43	27	11	27	46	26	40
TZ	80	100	94	86	88	64	100	100	92	85	91	83
SXT	40	83	60	71	56	50	58	0	46	31	35	55
MEM	100	100	100	100	100	100	100	100	98	100	100	100

AUG, amoxicillin-clavulanic acid; A, amikacin; GN, gentamicin; NIT, nitrofurantoin; CIP, ciprofloxacin; CEF, cefepime; TZ, piperacillin/tazobactam; SXT, trimethoprim-sulfamethoxazole; MEM, meropenem.

tance patterns of uropathogens causing UTIs in children in Kuwait.

Our results showed that only 13.7% of the urine samples yielded significant bacteriuria. However, studies done by Mashouf et al. [13] in Iran and Badhan et al. [14] in India showed a higher culture positivity of (34.2%) and (26.7%), respectively. The explanation for lower positivity rate in our cultures is possibly because we were very strict in our inclusion criteria to capture definite UTIs. Urine specimens with bacterial growth of ≥100,000 colony-forming units/mL were regarded as significant bacteriuria. A majority of the UTIs in our study occurred in female patients (76%), confirming the previous report that female patients had a higher prevalence of UTI than male patients, principally owing to anatomic and physical factors [15].

The bacteriologic profile and resistance patterns of uropathogens found in our study differ from those causing pediatric bacteremia in our hospital. The primary causative pathogens of pediatric UTIs were Gram-negative bacteria (87%), among which *E. coli* was the most common pathogen (67.3%), followed by *K. pneumoniae* (6.5%) and *Enterococcus* spp. However, the primary causative pathogens of pediatric bacteremia were Gram-positive bacteria (55%), among which *Streptococcus pneumoniae* was the most common pathogen (16.7%), followed by *E. coli* (14.4%), *S. aureus* (10.0%), and Group B streptococci (10.0%) (unpublished data). Analysis of our results showed that the bacteriologic profile of uropathogens in our study is different from those causing UTI infections in adults in our hospital. The primary causative pathogens of UTIs in adults were Gram-negative bacteria (73%), among which *E. coli* was the most common pathogen (30.2%), followed by *K. pneumoniae* (15.1%) and Group B streptococci (8.3%). Generally, Gram-negative bacteria from adult patients were more resistant to antimicrobials than those from children in our hospital (unpublished data).

In our study, UTIs were widely distributed in all age groups; however, the largest proportion was in children <1 year of age (353 patients, 26%). The age-specific gender distribution showed that significantly more male infants (age <1 year) were diagnosed with UTIs than female infants (66% male, 34% female), and the female contribution of infections increased in older age groups. The explanation is that males are more likely to be born with structural abnormalities of the urinary tract [16]. The etiological agents of UTI identified in the present study essentially correlate well with the most recently published regional studies in children from Saudi Arabia, Turkey, Iran, and Oman [17–20]. Our data indicate that *E. coli* is still the most frequent uropathogen causing UTI in the community and in hospital settings. Thus, our finding is consistent with those of previous studies in which *E. coli* was the predominant pathogen isolated from both community-acquired UTI (CA-UTI) and hospital-acquired UTI [5, 9, 21]. Also, our study showed that *K. pneumoniae was* the second most common isolates from pediatric patients with UTI. Thus, our study showed that *E. coli* and *K. pneumoniae* were responsible for 76% of all UTIs in children.

About 62% of *E. coli* was resistant to ampicillin, and 77% of all non-*E. coli* coliform bacteria were resistant to ampicillin. High rates of *E. coli* were resistant to SXT (37%), amoxicillin-clavulanic acid (29%), cephalothin (32%), and cefuroxime (28%). These antibiotics are frequently used in Kuwait for empirical treatment of CA-UTI in children. Based on these data, the use of these agents for empirical treatment of a suspected UTI, or prevention of recurrent UTI, would not cover the majority of pathogens. Although nitrofurantoin has activity against 96% of *E. coli* isolates, its poor renal parenchymal penetration precludes its use for pyelonephritis [19]. However, nitrofurantoin can be used for empiric therapy in uncomplicated UTI, particularly in the community setting. Resistance rates to meropenem, amikacin, and piperacillin-tazobactam were remarkably low. The same results were shown in numerous studies [17, 18, 20]. Due to the small number of other uropathogens found in our study, the antibiotic sensitivity pattern might not be conclusive and was thus not compared with other reports.

The high prevalence of ESBL-producing *E. coli* and *K. pneumoniae* causing UTI in our hospital has reached an alarming proportion. There was an increasing trend in ESBL-producing *E. coli* isolates from 18% in 2017 to 37% in 2019 and 22% in 2021. The trend in *K. pneumoniae* resistance increased from 33% in 2017 to 50% in 2019 and 42% in 2021. A compounding finding was that most of our ESBL-producing *E. coli* and *K. pneumoniae* strains were multiresistant. Specifically, most were resistant to the amoxicillin-clavulanic acid and SXT. This associated resistance to other classes of antimicrobials is especially problematic in urinary isolates and underscores the therapeutic challenge they represent. This study shows that there was a relatively high prevalence of *E. coli* and *K. pneumoniae* in Al-Amiri Hospital, which was higher than that reported from other countries in this region [17, 18, 20].

The current data may reflect the increased use of orally prescribed agents in our country, to treat hospital- or community-acquired infections, such as UTIs or respiratory tract infections. This overuse may select for multidrug-resistant *E. coli* phenotypes, harboring the potential to disseminate within our country. Further antimicrobial consumption studies at the community level are needed in our country to verify this assumption. In general, carbapenems, piperacillin-tazobactam, and amikacin agents showed excellent in vitro coverage of the uropathogens isolated in this study. This information will be useful in choosing empiric therapy for seriously ill hospitalized patients with suspected urosepsis.

We are aware that many CA-UTIs are treated without bacteriological testing, and most isolates from the community that are tested in our laboratory may be predominantly from patients for whom previous antimicrobial treatment failed or patients with other underlying risk factors. Therefore, the results of our study may not represent the actual distribution and antibiotic resistance pattern of the uropathogens causing acute uncomplicated CA-UTIs and may not necessarily serve as a basis for developing guidelines for the empirical treatment of CA-UTIs. However, we emphasize the need to investigate the distribution and susceptibility pattern of pathogens causing uncomplicated CA-UTI which would expectedly indicate the most appropriate antibiotic for empirical treatment of this condition. In addition, the results of our study increased our knowledge about the types of pathogens responsible for UTI in hospitalized patients with CA-UTI and hospital-acquired UTI and their resistance patterns to antibiotic drugs. This knowledge would help clinicians choose the proper empirical treatment, particularly in the hospital setting.

Conclusions

This study demonstrated that *E. coli* remains the most common pediatric uropathogen. A high percentage of the uropathogens causing UTI in children in Al-Amiri Hospital, Kuwait, was highly resistant to the first- and second-line antibiotics for the therapy of UTI, but the carbapenems, piperacillin/tazobactam, and amikacin demonstrated excellent in vitro coverage for the uropathogens. Nitrofurantoin is the only oral agent that remains relatively active against most uropathogens and can be used for empiric therapy in uncomplicated UTI, particularly in the community setting. We observed that a large number of *E. coli* and *K. pneumonia* were ESBL producers and multidrug resistant. Monitoring of ESBL production and antimicrobial susceptibility testing are necessary to avoid treatment failure in patients with UTI. To optimize the use of empirical therapy, evidence-based guidelines for antibiotics use, guided by surveillance studies of target bacteria, need to be developed and implemented.

Statement of Ethics

The strains used in this study were obtained as part of routine diagnostic services. Therefore, no ethical approval was required.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

Author Contributions

Khalifa Al Benwan and Wafaa Jamal contributed to the study design, data collection, data entry, data analysis, data interpretation, and drafting of the manuscript and edited and approved the final version of the manuscript.

Data Availability Statement

All relevant data are available in the manuscript.

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