Etiology and Antibiotic Susceptibility Patterns of Community- and Hospital-Acquired Urinary Tract Infections in a General Hospital in Kuwait

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Key Words

Etiology • Antibiotic susceptibility • Urinary tract infection • Community • Hospital, Kuwait

Abstract

Objective: Our purpose was to determine the bacterial profile and prevalence of antibiotic resistance patterns of uropathogens, as well as evaluate the problem with extended-spectrum β -lactamase (ESBL) producing isolates, causing urinary tract infections (UTIs) in Al-Amiri Hospital, Kuwait, over a 3-year period. **Materials and Methods:** Isolates (56,505) from symptomatic UTI cases from January 2005 to December 2007 were identified by conventional methods and the VITEK identification card system. Antimicrobial susceptibility testing was performed by disk diffusion method for Gram-positive organisms and an automated VITEK 2 machine for Gram-negative organisms. ESBL production by the Enterobacteriaceae was detected by the double-disk diffusion method and VITEK-2 system. **Results:** Significant bacteriuria was detected in 15,064 (26.6%) of the 56,505 urine samples. *Escherichia coli* accounted for 4,876 (54.9%) from community-acquired UTI (CA-UTI) and 2,253 (36.4%) from hospital-acquired UTI (HA-UTI), followed by *Streptococcus agalactiae* (1,129, 12.7%) and *Klebsiella pneumoniae* (962, 10.8%) from CA-UTI cases. *Candida* spp. (973, 15.7%) and *K. pneumoniae* (747, 12.1%) were the second and third most prevalent isolates, respectively, in HA-UTI. High resistance rates were observed among the Enterobacteriaceae against ampicillin, cephalothin, ciprofloxacin, piperacillin and tri-

methoprim-sulfamethoxazole. About 855 (12%) and 291 (17%) of *E. coli* and *K. pneumoniae*, respectively, were resistant to ≥ 4 antibiotics. The prevalence of ESBL-producing *E. coli* and *K. pneumoniae* in CA-UTI was 12 and 17% and in HA-UTI 26 and 28%, respectively. **Conclusion:** A high percentage of the uropathogens causing UTI in the Al-Amiri Hospital setting was highly resistant to the first- and second-line antibiotics for the therapy of UTI. ESBL-producing bacteria are highly prevalent in our hospital.

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Introduction

Urinary tract infections (UTIs) are one of the common bacterial infections encountered by both general practitioners and hospital doctors [1]. Acute UTIs are associated with substantial morbidity and problems of recurrent infections. Studies have shown that approximately 25% of the women with the first UTI will have another attack within 6 months [2]. In addition, UTIs are an important cause of septicemia resulting in high mortality rates, prolonged hospital stays and increased healthcare costs [2]. In almost all cases, treatment must be initiated before the final bacteriological results are available particularly in the outpatient setting. To optimize the use of empiric antibacterial therapy for UTI, current 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

Table 1. Gender and age distribution of patients with UTIs in a general hospital in Kuwait (percentages in parentheses)

Gender	Age, years							Total
	0–9	10–19	20–29	30–39	40–49	50–59	≥60	
Female	1,157 (79)	514 (83)	1,928 (89)	1,671 (82)	951 (72)	1,466 (65)	3,393 (65)	11,080 (73)
Male	308 (21)	103 (17)	231 (11)	360 (18)	360 (28)	771 (35)	1,851 (35)	3,984 (27)
Total	1,465 (10)	617 (4)	2,159 (14)	2,031 (13)	1,311 (9)	2,237 (15)	5,244 (35)	15,064 (100)

uropathogens have been changing over the past years, both in community and nosocomial infections [3]. However, the information on the etiology and resistance pattern of UTI isolates in Kuwait is not current.

The aim of the study was to determine the local bacterial species distribution of UTI isolates and their susceptibility pattern to antibiotics.

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 general intensive care unit, urology unit, renal dialysis and kidney transplant units. Al-Amiri Hospital serves a population of approximately 400,000 people of different nationalities and provides clinical laboratory services to 22 polyclinics. To reduce the bias due to different pathogen distributions and the susceptibility profile associated with in-/outpatient status, patients were assigned to 2 categories: CA-UTI and HA-UTI. The samples (56,505) were collected between January 2005 and December 2007 from both the inpatients and the outpatients. In the laboratory, all samples were inoculated onto a set of CLED (Oxoid, Basingstoke, UK) and blood agar (Oxoid) plates and incubated in air at 37°C for 24 h. Urine specimens with bacterial growth of $\geq 10^4$ cfu/ml were regarded as significant bacteriuria [4].

All Gram-negative bacteria were identified and antibiotic susceptibility testing was performed by an automated VITEK-2 machine (bioMérieux, Marcy-l'Étoile, France); A VITEK 2 GN card was used for identification and an AST-N020 card for susceptibility testing (bioMérieux). All Gram-positive bacteria were identified by standard biochemical tests and sensitivity of the organisms determined by Kirby-Bauer method. The results were interpreted according to the recommendation of the Clinical and Laboratory Standards Institute [5]. Extended-spectrum β -lactamase (ESBL) activity was detected by the double-desk synergy method using amoxicillin/clavulanic acid and cefotaxime and ceftazidime disks. The ESBL-producing strains were confirmed with the automated VITEK-2 system according to the manufacturer's instructions. For the quality control of susceptibility tests *E. coli* ATCC 25922, *Pseudomonas aeruginosa* ATCC 27853, *Staphylococcus aureus* ATCC 25923 and *Enterococcus faecalis* ATCC929212 strains were used. Discrete variables were expressed as percentages and the χ^2 test was used to compare proportions.

Results

Of the 56,505 urine samples processed during the study period, 15,064 (26.6%) yielded significant bacteriuria. Of the 15,064 samples, 6,180 (41.0%) were from inpatients (HA-UTI) and 8,884 (59.0%) were from outpatients (CA-UTI). Most cases of UTIs were recorded among young and middle age patients (20–59 years, 51%). Pediatric patients (0–19 years) comprised 2,082 (14%) and elderly (≥ 60) constituted 5,244 (35%) of the total number of UTIs. A significantly higher incidence of UTI was observed in females compared with males, 11,080 (73%) and 3,984 (27%), respectively (table 1).

Etiological Isolates

Gram-negative aerobic rods accounted for 10,726 (71.2%) of the total pathogens, Gram-positive cocci for 3,179 (21.1%) and *Candida* spp. for 1,160 (7.7%). The detailed analysis of the etiological agents is shown in table 2. *E. coli* was the predominant pathogen in both CA-UTI and HA-UTI cases, accounting for 4,876 (54.9%) and 2,253 (36.4%) of the causative agents, respectively. The next top 5 uropathogens, after *E. coli*, causing HA-UTI in our hospital were *Candida* spp.: 973 (15.7%); *K. pneumoniae*: 747 (12.0%); *Enterococcus* spp.: 713 (11.5%); *P. aeruginosa*: 609 (9.8%) and *S. agalactiae*: 326 (5.2%), while those causing CA-UTI were *S. agalactiae* (1,129, 12.7%); *K. pneumoniae* (962, 10.8%); *Enterococcus* spp. (709, 7.9%); *P. aeruginosa* (386, 4.3%) and *Candida* spp. (178, 2.3%).

Antimicrobial Susceptibility Pattern

The susceptibility of the Gram-negative bacterial isolates, expressed as resistance rates, is shown in table 3. Generally, Gram-negative bacteria from inpatients were more resistant to antimicrobials than those from outpatients.

Enterobacteriaceae. The *E. coli* resistance rates against the so-called first-line antibiotics were: amoxicillin (66

Table 2. Microbial uropathogens isolated from urines of inpatients and outpatients with urinary tract infection (UTI)

Microorganism	Number (%) of micro-organisms isolated from UTI					
	inpatients			outpatients		
	2005	2006	2007	2005	2006	2007
Gram-negative						
<i>E. coli</i>	752 (36.8)	731 (34.9)	770 (37.7)	1,555 (53.5)	1,576 (55.3)	1,745 (55.8)
<i>Klebsiella</i> spp.	242 (11.8)	288 (13.8)	217 (10.6)	289 (9.9)	320 (11.2)	353 (11.3)
<i>P. aeruginosa</i>	207 (10.1)	206 (9.8)	196 (9.6)	130 (4.5)	137 (4.8)	119 (3.8)
<i>Proteus</i> spp.	51 (2.5)	50 (2.4)	39 (1.9)	62 (2.1)	66 (2.3)	42 (1.3)
<i>Acinetobacter</i> spp.	46 (2.2)	35 (1.7)	45 (2.2)	32 (1.1)	23 (0.8)	30 (1.0)
<i>Enterobacter</i> spp.	42 (2.1)	36 (1.7)	42 (2.1)	47 (1.6)	39 (1.4)	60 (1.9)
<i>Citrobacter</i> spp.	7 (0.3)	21 (1.0)	10 (0.5)	9 (0.3)	20 (0.7)	5 (0.2)
<i>S. maltophilia</i>	5 (0.2)	4 (0.2)	15 (0.7)	3 (0.1)	1 (0.04)	14 (0.4)
Gram-positive						
<i>Enterococcus</i> spp.	231 (11.3)	245 (11.7)	237 (11.6)	222 (7.6)	185 (6.5)	302 (9.7)
<i>S. agalactiae</i>	125 (6.1)	108 (5.2)	93 (4.6)	412 (14.2)	366 (12.8)	351 (11.2)
<i>S. aureus</i>	14 (0.7)	27 (1.3)	32 (1.7)	41 (1.4)	37 (1.3)	38 (1.2)
<i>S. epidermidis</i>	21 (1.0)	5 (0.2)	9 (0.4)	23 (0.8)	10 (0.4)	11 (0.4)
<i>S. saprophyticus</i>	1 (0.05)	2 (0.1)	0 (0)	9 (0.3)	9 (0.3)	13 (0.4)
Yeast						
<i>C. albicans</i>	147 (7.2)	99 (4.7)	137 (6.7)	37 (1.3)	18 (0.6)	22 (0.7)
<i>Candida</i> spp.	154 (7.5)	235 (11.2)	201 (9.8)	37 (1.3)	42 (1.5)	22 (0.7)
Total	2,045	2,092	2,043	2,908	2,849	3,127

vs. 75%), trimethoprim-sulfamethoxazole (TMP-SMX) (47 vs. 52%), ciprofloxacin (28 vs. 46%), cephalothin (47 vs. 60%), amoxicillin-clavulanic acid (27 vs. 41%) and cefotaxime (12 vs. 26%). Amikacin (1 vs. 3%), piperacillin-tazobactam (1 vs. 4%) and nitrofurantoin (7 vs. 8%) had excellent activities against *E. coli*. Overall, *K. pneumoniae* causing CA-UTI as well as HA-UTI had high resistance rates against TMP-SMX (26 vs. 29%), ciprofloxacin (23 vs. 37%), cephalothin (27 vs. 41%), amoxicillin-clavulanate (21 vs. 33%) and cefotaxime (17 vs. 28%). The resistance rates of *K. pneumoniae* to piperacillin-tazobactam were 6 vs. 16% and to amikacin 2 vs. 6%.

Nonfermenting Gram-Negative Bacterial Isolates. As for the *P. aeruginosa* isolates from both CA-UTI and HA-UTI, the resistance rates to amikacin were 10 and 15%, to piperacillin-tazobactam 10 and 14%, and to ciprofloxacin 30 and 28%, respectively. *Acinetobacter* isolates from CA-UTI were less resistant than those from HA-UTI to several antibiotics. For example, compared to isolates from CA-UTI, the resistance rates of those from HA-UTI were 7 vs. 28% against amikacin, 10 vs. 42% to piperacillin-tazobactam, 12 vs. 47% to ciprofloxacin and 7 vs. 33% to TMP-SMX.

Gram-Positive Bacterial Isolates. The resistance rates of Gram-positive bacterial isolates are shown in table 4. All the Gram-positive isolates were susceptible to vancomycin. None of the *S. agalactiae* isolates was resistant to penicillin. Although all the *Enterococcus* spp. were susceptible to vancomycin, teicoplanin and nitrofurantoin, the resistance rates to penicillin by isolates from CA-UTI and HA-UTI were 24 and 35%, respectively. The majority of both CA-UTI and HA-UTI isolates of *S. aureus* exhibited high susceptibility rates; the resistance rates of cephalalexin were 0 and 2%, to cloxacillin 0 and 3% and to TMP-SMX 3 and 2%.

Prevalence of ESBL-Producing Isolates

The number of the members of the family of Enterobacteriaceae that were positive for ESBL production by the double disc synergy (DDS) test essentially tallied with those detected by the VITEK-2 system. Approximately 585 (12%) of the *E. coli* isolated from CA-UTI and 586 (26%) from HA-UTI were ESBL producers. A relatively high proportion of *K. pneumoniae* from CA-UTI 164 (17%) and HA-UTI 209 (28%) were also ESBL producers. The resistance of ESBL-producing *E. coli* and *K. pneumoniae* is shown in table 5.

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

Bacteria	Year	CA/HA	Percentage of CA vs. HA bacteria resistant to												
			A	AUG	AMP	CF	CTX	CXM	CIP	SXT	GN	NA	NIT	PIP	TZ
<i>E. coli</i>	2005	1,555/752	1/1	27/43	66/72	47/60	9/30	27/33	26/43	47/47	12/23	10/18	5/7	43/57	1/5
	2006	1,576/731	2/6	25/36	65/76	43/57	10/21		27/44	47/55	14/25	10/18	7/8	60/70	2/4
	2007	1,745/770	1/3	28/44	68/78	50/62	17/27		30/50	47/53	15/26	44/62	9/8	48/59	1/4
		4,876/2,253	1/3	27/41	66/75	47/60	12/26	9/11	28/46	47/52	14/25	22/33	7/8	50/62	1/4
<i>K. pneumoniae</i>	2005	289/242	1/2	18/37	100/100	20/40	11/17	12/37	16/29	29/30	10/27	7/14	58/57	74/80	6/19
	2006	320/288	5/8	19/33	100/100	28/46	19/33		27/40	22/27	13/25	9/16	43/68	92/92	5/14
	2007	353/217	1/7	24/29	100/100	31/34	20/33		26/43	26/32	14/13	28/33	65/66	88/84	6/14
		962/747	2/6	21/33	100/100	27/41	17/28	4/12	23/37	26/29	12/22	15/20	56/64	85/86	6/16
<i>P. aeruginosa</i>	2005	130/207	10/21	–	–	–	–	–	33/30	–	23/27	–	–	16/24	9/16
	2006	137/206	7/9	–	–	–	–	–	22/25	–	15/17	–	–	13/19	7/11
	2007	119/196	13/14	–	–	–	–	–	35/30	–	31/21	–	–	17/24	13/16
		386/609	10/15	–	–	–	–	–	30/28	–	23/22	–	–	15/22	10/14
<i>A. baumannii</i>	2005	32/46	12/40	54/76	96/95	100/98	65/81	–	15/67	12/56	12/57	22/61	100/100	31/74	12/55
	2006	23/35	5/15	67/76	100/10	100/10	76/85	–	19/35	0/21	10/29	21/23	100/100	14/41	10/38
	2007	30/45	4/27	77/86	92/97	100/10	88/95	–	4/35	8/19	4/22	24/44	100/00	31/57	8/32
		85/126	7/28	66/80	96/72	100/42	76/87	–	12/47	7/33	9/37	22/44	100/100	26/59	10/42
<i>P. mirabilis</i>	2005	62/51	0/0	0/0	35/35	11/10	0/0	–	31/25	48/35	16/16	2/9	98/100	10/4	0/0
	2006	66/50	0/4	5/16	23/54	12/28	3/14	–	18/42	32/52	14/26	9/21	97/100	18/32	2/0
	2007	42/39	3/0	3/6	34/25	8/6	3/8	–	11/28	32/36	11/14	21/34	67/100	8/8	0/0
		170/140	1/1	3/7	30/39	11/15	2/7	–	21/32	38/41	14/19	9/20	90/100	13/15	1/0
<i>Enterobacter</i> spp.	2005	47/42	0/0	100/98	100/100	98/98	22/45	–	13/24	29/59	18/24	4/11	62/29	28/59	13/50
	2006	39/36	0/11	92/100	100/10	97/100	10/45	–	10/17	18/28	2/20	6/5	46/40	18/45	5/25
	2007	60/42	0/3	87/90	97/94	96/100	25/49	–	4/12	7/9	8/9	12/21	51/36	30/48	7/27
		146/120	0/4	93/96	99/98	97/99	20/46	–	9/18	14/32	10/18	8/13	53/35	26/51	8/34
<i>Citrobacter</i> spp.	2005	9/7	0/14	91/100	91/100	100/10	0/71	–	0/14	22/43	0/43	0/0	0/0	11/71	0/29
	2006	20/21	5/11	90/85	95/90	100/10	40/50	–	25/15	35/15	20/20	0/24	5/16	40/65	25/20
	2007	5/10	0/2	75/70	100/92	100/82	0/2	–	0/4	25/11	25/15	25/36	0/11	25/32	0/0
		34/38	3/9	88/85	95/94	100/34	24/41	–	15/11	30/23	15/26	4/20	3/9	30/56	15/16

A = Amikacin; AUG = amoxicillin/clavulanic acid; AMP = ampicillin; CF = cephalothin; CTX = cefotaxime; CXM = cefuroxime; CIP = ciprofloxacin; SXT = cotrimoxazole; GN = gentamicin; NA = nalidixic acid; NIT = nitrofurantoin; PIP = piperacillin; TZ = piperacillin/tazobactam.

Discussion

Analysis of our results showed that 26.6% of the urine samples from inpatients and outpatients yielded significant bacteriuria. A majority of the UTIs in our study occurred in adult patients (51%), mainly women (73%), thereby confirming the previous report that adult women have a higher prevalence of UTI than men, principally owing to anatomic and physical factors [1]. The prevalence encountered in the present study was 26.6%; a finding considerably higher than other reports of studies [6, 7] emanating from Kuwait which demonstrated the prevalence of significant bacteriuria as 9.7% [6] and 11.4% [7]. The explanation for this is partly due to the fact that the criterion used for determining significant bacteriuria

was lower ($\geq 10^4$ CFU/ml) in the current study than that used in other studies ($\geq 10^5$ CFU/ml). In addition, growth of 2 bacteria was also categorized as significant if both were present at $\geq 10^4$ CFU/ml of urine. In this study, the etiological agents of UTI essentially correlate well with a previous study from Kuwait [6].

Our data indicate that *E. coli* is still the most frequent uropathogen causing UTI in the community and hospital settings. Thus, our finding is consistent with those of previous studies in which *E. coli* was the predominant pathogen isolated from both CA-UTI and HA-UTI [6, 7]. Also our study showed that *Candida* spp. were the second most common isolates from patients with nosocomial UTI, a finding in concordance with data from other studies that have reported an increase in the number of *Candida* spp.

Table 4. Frequency and percentage of resistant Gram-positive uropathogens isolated from outpatient vs. inpatient UTI cases

Bacteria	Year	Total No. of isolates CA/HA	Percentage of resistant uropathogens of CA-UTI vs. HA-UTI								
			AMP	CF	CC	Clox	SXT	P	Van	E	NIT
<i>S. agalactiae</i>	2005	412/125	0/0	–	0/0	–	–	0/0	0/0	10/10	0/0
	2006	351/93	0/0	–	0/0	–	–	0/0	0/0	21/18	0/0
	2007	366/108	0/0	–	0/0	–	–	0/0	0/0	17/17	0/0
			0/0	–	0/0	–	–	0/0	0/0	16/15	0/0
<i>Enterococcus</i> spp.	2005	222/231	1/3	–	–	–	–	7/11	0/0	–	2/1
	2006	302/237	2/1	–	–	–	–	32/39	0/0	–	2/3
	2007	185/245	1/4	–	–	–	–	30/55	0/0	–	2/4
			1/3	–	–	–	–	24/35	0/0	–	2/3
<i>S. aureus</i>	2005	41/14	–	0/0	0/0	0/0	2/4	78/93	0/0	2/14	0/0
	2006	38/32	–	0/0	9/14	0/0	3/0	91/90	0/0	11/17	0/0
	2007	37/28	–	0/4	3/21	0/7	11/4	86/93	0/0	6/35	0/0
			–	0/2	4/14	0/3	3/2	85/92	0/0	4/23	0/0
<i>S. epidermidis</i>	2005	23/21	–	60/67	50/33	60/67	0/33	80/83	0/0	60/50	0/0
	2006	11/9	–	43/75	29/0	43/75	18/100	71/100	0/0	29/25	0/0
	2007	10/5	–	83/67	50/33	83/67	20/40	83/90	0/0	67/–	0/0
			–	61/69	45/25	61/69	10/51	78/88	0/0	54/46	0/0
<i>S. saprophyticus</i>	2005	9/1	–	0/0	0/0	0/0	0/0	78/0	0/0	62/0	0/0
	2006	13/–	–	0/–	0/–	0/–	0/–	83/–	0/–	33/–	0/–
	2007	9/2	–	33/50	11/50	33/50	0/0	78/100	0/0	44/50	0/0
			–	10/33	3/33	10/33	0/0	80/67	0/0	45/33	0/0

AMP = Ampicillin; CF = cephalothin; CC = clindamycin; Clox = cloxacillin; SXT = cotrimoxazole; P = penicillin; Van = vancomycin; E = erythromycin; NIT = nitrofurantoin; – = not tested.

Table 5. Percentage of susceptible isolates of ESBL-producing *E. coli* and ESBL-producing *K. pneumoniae* to antimicrobials (inpatients/outpatients)

	2005		2006		2007	
	ESBL-positive isolates, %		ESBL-positive isolates, %		ESBL-positive isolates, %	
	<i>E. coli</i>	<i>K. pneumoniae</i>	<i>E. coli</i>	<i>K. pneumoniae</i>	<i>E. coli</i>	<i>K. pneumoniae</i>
Amc	12/41	35/38	33/47	40/47	60/10	9/39
NA	26/30	80/94	23/40	73/83	16/21	14/6
A	97/100	100/100	96/99	79/70	96/96	94/100
GN	40/47	20/28	54/54	37/50	54/40	58/37
NIT	84/88	45/31	90/88	7/13	89/81	22/9
CIP	4/12	40/19	32/3	10/20	29/24	9/3
PIP	1/3	0/6	3/3	20/3	1/1	0/3
TZ	91/94	85/100	95/100	85/93	85/97	72/91
SXT	53/30	50/31	33/18	69/60	37/43	47/74
Fox	80/100	95/100	82/78	73/90	83/78	72/97
Mem	100/100	100/100	100/100	100/100	100/100	100/100

Amc = Amoxicillin-clavulanic acid; NA = nalidixic acid; A = amikacin; GN = gentamicin; NIT = nitrofurantoin; CIP = ciprofloxacin; PIP = piperacillin; TZ = piperacillin/tazobactam; SXT = cotrimoxazole; Fox = ceftiofur; Mem = meropenem.

in nosocomial UTI [6, 8]. The high prevalence of yeast as a cause of UTI may be related to the type of patients, advances in surgical and medical management of the patients as well as excessive use of broad-spectrum antibiotics, high prevalence of diabetes mellitus and obesity in the Kuwait population [9]. This is supported by the findings in the 2001 ESCMID Study Group report on a European perspective study on nosocomial UTI, where *Candida* spp. were the third most commonly isolated pathogen [8]. It is noteworthy that the high prevalence rate of *S. agalactiae* in CA-UTI and HA-UTI at Al-Amiri Hospital is consistent with the findings of previous studies in Kuwait which also showed high prevalence rates of *S. agalactiae* [6, 7]. However, there is scarcely any other report that has published such a high prevalence rate of *S. agalactiae* in UTI as observed in our study. For example, the ESCMID Study Group report demonstrated only a 1.6% prevalence rate of *S. agalactiae* in UTI among patients in the non-EU countries [8]. The explanation for this observation may be related to the high prevalence of diabetes mellitus among the Kuwaiti population [9]. In a previous study, 36% of the patients with UTI had diabetes mellitus [10] and this disease is a known predisposing factor for *S. agalactiae* infection in adults. In addition, previous experience shows that there is a high vaginal colonization rate of pregnant and nonpregnant individuals by *S. agalactiae* in Kuwait [11]. Enterococci were the fourth most common isolate causing UTI in hospitalized patients, which is slightly different from the findings in previous studies in Kuwait that showed that enterococci ranked fifth among the UTI pathogens. There was a low prevalence of *S. saprophyticus* (0.3%), which is less than the previous reports of 2% each from Kuwait [6] and the UK [2]. However, recent reports from the USA have found this pathogen to be present in 4.0–9.7% of the women with uncomplicated cystitis [12]. This finding may indicate a distinct pattern of Gram-positive uropathogen distribution in our area. The finding of uropathogens resistant to many commonly used antibiotics is a new experience in this hospital. In general, the resistance rates of Gram-negative bacteria were relatively lower in outpatients than those of inpatients, a finding which is consistent with observations all over the world [11, 13]. The differences in antibiotic susceptibility between isolates from community and hospital patients may be attributable to the presence of additional risk factors for antibiotic resistance in the latter group. These include frequent antibiotic use, underlying pathology and presence of invasive devices. The high resistance rates of *E. coli* and other members of the family Enterobacteriaceae to several

commonly used antibiotics are alarming. For example, the resistance of *E. coli* from CA-UTI and HA-UTI to commonly used oral antibiotics is at an unacceptably high level. The fluoroquinolone resistance in *E. coli* was much higher than those reported in several recent studies in Kuwait [6], Europe and Canada [14]. This high resistance level might have been driven by prior exposure to fluoroquinolones which has been recently acknowledged as an independent risk factor for ciprofloxacin-resistant *E. coli* from CA-UTI [15]. Ciprofloxacin is one of the most prescribed antibiotics in Kuwait particularly by the general practitioners. This study shows that there is a relatively high prevalence of *E. coli* and *K. pneumoniae* in Al-Amiri Hospital which is higher than that reported from other countries in this region [16, 17].

Our data showed a substantial reduction in susceptibility to antibiotics frequently used in the community. Ampicillin, amoxicillin-clavulanic acid, cephalothin, TMP-SMX and ciprofloxacin did not have good in vitro coverage for many of the uropathogens isolated in this study. Because of this, they are of little use as empirical therapeutic options in outpatient departmental setting. 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. However, nitrofurantoin is not traditionally used in UTI with any significant tissue involvement such as pyelonephritis or infections caused by *K. pneumoniae* or *Proteus* spp. The current data may reflect the increased use of orally prescribed agents in our region, to treat hospital- or community-acquired infections, such as UTI or respiratory tract infections. This overuse may select for multidrug-resistant *E. coli* phenotypes, harboring the potential to disseminate within our region. Further antimicrobial consumption studies at the community level are needed in our region 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 from 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 to develop

guidelines for the empirical treatment of CA-UTIs. However, they 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 pathogen responsible for UTI in hospitalized patients with CA-UTI and HA-UTI and their resistance patterns to antibiotic drugs. This knowledge would help clinicians choose the right empirical treatment, particularly in the hospital setting.

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 outpatients from 9% in 2005 to 17% in 2007. The prevalence of the inpatient isolates decreased from 30% in 2005 to 27% in 2007. However, the trend in *K. pneumoniae* resistance increased from 12% in CA-UTI in 2005 to 19% in 2007 and from 17% in HA-UTI in 2005 to 33% in 2007. A compounding finding is the fact that the majority of our ESBL-producing *E. coli* and *K. pneumoniae* strains were multiresistant. Specifically, most were resistant to the quinolones, amoxicillin-clavulanic acid and TMP-SMX. This associated

resistance to other classes of antimicrobials is especially problematic in urinary isolates and underscores the therapeutic challenge that they represent.

Conclusion

This study demonstrated that almost a third of all the Gram-negative isolates reported in this study were resistant to ≥ 4 antibiotics, 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. In the present study a large number of *E. coli* and *K. pneumoniae* was 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.

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