ORIGINAL ARTICLE

Multidrug resistance and extended-spectrum β-lactamases genes among *Escherichia coli* from patients with urinary tract infections in Northwestern Libya

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Introduction: Multidrug resistance (MDR) and emergence of extended-spectrum β-lactamases (ESBLs) that mediate resistance to β-lactam drugs among *Escherichia coli* and other uropathogens have been reported worldwide. However, there is little information on the detection of ESBLs genes in *E. coli* from patients with urinary tract infections (UTIs) in the Arab countries using polymerase chain reaction (PCR), and in Libya such information is lacking.

Methods: All patients attending Zawiya Teaching Hospital in Zawiya city between November 2012 and June 2013 suspected of having UTIs and from whom midstream urine samples were taken as part of the clinical workup were included in this prospective study. Samples were examined for uropathogens by standard bacteriological procedures. VITEK-2 automated microbiology system was used to identify the isolated uropathogens and determine the susceptibility of *E. coli* and *Klebsiella* spp. isolates to antimicrobials. In addition, phenotypically ESBLs-positive *E. coli* isolates were tested for ESBLs genes by PCR.

Results: The present study enrolled 1,790 patients with UTIs. Uropathogens were found in 371 (20.7%) urine specimens examined. Mixed pathogens were detected in two specimens with 373 total pathogens isolated. *E. coli* and *Klebsiella* spp. were the predominant uropathogens at 55.8% (208/373) and 18.5% (69/373), respectively. Other pathogens were detected in 25.7% (96/373) of urine samples. Of the *E. coli* and *Klebsiella* spp. tested, 69.2 and 100% were resistant to ampicillin, 6.7 and 33.3% to ceftriaxone, and 23.1 and 17.4% to ciprofloxacin, respectively. MDR (resistance to ≥ 3 antimicrobial groups) was found in 69 (33.2%) of *E. coli* and in 29 (42%) of *Klebsiella* spp. isolates. ESBLs were detected phenotypically in 14 (6.7%) of *E. coli* and in 15 (21.7%) of *Klebsiella* spp. isolates. Thirteen out of the 14 phenotypically ESBL-positive *E. coli* were positive for ESBL genes by PCR. bla_{TEM} gene was detected in seven isolates, bla_{OXA} gene in 10 isolates and bla_{CTX-M} gene in six isolates. bla_{SHV} gene was not detected in the present study.

Conclusion: The isolation of MDR ESBL-producing uropathogens undoubtedly will limit the choices clinicians have to treat their patients with UTIs. Therefore, there is an urgent need for surveillance studies on antimicrobial resistance and prevalence of ESBLs among uropathogens to guide the clinical treatment of UTIs in Libya in the future.

Keywords: *urinary tract infections*; Escherichia coli; *extended-spectrum β-lactamases*; *multidrug resistance*; *Libya*

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One of the most common reasons that patients in the community seek medical care and prescribed antibiotics is urinary tract infections (UTIs) (1). Most UTIs are caused by members of the family *Enterobacteriaceae* mainly *Escherichia coli* and *Klebsiella* spp. High resistance rates to antimicrobials used in the treatment of UTIs among *E. coli* and other uropathogens have been reported worldwide, particularly in developing countries including Libya (2). In recent years, the problem worsened due to the emergence of extended-spectrum β-lactamases (ESBLs) that mediate resistance to β-lactam antimicrobials, especially third generation cephalosporins

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among these organisms. Genes responsible for ESBLs production arise by point mutation at the active site of the earlier β-lactamases (e.g. TEM-1 and SHV-1 enzymes), and they are usually plasmid mediated (3, 4). In addition, ESBLs-positive Gram-negative bacteria often carry genes that confer high levels of resistance to many other antibiotics (e.g. fluoroquinolones and aminoglycosides) (5). Previous use of penicillins, cephalosporins or quinolones is found to be a risk factor, among others, for the development of ESBLs-producing bacteria in non-hospitalized patients with community-acquired UTIs (6).

The epidemiology of antibiotic resistant bacteria, however, varies from region to region, from speciality to speciality, from infection type to infection type, and from year to year (7). Therefore, identification and determination of antimicrobial susceptibility of bacterial pathogens in the local healthcare setting may aid the clinician in selecting the appropriate antimicrobial agent (s) to treat his patients.

Studies on the causative agents of UTIs in Libya and their susceptibility to antimicrobial are few and were mainly carried out in the two main cities in Libya (i.e. Tripoli and Benghazi) (8, 9). Furthermore, there is little information on the detection of ESBLs genes in *E. coli* from patients with UTIs in the Arab countries using molecular methods and in Libya such information is lacking. Therefore, the aim of the present investigation was to determine the prevalence of organisms associated with UTIs in patients attending Zawiya Teaching Hospital (ZTH), their susceptibility to antimicrobial agents, and the presence of ESBLs genes in *E. coli* isolates using polymerase chain reaction (PCR).

Methods

Patients
All patients attending Zawiya Teaching Hospital in Zawiya city suspected of having UTIs and from whom urine samples were taken as part of the clinical workup were included in this prospective study. The study was carried out between November 2012 and June 2013. Zawiya city is located in northwestern Libya, situated on the Libyan coastline of the Mediterranean Sea about 45 km west of Tripoli with an estimated population of about 200,000 people. ZTH has 400 beds and frequented mainly by inhabitants of Zawiya city and surrounding cities and villages.

In this investigation, urine specimens were collected under approved ethical standards and the study was reviewed and approved by the Academy of Graduate Studies, Janzour, Tripoli, Libya.

Specimen collection
Urine specimens were obtained from all patients included in the study with the assistance of a medical doctor or

senior nurse. Midstream urine was collected from patients aged more than 1 year in a sterile container and processed in the laboratory within 2 h of collection. Urine specimens were obtained by suprapubic aspiration from children who are not toilet trained and proceed as above. The consent of the patients or that of their guardians was obtained before urine specimens were collected.

Isolation and identification of uropathogens
Using calibrated loops (10^{-3} ml, Last Loop Sp, Italiana, Italy), urine specimens were inoculated on to MacConkey and blood agar plates. After 18–24 h incubation at 37°C, the number of colony forming units (cfu) was counted, and urine samples giving $\geq 10^5$ cfu/ml of urine were considered significant. Isolated colonies from significant plates were identified using the VITEK-2 automated microbiology system (bioMérieux, Inc., Durham, NC, USA) employing the GN and GP colorimetric reagent cards that are incubated and interpreted automatically. The GN card is used for identification of Gram-negative fermenting and non-fermenting bacilli, and the GP card is used for identification of Gram-positive cocci and non-spore forming bacilli.

Reference strains of *E. coli* ATCC 25922 and *Pseudomonas aeruginosa* ATCC 27853 were used as controls for the Gram-negative bacteria. *Staphylococcus aureus* ATCC 25923 and *Enterococcus faecalis* ATCC 929212 were used as Gram-positive control strains.

Antimicrobial susceptibility testing
The VITEK-2 Gram-negative antimicrobial susceptibility testing card (GN AST, bioMérieux, Inc.) was used to determine the susceptibility of *E. coli* and *Klebsiella* spp. isolates to different antimicrobial agents. *E. coli* ATCC 25922 was used as a control organism. VITEK 2 provides AST results for antimicrobials as susceptible, intermediate susceptible, and resistant and is interpreted according to CLSI criteria (10). In the present study, only resistant results were presented.

ESBLs testing
Production of ESBLs by *E. coli* and *Klebsiella* spp. isolates was determined phenotypically by VITEK 2 (bioMérieux, Inc.). *E. coli* isolates positive for ESBLs phenotypically were tested by PCR technique for ESBLs genes as previously reported (11, 12). Briefly, whole cell lysate of an overnight bacterial culture was prepared by boiling method as described previously (13). Amplification was done in a 50-ul reaction mixture containing 50 pmol primers (as listed in Table 1), 0.25 mM deoxyribonucleotide, 1.5 mM $MgCl_2$, 1X GoTaq reaction buffer (Promega, Madison, WI, USA), and 0.2 U GoTaq DNA polymerase. Amplification conditions included 30 cycles of 95°C for 30 sec, 55°C for 1 min and 72°C for 1 min. This was followed by a final extension step at 72°C 30 cycles. PCR products were visualized by gel electrophoresis on a 2.0% agarose

Table 1. Polymerase chain reaction (PCR) primer sequences for the detection of extended-spectrum β-lactamases genes in *E. coli*

Target gene	Oligonucleotide primer sequences (5′ to 3′)	Amplicon size (bp)	Reference
bla_{TEM}-1F	CAGCGGTAAGATCCTTGAGA	643	11
bla_{TEM}-1R	ACTCCCCGTCGTGTAGATAA		
bla_{SHV}-1F	GGCCGCGTAGGCATGATAGA	714	11
bla_{SHV}-1R	CCCGGCGATTTGCTGATTTC		
bla_{OXA}-1F	AATGGCACCAGATTCAACTT	599	11
bla_{OXA}-1R	CTTGGCTTTTATGCTTGATG		
bla_{CTX-M}-1F	GAAGGTCATCAAGAAGGTGCG	560	12
bla_{CTX-M}-1R	GCATTGCCACGCTTTTCATAG		

(Sigma-Aldrich, Steinheim, Germany) using 1X Tris-acetate-EDTA buffer.

Statistical analysis

For statistical analysis, Epi Info 2000 software (Centers for Disease Control and Prevention) was employed. *P*-values were calculated using the Chi-square test. $P < 0.05$ was considered to be statistically significant.

Results

The present study enrolled 1,790 patients (1,151 females and 639 males) with UTIs. The age of the patients ranged from 3 days to 93 years (mean 25 years). Of these patients, 1,134 were outpatients and 656 inpatients.

Uropathogens were isolated from 371 (20.7%) urine specimens examined. Co-infection was determined in two patient's urine specimens as two different organisms were isolated from each of them with a total of 373 uropathogens being isolated. Predominance of *E. coli* and *Klebsiella* spp. among isolated uropathogens was observed at 55.8% (208/373) and 18.5% (69/373), respectively. Table 2 shows the uropathogens isolated from patients with UTIs attending ZTH.

According to gender and type of hospital admission, *E. coli* and total uropathogens were significantly detected in female patients compared with male patients and in outpatients compared with inpatients with UTIs. Distribution of *E. coli*, *Klebsiella* spp., and other uropathogens isolated from patients with UTIs according to gender and to type of hospital admission is shown in Table 3.

Only *E. coli* and *Klebsiella* spp. isolates were tested for antimicrobial susceptibility and ESBL production. Of the *E. coli* and *Klebsiella* spp. tested, 69.2 and 100% were resistant to ampicillin, 30.8 and 31.9% to ampicillin/sulbactam, 6.7 and 33.3% to ceftriaxone, 23.1 and 17.4% to ciprofloxacin, and 37 and 24.6% to trimethoprim/sulfamethoxazole, respectively. Nitrofurantoin showed good activity against *E. coli* isolates (1.9% resistant) but not against *Klebsiella* spp. (30.4% resistant). Table 4 shows the antimicrobial resistance patterns of *E. coli* and *Klebsiella* spp. from patients with UTIs attending ZTH.

From Table 4 it can be observed that *Klebsiella* spp. isolates were significantly more resistant to most of the antimicrobial agents tested than *E. coli* isolates. In addition, multi-drug resistance (MDR, resistance to three or more antimicrobial groups) was found in 69 (33.2%) of 208 *E. coli* isolates and in 29 (42%) of 69 *Klebsiella* spp. isolates.

ESBLs were detected in 6.7% (14/208) of *E. coli* and in 21.7% (15/69) of *Klebsiella* spp. isolates using phenotypic procedure. The detection rate of ESBLs among *Klebsiella* spp. is significantly higher than the detection rate of

Table 2. Uropathogens isolates from patients ($n = 1,790$) with UTIs

Organism	No. (%) positive
E. coli	208 (12)
Klebsiella spp.	69 (3.8)
K. pneumoniae	67 (3.7)
K. oxytoca	2 (0.1)
Enterobacter spp.	18 (1.0)
E. aerogenes	5 (0.3)
E. cloacae	13 (0.7)
Proteus mirabilis	22 (1.2)
Citrobacter spp.	12 (0.7)
C. freundii	5 (0.3)
C. koseri	7 (0.4)
Morganella morganii	6 (0.3)
Serratia marcescens	1 (0.05)
Aeromonas hydrophila/caviae	1 (0.05)
Pseudomonas aeruginosa	4 (0.2)
Acinetobacter spp.	8 (0.4)
A. baumannii	6 (0.3)
A. haemolyticus	1 (0.05)
A. lwoffii	1 (0.05)
Staphylococcus spp.	14 (0.8)
Enterococcus faecalis	4 (0.2)
Streptococcus agalactiae	6 (0.3)
Total	373 (20.8)[a]

[a]In two patients, two different organisms were isolated from each of them.

Table 3. Distribution of *E. coli*, *Klebsiella* spp., and other uropathogens isolated from patients with UTIs according to gender and type of hospital admission

Organism	No. (%) positive			
	Female (*n* = 1,151)	Male (*n* = 639)	Outpatients (*n* = 1,134)	Inpatients (*n* = 656)
E. coli	163 (14.2)[a]	45 (7.0)	155 (13.7)[b]	53 (8.1)
Klebsiella spp.	43 (3.7)	26 (4.1)	41 (3.6)	28 (4.3)
Other bacteria	65 (5.6)	31 (4.9)	68 (6.0)	28 (4.3)
Total	271 (23.5)[c]	102 (16)	264 (23.3)[d]	109 (16.6)

[a]Significantly higher than in male patients ($P < 0.000007$, odds ratio [OR] = 2.18); [b]significantly higher than in inpatients ($P < 0.0004$, OR = 1.80); [c]significantly higher than in male patients ($P < 0.0002$, OR = 1.62); [d]significantly higher than in inpatients ($P < 0.0009$, OR = 1.52).

ESBLs among *E. coli* isolates ($P < 0.0005$, OR = 3.85). Thirteen of the 14 phenotypically ESBLs-positive *E. coli* were positive for ESBLs genes by PCR. bla_{TEM} gene was detected in seven isolates, bla_{OXA} gene in 10 isolates and bla_{CTX-M} gene in six isolates (Fig. 1). bla_{SHV} gene was not detected in the present study. Combination of two ESBL genes in a single isolate occurred in four isolates (bla_{TEM} and bla_{OXA} in 1, bla_{TEM} and bla_{CTX-M} in 2, and bla_{OXA} and bla_{CTX-M} in 1) and three ESBL genes combination in three isolates (bla_{TEM}, bla_{OXA}, and bla_{CTX-M} in 3). Distribution of ESBLs genes among 14 phenotypically ESBLs-positive *E. coli* from patients with UTI is shown in Supplementary Table 1.

Discussion

In the present investigation, uropathogens were detected in more than 20% of patients with UTIs attending ZTH with a predominance of *E. coli* and *Klebsiella* spp. Previous studies from different countries reported different rates of uropathogens among patients with UTIs. A study from Kuwait reported uropathogens in 9.2% (4,696/51,562) that cause UTIs in two large teaching hospitals over a period of 1 year (14). The authors reported the predominance of *E. coli* (47%) followed by *Candida* spp. (10.8%) and *Klebsiella* spp. (9.6%). Bercion et al. (15) performed a retrospective analysis of all cases of confirmed UTIs due to *Enterobacteriaceae* in outpatients attending the Institut Pasteur de Bangui, Central African Republic, between 2004 and 2006. They found bacterial pathogens in 560 of the 5,128 (10.9%) patients with predominance of *E. coli* (64%) and *Klebsiella* spp. (10%). Kashef et al. (16) examined 13,333 mid-stream urine samples collected from suspected cases of UTI in Tehran, Iran. Uropathogens were found in 6.3% (840/13,333) with

Table 4. Antimicrobial resistance patterns of *E. coli* and *Klebsiella* spp. from patients with UTIs

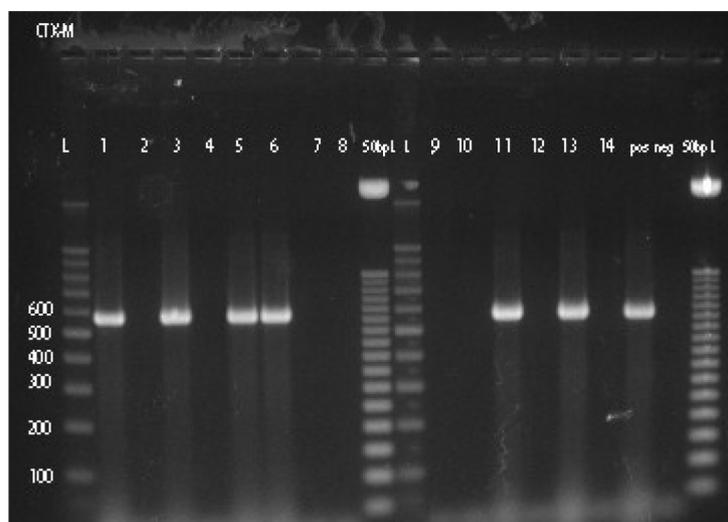| Antimicrobial agent	No. (%) resistant to		
	E. coli (*n* = 208)	*Klebsiella* spp. (*n* = 69)	*P* (odds ratio)
Ampicillin	144 (69.2)	69 (100)	0.0000001 (Undefined)
Ampicillin/sulbactam	64 (30.8)	22 (31.9)	NS
Cefazoline	45 (21.6)	26 (37.7)	<0.008 (2.19)
Cefoxitin	8 (3.8)	4 (5.8)	NS
Ceftazidime	14 (6.7)	22 (31.9)	0.0000001 (6.49)
Ceftriaxone	14 (6.7)	23 (33.3)	0.0000000 (6.93)
Cefepime	13 (6.3)	22 (31.9)	0.0000000 (7.02)
Imipenem	1 (0.5)	4 (5.8)	<0.005 (12.74)
Meropenem	1 (0.5)	3 (4.3)	<0.02 (9.41)
Amikacin	0 (0.0)	1 (1.4)	NS
Gentamicin	23 (11.1)	16 (23.2)	<0.02 (2.43)
Tobramycin	17 (8.2)	9 (13)	NS
Ciprofloxacin	48 (23.1)	12 (17.4)	NS
Levofloxacin	40 (19.2)	9 (13)	NS
Nitrofurantoin	4 (1.9)	21 (30.4)	0.0000000 (22.31)
Trimethoprim/sulfamethoxazole	77 (37)	17 (24.6)	NS

Fig. 1. PCR products of bla_{CTX-M} (lines 1–8 and 9–14); L 100 bp ladder and 50 bp ladder. pos = positive control and neg = negative control.

a predominance of *E. coli* (68.8%, 578/840) followed by *Proteus* spp. (12.4%, 104/840), and *Klebsiella* spp. (9.6%, 81/840).

Other uropathogens isolated from ZTH patients include *P. mirabilis* (5.9%), *Enterobacter* spp. (4.8%), and *Citrobacter* spp. (3.2%). A study from Ife, Nigeria reported uropathogens in 36 (12%) of the 301 patients with UTIs (17). The majority of 36 bacterial isolates obtained were *E. coli* leading to 52.8% of the cases of UTIs, followed by *Klebsiella* spp. (25%), *P. mirabilis* (13.9%), *Strep.*(*Enterococcus*) *faecalis* (5.6%), and *Ps. aeruginosa* (2.8%).

We found *E. coli* and total uropathogens were significantly isolated from female patients compared to male patients (Table 3). Other investigators found no significant difference in the distribution of isolated uropathogens between genders (15, 18). However, an Iranian study reported that *E. coli* occurred significantly more frequently in women (76.5% in women compared to 62.4% in men; $P < 0.05$), whereas the prevalence of UTIs due to *K. pneumoniae* and *Ps. aeruginosa* was higher in men than in women (22.6 and 7.5% in men compared to 9.9 and 1.4% in women, respectively; $P < 0.01$) (19). No significant differences ($P > 0.05$) in the distribution of *Klebsiella* spp. and other uropathogens between genders were observed in this study. Also, *E. coli* and total uropathogens were significantly isolated from outpatients than from inpatients with UTIs frequenting ZTH. Other studies found no significant difference in the isolation of uropathogens from outpatients and inpatients with UTIs (20).

Differences in the reported isolation rates of uropathogens from different regions may be due to differences in age, gender and number of patients examined, types of uropathogens examined (e.g. some studies did not include *Candida* spp. in their search as in the present study), and

types and number of media used in the isolation of uropathogens. Some studies used blood and MacConkey agars (present study) or blood agar and eosin methylene blue agar plates (16). Other studies used only bromocresol purple agar (15).

In the present study, antimicrobial susceptibility testing showed high resistance rates to ampicillin among *E. coli* and *Klebsiella* spp. isolates. However, lower resistance rates than previously reported from Libya to trimethoprim/sulfamethoxazole among *E. coli* (37%) and *Klebsiella* spp. (24.6%) were observed. In the mid-1990s, Ghenghesh et al. examined 538 *E. coli* isolates from patients with UTIs in Tripoli for their susceptibility to antimicrobial agents (8). Of the isolates examined 74% were resistant to ampicillin, 7% to gentamicin, 25% to nitrofurantoin, and 45% to trimethoprim/sulfamethoxazole. Tobgi et al. tested the susceptibility of 148 *E. coli* isolated from urine specimens from outpatients attending Al-Jalla Hospital in Benghazi to antibiotics (9). They reported that 75% of them were resistant to ampicillin, 18% to gentamicin and 81% to trimethoprim/sulfamethoxazole.

The lower rates observed with trimethoprim/sulfamethoxazole may be due to less use of the drug in treating bacterial infections (including UTIs) in Libya. Newer antibiotics like third generation cephalosporins (e.g. ceftriaxone and cefotaxime) and fluoroquinolones (e.g. ciprofloxacin and norfloxacin) have been more widely used in recent years. This observation can be supported by the findings of the present investigation of high resistance rates to ciprofloxacin among *E. coli* and *Klebsiella* spp., and to the cephalosporins such as ceftazidime, ceftriaxone, and cefepime among *Klebsiella* spp. (Table 4).

Studies from other countries also reported high resistance rates to different classes of antimicrobials. A study from Mexico examined 119 *E. coli* isolates obtained from

urine specimens of outpatients with clinical diagnosis of uncomplicated UTIs from 2004 to 2007 (21). Resistance to ampicillin was found in 83.7% of the isolates, to the fluoroquinolone group (i.e. ciprofloxacin, nalidixic acid, ofloxacin, and norfloxacin) in 55.5–60.6%, and to trimethoprim/sulfamethoxazole in 56.4%. In addition, 30.2% of isolates were multidrug-resistant.

MDR was detected in 32.2% of *E. coli* and 42% of *Klebsiella* spp. isolated from patients with UTIs attending ZTH. Alzohairy and Khadri reported higher rates of MDR among *E. coli* (53.6%) and *Klebsiella* spp. (50%) isolated from community and hospital-acquired UTIs in Qassim province, Saudi Arabia (22).

A previous study from Benghazi examined 119 strains of *E. coli* isolated from patients with UTIs (14 from HIV-positive patients) for ESBLs production using phenotypic method (23). Only four (3.4%) *E. coli* strains (two from HIV-negative and two from HIV-positive patients) were found positive for ESBLs. In the present study, ESBLs were detected at a higher rate of 6.7% among *E. coli* isolates from patients with UTIs attending ZTH using phenotypic techniques.

Other investigators from the Middle East and Africa reported similar findings. A study from Saudi Arabia reported ESBLs in 6.1% (570/9,409) (24). ESBLs were detected in 8.1% (29/357) of *E. coli* strains isolated from outpatients with suspected uncomplicated UTIs in Central African Republic (15). However, much higher rates of ESBLs have been reported from other countries in Africa. Ejikeugwu et al. examined a total of 83 non-duplicate *Escherichia coli* isolates from urine specimens of patients suspected of having community-acquired UTIs in Enugu State, Nigeria, from August 2010 to July 2011 (25). They detected ESBLs in 23 (27.7%) of the isolates investigated using the double disk synergy test method. Although the prevalence of ESBLs-producing bacteria is a worldwide problem, the geographical distribution can vary according to countries and institutions (26).

Several studies suggested that urine can be an important source of ESBLs-producing *E. coli* (27, 28). To our knowledge, this the first report of ESBLs detection in *E. coli* isolates from UTIs in Libya using PCR. Predominance of bla_{OXA} (10/13) followed by bla_{TEM} (7/13) and bla_{CTX-M} (6/13) was observed in this study. Bourjilat et al. detected seven (1.3%) ESBLs-producing *E. coli* among 535 *E. coli* isolates from urine specimens of patients with community-acquired urinary infections in Casablanca, Morocco, during July 2004 to July 2007 (29). Employing PCR the investigators detected genes encoding bla_{CTX-M} in most of them (6/7).

The findings of this study showed that *E. coli* and *Klebsiella* spp. were the predominant uropathogens causing UTIs in patients frequenting ZTH. High rates of resistance to commonly used and newer antimicrobial agents were observed among these organisms; with *Klebsiella* spp. isolates being significantly more resistant to these drugs than *E. coli* isolates. ESBLs and high rates of MDR were observed in *E. coli* and *Klebsiella* spp. isolates. In addition, genes coding for ESBLs were detected in *E. coli* using PCR with a predominance of bla_{OXA} followed by bla_{TEM} and bla_{CTX-M}.

The isolation of MDR ESBLs-producing uropathogens from UTIs patients undoubtedly will limit the choices clinicians have to treat their patients. Of the antimicrobial tested imipenem, meropenem, amikacin, and cefoxitin showed excellent activity against both *E. coli* and *Klebsiella* spp. isolates. In addition, third generation cephalosporins and nitrofurantoin demonstrated good activity against *E. coli* isolates. However, treatment should be guided by the results of antimicrobial susceptibility testing for each individual patient.

Antimicrobial resistance among uropathogens is a serious health problem. Education of clinicians and other healthcare workers on the health risks associated with the problem and on the benefits of prudent use of antimicrobials will help in tackling such a problem. Furthermore, there is an urgent need for surveillance studies on antimicrobial resistance and prevalence of ESBLs among uropathogens to guide the clinical treatment of UTIs in Libya in the future.

Conflict of interest and funding

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