Mieret et al. *Afr. J. Clin. Exper. Microbiol.* 2024; 25 (3): 286 - 294 https://www.afrjcem.org

African Journal of Clinical and Experimental Microbiology. ISSN 1595-689X Jul 2024; Vol.25 No.3
AJCEM/2312. https://www.ajol.info/index.php/ajcem

Original Article **Open Access**

Antibiotic resistance in uropathogenic *Escherichia coli* strains at Brazzaville University Hospital, Congo and the therapeutic consequences

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Abstract:

Background: Urinary tract infections (UTIs) are a very frequent reason for consultations and antibiotic prescriptions in everyday practice. Excessive and inappropriate use of antibiotics is responsible for the emergence and spread of multidrug-resistant (MDR) uropathogenic bacteria. The aim of this study was to determine the frequency of isolation and antibiotic resistance of uropathogenic strains of *Escherichia coli* (UPEC) isolated in the bacteriology-virology laboratory of the University Hospital Centre (CHU) in Brazzaville, Congo.
Methodology: This was a descriptive retrospective study over a 6-month period (from 1 April to 31 September 2022) that included all non-redundant uropathogenic UPEC strains isolated from urine samples of patients with UTIs referred to the bacteriology-virology laboratory of the University Hospital of Brazzaville, Congo. The strains were isolated from urine samples after inoculation onto Cystine Lactose Electrolyte Deficient agar (CLED), and incubating aerobically at 37°C for 24 hours. Identification was carried out using BioMérieux API 20 E galleries and antibiotic susceptibility testing was performed on Mueller Hinton agar medium using selected antibiotic discs. Extended spectrum β-lactamase (ESBL) production by the isolates was confirmed by double disc synergy test. Data were analysed using Microsoft Office Excel 2013.
Results: Of the 187 non-repetitive uropathogenic *Enterobacteriaceae* isolated from urine samples of 187 patients with clinical UTIs, 81 were strains of UPEC, giving an overall frequency of UPEC isolation of 43.0%. The modal age of patients from whom UPEC strains were isolated was 57 years (age range 2 to 86 years), with 49 from females and 32 from males (F: M ratio of 1.5). The UPEC strains showed high rates of resistance to amoxicillin (94.0%), amoxicillin-clavulanic acid (84.0%), piperacillin-tazobactam (73.0%), ceftriaxone (52.0%), cefixime (54.0%), cefotaxime (55.0%), ceftazidime (58.0%), gentamicin (42.0%), ciprofloxacin (55.0%) and sulfa-methoxazole-trimethoprim (90.0%) but relatively low resistance rates were observed with imipenem (4.0%), fosfomycin (8.0%) and amikacin (18.0%). The ESBL-producing strains accounted for 24.5% (46/187) of all uropathogenic *Enterobacteriaceae* isolates, and compared to the non-ESBL producing strains, had significantly higher resistance rates to gentamicin (p=0.018), ciprofloxacin (p=0.0003), ceftazidime (p<0.0001), ceftriaxone (p<0.0001), cefixime (p<0.0001), cefotaxime (p<0.0001), piperacillin-tazobactam (p=0.0006), and amoxicillin-clavulanate (p=0.0024).
Conclusion: Our results show high rates of *in vitro* resistance of UPEC strains to commonly used antibiotics, which potentially limits therapeutic options and therefore a real public health challenge in Congo.

Key words: Antibiotic, Uropathogenic strains, *Escherichia coli*, Antibiotic Resistance.

Received Nov 22, 2023; Revised Jun 5, 2024; Accepted Jun 6, 2024

Résistance aux antibiotiques des souches uropathogènes d'*Escherichia coli* au CHU de Brazzaville, Congo et conséquences thérapeutiques

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Résumé:

Contexte: Les infections des voies urinaires (IVU) constituent un motif de consultation et de prescription très fréquente d'antibiotiques dans la pratique quotidienne. L'utilisation excessive et inappropriée d'antibiotiques est responsable de l'émergence et de la propagation de bactéries uropathogènes multirésistantes (MDR). Le but de cette étude était de déterminer la fréquence d'isolement et la résistance aux antibiotiques des souches uropathogènes d'*Escherichia coli* (UPEC) isolées au laboratoire de bactériologie-virologie du Centre Hospitalier Universitaire (CHU) de Brazzaville au Congo.
Méthodologie: Il s'agissait d'une étude rétrospective descriptive sur une période de 6 mois (du 1er avril au 31 septembre 2022) ayant inclus toutes les souches d'UPEC non redondantes isolées à partir d'échantillons d'urine de patients atteints d'infections urinaires adressés au laboratoire de bactériologie-virologie du CHU de Brazzaville, au Congo. Les souches ont été isolées à partir d'échantillons d'urine après inoculation sur une gélose cystine lactose déficiente en électrolytes (CLED) et incubés en aérobiose à 37°C pendant 24 heures. L'identification a été réalisée à l'aide des galeries API 20 E de BioMérieux et des tests de sensibilité aux antibiotiques ont été réalisés sur milieu gélosé Mueller Hinton à l'aide de disques d'antibiotiques sélectionnés. La production de β-lactamases à spectre étendu (BLSE) par les isolats a été confirmée par un test de synergie à double disque. Les données ont été analysées à l'aide de Microsoft Office Excel 2013.
Résultats: Parmi les 187 Entérobactéries uropathogènes non redondantes isolées à partir d'échantillons d'urine de 187 patients présentant des signes cliniques d'infections urinaires, 81 étaient des souches d'UPEC, ce qui donne une fréquence globale d'isolement d'UPEC de 43,0%. L'âge modal des patients chez lesquels les souches d'UPEC ont été isolées était de 57 ans (tranche d'âge de 2 à 86 ans), dont 49 chez les femmes et 32 chez les hommes (rapport F: M de 1,5). Les souches d'UPEC ont montré des taux élevés de résistance à l'amoxicilline (94,0%), à l'amoxicilline-acide clavulanique (84,0%), à la pipéracilline-tazobactam (73,0%), à la ceftriaxone (52,0%), au céfixime (54,0%), au céfotaxime (55,0%), à la ceftazidime (58,0%), à la gentamicine (42,0%), à la ciprofloxacine (55,0%) et au sulfaméthoxazole-triméthroprime (90,0%). Des taux de résistance relativement faibles ont été observés avec l'imipénème (4,0%), la fosfomycine (8,0%) et l'amikacine (18,0%). Les souches productrices de BLSE représentaient 24,5% (46/187) de tous les isolats d'Entérobactéries uropathogènes. Comparées aux souches d'UPEC non productrices de BLSE, les souches d'UPEC productrices de BLSE présentaient des taux de résistance significativement plus élevés à la gentamicine (p=0,018), à la ciprofloxacine (p=0,0003), à la ceftazidime (p<0,0001), à la ceftriaxone (p<0,0001), au céfixime (p<0,0001), au céfotaxime (p<0,0001), à la pipéracilline-tazobactam (p=0,0006) et à l'amoxicilline-acide clavulanique (p=0,0024).
Conclusion: Nos résultats montrent des taux élevés de résistance in vitro des souches UPEC aux antibiotiques couramment utilisés, ce qui limite potentiellement les options thérapeutiques et donc un véritable défi de santé publique au Congo.

Mots clés: Antibiotique, Souches uropathogènes, *Escherichia coli*, Résistance aux antibiotiques

Introduction:

Urinary tract infections (UTIs) refer to inflammatory response in the urinary system resulting from invasion of the urinary tract by microbial pathogens (1,2). Urinary tract infections are a very frequent reason for consultations and medical prescriptions in everyday practice (3). Worldwide, 150 million cases of UTIs are diagnosed each year, and it is estimated that 20-40% of women over the age of 18 years will suffer at least once from UTI in their lifetime (4). Over 90% of UTIs are of monomicrobial aetiology, with *Escherichia coli* being the most common uropathogen, responsible for 75-90% of cases (5,6).

The overuse and misuse of antibiotics such as fluoroquinolones and third-generation cephalosporins in the treatment of UTIs was rapidly followed by the emergence of multidrug-resistant (MDR) strains. One of the factors responsible for the variation in antibiotic sensitivity of uropathogens is the acquisition of resistance mechanisms such as *Enterobacteriaceae* producing the enzymes extended-spectrum beta-lactamases (ESBL), which are capable of hydrolyzing the beta-lactam antibiotics. In many situations, these resistance events have compromised the use of these antimicrobial molecules of choice in the treatment of MDR infection, resulting in therapeutic failures and increased treatment costs (7,8).

Urinary tract infections caused by *E. coli* are a priority for antibiotic resistance surveillance, given their high frequency of occurrence and sometimes, severity of infection. The aim of this study was to determine the frequency of isolation and antibiotic susceptibility of UPEC strains from clinical *Enterobacteriaceae* isolates in the bacteriology-virology laboratory of the University Hospital Centre (CHU) in Brazzaville, Congo

Materials and method:

Study design and setting:

This was a descriptive retrospective study of patients with confirmed *Escherichia coli* UTIs over a period of 6 months (April 1 September 31, 2022) at the bacteriology-virology laboratory of Brazzaville University Hospital, Congo.

Sample collection and culture isolation

Voided midstream urine samples were obtained from a total of 187 hospitalized patients referred to the bacteriology-virology lab-

oratory at Brazzaville University Hospital for microbiological culture. About 10 microlitres of the urine samples were inoculated onto Cystine Lactose Electrolyte Deficient agar (CLED) and incubated at 37°C for 24 hours. Yellow, opaque colonies with a slightly darker center observed on CLED agar were preliminarily identified as *E. coli*. Urine samples with significant bacteriuria ($\geq 10^5$ CFU/ml) in the presence of leukocyturia ($\geq 10^4$ leukocytes/ml) were included for further analysis.

In culture plates where more than 2 different colony types were isolated, further analysis was discontinued except in special situations and in consultation with the clinicians. Urine sample with bacteriuria threshold of 10^3 CFU/ml for *E. coli* cystitis was also included.

Identification of *E. coli* isolates and antibiotic susceptibility testing:

Biochemical identification of *E. coli* isolates to species level was carried out using the Analytical Profile Index (API 20E) strips (BioMérieux), with the following biochemical characteristics; indole positive, urease negative, arginine dihydrolase negative, Simmon's citrate negative, Voges-Proskauer (VP) test negative, and fermentation of glucose to produce acid and gas.

Antibiotic susceptibility testing (AST) was performed on Mueller Hinton agar using the Kirby-Bauer disc diffusion method. The antibiotic discs tested were amoxicillin (25µg), amoxicillin-clavulanic acid (20/10µg), piperacillin-tazobactam (30/6µg), imipenem (10µg), cefixime (5µg), ceftriaxone (30µg), cefotaxime (30µg), ceftazidime (30µg), ciprofloxacin (5µg), gentamicin (10µg), amikacin (30µg), sulfamethoxazole-trimethoprim (1.25/23.75µg) and fosfomycin (50µg).

Sensitivity and resistance were determined by measuring the diameter of the zones of inhibition of bacterial growth with a calibrated ruler, then compared with the interpretive breakpoints. The criteria for performing, reading and interpreting the tests were those of the French Microbiology Society CA-SFM 2020 committee. Where *E. coli* was isolated more than once from the same patient with the same antibiotic susceptibility profile, only one was considered.

Phenotypic detection of ESBL:

The production of ESBL, which cause hydrolysis of all beta-lactam antibiotics, was confirmed by the 'double disc synergy test' (DDST) using the combination of amoxicillin and clavulanic acid and a third- or fourth-generation cephalosporin and/or aztreonam. The synergy was characterized by the appearance of a "champagne cork" image, which indicates the presence of ESBL.

Data analysis:

Data were entered and analysed using Microsoft Office Excel 2013. The Fisher's exact test was used to compare the antimicrobial resistance profiles of ESBL-producing and non-ESBL-producing *E. coli* strains. The significance level was less than 5%.

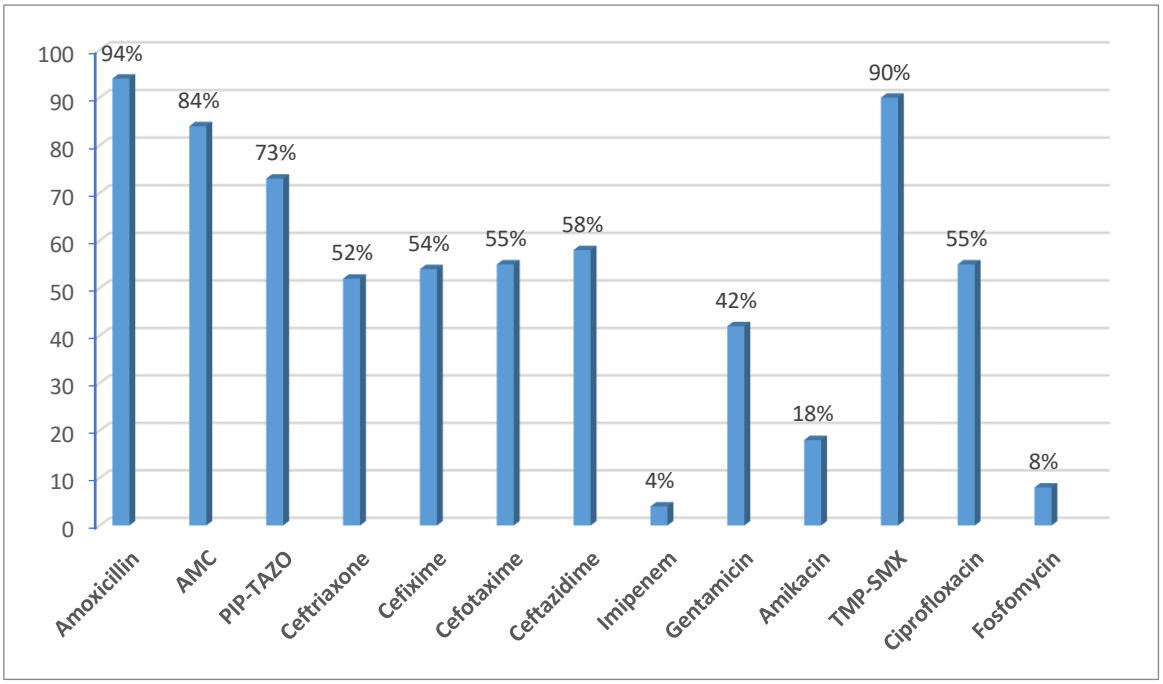
Results:

A total of 187 non-repetitive uropathogenic *Enterobacteriaceae* were isolated from 187 patients with UTI, out of which 81 were uropathogenic *E. coli* (UPEC) strains, giving an overall UPEC isolation frequency of 43.0%. Forty-nine (60.0%) the 81 patients with UPEC UTIs (60.0%) were females while 32 (40.0%) were males, with female to male ratio of 1.5. The modal age of the patients was 57 years with age range of 2 to 86 years. The distribution of the population by age group showed that 3 (3.7%) patients were under 18 years of age, 46 (56.8%) were 18-60 years of age and 32 (39.5%) were over 60 years of age

Among the ESBL-producing UPEC isolates, 23 (50.0%) were from female and 23 (50.0%) from male patients. Four (8.6%) were isolated from patients less than 18 years of age, while 21 (47.7%) each were from patients aged 18-60 years and age over 60 years. Of the non-ESBL-producing UPEC strains, 26 (74.3%) were from female and 9 (25.7%) were from male patients, while 25 (71.4%) and 10 (28.6%) were isolated from patients in the age group 18-60 years and age over 60 years respectively.

Antibiotic resistance profile of UPEC strains:

The resistance profile of the uropathogenic *E. coli* strains to the antibiotics tested showed very high rates of resistance to amoxicillin (94.0%), amoxicillin-clavulanic acid (84%), piperacillin-tazobactam (73.0%), and sulfamethoxazole-trimethoprim (90.0%) (Fig 1).



AMC = Amoxicillin-clavulanic acid; PIP-TAZO = Piperacillin-tazobactam; TMP-SMX = Sulfamethozole-trimethroprim.

Fig 1: The trend in antibiotic resistance in UPEC strains

Table 1: Comparative antibiotic resistance rates of ESBL and non-ESBL-producing UPEC strains

Antibiotics (no of isolates tested)	**ESBL producing UPEC (%) (n=46)**		**Non-ESBL producing UPEC (%) (n=35)**		**OR (95% CI)**	***p* value**
	Resistant	Sensitive	Resistant	Sensitive		
Imipenem (n=59)	3 (8.8)	31 (91.2)	1 (4.0)	24 (96.0)	2.32 (0.23-23.8)	0.43*
Fosfomycin (n=74)	3 (7.5)	37 (92.5)	0	34 (100.0)	6.44 (0.32-129.3)	0.15*
Amikacin (n=50)	8 (25.0)	24 (75.0)	1 (5.6)	17 (94.4)	5.67 (0.65-49.6)	0.13*
Gentamicin (n=45)	15 (57.7)	11 (42.3)	4 (21.1)	15 (78.9)	5.11 (1.33-19.7)	0.018**
Ciprofloxacin (n=49)	23 (76.7)	7 (23.3)	4 (21.1)	15 (78.9)	12.3 (3.07-49.5)	0.0003 **
Ceftazidime (n=80)	45 (100.0)	0	2 (5.7)	33 (94.3)	1219 (56.6-26261)	<0.0001**
Ceftriaxone (n=21)	11 (100.0)	0	0	10 (100.0)	483 (8.8-26615)	<0.0001**
Cefixime (n=48)	26 (100.0)	0	0	22 (100.0)	2385 (45.4-125232)	<0.0001**
Cefotaxime (n=58)	31 (100.0)	0	1 (3.7)	26 (96.3)	1113 (43.5-28500)	<0.0001**
Piperacillin-tazobactam (n=45)	25 (92.6)	2 (7.4)	8 (44.4)	10 (55.6)	15.63 (2.8-86.8)	0.0006**
Amoxicillin-clavulanate (n=43)	23 (100.0)	0	13 (65.0)	7 (35.0)	26.11 (1.38-494.2)	0.0024**
Amoxicillin (n=49)	28 (100.0)	0	18 (85.7)	3 (14.3)	10.78 (0.53-221.2)	0.072*

* = Non-significant difference; ** = Significant difference; OR = Odds ratio; CI = Confidence interval

Comparative antibiotic resistance of ESBL and non-ESBL producing UPEC strains:

The ESBL-producing UPEC strains accounted for 24.5% (46/187) of all uropathogenic *Enterobacteriaceae* isolated. These isolates had very high resistance rates of up to 100.0% for ceftazidime, ceftriaxone, cefixime, cefotaxime, amoxicillin-clavulanic acid and amoxicillin (Table 1).

Comparative analysis of the antibiotic resistance rates between ESBL and non-ESBL-producing UPEC strains showed no significant difference for imipenem (p=0.43), fosfomycin (p=0.15), amikacin (p=0.13), and amoxicillin (p>0.072) while the resistance rates of ESBL-producing strains were significantly higher for gentamicin (p=0.018), ciprofloxacin (p=0.0003), ceftazidime (p<0.0001), ceftriaxone (p<0.0001), cefixime (p<0.0001), cefotaxime (p<0.0001), piperacillin-tazobactam (p=0.0006), and amoxicillin-clavulanate (p=0.0024), compared to non-ESBL producing UPEC strains.

Discussion:

Urinary tract infections are associated with overuse and misuse of antimicrobial agents. The latter have implications for bacterial ecology and the spread of antibiotic resistance, especially when it arises from empirical antimicrobial treatment of recurrent UTIs (9). *Escherichia coli* is a major cause of UTIs (5, 6). The evolution of resistance in *E. coli* is a testament to the effectiveness of antibiotic management policies in community and hospital medicine. These policies include recommendations for the management and empiri-

cal treatment of UTIs (10). Thus, for simple cystitis, an antibiotic will be recommended for empirical therapy if the resistance rate of the bacteria responsible is less than 20.0%. Given the possible complications, in cystitis at risk of complication, acute pyelonephritis, gestational cystitis, and male infections, this rate should be less than 10% (11).

In the present study, 60.0% of the female gender was represented, with a female to male ratio of 1.5. The majority of UTIs were seen in patients over 40 years of age, with a predominance of female patients (58.0%). Indeed, female predominance is generally reported (12,13,14) and is linked to the nature of the female urogenital tract, which is close to the anus and lacks the bacteriostatic character of male prostate secretions (15,16,17). Other host-related factors such as catheterization, pregnancy, sexual activity, urinary tract obstruction have been reported as important causes. In females over 40 years of age, recurrent UTIs could be associated with vaginal prolapse after menopause, which could increase the risk of bacteriuria as vaginal pH increases due to decreased lactobacilli in the birth canal, giving other uropathogens a chance to colonize (18). The results of this study showed a strong involvement of *E. coli* strains in 43.0% of uropathogens causing UTIs. Our findings are consistent with previous studies conducted in different geographic areas (15, 19). However, our results disagree with that of a study from southwestern Nigeria, which reported that *Klebsiella* spp was the most prevalent uropathogen involved in UTIs. This difference could be attributed to differences in study design and environmental factors.

The study of antibiotic resistance in uropathogenic *E. coli* strains showed varying rates of resistance to the antibiotics tested. Among the antibiotics tested, resistance was highest to amoxicillin (94.0%), amoxicillin-clavulanic acid (84.0%), piperacillin-tazobactam (73.0%) and trimethoprim-sulfamethoxazole (90.0%). A similar rate (94.1%) of amoxicillin resistance was reported in Antananarivo, Madagascar by Rakotovao-Ravahatra (20). High rates of resistance to amoxicillin have been reported in numerous studies (21,22,23). This resistance is acquired and is thought to be the consequence of selection pressure linked to the misuse of these antibiotics in developing countries (24). The emergence of amoxicillin-clavulanic acid resistance is a global phenomenon, reported widely at varying rates (22). This antibiotic is known to have an impact on the digestive flora. Thus, the combination of amoxicillin and clavulanic acid is not indicated for empirical treatment of UTIs but only on documentation in the few cases where the strain will be susceptible. The high resistance rates of the uropathogenic *E. coli* strains in our study to these antibiotic molecules justify that they (amoxicillin, amoxicillin–clavulanic acid) are no longer recommended for empirical treatment of UTIs (10,25).

About 73% (33/45) of the UPEC in our study were resistant to piperacillin-tazobactam. Very low rates of resistance to this antibiotic have been reported in many studies, ranging from 6.6% to 27.8% (26,27,28,29). UPEC has the ability to form biofilm (30). Bacteria in a biofilm can be 10 to 1000 times more resistant to antimicrobial agents (31,32) than the same bacteria in planktonic form. Several factors can explain this high resistance or tolerance, including the polymer matrix that acts as a barrier, reducing or preventing the spread of antimicrobial agents. Electrostatic charges on the surface of the polymer matrix can also bind some antimicrobial agents. The metabolism of bacteria in biofilm also plays a very important role. Given the low concentration of certain nutrients and the oxygen gradient, some biofilm cells will be metabolically inactive and may even be dormant. These dormant bacterial cells are likely responsible for much of the tolerance associated with biofilms (33). Ponnusamy et al., (34) reported resistance rate of 83.0% among biofilm-producing UPECs. This result is not so different from ours.

Escherichia coli is naturally susceptible to third-generation cephalosporins and resistance is mainly due to ESBL production. High rates of resistance to ceftriaxone (52.0%), cefixime (54.0%), cefotaxime (55.0%) and ceftazidime (58.0%) were seen in our study. Resistance to third-generation cephalosporins has increased significantly in some geographic areas. Resistance rates similar to that found in our study have also been reported in various studies with rates up to 97.1% for ceftriaxone and 61.8% for cefixime, 87.0% for cefotaxime and ceftazidime (27,35,36). It should also be remembered that these antibiotics are selective for the microbiota. The high frequency of resistance to third-generation cephalosporins could be related to the overuse of these antibiotics without microbiological investigations since most clinicians depend on empiric therapy as a first decision or even on self-prescription of antibiotics by patients themselves in the case of orally administered third-generation cephalosporins (cefixime) and the incomplete duration of treatment.

Low resistance rate was demonstrated to amikacin compared to gentamicin at 18.0%

and 42.0% respectively. In India, gentamicin resistance rates were 48.8% (37). Leski et al., (38) in 2016 reported high resistance rate of 72.9% to gentamicin in their study. Resistance rates of 81.3% to gentamicin and 27.0% to amikacin have been recorded in Iran (39). All of these studies differed in the resistance rates of the bacteria that cause UTIs, which could be attributed to many factors, such as the study population and differences in geographic location.

The rate of resistance to ciprofloxacin (55.0%) was also high in our study. This rate of resistance to ciprofloxacin is indicative of the high level of resistance to fluoroquinolones in our country. Fluoroquinolone resistance has become a global concern (10). Mohamed, in Somalia, reported ciprofloxacin resistance rate of 67.6%. Significant rates of resistance to ciprofloxacin have been identified in various studies (12,13,40,41,42). The fluoroquinolones induce resistance by accumulating mutations in DNA gyrase and topoisomerase genes, justifying a policy of sparing. It is now established that *E. coli* resistance to quinolones is correlated with outpatient quinolone use at the state, hospital, general practice, and community levels (43). Strict adherence to antibiotic therapy recommendations for common infections should make it possible to drastically limit the use of quinolones in UIIs by limiting the indications and durations of treatment, and by practicing therapeutic de-escalation when the susceptibility test allows it.

Antibiotic molecules with urinary specificity deserve particular attention, in this case fosfomycin. It is active against several species of *Enterobacteriaceae*, including ESBL-producing strains. These are antibiotics that are not selective for the gut microbiota. Their activity persists at a high rate in older patients. In this study, the resistance rate to this molecule was 8.0%. Resistance rates reported in the literature are highly variable but less than 15.0% (44). Their prescription should be limited to simple acute cystitis because of its activity. Trimethoprim-sulfamethoxazole is a first-line antimicrobial used in the treatment of simple cystitis. However, increasing resistance to this molecule has recently been observed in many countries. The majority of studies show resistance at or above the accepted level of 20.0% (21,22,23). A high rate of resistance to trimethoprim-sulfamethoxazole (90.0%) was found in our study. These data justify that this molecule is no longer recommended for empirical treatment of UTIs (10,25). On the other hand, relatively low resistance rates were recorded to imipenem (4.0%). These low rates of imipenem resistance are corroborated by many studies (19,23).

Among the resistance mechanisms of *E. coli* to antibiotics, the production of ESBL is the primary mechanism (45). Beta-lactamases are enzymes that hydrolyse the amide bond of the four-chain β-lactam ring of the β-lactam antibiotics (penicillins, cephalosporins, monobactams and carbapenems) (46) thus conferring resistance to β-lactams (all penicillins, cephalosporins and monobactams), with the exception of carbapenems, cephamycins and β-lactamase inhibitors (47). In our study, 56.8% (46/81) of *E. coli* strains were ESBL-producing. The frequency of ESBL-producing *E. coli* differs in different parts of the world and sometimes even in different hospitals across the country. El Bouamri (21) had reported rate of 6.0% in Marrakech. In Poland and France, rates of 8.0% and 7.6% were reported respectively (48,49). High levels of ESBL-producing *E. coli* are particularly detected in developing countries such as Iran-37.1%, Nepal-38.9%, Pakistan-40% and Jordan-50% (50,51,52). These high rates of ESBL production by UPEC strains confirm the widespread of this resistance phenomenon in hospitals (15,53).

For the comparison of antibiotic resistance rates of ESBL-producing versus non-ESBL-producing strains, the difference was not statistically significant for imipenem, fosfomycin, amikacin and amoxicillin. However, significantly higher resistance rates of up to 100% were observed among ESBL-producing compared to non-ESBL-producing *E. coli* strains for cephalosporins (ceftazidime, ceftriaxone, cefixime, cefotaxime) and aminopenicillins (amoxicillin). Also, significantly higher resistance rates to penicillins combined with inhibitors (amoxicillin-clavulanic acid-100.0%, piperacillin-tazobactam-92.6%), and to ciprofloxacin (76.7%), gentamicin (57.7%) and amikacin (25.0%) were observed. This higher resistant rate of ESBL-producing UBEC strains could be explained by the fact that ESBL genes, usually carried by plasmids, are often associated with other antibiotic resistance genes, including resistance to aminoglycosides and fluoroquinolones (42,54). A lower resistance rate was observed with imipenem (8.8%), which confirms that ESBL-producing strains of *E. coli* remain highly susceptible to the carbapenems. However, in order to preserve this class of 'last resort' antibiotic as much as possible, alternatives should be prioritized whenever possible.

One of the limitations of our study is the fact that clinical data, which are part of the case definition of the different clinical pictures of UTIs, were not collected. Also, the data obt-

ained in this study are global and do not allow us to highlight possible differences in resistance phenotypes according to clinical presentations. It would seem interesting to support the findings of our study with a larger-scale study that includes clinical data.

Conclusion:

The emergence and spread of multi-drug-resistant uropathogenic bacteria are public health problems and real challenge for medical practitioners. This prompts reflection on the management of patients with UTIs. Indeed, the treatment of UTIs should be the subject of therapeutic consensus, taking into account, the national situation of antibiotic resistance. In addition, the adoption of a policy for the proper use of antibiotics, updated by regular programmes to monitor the antibiotic susceptibility of bacteria isolates, remains one of the key tools for reducing antimicrobial resistance in bacterial uropathogens.

Contributions of authors:

MT designed the study, and contributed to the writing of the entire manuscript at its different stages (initial drafting, critical revision, editorial finalization); ONEN was involved in the study design and supervision; AA was involved in bibliographic prospecting; OIBR was involved in proofreading of the manuscript; and OAWS was involved in proofreading and validation of the manuscript. All authors approved the final version of the manuscript submitted for publication.

Source of funding:

No funding was received for the study

Conflict of interest:

Authors declare no conflict of interest

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