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## Community-Associated Extended-Spectrum Beta-Lactamase-Producing *Escherichia coli* in a Nephrology Center

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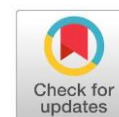
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### ABSTRACT

Urinary tract infections caused by extended-spectrum beta-lactamase (ESBL)-producing *Escherichia coli* are increasingly difficult to manage, particularly among patients with repeated healthcare exposure. This study characterized uropathogens and determined the prevalence and antimicrobial susceptibility of ESBL-producing *E.coli* among hospital- and community-associated urinary tract infections in Benghazi, Libya. A cross-sectional laboratory investigation was conducted from April to December 2023 among 120 symptomatic patients attending Al-Hawari Nephrology Hospital and community outpatient services. Midstream urine specimens were cultured on blood and MacConkey agars; isolates were identified by colony morphology, Gram staining, and conventional biochemical tests. Antimicrobial susceptibility was evaluated by disk diffusion, and ESBL production in *E.coli* was confirmed phenotypically using double-disk synergy and combination-disk tests. Gram-negative organisms accounted for 70% of isolates and *E.coli* was the predominant uropathogen (50%, 60/120). Of the *E.coli* isolates, 27% (16/60) were ESBL producers. ESBL-positive isolates were more frequent among inpatients (63%) than outpatients (37%) and among females (56%) than males (44%). Resistance among ESBL-producing isolates was highest to ciprofloxacin (94%), cefotaxime (90%), ceftazidime (85%), cefuroxime (80%), and colistin (70%). Susceptibility remained high to ertapenem (95%), amikacin (90%), and nitrofurantoin (75%). These findings demonstrate a clinically important ESBL burden and support routine susceptibility testing, strengthened infection-control measures, and antimicrobial stewardship guided by local resistance data.

### 1. INTRODUCTION

Urinary tract infections (UTIs) are among the most frequent bacterial infections and impose a substantial burden in both community and healthcare settings. Uropathogenic *Escherichia coli* is consistently the leading etiological agent because its virulence repertoire facilitates adhesion, invasion, persistence, and recurrence within the urinary tract (Lee *et al.*, 2018; Nielubowicz & Mobley, 2010). The clinical challenge is amplified by the global expansion of antimicrobial resistance, which increasingly compromises standard empirical therapy.

Extended-spectrum beta-lactamases (ESBLs) hydrolyze penicillins, third-generation cephalosporins, and monobactams and are commonly encoded on transferable plasmids. CTX-M-type enzymes have become particularly widespread, while TEM and SHV variants remain epidemiologically relevant (Bradford, 2001; Castanheira *et al.*, 2021). Plasmid co-localization of resistance determinants also promotes multidrug-resistant phenotypes, frequently including reduced susceptibility to fluoroquinolones and aminoglycosides. Although ESBL-producing organisms were initially associated with hospitals, community-onset infections are now widely documented. Recent hospitalization, recurrent antibiotic exposure, invasive devices, chronic disease, and frequent contact with healthcare services increase the risk of carriage and infection (Pitout & Laupland, 2008; Woerther *et al.*, 2013). Patients receiving nephrology care are particularly vulnerable because immune dysfunction, repeated hospital visits, dialysis-related procedures, and cumulative antimicrobial exposure create opportunities for both acquisition and transmission. Local surveillance is therefore essential. Empirical regimens based on resistance patterns from other regions may result in treatment failure and further selection of resistant strains. Data from Libya remain limited, despite reports of CTX-M-15-producing uropathogenic *E.coli* in major hospitals (Ejaz *et al.*, 2017). This study addressed that gap by characterizing uropathogens among symptomatic patients in Benghazi and comparing ESBL-producing *E.coli* recovered from hospital- and community-associated infections.

### 1.1 Study objectives

1. To characterize bacterial pathogens associated with symptomatic UTIs among patients attending Al-Hawari Nephrology Hospital and community outpatient services in Benghazi.
2. To identify the predominant uropathogen and describe its distribution by hospitalization status, sex, and age group.
3. To determine the phenotypic prevalence of ESBL production among *E.coli* isolates.
4. To compare the antimicrobial susceptibility patterns of ESBL-producing and non-ESBL-producing *E.coli* and identify potentially effective therapeutic options.

## 2. METHOD

### 2.1 Study design, setting, and participants

A cross-sectional laboratory-based study was conducted from April to December 2023 at Al-Hawari Nephrology Hospital in Benghazi, Libya. The study enrolled 120 patients with one or more symptoms compatible with UTI, including dysuria, urinary frequency, and changes in urine color or odor. Participants were classified by hospitalization status as inpatients with hospital-associated infections or outpatients with community-associated infections. The sample contained equal numbers of males and females, and participants were grouped into the age categories 30–49 years and 50–70 years. Patients who had received antibiotics during the two days preceding sample collection were excluded. Specimens with fewer than  $10^5$  pus cells per high-power field and absent or minimal bacteriuria were also excluded according to the criteria reported in the source study.

### 2.2 Specimen collection and microbiological identification

Participants provided first-morning, clean-catch midstream urine in sterile labeled containers after receiving standardized hygiene instructions. Samples were transported to the microbiology laboratory. Urine sediment was examined microscopically after centrifugation at 4,000 rpm for five minutes. The remaining specimen was inoculated onto blood agar and MacConkey agar and incubated at 37°C for 24–48 hours. Growth of at least  $10^5$  colony-forming units/mL was interpreted as significant bacteriuria (Cheesbrough, 2006). Isolates were identified by colony morphology, Gram staining, and conventional biochemical testing, including catalase, coagulase, oxidase, urease, indole, citrate, triple sugar iron, and novobiocin tests, as appropriate. *E.coli* isolates were selected for subsequent ESBL screening and susceptibility analysis.

### 2.3 Antimicrobial susceptibility and ESBL confirmation

Antimicrobial susceptibility was assessed by the agar disk-diffusion method on Mueller-Hinton agar. The antibiotic panel included amikacin, gentamicin, ertapenem, cefotaxime, ceftazidime, cefuroxime, aztreonam, amoxicillin-clavulanic acid, colistin, nitrofurantoin, and ciprofloxacin. Reduced inhibition zones around cefotaxime or ceftazidime disks triggered phenotypic confirmation. ESBL production was evaluated using the double-disk synergy test and combination-disk test; an increase of at least 5 mm in the inhibition zone with clavulanate was interpreted as ESBL-positive.

## 2.4 Statistical analysis

Data were summarized using counts and percentages. Descriptive comparisons were made across organism groups, hospitalization status, sex, age group, ESBL phenotype, and antibiotic susceptibility categories. No inferential estimates or multivariable analyses were reported in the source study.

## 3. ETHICAL APPROVAL

The study was conducted within Al-Hawari Nephrology Hospital and used clinical urine specimens collected after patients received specimen-collection instructions. The source thesis did not report the name of the approving ethics committee, an approval number, or the consent procedure. These details should be verified in the institution's records before journal submission.

## 4. RESULTS

### 4.1 Distribution of uropathogens

All 120 collected specimens yielded bacterial growth. Gram-negative bacteria accounted for 84 isolates (70%), whereas Gram-positive bacteria accounted for 36 isolates (30%). *E.coli* was the predominant organism, representing 60 of 120 isolates (50%). *Staphylococcus aureus* was the second most frequent isolate (16%), followed by *Klebsiella spp.* and *Streptococcus spp.* (8% each). Other recovered organisms each represented 7% or less of the total collection.

**Table 1. Distribution of uropathogens isolated from 120 urine specimens**

| %  | n  | Organism                            |
|----|----|-------------------------------------|
| 50 | 60 | <i>Escherichia coli</i>             |
| 16 | 19 | <i>Staphylococcus aureus</i>        |
| 8  | 9  | <i>Klebsiella spp.</i>              |
| 8  | 9  | <i>Streptococcus spp.</i>           |
| 7  | 8  | <i>Staphylococcus saprophyticus</i> |
| 4  | 5  | <i>Enterobacter spp.</i>            |
| 4  | 5  | <i>Pseudomonas spp.</i>             |
| 2  | 2  | <i>Pseudomonas aeruginosa</i>       |
| 2  | 2  | <i>Acinetobacter spp.</i>           |
| 1  | 1  | <i>Proteus spp.</i>                 |

### 4.2 Epidemiological distribution of *E.coli*

Among the 60 *E.coli* isolates, 33 (55%) were recovered from inpatients and 27 (45%) from outpatients. Females accounted for 34 isolates (57%) and males for 26 (43%). The source study reported a greater proportion of *E.coli* infection in the 30–49-year group (69%) than in the 50–70-year group (31%).

**Table 2. Distribution of *E. coli* by hospitalization status and sex**

| %  | n  | Category           | Characteristic         |
|----|----|--------------------|------------------------|
| 45 | 27 | Outpatients (CAIs) | Hospitalization status |
| 55 | 33 | Inpatients (HAIs)  | Hospitalization status |
| 43 | 26 | Male               | Sex                    |
| 57 | 34 | Female             | Sex                    |

### 4.3 Prevalence and distribution of ESBL-producing *E. coli*

Phenotypic testing identified 16 ESBL-producing isolates, corresponding to 27% of all *E.coli*, while 44 isolates (73%) were ESBL-negative. Among ESBL-positive isolates, 10 (63%) originated from inpatients and six (37%) from outpatients. Nine (56%) were isolated from females and seven (44%) from males.

**Table 3. Phenotypic ESBL status and distribution of ESBL-positive *E. coli***

| %  | n  | Category   | Measure                          |
|----|----|------------|----------------------------------|
| 73 | 44 | Negative   | ESBL status among <i>E.coli</i>  |
| 27 | 16 | Positive   | ESBL status among <i>E.coli</i>  |
| 37 | 6  | Outpatient | Source of ESBL-positive isolates |
| 63 | 10 | Inpatient  | Source of ESBL-positive isolates |
| 44 | 7  | Male       | Sex of ESBL-positive patients    |
| 56 | 9  | Female     | Sex of ESBL-positive patients    |

### 4.4 Antimicrobial susceptibility

ESBL-producing *E.coli* showed the greatest resistance to ciprofloxacin (94%), cefotaxime (90%), ceftazidime (85%), and cefuroxime (80%). Resistance to colistin was also high (70%). By contrast, ertapenem, amikacin, and nitrofurantoin retained the highest reported activity, with susceptibility rates of 95%, 90%, and 75%, respectively. Non-ESBL-producing *E.coli* showed broader susceptibility across the tested drugs.

**Table 4. Antimicrobial susceptibility of ESBL-producing *E.coli* (n = 16)**

| Susceptible (%) | Resistant (%) | Antimicrobial               |
|-----------------|---------------|-----------------------------|
| 90              | 10            | Amikacin                    |
| 69              | 31            | Gentamicin                  |
| 95              | 5             | Ertapenem                   |
| 10              | 90            | Cefotaxime                  |
| 15              | 85            | Ceftazidime                 |
| 20              | 80            | Cefuroxime                  |
| 63              | 37            | Amoxicillin-clavulanic acid |
| 30              | 70            | Colistin                    |
| 75              | 25            | Nitrofurantoin              |
| 6               | 94            | Ciprofloxacin               |

**Table 5. Reported susceptibility of ESBL-negative *E. coli***

| Susceptible (%) | Resistant (%) | Antimicrobial               |
|-----------------|---------------|-----------------------------|
| 88              | 12            | Amikacin                    |
| 66              | 34            | Gentamicin                  |
| 94              | 6             | Ertapenem                   |
| 67              | 33            | Cefotaxime                  |
| 73              | 23            | Ceftazidime                 |
| 64              | 36            | Cefuroxime                  |
| 60              | 40            | Amoxicillin-clavulanic acid |
| 63              | 37            | Colistin                    |
| 70              | 30            | Nitrofurantoin              |
| 65              | 35            | Ciprofloxacin               |

The predominance of *E.coli* in this study is consistent with its established role as the principal cause of community- and healthcare-associated UTIs. Its biological fitness in the urinary tract, combined with the capacity of successful lineages to acquire and disseminate resistance plasmids, explains its recurrent dominance in surveillance studies (Nielubowicz & Mobley, 2010; Lee *et al.*, 2018). The 50% prevalence observed here therefore supports organism-directed surveillance as a central component of UTI management in Benghazi.

The ESBL prevalence of 27% among *E.coli* isolates represents a clinically important burden. Comparable rates have been reported in some hospital and community series, although ESBL frequency varies substantially by patient population, antimicrobial exposure, diagnostic approach, and geography (Pitout & Laupland, 2008; Kettani Halabi *et al.*, 2021). The higher proportion among inpatients in the current study is biologically plausible given repeated healthcare contact, underlying renal disease, invasive procedures, and antibiotic selection pressure. Nevertheless, the presence of ESBL-positive isolates among outpatients confirms that resistant organisms are not confined to hospital environments.

The resistance profile has direct therapeutic implications. High resistance to cefotaxime, ceftazidime, and cefuroxime is expected among ESBL producers and reinforces the unreliability of cephalosporins for suspected ESBL infection. Ciprofloxacin resistance of 94% further restricts oral empirical options and is consistent with the frequent co-selection of quinolone resistance on multidrug-resistance plasmids. Similar treatment challenges have been documented for virulent ESBL-producing *E.coli* in UTIs (Naziri *et al.*, 2020).

Ertapenem and amikacin demonstrated the highest in-vitro activity, while nitrofurantoin retained useful activity for lower-tract infection when clinically appropriate. These results should guide, but not replace, individual culture and susceptibility testing. Carbapenem use should remain carefully controlled to avoid accelerating carbapenem resistance. The reported colistin resistance also warrants cautious interpretation because disk diffusion is not the preferred method for colistin susceptibility; confirmation by broth microdilution would be necessary before clinical or epidemiological conclusions are drawn.

The female predominance is compatible with well-established anatomical and behavioral risk factors for UTI. The greater frequency among adults aged 30–49 years should be interpreted cautiously because the source thesis reports age percentages without an internally consistent *E.coli*-specific denominator. Future studies should preserve patient-level data and apply inferential analyses to distinguish true risk factors from differences in recruitment.

## 5. DISCUSSION

### 5.1 Clinical and public health implications

1. Culture and antimicrobial susceptibility testing should precede definitive therapy whenever clinically feasible, particularly among nephrology patients and those with prior healthcare exposure.
2. Empirical use of third-generation cephalosporins and fluoroquinolones should be reviewed against current local antibiograms.
3. Infection-prevention measures in nephrology and dialysis settings should emphasize hand hygiene, equipment decontamination, contact precautions when indicated, and surveillance of resistant organisms.
4. Regional antimicrobial-resistance surveillance should link laboratory results with prior antibiotic exposure, comorbidities, hospitalization duration, recurrence, and clinical outcomes.

### 5.2 Limitations

This was a single-center, cross-sectional study with a modest sample size, which limits generalizability and prevents assessment of temporal trends. ESBL production was determined phenotypically without molecular confirmation of blaCTX-M, blaTEM, blaSHV, or other resistance genes. Patient-level clinical variables were limited, and no multivariable analysis was reported. Some source tables contained inconsistent raw counts or overlapping organism labels; the present article therefore prioritized internally coherent denominators and clearly identified where only reported percentages could be retained. Finally, colistin susceptibility requires confirmation using a validated broth microdilution method.

## 6. CONCLUSION

*E. coli* was the predominant uropathogen among symptomatic patients in Benghazi, accounting for half of all isolates. More than one-quarter of *E. coli* isolates were phenotypic ESBL producers, with a greater proportion among inpatients and females. ESBL-positive isolates showed extensive resistance to cephalosporins and ciprofloxacin, whereas ertapenem, amikacin, and nitrofurantoin retained the highest reported activity. These findings support routine culture-based diagnosis, locally informed prescribing, strengthened infection control in nephrology settings, and coordinated antimicrobial-stewardship programs. Larger multicenter investigations using standardized susceptibility methods and molecular characterization are needed to define the regional epidemiology and monitor the emergence of carbapenem and colistin resistance.

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