

Clinical and Healthcare Related Factors Associated with ESBL and AmpC-Producing Uropathogenic *Escherichia coli* in Inpatient and Outpatient Settings

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ABSTRACT

Background: Extended-spectrum β -lactamase (ESBL)- and AmpC-producing uropathogenic *Escherichia coli* (UPEC) complicate treatment of urinary tract infections. This study evaluated clinical and healthcare-related factors associated with these resistance phenotypes in inpatient and outpatient settings. **Methods:** A prospective observational study was conducted at a tertiary-care teaching hospital in southern Haryana from February 2020 to January 2021. Seventy-one resistant UPEC isolates with complete clinical and microbiological data were analysed. Associations with ESBL and AmpC production were assessed using univariable and multivariable logistic regression. **Results:** ESBL production was identified in 45.1% and AmpC production in 62.0% of isolates. ESBL-producing isolates were more frequent among outpatients (61.1% vs 28.6%), whereas AmpC-producing isolates predominated among inpatients (74.3% vs 50.0%). Outpatient status (aOR 3.72; 95% CI 1.07–12.92) and prior antibiotic exposure (aOR 4.47; 95% CI 1.41–14.17) independently predicted ESBL production. Prior antibiotic exposure was associated with lower odds of AmpC production (aOR 0.29; 95% CI 0.09–0.94). **Conclusion:** ESBL and AmpC production showed distinct epidemiological patterns, supporting phenotype-specific surveillance and consideration of recent antibiotic and healthcare exposure in UTI management.

Keywords: Uropathogenic *Escherichia coli*; ESBL; AmpC β -lactamase; urinary tract infection; antimicrobial resistance

INTRODUCTION

Urinary tract infection (UTI) is one of the most common bacterial infections in the community and in health care facilities, and is a significant driver of antimicrobial use globally. *E. coli* is the most common cause of uncomplicated and complicated UTIs, especially uropathogenic *E. coli* (UPEC). UPEC can colonize the periurethral area, attach to uroepithelial cells, resist host immunity, and survive in the urinary tract, which are all important advantages leading to the occurrence of acute infection and recurrence [1]. The burden of UTI is especially high in females, but age, urinary tract abnormalities, underlying disease, instrumentation and

healthcare exposure influence the risk and clinical presentation of UTI [2].

UTIs are becoming more difficult to empirically manage because of the increased resistance of UPEC. Particularly concerning is resistance due to extended-spectrum β -lactamases (ESBLs) and AmpC β -lactamases. ESBLs hydrolyse extended-spectrum cephalosporins and aztreonam, but are typically inhibited by β -lactamase inhibitors such as clavulanic acid; the spread of ESBLs in *E. coli* has significantly reduced the effectiveness of some commonly used β -lactam antibiotics [3]. Another mechanism of resistance is the presence of AmpC β -lactamases, which confer resistance to most penicillins and cephalosporins,

including cephamycins, and are generally not inhibited by clavulanate [4]. The production of AmpC may be either chromosomal or acquired through plasmid-mediated determinants, which can allow for the spread of AmpC between strains. The concurrent detection of ESBL and AmpC enzymes could also further complicate phenotypic detection and therapy decisions.

There has also been a significant change in the epidemiology of *E. coli* that produce ESBL. ESBL-producing Enterobacterales, especially CTX-M-producing *E. coli*, primarily were seen as a problem in healthcare-associated infections, but now have been found in community reservoirs. The spread of CTX-M enzymes and colonization of the intestinal flora of healthy people have gradually blurred the traditional distinction between hospital- and community-associated antimicrobial resistance [5]. Thus, community-onset UTI with ESBL-producing *E. coli* has become a significant therapeutic challenge. Studies of community-onset ESBL-producing *E. coli* UTI have identified previous hospitalization and prior antimicrobial exposure among associated factors, with previous exposure to second-generation cephalosporins emerging as an important independent predictor in one study [6]. Recurrent UTI has also been associated with ESBL-producing UPEC in community-acquired infection, with more than three UTI episodes in the preceding year and β -lactam use during the preceding 3 months associated with ESBL positivity [7].

However, the distribution of these risk factors is not necessarily uniform over geographical regions or resistance mechanisms. Different exposure events to antimicrobials and to hospitalizations, recurrent UTI, or urinary catheters can impose different selective pressures on resistant organisms, and resistance in community *E. coli* can lead to significant resistance amongst patients despite not having common healthcare-associated risk factors. This distinction becomes important when the two types of resistance, ESBL and AmpC, are discussed separately, as the epidemiology and selective pressures for the two resistance types can be different. Therefore, grouping all cephalosporin-resistant *E. coli* together may mask clinically important associations and may limit the usefulness of epidemiological data for empirical treatment and antimicrobial stewardship decisions.

In India, this is particularly relevant as studies of urinary pathogens have shown that there is a high degree of association of different antimicrobial-resistance determinants, including β -lactamases. In an investigation of uropathogens from Northern India, the presence of AmpC and carbapenemase genes in ESBL-positive isolates was found, highlighting the multiple resistance mechanisms found in this region [8]. A more recent prospective study of urinary *E. coli* from north India recorded ESBL, AmpC and metallo- β -lactamase

phenotypes, including isolates with co-production of multiple β -lactamases [9]. The results underscore the importance of local surveillance but do not provide evidence to identify the relationship between microbiological characterisation and patient-related and healthcare-associated factors at the individual patient level.

Thus, in the present study, resistant UPEC isolates were evaluated from patients attending a tertiary-care teaching hospital in the southern part of Haryana for suspected UTI in both inpatient and outpatient services. The study was designed to compare demographic, clinical and healthcare-related characteristics of the two care settings, to assess the distribution of ESBL- and AmpC-producing resistance phenotypes and to recognise factors independently associated with ESBL and AmpC production. Clarification of these correlations could aid in the recognition of patients with an elevated risk of infection with individual β -lactamase-producing UPEC phenotypes and inform locally driven empirical therapy, diagnostic approaches and antimicrobial stewardship measures.

MATERIALS AND METHODS

Study design and setting

A prospective observational study was conducted in the Department of Microbiology at a tertiary care teaching hospital in Southern Haryana from February 2020 to January 2021. Patients attending the inpatient and outpatient departments with clinically suspected urinary tract infection were screened during the study period.

Study population

Patients from whom clinically significant, non-duplicate uropathogenic *Escherichia coli* isolates were recovered were considered for inclusion. The present analysis included 71 resistant UPEC isolates with corresponding demographic, clinical, healthcare-exposure, and microbiological data.

Inclusion criteria

Patients were included if they:

- were attending inpatient or outpatient services with suspected urinary tract infection;
- had been advised urine examination;
- yielded a clinically significant *E. coli* isolate; and
- had complete demographic, clinical, and microbiological information available for analysis.

Exclusion criteria

The following were excluded:

- repeat urine specimens from the same patient;
- patients unwilling to participate; and

- isolates with incomplete resistance-phenotype or clinical information.

Clinical and epidemiological data collection

Patient information was recorded using a structured proforma. Variables collected included age, sex, inpatient or outpatient status, previous hospitalization, prior antibiotic exposure, previous urinary tract infection, urinary catheterization, duration of catheterization, duration of hospital stay, diabetes mellitus, anaemia, hypertension, and chronic kidney disease.

Previous hospitalization was defined as hospitalization within the preceding 6 months, while prior antibiotic exposure was defined as receipt of systemic antibiotics within the preceding 3 months. A history of previous UTI within the preceding 12 months was also recorded.

For hospitalized patients, duration of hospital stay was recorded in days. In catheterized patients, catheter duration was recorded from insertion until specimen collection or catheter removal, as applicable.

Microbiological processing

Urine specimens were cultured semi-quantitatively on cystine-lactose-electrolyte-deficient agar. Clinically significant growth was identified using standard microbiological methods. *E. coli* identification was based on colony morphology, Gram staining, motility, and conventional biochemical reactions.

Antimicrobial susceptibility testing was performed by the Kirby-Bauer disk diffusion method on Mueller-Hinton agar and interpreted according to Clinical and Laboratory Standards Institute 2019 recommendations.

Phenotypic detection of β -lactamases

ESBL production was assessed using phenotypic confirmatory testing with ceftazidime and ceftazidime-clavulanate, with additional confirmation by E-test where performed.

AmpC β -lactamase production was assessed using the AmpC disk test and an inhibitor-based method using cloxacillin.

MBL production was evaluated using imipenem-EDTA-based phenotypic methods.

For analysis, isolates were classified into the following mutually exclusive phenotypes:

- ESBL only;
- AmpC only;
- ESBL + AmpC co-production; and

- AmpC + MBL co-production.

Binary variables were also created for any ESBL production and any AmpC production, irrespective of co-production.

Outcome measures

The primary outcomes were:

1. differences in demographic, clinical, and healthcare-related characteristics between inpatient and outpatient cases;
2. factors associated with ESBL and AmpC production; and
3. independent predictors of ESBL and AmpC production.

MBL-producing isolates were summarized descriptively because of their low frequency.

Statistical analysis

Categorical variables were summarized as n (%). Continuous variables were presented as mean $\pm$ SD or median (interquartile range) according to distribution.

Comparisons between inpatient and outpatient groups were performed using the Pearson chi-square test or Fisher exact test for categorical variables. Continuous variables were compared using the independent-samples t-test or Mann-Whitney U test, as appropriate.

Associations between demographic, clinical, and healthcare-related variables and ESBL or AmpC production were first evaluated using univariable analysis. Crude odds ratios (ORs) with 95% confidence intervals (CIs) were calculated.

Variables considered clinically relevant or associated with the outcome on univariable analysis were entered into separate multivariable binary logistic regression models for ESBL and AmpC production. Adjusted odds ratios (aORs) with 95% CIs and p-values were reported. The number of predictors included in each model was restricted according to the number of outcome events to minimize overfitting. All tests were two-sided, and $p < 0.05$ was considered statistically significant.

Ethical considerations

The study was conducted after approval from the institutional ethics committee. Written informed consent was obtained from eligible participants before enrollment, and patient confidentiality was maintained throughout data collection and analysis.

RESULTS

Patient characteristics

The analysis included 71 patients with resistant uropathogenic *Escherichia coli* isolates, comprising 35 (49.3%) inpatients and 36 (50.7%) outpatients. Females accounted for 48 (67.6%) participants, and 36 (50.7%) were aged ≤ 20 years. Previous hospitalization, urinary catheterization, and anaemia were more frequent among inpatients, whereas the remaining demographic and clinical characteristics were broadly comparable between care settings (Table 1).

Table 1. Demographic and clinical characteristics according to care setting

Characteristic	Overall (N=71)	Inpatient (n=35)	Outpatient (n=36)	Test statistic	p-value
Age group, years				Fisher-Freeman-Halton exact	0.691
≤ 20	36 (50.7)	18 (51.4)	18 (50.0)		
21–40	25 (35.2)	12 (34.3)	13 (36.1)		
41–60	6 (8.5)	4 (11.4)	2 (5.6)		
61–80	4 (5.6)	1 (2.9)	3 (8.3)		
Female sex	48 (67.6)	25 (71.4)	23 (63.9)	$\chi^2=0.46$	0.497
Previous hospitalization within 6 months	24 (33.8)	16 (45.7)	8 (22.2)	$\chi^2=4.38$	0.036
Prior antibiotic exposure within 3 months	34 (47.9)	14 (40.0)	20 (55.6)	$\chi^2=1.72$	0.190
Previous UTI within 12 months	25 (35.2)	12 (34.3)	13 (36.1)	$\chi^2=0.03$	0.872
Urinary catheterization	23 (32.4)	18 (51.4)	5 (13.9)	$\chi^2=11.42$	<0.001
Diabetes mellitus	9 (12.7)	7 (20.0)	2 (5.6)	Fisher exact	0.085
Anaemia	23 (32.4)	19 (54.3)	4 (11.1)	$\chi^2=15.10$	<0.001
Hypertension	2 (2.8)	1 (2.9)	1 (2.8)	Fisher exact	1.000
Chronic kidney disease	2 (2.8)	1 (2.9)	1 (2.8)	Fisher exact	1.000

Values are n (%) unless otherwise indicated. UTI, urinary tract infection.

Among catheterized patients, the median catheter duration was 6.0 days (IQR 4.0–7.5) and did not differ significantly between care settings (Mann-Whitney U=39.0, p=0.674). Among inpatients, the median duration of hospitalization was 10.0 days (IQR 7.5–11.5).

Distribution of β -lactamase resistance phenotypes

AmpC-only production was the most frequent phenotype, identified in 36 (50.7%) isolates, followed by ESBL-only production in 27 (38.0%). ESBL+AmpC co-production occurred in 5 (7.0%), while 3 (4.2%) isolates demonstrated AmpC+MBL co-production. The overall phenotype distribution differed significantly between inpatient and outpatient isolates (Fisher-Freeman-Halton exact p=0.017). ESBL-containing phenotypes were more frequent among outpatients, whereas AmpC-containing phenotypes predominated among inpatients (Table 2; Figure 1).

Table 2. Distribution of β -lactamase resistance phenotypes according to care setting

Resistance phenotype	Overall (N=71)	Inpatient (n=35)	Outpatient (n=36)	Test statistic	p-value
Mutually exclusive phenotype distribution				Fisher-Freeman-Halton exact	0.017
ESBL only	27 (38.0)	9 (25.7)	18 (50.0)		
AmpC only	36 (50.7)	22 (62.9)	14 (38.9)		
ESBL + AmpC	5 (7.0)	1 (2.9)	4 (11.1)		
AmpC + MBL	3 (4.2)	3 (8.6)	0 (0)		
Any ESBL production	32 (45.1)	10 (28.6)	22 (61.1)	$\chi^2=7.59$	0.006
Any AmpC production	44 (62.0)	26 (74.3)	18 (50.0)	$\chi^2=4.44$	0.035
Any MBL production	3 (4.2)	3 (8.6)	0 (0)	Fisher exact	0.115

ESBL, extended-spectrum β -lactamase; MBL, metallo- β -lactamase. 'Any' enzyme-production categories include co-producers and are therefore not mutually exclusive.

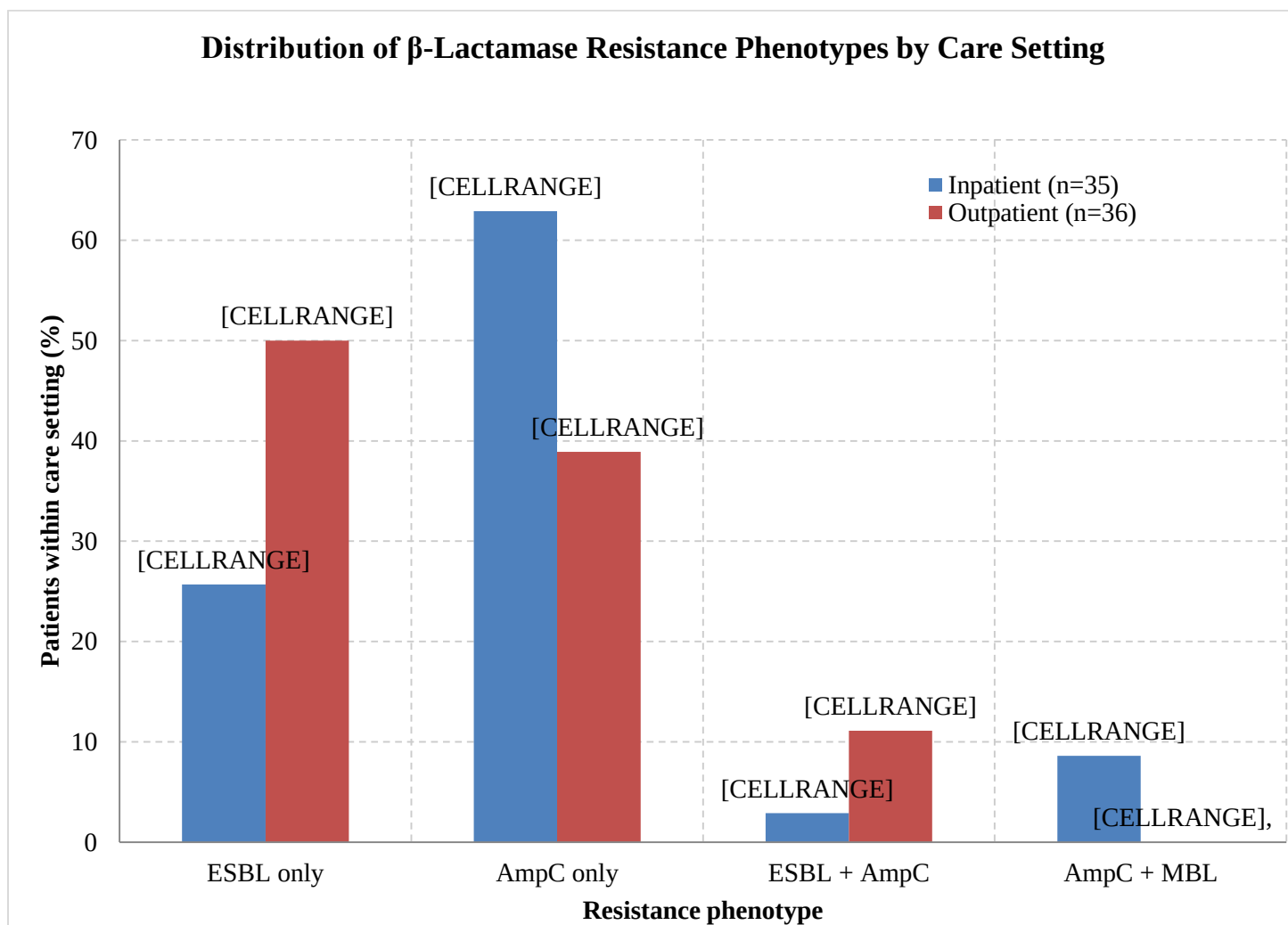


Figure 1. Distribution of β -lactamase resistance phenotypes according to inpatient and outpatient setting.

Factors associated with ESBL production

Any ESBL production was identified in 32 (45.1%) isolates. On univariable analysis, ESBL production was more frequent among outpatients, patients with prior antibiotic exposure, and those with a previous UTI. Urinary catheterization was associated with lower crude odds of ESBL production, while age, sex, diabetes mellitus, and anaemia were not significantly associated with ESBL status (Table 3).

Table 3. Univariable factors associated with ESBL production

Factor	ESBL among exposed, n/N (%)	ESBL among reference, n/N (%)	Crude OR (95% CI)	Test statistic	p-value
Age, per 10-year increase	—	—	1.02 (0.79–1.31)	Wald z=0.16	0.872
Female vs male	23/48 (47.9)	9/23 (39.1)	1.43 (0.52–3.93)	$\chi^2=0.48$	0.486
Outpatient vs inpatient	22/36 (61.1)	10/35 (28.6)	3.93 (1.45–10.61)	$\chi^2=7.59$	0.006
Previous hospitalization	7/24 (29.2)	25/47 (53.2)	0.36 (0.13–1.04)	$\chi^2=3.70$	0.054
Prior antibiotic exposure	23/34 (67.6)	9/37 (24.3)	6.51 (2.30–18.39)	$\chi^2=13.43$	<0.001
Previous UTI	17/25 (68.0)	15/46 (32.6)	4.39 (1.55–12.45)	$\chi^2=8.19$	0.004
Urinary catheterization	6/23 (26.1)	26/48 (54.2)	0.30 (0.10–0.89)	$\chi^2=4.95$	0.026
Diabetes mellitus	3/9 (33.3)	29/62 (46.8)	0.57 (0.13–2.48)	Fisher exact	0.500
Anaemia	8/23 (34.8)	24/48 (50.0)	0.53 (0.19–1.49)	$\chi^2=1.45$	0.228

OR, odds ratio; CI, confidence interval; UTI, urinary tract infection.

Factors associated with AmpC production

Any AmpC production was identified in 44 (62.0%) isolates. AmpC production was more frequent among inpatients and among patients with previous hospitalization. Prior antibiotic exposure and previous UTI were associated with lower crude odds of AmpC production. Urinary catheterization showed a borderline association with AmpC positivity (Table 4).

Table 4. Univariable factors associated with AmpC production

Factor	AmpC among exposed, n/N (%)	AmpC among reference, n/N (%)	Crude OR (95% CI)	Test statistic	p-value
Age, per 10-year increase	—	—	1.02 (0.79–1.32)	Wald z=0.16	0.870
Female vs male	28/48 (58.3)	16/23 (69.6)	0.61 (0.21–1.76)	$\chi^2=0.83$	0.362
Outpatient vs inpatient	18/36 (50.0)	26/35 (74.3)	0.35 (0.13–0.94)	$\chi^2=4.44$	0.035
Previous hospitalization	19/24 (79.2)	25/47 (53.2)	3.34 (1.07–10.45)	$\chi^2=4.55$	0.033
Prior antibiotic exposure	15/34 (44.1)	29/37 (78.4)	0.22 (0.08–0.61)	$\chi^2=8.83$	0.003
Previous UTI	10/25 (40.0)	34/46 (73.9)	0.24 (0.08–0.66)	$\chi^2=7.90$	0.005
Urinary catheterization	18/23 (78.3)	26/48 (54.2)	3.05 (0.97–9.54)	$\chi^2=3.83$	0.050
Diabetes mellitus	7/9 (77.8)	37/62 (59.7)	2.36 (0.45–12.33)	Fisher exact	0.467
Anaemia	16/23 (69.6)	28/48 (58.3)	1.63 (0.57–4.70)	$\chi^2=0.83$	0.362

OR, odds ratio; CI, confidence interval; UTI, urinary tract infection.

Multivariable analysis

In the multivariable model for ESBL production, outpatient status and prior antibiotic exposure remained independently associated with ESBL positivity. Previous UTI showed a positive association that approached statistical significance. In the AmpC model, prior antibiotic exposure remained independently associated with lower odds of AmpC positivity. Both regression models were statistically significant overall (Table 5).

Table 5. Multivariable logistic regression models for ESBL and AmpC production

Outcome / predictor	Adjusted OR	95% CI	Wald z	p-value
ESBL production				
Outpatient vs inpatient	3.72	1.07–12.92	2.07	0.038
Prior antibiotic exposure	4.47	1.41–14.17	2.54	0.011
Previous UTI	3.33	0.95–11.70	1.88	0.060
Urinary catheterization	0.64	0.17–2.35	−0.68	0.497
AmpC production				
Outpatient vs inpatient	0.42	0.13–1.31	−1.49	0.136
Previous hospitalization	2.93	0.80–10.78	1.62	0.106
Prior antibiotic exposure	0.29	0.09–0.94	−2.06	0.040
Previous UTI	0.34	0.10–1.09	−1.81	0.070

ESBL model: likelihood-ratio $\chi^2(4)=24.41$, $p<0.001$; pseudo- $R^2=0.250$.

AmpC model: likelihood-ratio $\chi^2(4)=19.18$, $p<0.001$; pseudo- $R^2=0.203$.

OR, odds ratio; CI, confidence interval.

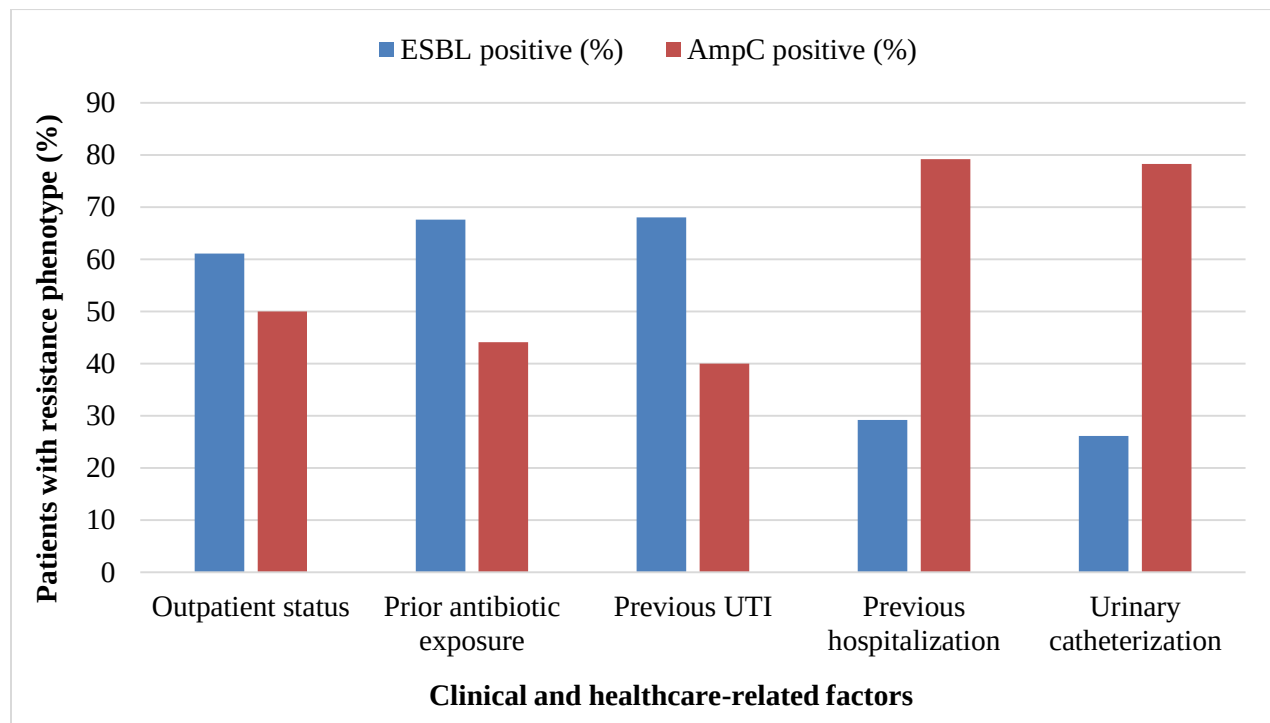


Figure 2. Distribution of ESBL and AmpC production according to selected clinical and healthcare-related factors.

DISCUSSION

The present study revealed different clinical and epidemiological patterns for ESBL- and AmpC-producing UPEC. ESBL production was found in 45.1% and AmpC production in 62.0% of the 71 resistant isolates. ESBL-producing isolates were significantly more common in outpatients, while AmpC-producing isolates were more common in inpatients. Multivariable analysis revealed that outpatient status (aOR 3.72) and prior antibiotic exposure (aOR 4.47) were independently associated with ESBL production, while previous UTI showed a positive association with borderline statistical significance. Conversely, previous antibiotic use was independently associated with reduced odds of AmpC production (aOR 0.29). The results indicate that the epidemiology of ESBL and AmpC resistance in UPEC may differ and that these should not be regarded as a single resistance phenotype.

The increased prevalence of ESBL among outpatients reinforces the emerging significance of ESBL in non-hospital environments. In a primary-care study of 98 ESBL-producing *E. coli* UTIs, Hertz et al. [10] identified recent hospital admission as an independent risk factor for ESBL infection, with odds ratios of approximately 4–5 depending on the comparator group, but no consistent difference between ESBL and other resistant *E. coli* was seen with recent antibiotic exposure. ESBL production was reported by Kumar et al. [11] in 46.6% of community-onset urinary *E. coli* isolates in India, which is similar to the 45.1% found in the present resistant cohort. Previous antibiotic use (OR 11.03), hospitalization (OR 7.1) and diabetes (OR 15.3) were independent predictors in their study. Diabetes and age were not significantly associated with ESBL production in our study, but the strong association with previous antibiotic use was similar in both studies.

Previous UTI was also significantly associated with ESBL production in our univariable analysis and remained clinically relevant after adjustment (aOR 3.33, $p=0.060$). Goyal et al. [12] also found significant associations with recurrent UTI (aOR 6.40), previous outpatient antibiotic use (aOR 7.98), and urinary catheterization (aOR 2.36) in a matched study of 251 community-acquired ESBL UTIs and 251 controls. These results suggest that recurrent UTI may be a marker of repeated exposure to antimicrobials, persistent colonization, or repeated exposure to resistant organisms. The borderline statistical significance in our adjusted model might thus reflect limited statistical power rather than the absence of an underlying association.

The pattern was different for urinary catheterization. Catheterization was more prevalent in inpatients and was associated with lower crude odds of ESBL production,

but was not independently associated after adjustment. However, Köksal et al. [13] found that 37.1% of community-acquired *E. coli/Klebsiella* isolates were ESBL producers and that previous catheterization (OR 2.32), invasive urological procedures (OR 3.22), and urolithiasis (OR 3.00) were independent risk factors. This difference could be attributed to the strong association between catheterization and hospitalization in our study population, together with the predominance of AmpC rather than ESBL among hospitalized patients. In the current study, AmpC production was common and was more prevalent among inpatients. This is in line with Rehana et al. [14], who reported AmpC production in 118 UPEC isolates from western Uttar Pradesh, 73% of which were from hospitalized patients. Of the plasmid-mediated AmpC-positive isolates, CIT-type determinants were the most common (57.1%). These findings support the importance of healthcare-associated selection in AmpC-producing UPEC and are consistent with the inpatient predominance of AmpC observed in our study.

The inverse relationship between previous antibiotic use and AmpC production should, however, be interpreted with caution. It should not be considered evidence that antibiotic exposure protects against AmpC-producing infection. Pascual et al. [15] found AmpC-producing *E. coli* in 1.1% of over 21,000 clinical isolates; 73.8% of the evaluated cases had acquired AmpC mechanisms, and prior exposure to fluoroquinolones was an independent risk factor for AmpC infection (OR 2.6). Similarly, Lee et al. [16] reported that prior fluoroquinolone use (OR 4.05) and prior cephamycin use (OR 9.68) were independently associated with community-onset AmpC-producing Enterobacteriaceae UTI. In our study, antibiotic exposure was not recorded by antimicrobial class, and all isolates were already resistant. The observed inverse relationship may thus be due to the relative distribution of competing resistance phenotypes in a selected resistant population, especially as prior antibiotic use was strongly associated with ESBL production.

The difference in the distribution of ESBL and AmpC between outpatient and inpatient settings is an important finding. Both mechanisms are involved in cephalosporin resistance, but their epidemiological associations may differ. The finding of ESBL+AmpC and AmpC+MBL co-production is another example of the complexity of β -lactam resistance in UPEC. The limited number of co-producing isolates, however, did not allow for meaningful analysis of clinical predictors. Larger cohorts with molecular characterization would help determine whether specific resistance genes, plasmids, or clonal lineages contribute to these differences.

The clinical relevance of the association between previous antibiotic use and ESBL production is of particular interest. Our results, along with those of Kumar et al. [11] and Goyal et al. [12], suggest that recent antimicrobial use should be taken into account when choosing empirical treatment for suspected UTI, even in outpatients. However, outpatient presentation does not imply lack of healthcare exposure, as prior hospitalization, recurrent infection, and recent antimicrobial use can all affect the likelihood of resistant UPEC.

There are some limitations to this study. The relatively small sample size and single-centre design resulted in wide confidence intervals and limited the number of variables that could be included in the multivariable models. The analysis was restricted to resistant UPEC, and therefore the associations reported are for ESBL and AmpC phenotypes within a resistant population and should not be interpreted as population-level risk factors for resistant UTI. Antibiotic exposure was not analysed by drug class, duration, or cumulative exposure, which may be relevant to AmpC-associated risk. Furthermore, β -lactamase classification was based mainly on phenotypic methods, and the small number of co-producing isolates did not allow for further subgroup analysis.

CONCLUSION

ESBL- and AmpC-producing UPEC showed distinct epidemiological patterns in this cohort. ESBL production was independently associated with outpatient status and prior antibiotic exposure, whereas AmpC production was more frequent among inpatients. The inverse association between prior antibiotic exposure and AmpC positivity should be interpreted within the context of the selected resistant study population rather than as a protective relationship. These findings support phenotype-specific surveillance and highlight the importance of recent antibiotic and healthcare exposure when evaluating patients with UTI. Larger multicentre studies incorporating susceptible comparator isolates, antimicrobial-class-specific exposure data, and molecular characterization are required to validate these observations.

DECLARATIONS

Ethics Approval and Consent to Participate

The study was conducted after approval from the institutional ethics committee. Written informed consent was obtained from all eligible participants before enrollment.

Consent for Publication

Not applicable.

Competing Interests

The authors declare that they have no competing interests.

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No specific funding was received for this study.

Authors' Contributions

Both authors contributed to the conception and design of the study, data collection, analysis and interpretation of the findings, manuscript preparation, critical revision, and approval of the final manuscript.

Data Availability

The data supporting the findings of this study are available from the corresponding author upon reasonable request, subject to applicable ethical and institutional restrictions.

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AI Use Disclosure

The authors declare that no generative artificial intelligence tools were used to generate or substantially modify the scientific content of this manuscript.

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