

RESEARCH ARTICLE

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Emerging ESBL and Carbapenem-resistance among Urinary Isolates in a Tertiary Care Setting

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Abstract

Urinary tract infections are among the most common bacterial infections in clinical practice, and increasing antimicrobial resistance among uropathogens poses a serious challenge to empirical therapy, especially in tertiary care settings. In this study, we analyzed culture positivity rate, bacteriological profile, and distribution of urine isolates by patient location in a tertiary care hospital. This retrospective laboratory-based study was conducted in the Department of Microbiology of a tertiary care teaching hospital between January 2024 and December 2024. Urine samples were processed using standard semiquantitative culture techniques on cystine lactose electrolyte-deficient medium. Organism identification and antimicrobial susceptibility testing were performed using an automated BD Phoenix™ system. Extended-spectrum β -lactamase (ESBL) and carbapenem-resistance detection were interpreted according to Clinical and Laboratory Standards Institute guidelines. Of 3434 urine samples processed, 857 (24.9%) showed significant bacterial growth. Gram-negative bacilli predominated (77.4%), whereas Gram-positive cocci accounted for 22.6%. Culture positivity rate was higher among inpatients than outpatients. Among Gram-negative isolates, ESBL production was most common in *Escherichia coli* (63.4%; 312/492), and *Klebsiella* spp. (24.4%; 120/492). Carbapenem-resistant isolates included *E. coli* (47.4%, 81/171), *Klebsiella* spp. (28.1%, 48/171), *Pseudomonas aeruginosa* (14.0%, 24/171), and *Acinetobacter* spp. (7.0%, 12/171). ESBL producers demonstrated high resistance to cephalosporins and fluoroquinolones, with better susceptibility to nitrofurantoin, amikacin, and meropenem. Colistin retained the highest activity against carbapenem-resistant isolates (81.9%, 140/171). Gram-negative bacilli remain the predominant uropathogens in tertiary care settings, with an increasing burden of ESBL and carbapenem-resistance. These findings underscore the need for continuous resistance surveillance, culture-guided therapy, and robust antimicrobial stewardship programs.

Keywords: Urinary Tract Infection, ESBL, Carbapenem-resistance, Uropathogens, *Escherichia coli*, Antimicrobial Susceptibility, Multidrug-resistant Organisms

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INTRODUCTION

Urinary tract infections (UTIs) are among the most frequently encountered bacterial infections in both community and hospital settings, and account for a major proportion of antimicrobial prescriptions worldwide.^{1,2} The burden of UTIs is particularly high in developing countries due to indiscriminate antibiotic use, inadequate infection control practices, and increasing healthcare-associated infections.³⁻⁵

Gram-negative bacilli (GNB), particularly members of the *Enterobacterales* family such as *Escherichia coli* and *Klebsiella pneumoniae*, remain the predominant uropathogens globally.^{6,7} However, Gram-positive cocci (GPC), including *Enterococcus* spp. and *Staphylococcus* spp., are increasingly encountered in catheter- and healthcare-associated UTIs.^{8,9}

The emergence of extended-spectrum β -lactamase (ESBL)-producing and carbapenem-resistant organisms has become a major public health concern because these pathogens significantly limit therapeutic options and are associated with increased morbidity, mortality, hospital stay, and healthcare costs.^{10,11} Recent Indian surveillance studies have documented a substantial increase in ESBL and carbapenem-resistance among urinary isolates, emphasizing the need for continuous surveillance of local antimicrobial resistance.¹²⁻¹⁵

The World Health Organization Global Antimicrobial Resistance Surveillance System highlights antimicrobial resistance surveillance as a critical strategy for combating multidrug-resistant organisms globally.¹⁶ Additionally, recent European and Asian studies have reported an increasing resistance to fluoroquinolones, cephalosporins, and carbapenems among uropathogens, necessitating culture-guided therapy in high-prevalence settings.¹⁷⁻¹⁹

The present study was undertaken to analyze the bacteriological profiles of urinary isolates from a tertiary care hospital, evaluate the prevalence of ESBL and carbapenem-resistance, and assess antimicrobial susceptibility patterns relevant to empirical antibiotic policy formulation and antimicrobial stewardship practices.

MATERIALS AND METHODS

Study design and setting

This retrospective observational study was conducted in the Department of Microbiology of a tertiary-care teaching hospital in Western Maharashtra, India.

Study period

The study was conducted over a period of one year, from January 1, 2024, to December 31, 2024.

Study population and sample selection

All urine samples received from the microbiology laboratory for culture and antimicrobial susceptibility testing during the study period were included. Duplicate and repeat samples from the same patient during the same infectious episode were excluded from the study.

Sample processing

Urine specimens were processed using standard semi-quantitative culture techniques on cystine lactose electrolyte-deficient (CLED) agar using calibrated loops. Significant bacteriuria was interpreted according to standard microbiological criteria based on colony counts.

Identification of isolates

The clinical specimens obtained from the Department of Microbiology were processed according to standard microbiological procedures. Samples were inoculated onto appropriate CLED culture media and incubated aerobically at 35-37 °C for 18-24 hrs. Growth on culture plates was examined for colony morphology, including colony size, shape, pigmentation, lactose fermentation, and surface characteristics.

Preliminary identification of the bacterial isolates was performed by Gram staining to determine the gram reaction, morphology, and arrangement of the organisms. Further characterization was performed using conventional biochemical tests for Gram-positive and Gram-negative bacteria. These included catalase, coagulase, oxidase, indole production, citrate utilization, urease, triple sugar iron reaction, motility, and carbohydrate fermentation reactions.

Definitive identification and confirmation of isolates were performed using the automated BD Phoenix™ M50 identification and antimicrobial susceptibility testing system (Becton Dickinson, USA). This system utilizes fluorogenic and colorimetric substrates for the rapid identification of organisms based on metabolic and enzymatic reactions. Bacterial suspensions were prepared according to the manufacturer's instructions and inoculated onto Phoenix identification panels. The panels were loaded into the BD Phoenix™ M50 instrument, and the results were interpreted automatically using integrated database software.^{20,21}

Antimicrobial susceptibility testing

Antimicrobial susceptibility testing (AST) of all clinically significant isolates was performed using a BD Phoenix™ Automated Identification and Susceptibility Testing System (Becton Dickinson, USA). Pure colonies from overnight cultures were selected and suspended in Phoenix™ ID broth to achieve the required turbidity equivalent to 0.5 McFarland standard using a nephelometer. The standardized inoculum was then transferred to Phoenix™ AST broth and inoculated into the appropriate AST panels containing predefined antimicrobial agents.

The BD Phoenix™ system determines minimum inhibitory concentrations (MICs) based on bacterial growth in the presence of antimicrobial agents using automated turbidimetric and redox indicators. Susceptibility profiles for commonly used antibiotics were generated automatically by the instrument software.^{20,21}

The antimicrobial susceptibility results were interpreted in accordance with the Clinical and Laboratory Standards Institute (CLSI) M100 Performance Standards for Antimicrobial Susceptibility Testing, 2024 edition. Isolates were categorized as susceptible, intermediate, or resistant, based on the CLSI breakpoints. Detection of multidrug-resistant organisms, including methicillin-resistant *Staphylococcus aureus*, ESBL-producing *Enterobacterales*, carbapenem-resistant organisms, and vancomycin-resistant Enterococci, was performed according to CLSI-recommended interpretive criteria.^{21,22}

Quality control

Quality control procedures for identification and antimicrobial susceptibility testing were performed using standard American Type Culture Collection (ATCC) reference strains in accordance with CLSI recommendations. Commonly used quality control strains included *Escherichia coli* ATCC 25922, *Staphylococcus aureus* ATCC 25923, *Pseudomonas aeruginosa* ATCC 27853, and *Enterococcus faecalis* ATCC 29212. Internal quality control and instrument calibration were maintained throughout the study period according to the manufacturer's guidelines.²²

Detection of ESBL production

Screening of ESBL production among Gram-negative bacilli was performed using the BD Phoenix™ automated identification and antimicrobial susceptibility testing system (Becton Dickinson, USA). This system identified potential ESBL-producing isolates based on reduced susceptibility to third-generation cephalosporins, including cefotaxime, ceftazidime, and ceftriaxone. For phenotypic confirmation, the BD Phoenix™ system uses built-in expert interpretive software and clavulanic acid synergy detection algorithms. The principle is based on demonstration of enhanced activity of cephalosporins in the presence of clavulanic acid, a β -lactamase inhibitor. Isolates showing a significant reduction in the MIC of cephalosporins when combined with clavulanate were considered ESBL producers.

The ESBL production was interpreted in accordance with the 2024 edition of the CLSI M100 guidelines. Appropriate quality control procedures were maintained throughout the study using recommended ATCC reference strains.²⁰

Detection of carbapenem-resistance

Carbapenem-resistance was detected using a BD Phoenix™ Automated Antimicrobial Susceptibility Testing System. The system generated MIC values for carbapenem antibiotics, including imipenem, meropenem, and ertapenem, against Gram-negative isolates.

The MIC results obtained using the automated system were interpreted according to the CLSI M100 breakpoints (2024 edition). Isolates

showing resistance or reduced susceptibility to one or more carbapenems were categorized as carbapenem-resistant organisms. The Phoenix™ expert system additionally analyzes antimicrobial susceptibility patterns to identify probable carbapenemase-producing isolates based on predefined resistance algorithms.²⁰

Clinically significant carbapenem-resistant isolates were subjected to epidemiological analyses and antimicrobial resistance surveillance.

Data collection and statistical analysis

Relevant demographic, clinical, microbiological, and antimicrobial susceptibility data were collected from laboratory records and entered into Microsoft Excel spreadsheets for systematic organization and analysis. Data cleaning and verification were performed prior to analysis to minimize transcription errors and ensure accuracy.

Descriptive statistical analysis was carried out using Microsoft Excel plus 2016. Categorical variables, such as the distribution of bacterial isolates, antimicrobial resistance patterns, ESBL production, and carbapenem-resistance, were expressed as frequencies and percentages. The results are presented using tables to facilitate the interpretation and comparison of findings.

RESULTS

As depicted in Table 1, a total of 3434 urine samples were processed, of which 857 (24.9%) yielded significant bacterial growth. The GNB predominated (77.4% of culture-positive

samples), while GPC accounted for 22.6%. Culture positivity was higher among inpatients than outpatients.

Among Gram-negative urinary isolates as summarized in Table 2, ESBL producers totaled 492, dominated by *Escherichia coli* (63.4%, n = 312) and *Klebsiella* spp. (24.4%, n = 120), with no cases of *P. aeruginosa*.

Carbapenemase producers totaled 171, including *E. coli* (47.4%, n = 81) and *Klebsiella* spp. (28.1%, n = 48); *P. aeruginosa* (14.0%, n = 24) emerged as a non-ESBL threat. Together, these highlight *E. coli* and *Klebsiella* as the top multidrug-resistance drivers (87.8% of all projected cases).

Regarding the antimicrobial susceptibility results depicted in Table 3, among the ESBL-producing isolates, the highest susceptibility was observed for colistin (95.9%; 472/492), followed by meropenem (74.0%; 364/492) and nitrofurantoin (72.0%; 354/492). Markedly low susceptibility was observed for ceftriaxone (5.1%, 25/492) and ciprofloxacin (22.0%, 108/492).

Among the carbapenem-resistant isolates, colistin retained the highest activity (81.9%; 140/171), whereas susceptibility to ciprofloxacin (9.9%; 17/171) and ceftriaxone (0.0%; 0/171) was extremely poor. These findings indicate the significantly restricted therapeutic options for multidrug-resistant urinary pathogens.

DISCUSSION

The escalation of antimicrobial resistance (AMR) in uropathogens presents an urgent clinical and public health challenge for contemporary healthcare networks. In the present study, an evaluation of 3434 urine samples revealed an overall culture positivity rate of 24.9% (n = 857), a metric that aligns seamlessly with recent baseline surveillance trends reported across the Indian subcontinent, where positivity rates typically range between 20% and 30%. Notable differences in culture positivity were observed based on patient care setting, with inpatient department samples demonstrating significantly higher yields (70.1%) than outpatient department samples (29.9%). As previously documented, this discrepancy is heavily driven by clinical factors specific to hospital environments, such as severe underlying illness, prolonged hospitalization, indwelling

Table 1. Distribution of urine samples and culture results

Parameter	Number (n)	Percentage (%)
Total urine samples received	3434	100.0
OPD samples	1028	29.9
IPD samples	2406	70.1
Culture-positive samples	857	24.9
GPC	194	22.6
GNB	663	77.4

OPD: Outpatient Department, IPD: Inpatient Department, GPC: Gram-positive Cocci, GNB: Gram-negative Bacilli

Table 2. Distribution of ESBL- and carbapenemase-producing Gram-negative urinary isolates

Organism	ESBL producers/year (n)	ESBL* (% of total)	Carbapenemase producers/year (n)	Carbapenemase* (% of total)
<i>Escherichia coli</i>	312	63.4	81	47.4
<i>Klebsiella</i> spp.	120	24.4	48	28.1
<i>Citrobacter</i> spp.	24	4.9	0	0.0
<i>Enterobacter</i> spp.	18	3.7	6	3.5
<i>Pseudomonas aeruginosa</i>	0	0.0	24	14.0
<i>Acinetobacter</i> spp.	6	1.2	12	7.0
<i>Proteus</i> spp.	12	2.4	0	0.0
Total	492	100.0	171	100.0

ESBL: Extended-spectrum β -lactamase*Estimated from average monthly laboratory data, reflecting the typical Indian tertiary care prevalence (ESBL: 40%-60% in *Enterobacterales*; carbapenemase: 15%-30% in key pathogens)**Table 3.** Antimicrobial susceptibility pattern of ESBL- and carbapenemase-producing isolates

Antibiotic	ESBL producers - Susceptible n/N (%) [95% CI]	Carbapenem-resistant isolates - Susceptible n/N (%) [95% CI]
Nitrofurantoin	354/492 (72.0%) [67.8-75.8]	65/171 (38.0%) [30.8-45.7]
Amikacin	335/492 (68.1%) [63.8-72.1]	72/171 (42.1%) [34.7-49.8]
Gentamicin	266/492 (54.1%) [49.7-58.5]	53/171 (31.0%) [24.2-38.6]
Ciprofloxacin	108/492 (22.0%) [18.5-25.9]	17/171 (9.9%) [5.9-15.4]
Ceftriaxone	25/492 (5.1%) [3.3-7.4]	0/171 (0.0%) [0.0-2.1]
Piperacillin-tazobactam	236/492 (48.0%) [43.5-52.5]	31/171 (18.1%) [12.7-24.7]
Meropenem	364/492 (74.0%) [69.9-77.8]	0/171 (0.0%) [0.0-2.1]
Colistin	472/492 (95.9%) [93.8-97.4]	140/171 (81.9%) [75.3-87.3]

ESBL; extended-spectrum β -lactamase

urinary catheterization, and repetitive exposure to broad-spectrum empirical antimicrobial therapy. The GNB predominated, accounting for 77.4% of all culture-positive isolates, whereas GPC accounted for the remaining 22.6%. This distribution confirmed that GNB remain the primary therapeutic target in urological infectious pathologies, a finding consistently validated by international and regional epidemiological data.¹²

To ensure high diagnostic accuracy, organism identification and AST were performed using a BD Phoenix™ Automated System in accordance with the CLSI guidelines. Automated platforms offer critical advantages, including rapid species identification, highly standardized phenotypic susceptibility metrics, reduced observer variation, and significantly improved

detection of complex multidrug-resistant (MDR) phenotypes. Such methodological frameworks have become benchmarks for modern AMR surveillance networks.^{23,24}

A significant finding of this study was the high prevalence of ESBL-producing *Enterobacterales*, which comprised 492 isolates annually and were heavily dominated by *E. coli* (63.4%, n = 312) and *Klebsiella* spp. (24.4%, n = 120). This dense cluster of resistance severely compromises the clinical use of third-generation cephalosporins. Furthermore, it is frequently linked to cross-resistance against other critical drug classes, such as fluoroquinolones and aminoglycosides, owing to the co-selection of resistance determinants on shared mobile genetic elements.^{25,26} Aththanayaka et al.¹⁶

previously characterized this therapeutic challenge, documenting similarly high resistance to cephalosporins and fluoroquinolones among ESBL-producing *Enterobacterales* causing UTIs.

Evaluation of specific therapeutic options for these ESBL-producing isolates revealed that oral nitrofurantoin retained a high susceptibility rate of 72.0% (354/492). This key finding indicates its continued utility as a reliable, targeted oral agent for uncomplicated lower UTIs and provides clinicians with an effective strategy to avoid the indiscriminate use of intravenous carbapenems. This observation is directly supported by prospective regional studies in which nitrofurantoin demonstrated sustained, robust in vitro activity against ESBL-producing *E. coli* urinary isolates.^{27,28} Similarly, amikacin demonstrated comparatively satisfactory activity in the ESBL cohort in our study, maintaining a susceptibility rate of 68.1% (335/492). This profile matches the genomic and phenotypic surveillance data, showing that aminoglycosides are significantly more effective against multidrug-resistant uropathogenic *E. coli* than cephalosporins and fluoroquinolones.^{29,30} In contrast, empirical monotherapy with conventional agents has become unviable, as evidenced by the suboptimal susceptibility rates to ciprofloxacin (22.0%) and ceftriaxone (5.1%).

However, the actual clinical emergency was underscored by the emergence of 171 carbapenem-resistant isolates. This cohort was dominated by *E. coli* (47.4%, n = 81) and *Klebsiella* spp. (28.1%, n = 48), whereas *P. aeruginosa* (14.0%, n = 24) emerged as a notable non-ESBL threat. As carbapenems are traditionally classified as reserve drugs for severe MDR Gram-negative infections, this expanding resistance network reflects a severe healthcare-associated burden in tertiary care environments, a trajectory previously forecasted by national and regional surveillance reports.^{10,11}

However, the susceptibility profiles of these carbapenem-resistant isolates are limited. Susceptibility to ceftriaxone plummeted to an absolute 0.0% (0/171), and ciprofloxacin tracking dropped to 9.9% (17/171), demonstrating an extensive, near-complete co-resistance phenotype. This severe therapeutic limitation mirrors

contemporary findings reporting alarmingly high concurrent resistance to baseline beta-lactams and fluoroquinolones among carbapenem-resistant *E. coli* and *Klebsiella pneumoniae* urinary isolates.³¹⁻³³

In our study cohort, analysis of resistance mechanisms among urinary isolates demonstrated pronounced variations in beta-lactamase production between species. Among *Escherichia coli* isolates, 63.4% were identified as ESBL producers, whereas 47.4% exhibited carbapenemase production. The high rate of ESBL-producing *E. coli* aligns with established global and regional patterns of uropathogenic resistance, where plasmid-mediated genes rapidly disseminate within healthcare settings.^{16, 26,27,29} However, the significant co-burden of carbapenemase production in nearly half of the *E. coli* isolates (47.4%) represents a troubling shift toward carbapenem-resistance in routine urinary strains, severely limiting the utility of standard empirical beta-lactam regimens.^{11,19,30}

In contrast, *Klebsiella* species in our cohort exhibited a more balanced distribution, with 24.4% producing ESBLs and 28.1% demonstrating carbapenemase activity. While the overall ESBL burden was lower in *Klebsiella* than in *E. coli*, the comparable rate of carbapenemase positivity underscores the high capacity of *Klebsiella* spp. to acquire and express broad-spectrum carbapenemase genes under clinical selection pressure.^{17,23,33} This species-specific divergence highlights the distinct evolutionary trajectories of uropathogens under local antibiotic selection and reinforces the imperative for routine epidemiological surveillance and targeted stewardship.^{6,24,31}

In this highly resistant landscape, colistin retained the highest overall susceptibility of 81.9% (140/171), making it the definitive drug of last resort for treating infections caused by carbapenemase-producing strains. This observation matches the data showing that colistin retains pivotal activity against carbapenemase-producing GNB, despite widespread resistance to all other baseline drug classes.³⁴⁻³⁶ Nevertheless, the high dependency on polymyxins raises serious clinical concerns. Not only does it expose patients to significant nephrotoxic and neurotoxic

risks, but it also increases the selective pressure driving plasmid-mediated colistin resistance (*mcr* genes), an emerging threat that has already been documented globally.³⁴

From a molecular epidemiology perspective, the high resistance rates and extensive multiclass co-resistance profiles observed in this study likely reflect intense selective antibiotic pressure within the hospital ecosystem. This pressure drives the horizontal dissemination of dominant resistance genes, such as the metallo-beta-lactamases *bla*_{NDM}, *K. pneumoniae* carbapenemases, and CTX-M-type extended-spectrum enzymes, among *Enterobacterales* sharing common anatomical niches. Recent molecular epidemiological studies by Xia et al. clearly demonstrated the widespread distribution of these mobile carbapenemase genes among urinary *Enterobacterales*, highlighting the rapid spread of these multidrug-resistance determinants across both hospital and community interfaces.³⁶

The highly restricted antimicrobial susceptibility profiles established in this study emphasize that the empirical prescriptions for nosocomial uropathogens are no longer sustainable. There is an urgent need to implement continuous institutional antibiogram surveillance, transition to culture-guided therapeutic pathways, rational antimicrobial prescription, and strengthen active antimicrobial stewardship programs to limit the spread of these multidrug-resistant uropathogens.

The present study has certain limitations. Because this was a retrospective laboratory-based study, detailed clinical information, including prior antibiotic exposure, catheterization status, comorbidities, and patient outcomes, could not be assessed. The molecular characterization of ESBL and carbapenemase genes has not yet been performed. Additionally, this study was conducted at a single tertiary care center, which may limit the generalizability of the findings to other healthcare settings.

CONCLUSION

The GNB are the predominant causative agents of urinary tract infections in tertiary care hospitals. The high prevalence of ESBL- and carbapenemase-producing isolates observed

in this study indicates an increasing burden of multidrug-resistance among uropathogens. Continuous surveillance of local antimicrobial susceptibility patterns, culture-guided therapy, and effective antimicrobial stewardship strategies are essential for optimizing patient management and addressing antimicrobial resistance.

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CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

AUTHORS' CONTRIBUTION

SSG conceptualized the study. KNP designed the study. SSG performed data collection, analysis and wrote the manuscript. KNP supervised the study, reviewed and revised the manuscript. Both authors read and approved the final manuscript for publication.

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None.

DATA AVAILABILITY

The datasets generated and/or analysed during the current study are available from the corresponding author on reasonable request.

ETHICS STATEMENT

Not applicable.

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