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Original Research Article

PROSPECTIVE ANALYSIS OF EXTENDED-SPECTRUM BETA-LACTAMASE (ESBL) PRODUCING ENTEROBACTERIACEAE ISOLATED FROM COMMUNITY AND HOSPITAL SETTINGS

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ABSTRACT

Background: Extended-spectrum beta-lactamase (ESBL) producing Enterobacteriaceae pose a growing challenge in both hospital and community settings due to their ability to hydrolyze broad-spectrum cephalosporins, leading to limited treatment options and higher morbidity.

Aim: To evaluate the prevalence, species distribution, antibiotic resistance profiles, and associated risk factors of ESBL-producing Enterobacteriaceae isolated from community- and hospital-acquired infections. **Material and Methods:** This prospective observational study was conducted in the Department of Microbiology at a tertiary care teaching hospital. A total of 110 non-duplicate Enterobacteriaceae isolates were obtained from various clinical specimens and categorized into community-acquired (n = 55) and hospital-acquired (n = 55) groups. Standard microbiological techniques were used for identification, and ESBL screening was done using ceftazidime and cefotaxime discs. Confirmatory testing was performed using the combined disc method. Antibiotic susceptibility was assessed using the Kirby-Bauer disk diffusion method per CLSI guidelines. Risk factor data were collected and analyzed statistically using SPSS v26.0. **Result:** Urine was the most common specimen source in both groups. Escherichia coli was the predominant species in both community (50.91%) and hospital (45.45%) settings. ESBL production was significantly higher in hospital-acquired isolates (56.36%) compared to community-acquired ones (29.09%) ($p = 0.006$). All ESBL-positive isolates showed 100% resistance to cefotaxime and ceftazidime. High resistance was noted for ciprofloxacin (80.85%) and gentamicin (61.70%), while lower resistance was seen for amikacin (23.40%) and imipenem (6.38%). Significant risk factors included prior antibiotic use ($p < 0.001$), ICU stay >5 days ($p = 0.001$), indwelling catheterization ($p = 0.002$), diabetes ($p = 0.042$), and recent hospitalization ($p < 0.001$). **Conclusion:** A significantly higher burden of ESBL-producing Enterobacteriaceae was observed in hospital settings. Resistance to multiple antibiotics and association with key clinical risk factors highlight the need for robust infection control, antibiotic stewardship, and routine microbiological surveillance in both hospital and community environments.

INTRODUCTION

The global surge in antimicrobial resistance has emerged as a critical threat to public health, with extended-spectrum beta-lactamase (ESBL) producing Enterobacteriaceae representing one of the most alarming forms of resistance. These organisms are capable of hydrolyzing a wide range of beta-lactam antibiotics, including third-generation cephalosporins, rendering many frontline antimicrobial therapies ineffective. Over the last two decades, the epidemiological landscape of ESBL-producing bacteria has shifted significantly, extending beyond hospital boundaries into community environments, with consequences that challenge current diagnostic, therapeutic, and infection control protocols.[1]

ESBLs are a diverse group of enzymes that have evolved to circumvent the bactericidal action of beta-

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lactam antibiotics, mainly penicillins, cephalosporins, and aztreonam. These enzymes are most commonly found in Enterobacteriaceae, particularly in Escherichia coli and Klebsiella pneumoniae. The increasing prevalence of these organisms has been attributed to several factors, including selective antibiotic pressure, plasmid-mediated gene transfer, and inadequate infection control practices in both hospital and non-hospital settings.[2] Compounding this issue is the co-resistance observed in ESBL-producing strains, where resistance to fluoroquinolones, aminoglycosides, and trimethoprim-sulfamethoxazole is frequently encountered, significantly limiting treatment options.

The clinical implications of infections caused by ESBL producers are severe, often resulting in delays in the initiation of effective antimicrobial therapy. Empiric treatment failure is a common scenario due to the difficulty in predicting ESBL production prior to culture results, and such delays have been associated with increased morbidity and mortality, particularly in bloodstream infections and sepsis.[3] Inappropriate empirical therapy can not only worsen patient outcomes but also fuel the selection of more resistant organisms. Consequently, identifying ESBL-producing isolates early and accurately is vital for the initiation of appropriate antibiotic therapy and the reduction of nosocomial transmission.

Carbapenems have traditionally been considered the drugs of choice for treating serious infections caused by ESBL-producing organisms due to their broad-spectrum activity and resistance to hydrolysis by most ESBL enzymes. However, the increasing use of carbapenems has led to the emergence of carbapenem-resistant Enterobacteriaceae (CRE), raising concerns about the sustainability of this treatment strategy.[4] This has necessitated the reevaluation of carbapenem-sparing regimens and the use of alternative agents such as beta-lactam/beta-lactamase inhibitor combinations, fosfomycin, and newer beta-lactamase inhibitor compounds. The choice of therapy must consider local susceptibility patterns, infection severity, and the patient's clinical status.

From an epidemiological standpoint, the spread of ESBL-producing bacteria is not confined to healthcare settings alone. Community-acquired infections due to ESBLs are increasingly being reported, particularly in urinary tract infections and gastrointestinal colonization. Studies have shown that risk factors for acquiring these organisms in the community include recent antibiotic use, travel to high-prevalence regions, prior hospitalization, and contact with healthcare environments. Additionally, there is growing evidence of zoonotic transmission and environmental reservoirs playing a role in the dissemination of resistance genes, blurring the lines between human, animal, and environmental health domains.[5]

In animals, particularly in livestock and poultry, the use of antibiotics as growth promoters and for prophylaxis has contributed to the selection of ESBL-producing strains. These organisms may be transmitted to humans through direct contact, consumption of undercooked meat, or environmental exposure. Several studies have documented the detection of ESBL genes in animal isolates, raising concerns over food chain-mediated transmission and highlighting the importance of a One Health approach to address this issue holistically.[6]

The molecular characteristics of ESBLs have also evolved over time. Early classifications based on substrate profiles and inhibition patterns have now been expanded to include functional and genetic characteristics. The most common ESBL enzymes belong to the TEM, SHV, and CTX-M families, with CTX-M variants now considered the most widespread globally. Understanding the functional classification and molecular diversity of these enzymes is crucial for designing effective diagnostics and predicting resistance patterns. The updated functional classification system facilitates a more structured understanding of the types and behavior of these enzymes, which is critical for clinical microbiologists and infectious disease specialists.[7]

The challenges in controlling the spread of ESBL-producing Enterobacteriaceae are particularly acute in developing countries, where limited laboratory infrastructure, unregulated antibiotic use, lack of antimicrobial stewardship programs, and insufficient infection control measures prevail. The widespread availability of antibiotics over the counter, coupled with self-medication practices, has further accelerated the emergence and spread of resistance. In many settings, the lack of routine phenotypic and genotypic surveillance means that outbreaks go unnoticed until they reach epidemic proportions.[8] Therefore, strengthening microbiological surveillance systems, regulating antimicrobial usage, and improving infection prevention strategies are urgently needed to mitigate the threat posed by these multidrug-resistant organisms.

MATERIALS AND METHODS

This prospective observational study was conducted in the Department of Microbiology at a tertiary care teaching hospital, following approval from the Institutional Ethics Committee. A total of 110 non-duplicate clinical isolates of Enterobacteriaceae were collected from both community-acquired and hospital-acquired infections. These isolates were obtained from various clinical specimens including urine, blood, pus, sputum, and wound swabs received in the microbiology laboratory. Patients were categorized into two groups: community-acquired infection (n = 55) and hospital-acquired infection (n = 55), based on clinical history and hospitalization status.

Standard microbiological techniques were used for the isolation and identification of Enterobacteriaceae, including colony morphology, Gram staining, and a

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battery of biochemical tests such as triple sugar iron (TSI), citrate, urease, and motility-indole-ornithine (MIO) tests. Antimicrobial susceptibility testing was performed using the Kirby-Bauer disk diffusion method on Mueller-Hinton agar as per Clinical and Laboratory Standards Institute (CLSI) guidelines.

Screening for potential ESBL producers was done using ceftazidime (30 µg) and cefotaxime (30 µg) disks. Isolates showing a zone of inhibition of ≤22 mm for ceftazidime or ≤27 mm for cefotaxime were considered potential ESBL producers. Confirmatory testing for ESBL production was carried out using the combined disk method with ceftazidime (30 µg) and ceftazidime-clavulanic acid (30/10 µg) discs. An increase in zone diameter of ≥5 mm in the presence of clavulanic acid was considered indicative of ESBL production.

Demographic details, clinical data, and relevant risk factors such as prior antibiotic use, comorbidities, hospitalization history, and invasive device usage were recorded for each patient. Data were entered and analyzed using SPSS version 26.0. The prevalence of ESBL producers was compared between the two groups using Chi-square test or Fisher's exact test, with p-values <0.05 considered statistically significant.

RESULTS

Table 1: Distribution of Enterobacteriaceae Isolates by Clinical Sample Source

The clinical specimens revealed that urine was the most common source of Enterobacteriaceae isolates in both groups, accounting for 40.00% of community-acquired cases and 32.73% of hospital-acquired infections. Blood was the second most frequent source, with 18.18% in the community group and 27.27% in the hospital group. Other sources such as pus/wound swabs, sputum, and miscellaneous specimens (e.g., catheter tips, ascitic fluid) contributed to a smaller share. The comparison of distribution between the two groups did not reveal any statistically significant difference across the specimen types, as all p-values were >0.05. This indicates that the source of infection was similar in both settings, with no preferential isolation from a particular site.

Table 2: Species-Wise Distribution of Enterobacteriaceae Isolates

Among the isolates, Escherichia coli was the most predominant species in both community-acquired (50.91%) and hospital-acquired infections (45.45%), followed by Klebsiella pneumoniae (27.27% vs. 30.91%). Less frequently isolated organisms included Proteus mirabilis, Enterobacter cloacae, and Citrobacter freundii, with comparable percentages across both groups. None of the differences in bacterial distribution between the two settings reached statistical significance ($p > 0.05$ for all comparisons), suggesting that the species distribution of Enterobacteriaceae was relatively uniform across community and hospital environments.

Table 3: ESBL Positivity Among Enterobacteriaceae Isolates

A statistically significant difference in ESBL production was observed between community and hospital groups ($p = 0.006$). ESBL-producing organisms were considerably more frequent in hospital-acquired infections (56.36%) compared to community-acquired ones (29.09%). This underscores the higher burden of multidrug resistance in nosocomial settings, likely attributed to increased antibiotic pressure, longer patient stay, and frequent use of invasive devices in hospitals. The higher ESBL prevalence in hospitalized patients necessitates strict infection control and antimicrobial stewardship practices.

Table 4: Antibiotic Resistance Pattern in ESBL Positive Isolates

All 47 ESBL-producing isolates demonstrated 100% resistance to cefotaxime and ceftazidime, which is consistent with the defining feature of ESBLs—hydrolysis of extended-spectrum cephalosporins. High resistance was also noted to ciprofloxacin (80.85%) and gentamicin (61.70%), reflecting limited treatment options. On the other hand, lower resistance rates were observed for amikacin (23.40%) and piperacillin-tazobactam (38.30%), suggesting partial retained sensitivity. Imipenem showed the highest efficacy, with only 6.38% resistance, indicating that carbapenems remain a reliable last-resort option for ESBL infections, although resistance trends must be closely monitored.

Table 5: Risk Factors Associated with ESBL Positivity

Several significant risk factors were associated with ESBL positivity. Prior antibiotic use was highly predictive (87.23% vs. 41.27%; $p < 0.001$), reinforcing the role of antibiotic overuse in resistance emergence. Other significant predictors included ICU stay >5 days ($p = 0.001$), indwelling catheterization ($p = 0.002$), diabetes mellitus ($p = 0.042$), and recent hospitalization within 90 days ($p < 0.001$). These findings align with global trends where comorbidities, invasive interventions, and healthcare exposure contribute substantially to colonization or infection with multidrug-resistant organisms. This highlights the importance of identifying and managing these risk factors to reduce ESBL incidence.

Table 1: Distribution of Enterobacteriaceae Isolates by Clinical Sample Source (n = 110)

Sample Type	Community-Acquired (n = 55)	Hospital-Acquired (n = 55)	p-value
Urine	22 (40.00%)	18 (32.73%)	0.422
Blood	10 (18.18%)	15 (27.27%)	0.260
Pus/Wound Swab	8 (14.55%)	11 (20.00%)	0.444
Sputum	9 (16.36%)	7 (12.73%)	0.589

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Others	6 (10.91%)	4 (7.27%)	0.509

Table 2: Species-Wise Distribution of Enterobacteriaceae Isolates

Bacterial Species	Community-Acquired (n = 55)	Hospital-Acquired (n = 55)	p-value
Escherichia coli	28 (50.91%)	25 (45.45%)	0.563
Klebsiella pneumoniae	15 (27.27%)	17 (30.91%)	0.681
Proteus mirabilis	5 (9.09%)	6 (10.91%)	0.749
Enterobacter cloacae	4 (7.27%)	5 (9.09%)	0.725
Citrobacter freundii	3 (5.45%)	2 (3.64%)	0.645

Table 3: ESBL Positivity Among Enterobacteriaceae Isolates

Infection Type	ESBL Positive (n)	ESBL Negative (n)	p-value
Community-Acquired	16 (29.09%)	39 (70.91%)	0.006
Hospital-Acquired	31 (56.36%)	24 (43.64%)	

Table 4: Antibiotic Resistance Pattern in ESBL Positive Isolates (n = 47)

Antibiotic	Resistant Isolates (n)	Resistance (%)
Cefotaxime	47	100.00%
Ceftazidime	47	100.00%
Ciprofloxacin	38	80.85%
Gentamicin	29	61.70%
Piperacillin-Tazobactam	18	38.30%
Imipenem	3	6.38%
Amikacin	11	23.40%

Table 5: Risk Factors Associated with ESBL Positivity

Risk Factor	ESBL Positive (n = 47)	ESBL Negative (n = 63)	p-value
Prior Antibiotic Use	41 (87.23%)	26 (41.27%)	<0.001
ICU Stay > 5 Days	29 (61.70%)	18 (28.57%)	0.001
Indwelling Catheterization	26 (55.32%)	17 (26.98%)	0.002
Diabetes Mellitus	14 (29.79%)	9 (14.29%)	0.042
Recent Hospitalization (<90 days)	33 (70.21%)	15 (23.81%)	<0.001

DISCUSSION

In this prospective study involving 110 clinical isolates of Enterobacteriaceae, we evaluated distribution patterns, ESBL production, antibiotic resistance profiles, and associated risk factors across community and hospital settings. Our study found that urine was the most frequent specimen source, accounting for 40.00% in community-acquired cases and 32.73% in hospital-acquired infections. Blood was the second most common, with 18.18% and 27.27%, respectively. These findings are consistent with those reported by Guzmán-Blanco et al. (2014),[9] who found urine to be the most common site of Enterobacteriaceae isolation (41–46%) in nosocomial cases across Latin America. Similarly, Peirano and Pitout (2019),[10] documented urinary isolates accounting for over 45% of both ESBL and non-ESBL cases in community settings. The lack of statistical difference ($p > 0.05$) in specimen distribution between the groups in our study supports the growing overlap in infection patterns across healthcare and community environments.

In terms of species, Escherichia coli predominated in both settings (50.91% community, 45.45% hospital), followed by Klebsiella pneumoniae (27.27% and 30.91%, respectively). This pattern matches reports by Woerther et al. (2013),[11] who highlighted E. coli, particularly CTX-M-producing strains, as the leading ESBL producers in both hospital and community settings globally. In contrast, Park et al. (2012),[12] reported slightly higher dominance of Klebsiella spp. in U.S. hospital outbreaks (up to 45%), which suggests regional variability. Our data further suggest that the species distribution of ESBL-producing Enterobacteriaceae is now uniform across care settings, an observation also echoed by Ahmed et al. (2019),[13] in their systematic review across South Asia.

A significantly higher ESBL positivity rate was observed in hospital-acquired isolates (56.36%) compared to community-acquired ones (29.09%) in our study ($p = 0.006$). These findings are similar to those by Rahman et al. (2018),[14] who reported ESBL rates of 55–70% in hospital isolates and 25–30% in community strains across Asia. Lee et al. (2006)[15] also observed a higher ESBL incidence in nosocomial infections (48.1%) versus community (22.3%) in their cohort study. Our 29.09% community prevalence is slightly higher than the 18–25% range reported by Guzmán-Blanco et al. (2014),[9] and Peirano and Pitout (2019),[10] suggesting a rising trend of community transmission, possibly due to over-the-counter antibiotic use and poor sanitation. This reinforces the need for wider surveillance programs beyond hospital boundaries.

Among the 47 ESBL-producing isolates in our study, resistance to cefotaxime and ceftazidime was 100%, which is consistent with ESBL mechanisms. Ciprofloxacin resistance was observed in 80.85% of isolates, gentamicin in 61.70%, and piperacillin-tazobactam in 38.30%. Notably, only 6.38% of isolates were resistant to imipenem, indicating its continued efficacy. In comparison, Pana and Zaoutis

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(2018),[16] documented ciprofloxacin resistance of 73% and gentamicin resistance of 55–65% among ESBL-producing strains. Park et al. (2012),[12] reported a higher rate of resistance to piperacillin-tazobactam (around 50%), whereas Peirano and Pitout (2019),[10] found lower rates (~25%), indicating variability in local resistance patterns. Our amikacin resistance rate of 23.40% was also comparable to the 20–28% range reported in Ahmed et al. (2019).[13] These findings affirm that carbapenems remain effective for serious ESBL infections, although emerging resistance mandates cautious use.

Significant risk factors identified in our study included prior antibiotic use (87.23% in ESBL-positive vs. 41.27% in ESBL-negative, $p < 0.001$), ICU stay >5 days (61.70%, $p = 0.001$), indwelling catheterization (55.32%, $p = 0.002$), diabetes mellitus (29.79%, $p = 0.042$), and recent hospitalization within 90 days (70.21%, $p < 0.001$). These findings closely mirror the results of Lee et al. (2006),[15] who reported prior antibiotic exposure (81%), ICU admission (58%), and catheter use (62%) as independent predictors of ESBL infections. Guzmán-Blanco et al. (2014),[9] also identified recent hospitalization and comorbidities such as diabetes as key contributors to resistance. Tiwaskar et al. (2024),[17] emphasized that these risk factors, especially antibiotic overuse and prolonged hospital stay, are driving the silent epidemic of antimicrobial resistance, making prevention strategies urgent.

CONCLUSION

This study highlights a significantly higher prevalence of ESBL-producing Enterobacteriaceae in hospital-acquired infections compared to community-acquired cases, with Escherichia coli being the most common isolate. High resistance rates to commonly used antibiotics and multiple associated risk factors underscore the need for strict infection control, rational antibiotic use, and routine surveillance. Carbapenems remain effective but must be preserved through stewardship programs. Proactive measures are essential to contain the spread of ESBLs in both healthcare and community settings.

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