e-ISSN: 0976-822X, p-ISSN:2961-6042

Available online on http://www.ijcpr.com/

International Journal of Current Pharmaceutical Review and Research 2025; 17(9); 1321-1323

Original Research Article

Antimicrobial Resistance Patterns and Clinical Implications of Extended-Spectrum Beta-Lactamase-Producing Gram-Negative Bacilli in Neonatal Sepsis: Evidence from a Kanpur Cohort

Kayyum Khan[1], Mohd Mohsin[2], Arpit Goel[3], Waqas Alauddin[4]

[1]Assistant Professor, Department of Microbiology, Naraina Medical College and Research Centre, Kanpur, India

[2]Assistant Professor, Department of Pediatrics, Naraina Medical College and Research Centre, Kanpur, India

[3]Assistant Professor, Department of Pediatrics, Naraina Medical College and Research Centre, Kanpur, India

[4]Assistant Professor, Department of Physiology, Naraina Medical College and Research Centre, Kanpur, India

Received: 01-06-2025 / Revised: 15-07-2025 / Accepted: 21-08-2025

Corresponding author: Dr. Arpit Goel

Conflict of interest: Nil

Abstract

Background: The rising prevalence of extended-spectrum beta-lactamase (ESBL)-producing Gram-negative bacteria poses a major challenge in neonatal septicemia, limiting therapeutic options and worsening outcomes. Evidence from semi-urban areas of northern India is scarce. This study explored the antimicrobial resistance patterns and clinical consequences of ESBL-producing Gram-negative bacilli in neonates with sepsis in Kanpur, India.

Methods: A prospective observational study was conducted between January and June 2025 in the neonatal intensive care unit (NICU) of a tertiary hospital in Kanpur. Blood cultures from neonates with suspected sepsis were processed using automated systems, and isolates were identified with standard biochemical tests and VITEK-2. Antimicrobial susceptibility was determined according to Clinical and Laboratory Standards Institute (CLSI) 2018 guidelines, with phenotypic confirmation of ESBL production. Clinical parameters, including NICU stay, ventilator use, and mortality, were compared between ESBL-positive and ESBL-negative infections.

Results: Of 500 cultures, 300 (60%) yielded growth, including 180 Gram-negative bacilli. Klebsiella spp. (42.2%) and Escherichia coli (36.6%) predominated. ESBL production was confirmed in 40 isolates (22.2%). These isolates demonstrated extensive resistance to third-generation cephalosporins (>90%), aztreonam (75%), and carbapenems (65%). Resistance to amikacin (28%) and colistin (<10%) was relatively lower. Clinically, neonates with ESBL-positive infections had longer NICU stays (18 vs 11 days), greater ventilator requirement (40% vs 22%), and higher mortality (28% vs 15%) compared with ESBL-negative cases ($p<0.05$).

Conclusion: ESBL-producing Gram-negative organisms significantly contribute to neonatal sepsis in Kanpur, with alarming resistance patterns and poorer outcomes. Strengthened antimicrobial stewardship, early detection, and rational empiric therapy are urgently required in NICUs.

Keywords: Extended-Spectrum Beta-Lactamase (ESBL), Neonatal Sepsis, Gram-Negative Bacilli, Antimicrobial Resistance.

Introduction

Neonatal sepsis continues to be a critical cause of morbidity and mortality, particularly in low- and middle-income countries where overcrowding, limited infrastructure, and unregulated antibiotic use exacerbate the problem [1]. The rapid emergence of antimicrobial resistance further complicates management. Among resistant organisms, ESBL-producing Gram-negative bacilli are of prime concern because of their ability to inactivate penicillins, third-generation cephalosporins, and aztreonam [2]. Outbreaks of ESBL-producing pathogens in NICUs have been linked to delayed initiation of effective antibiotics, prolonged hospital stays, increased costs, and higher case fatality rates [3,4]. Many ESBL-producing strains also carry plasmids conferring resistance to aminoglycosides and fluoroquinolones, restricting therapeutic choices to

last-resort agents such as carbapenems and colistin [5,6]. While studies from large metropolitan centers in India document a growing ESBL burden [7,8], evidence from semi-urban regions such as Kanpur remains sparse. Local surveillance is essential to guide empiric therapy and optimize neonatal care. This study aimed to characterize the resistance profiles of ESBL-producing Gram-negative organisms and assess associated clinical outcomes in neonates with septicemia admitted to a tertiary NICU in Kanpur.

Materials and Methods

Study Design and Population: A prospective observational study was performed at the NICU of a tertiary teaching hospital in Kanpur from January and June 2025. After written informed consent was secured from parents or guardians. All neonates with suspected sepsis (manifested by fever, apnea, poor feeding, respiratory distress, or lethargy) were eligible. Infants pre-treated with antibiotics for more than 48 hours prior to admission were excluded.

Sample Processing- Two milliliters of venous blood were aseptically collected and inoculated into pediatric blood culture bottles. Cultures were incubated in an automated detection system (BACTEC, Becton Dickinson). Positive samples were sub-cultured on MacConkey and blood agar. Identification was performed using biochemical tests and confirmed with VITEK-2 (bioMérieux).

Antimicrobial Susceptibility and ESBL Detection- Antibiotic susceptibility was assessed using the Kirby–Bauer disk diffusion method, interpreted according to CLSI 2018 standards. Drugs tested included cephalosporins, aztreonam, carbapenems, aminoglycosides, fluoroquinolones, piperacillin-tazobactam, and colistin. ESBL production was screened with ceftazidime and cefotaxime disks, and confirmed with clavulanate-based combination disk tests, with ≥5 mm increase in zone diameter considered positive.

Clinical Data Collection- Demographic and clinical data were collected, including gestational age, NICU length of stay, ventilator requirement, and survival outcome.

Statistical Analysis: Data were analyzed with SPSS version 22.0. Continuous variables were presented as mean ± standard deviation and compared using t-tests; categorical variables were analyzed using chi-square tests. A p-value <0.05 was considered significant.

Results

Microbiological Findings- of 500 cultures, 300 (60%) were positive. Gram-negative organisms accounted for 180 (60%) isolates, while Gram-positive bacteria comprised 120 (40%).

Klebsiella spp. (42.2%) and E. coli (36.6%) were predominant, followed by Acinetobacter spp. (12.7%) and Pseudomonas spp. (8.5%).

Table 1: Distribution of Gram-negative isolates and ESBL production

Organism	Total Isolates (n=180)	% of GN Isolates	ESBL Positive (n=40)	% of ESBL Isolates
Klebsiella spp.	76	42.2%	19	47.5%
Escherichia coli	66	36.6%	14	35.0%
Acinetobacter spp.	23	12.7%	5	12.5%
Pseudomonas spp.	15	8.5%	2	5.0%
Total	180	100%	40	22.2%

Antimicrobial Resistance

ESBL-positive isolates demonstrated:

- Resistance to third-generation cephalosporins >90%
- Resistance to aztreonam 75%
- Resistance to carbapenems 65%
- Resistance to gentamicin 55%
- Resistance to amikacin 28%
- Resistance to colistin <10%

Clinical Outcomes: Compared with ESBL-negative infections, neonates with ESBL-positive septicemia had significantly longer NICU stays (18 ± 4 vs 11 ± 3 days), higher ventilator requirement (40% vs 22%), and increased mortality (28% vs 15%).

Table 2: Clinical outcomes in neonates with ESBL-positive vs ESBL-negative infections

Clinical Parameter	ESBL-Positive (n=40)	ESBL-Negative (n=140)	p-value
Mean NICU stay (days)	18 ± 4	11 ± 3	<0.05*
Ventilator requirement	40%	22%	<0.05*
Mortality	28%	15%	<0.05*

*** P-value <0.05 is significant**

Discussion

This study highlights the significant prevalence of ESBL-producing Gram-negative organisms (22.2%) in neonatal sepsis in Kanpur. Similar rates (20–40%) have been reported in Indian NICUs [9,10]. Klebsiella spp. and E. coli were the leading ESBL producers, consistent with earlier studies [11,12]. Their plasmid-mediated ESBL genes facilitate rapid dissemination in neonatal units [13].

The resistance profile is alarming, with near-universal resistance to third-generation cephalosporins and substantial carbapenem resistance. Limited susceptibility to amikacin and colistin underscores the urgent need for judicious use of these drugs [14].

Clinically, ESBL infections were associated with prolonged NICU stays, higher ventilator needs, and increased mortality. These findings mirror global evidence linking ESBL bacteremia with delayed effective therapy and poorer outcomes [15].

From a clinical perspective, empirical reliance on cephalosporins in NICUs with high ESBL prevalence is no longer tenable.

Strengthened infection control, antimicrobial stewardship, and ongoing resistance surveillance are critical to mitigate this threat.

Conclusion

ESBL-producing Gram-negative bacilli represent a growing burden in neonatal septicemia in Kanpur. Their association with multidrug resistance, prolonged hospitalization, and higher mortality demands immediate action through rational antibiotic policies, robust infection prevention, and continuous microbiological monitoring.

References

1. Fleischmann-Struzek C, et al. Global incidence and mortality of neonatal sepsis: a systematic review. Arch Dis Child. 2018;103(1):14–20.
2. Paterson DL, Bonomo RA. Extended-spectrum beta-lactamases: a clinical update. Clin Microbiol Rev. 2005;18(4):657–686.
3. Tamma PD, Rodriguez-Baño J. The use of noncarbapenem β-lactams for the treatment of extended-spectrum β-lactamase infections. Clin Infect Dis. 2017;64(7):972–980.
4. Karanika S, et al. Clinical outcomes of infections caused by ESBL-producing Enterobacteriaceae: a systematic review and meta-analysis. Clin Infect Dis. 2016;63(6):7 59–766.
5. Nordmann P, et al. The real threat of Klebsiella pneumoniae carbapenemase-producing bacte ria. Lancet Infect Dis. 2009;9(4):228–236.
6. Logan LK, Weinstein RA. The epidemiology of carbapenem-resistant Enterobacteriaceae. J Infect Dis. 2017;215(suppl_1):S28–S36.
7. Roy S, et al. Prevalence and antimicrobial resistance patterns of Gram-negative bacteria in neonatal sepsis: an Indian NICU study. Indian J Med Microbiol. 2019;37(1):46–52.
8. Sundaram V, et al. Blood culture-confirmed bacterial sepsis in neonates in India: a multicenter study. Pediatr Infect Dis J. 2009;28(12):1079–1082.
9. Bhattacharya S. ESBL-producing Enterobacteriaceae in neonatal sepsis: Indian scenario. Indian Pediatr. 2013;50(7):583–587.
10. Dutta S, et al. Antimicrobial resistance in neonatal sepsis: multicenter NICU study. J Trop Pediatr. 2014;60(5):377–382.
11. Kaur P, et al. Prevalence of ESBL-producing Enterobacteriaceae in neonatal sepsis. Indian J Pathol Microbiol. 2017;60(4):541–546.
12. Bhat YR, Lewis LE. Bacterial pathogens and resistance patterns in neonatal sepsis in India. J Pediatr Infect Dis. 2011;6(4):227–234.
13. Stoll BJ, et al. Early-onset neonatal sepsis: epidemiology and risk factors. J Pediatr. 2011;159(1):72–78.
14. Tzialla C, et al. New insights into neonatal sepsis: impact of multidrug resistance. Front Pediatr. 2018; 6:285.
15. Schwaber MJ, Carmeli Y. Mortality and delay in effective therapy associated with ESBL bacteremia: a systematic review and meta-analysis. J Antimicrob Chemother. 2007;60 (5): 913–920.