RESEARCH PAPER

Sensitivity Profile of Ceftriaxone-Sulbactam Combination Against Gram-Negative ICU pathogens in a Tertiary Care Hospital.

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ABSTRACT

Background:
Antimicrobial resistance (AMR) among Gram-negative pathogens has become a major challenge in Intensive Care Units (ICUs), leading to increased morbidity, mortality, and healthcare costs. The emergence of multidrug-resistant organisms and rising carbapenem resistance necessitate the evaluation of effective carbapenem-sparing therapeutic alternatives. This study assessed the in-vitro sensitivity profile of the ceftriaxone–sulbactam combination against Gram-negative bacterial isolates recovered from ICU patients in a tertiary care hospital.

Methods:
A hospital-based cross-sectional observational study was conducted in the Department of Microbiology in collaboration with ICUs at Dr. B.S.K.I.M.S, Kanpur from December 2025 to May 2026. A total of 120 non-duplicate Gram-negative bacterial isolates obtained from blood, urine, respiratory specimens, pus/wound swabs, catheter tips, and body fluids were included. Isolates were identified using standard microbiological methods, and antimicrobial susceptibility testing was performed by the Kirby–Bauer disk diffusion method according to Clinical and Laboratory Standards Institute (CLSI) guidelines. The sensitivity profile of ceftriaxone–sulbactam was evaluated and compared with other commonly used antibiotics.

Results:
Among the 120 ICU patients, 78 (65.0%) were male and 42 (35.0%) were female. The majority of patients belonged to the 51–60 years age group (31.7%). Urine samples constituted the largest proportion of specimens (31.7%), followed by respiratory samples (26.7%) and blood cultures (20.0%). Klebsiella pneumoniae was the most frequently isolated pathogen (35.0%), followed by Escherichia coli (25.0%), Pseudomonas aeruginosa (18.3%), and Acinetobacter baumannii (15.0%). Overall sensitivity to ceftriaxone–sulbactam was 67.5% (81/120). The highest susceptibility was observed in Escherichia coli (80.0%) and Enterobacter spp. (80.0%), whereas Acinetobacter baumannii demonstrated the lowest sensitivity (50.0%). Comparative analysis revealed higher sensitivity rates for meropenem (85.0%), imipenem (83.3%), and amikacin (80.0%), while ciprofloxacin exhibited the lowest sensitivity (48.3%).

Conclusion:
Ceftriaxone–sulbactam demonstrated moderate in-vitro activity against Gram-negative ICU pathogens, with an overall sensitivity of 67.5%, suggesting its potential role as a carbapenem-sparing therapeutic option in selected infections. However, carbapenems and amikacin remained the most effective antimicrobial agents. Continuous surveillance of antimicrobial susceptibility patterns and implementation of robust antibiotic stewardship programs are essential to optimize empirical therapy and limit the spread of multidrug-resistant organisms in ICU settings.

Keywords: Antimicrobial resistance, Ceftriaxone–Sulbactam, Gram-negative bacteria, Intensive Care Unit, Antibiotic susceptibility, Carbapenem-sparing therapy, Klebsiella pneumoniae, Escherichia coli.

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Introduction

Antimicrobial resistance (AMR) has emerged as one of the most significant threats to global public health, resulting in increased morbidity, mortality, prolonged hospital stays, and escalating healthcare costs. Intensive Care Units (ICUs) are recognized as major reservoirs of multidrug-resistant (MDR) pathogens due to extensive antibiotic use, invasive procedures, prolonged hospitalization, and the presence of critically ill patients. Gram-negative bacteria such as Klebsiella pneumoniae, Escherichia coli, Acinetobacter

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baumannii, and Pseudomonas aeruginosa are among the most common causative agents of healthcare-associated infections in ICUs and are increasingly associated with resistance to multiple classes of antimicrobial agents. Recent studies have demonstrated a rising prevalence of extended-spectrum β-lactamase (ESBL)- and carbapenemase-producing Gram-negative organisms, limited available therapeutic options and posing a major challenge to clinicians. [1–3]

The increasing incidence of resistance to carbapenems, which are often considered the last line of defence against severe Gram-negative infections, has necessitated the search for effective carbapenem-sparing therapeutic alternatives. In India and other developing countries, antimicrobial resistance among ICU isolates has reached alarming levels, particularly among Acinetobacter and Klebsiella species. Recent multicentre studies from Indian ICUs have reported high rates of resistance to third-generation cephalosporins, fluoroquinolones, and even carbapenems among Gram-negative pathogens. [4,5]

Ceftriaxone is a third-generation cephalosporin with broad-spectrum activity against many Gram-negative organisms. However, its effectiveness has been significantly compromised due to the widespread production of β-lactamases by pathogenic bacteria. Sulbactam, a β-lactamase inhibitor, enhances the activity of ceftriaxone by inhibiting many plasmid-mediated β-lactamases and restoring susceptibility in certain resistant isolates. In addition to its β-lactamase inhibitory action, sulbactam possesses intrinsic antibacterial activity against Acinetobacter species, making the ceftriaxone-sulbactam combination a potentially useful therapeutic option in ICU settings. [6]

Several recent studies have evaluated the in-vitro activity of ceftriaxone-sulbactam-based combinations against Gram-negative pathogens. A study conducted among ICU isolates demonstrated that ceftriaxone-sulbactam-based therapy exhibited substantial activity against ESBL- and Metallo-β-lactamase (MBL)-producing organisms and could serve as a carbapenem-sparing alternative.[7] Another study from a tertiary care canter in North India reported susceptibility rates ranging from 51% to 95% among multidrug-resistant and non-MDR Gram-negative isolates, highlighting its potential utility against resistant pathogens.[8] Similarly, Chaudhuri and Gupta observed encouraging susceptibility patterns among respiratory, blood, and urinary isolates, particularly against Pseudomonas aeruginosa and Escherichia coli.[9]

Continuous surveillance of antimicrobial susceptibility patterns is essential because resistance profiles vary considerably across hospitals and geographical regions. Local antibiogram data are indispensable for guiding empirical therapy, optimizing antibiotic stewardship programs, and reducing the emergence of further resistance. Recent reports emphasize that ICU-specific antimicrobial susceptibility monitoring remains crucial for improving patient outcomes and informing infection-control strategies.[1,4,5]

Materials and Methods

Study Design and Setting

This hospital-based cross-sectional observational study was conducted in the Department of Microbiology in collaboration with the Intensive Care Units (ICUs) at Dr. B.S.K.I.M.S, Kanpur over a period of December 2025 to May 2026.

Study Population

Clinical specimens received from patients admitted to ICUs

Sample Size

A total of 120 patients non-duplicate Gram-negative bacterial isolates recovered from various clinical specimens were included in the study.

Inclusion Criteria

1. Patients aged 18–60 years admitted to the ICU.
2. Clinically significant Gram-negative bacterial isolates obtained from ICU patients.
3. Isolates recovered from blood, urine, respiratory samples, pus, wound swabs, body fluids, and other relevant clinical specimens.
4. First isolate obtained from each patient during the study period.

Exclusion Criteria

1. Patients aged below 18 years or above 60 years.
2. Duplicate isolates obtained from the same patient.
3. Environmental isolates and surveillance cultures.
4. Specimens showing mixed growth suggestive of contamination.
5. Gram-positive bacterial and fungal isolates.
6. Isolates lacking complete demographic or laboratory data.

Sample Collection and Processing

Clinical specimens were collected aseptically from ICU patients and transported promptly to the microbiology laboratory. Samples were processed according to standard microbiological procedures. Blood agar and MacConkey agar were used for primary isolation. The inoculated plates were incubated aerobically at 35–37°C for 18–24 hours.

Identification of Bacterial Isolates

Bacterial isolates were identified based on colony morphology, Gram staining characteristics, motility testing, and standard biochemical reactions. Where available, identification was confirmed using automated systems.

The commonly isolated Gram-negative pathogens included:

- Klebsiella pneumoniae
- Escherichia coli
- Pseudomonas aeruginosa
- Acinetobacter baumannii complex
- Enterobacter spp.
- Citrobacter spp.
- Proteus spp.

Antimicrobial Susceptibility Testing

Antimicrobial susceptibility testing (AST) was performed using the Kirby–Bauer disk diffusion method on Mueller–

Hinton agar according to the latest Clinical and Laboratory Standards Institute (CLSI) guidelines.
A bacterial suspension equivalent to 0.5 McFarland standard was prepared and inoculated onto Mueller–Hinton agar plates. Antibiotic discs were applied and plates were incubated at 35 ± 2°C for 16–18 hours.
Zone diameters were interpreted according to CLSI recommendations. Isolates were categorized as Sensitive (S), Intermediate (I), or Resistant (R).
Determination of Sensitivity Profile of Ceftriaxone–Sulbactam
The susceptibility of all Gram-negative isolates to the ceftriaxone–sulbactam combination was specifically analysed. Sensitivity rates were calculated separately for individual bacterial species and for the overall Gram-negative bacterial population isolated from ICU patients.

Data Collection
Demographic and clinical information including age, sex, ICU type, specimen source, bacterial isolate, and antimicrobial susceptibility pattern were recorded in a structured data collection form.

Result:

Table: 1 Gender distribution of the patients

Gender	Number of Patients (n)	Percentage (%)
Male	78	65.0
Female	42	35.0
Total	120	100.0

The study population showed a male predominance, with 78 patients (65.0%) being male and 42 patients (35.0%) being female, indicating a higher incidence of ICU admissions among males compared to females.

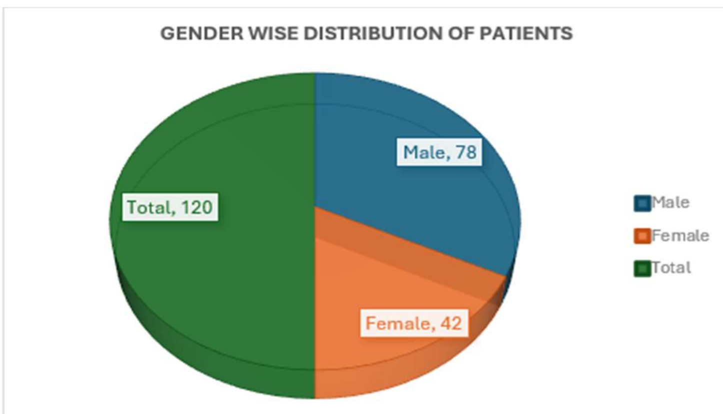

Fig: 1 Graphical represents gender wise distribution of patients

Table: 2 Age wise distribution of patients.

Age Group (Years)	Number of Patients (n)	Percentage (%)
18–30	20	16.7
31–40	28	23.3
41–50	34	28.3
51–60	38	31.7
Total	120	100.0

The age-wise distribution of patients showed that the majority belonged to the 51–60 years age group (31.7%), followed by 41–50 years (28.3%), 31–40 years (23.3%), and 18–30 years (16.7%). This indicates that ICU admissions with Gram-negative infections were more common in the older age groups, particularly among patients above 40 years.

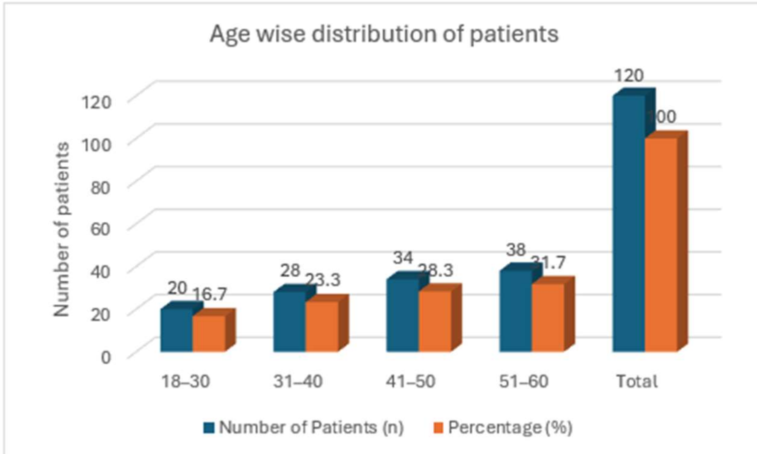

Fig: 2 Graphical represents age wise distribution of patients

Table: 3 BMI distribution of the patients.

BMI Category (kg/m²)	BMI Range	Number of Patients (n)	Percentage (%)
Underweight	<18.5	10	8.3
Normal Weight	18.5–24.9	52	43.3
Overweight	25.0–29.9	38	31.7
Obese	≥30.0		20
Total	-	120	100.0

Among the 120 study participants, the majority had normal BMI (43.3%), followed by overweight (31.7%) and obese individuals (16.7%). Underweight participants constituted 8.3% of the study population.

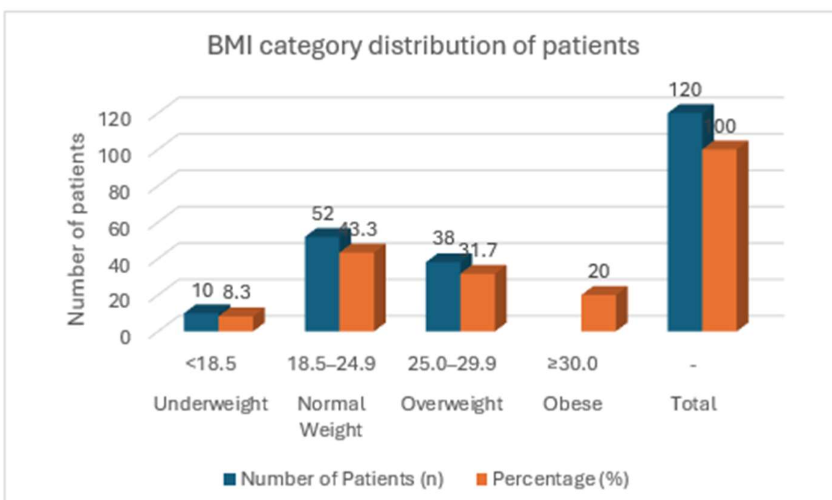

Fig: 3 BMI category distribution of patients

Table 4: Distribution of Clinical Specimens Received from ICU Patients (n = 120)

Specimen Type	Number of Isolates (n)	Percentage (%)
Urine	38	31.7
Blood	24	20.0
Endotracheal Aspirate/Sputum	32	26.7
Pus/Wound Swab	15	12.5
Catheter Tip	6	5.0
Body Fluids	5	4.1
Total	120	100.0

Urine specimens constituted the highest proportion of samples (31.7%), followed by endotracheal aspirates/sputum (26.7%) and blood samples (20.0%).

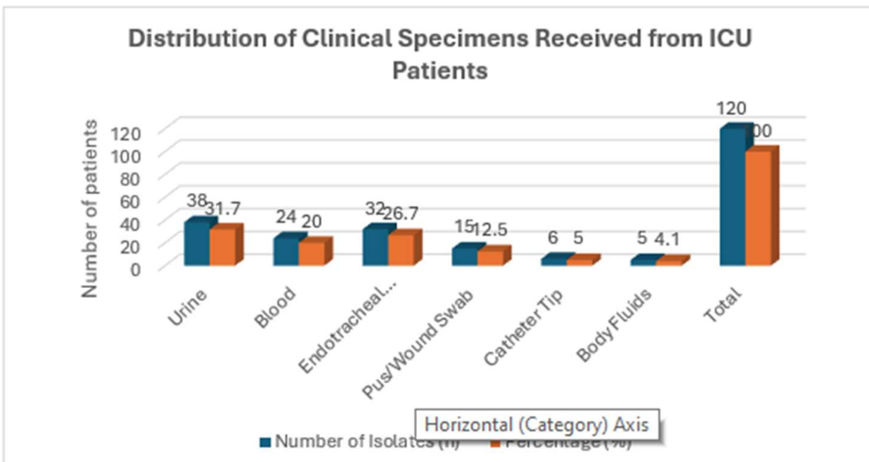

Fig: 4 Graphical represents distribution of clinical specimens received from ICU patients

Table 5: Distribution of Gram-Negative Bacterial Isolates (n = 120)

Organism Isolated	Number (n)	Percentage (%)
Klebsiella pneumoniae	42	35.0
Escherichia coli	30	25.0
Pseudomonas aeruginosa	22	18.3
Acinetobacter baumannii	18	15.0
Enterobacter spp.	5	4.2
Citrobacter spp.	3	2.5
Total	120	100.0

Klebsiella pneumoniae was the most commonly isolated Gram-negative pathogen (35.0%), followed by Escherichia coli (25.0%) and Pseudomonas aeruginosa (18.3%).

Table 6: Sensitivity Profile of Ceftriaxone–Sulbactam Against Gram-Negative Isolates

Organism	Sensitive n (%)	Resistant n (%)	Total
Klebsiella pneumoniae	28 (66.7)	14 (33.3)	42
Escherichia coli	24 (80.0)	6 (20.0)	30
Pseudomonas aeruginosa	14 (63.6)	8 (36.4)	22
Acinetobacter baumannii	9 (50.0)	9 (50.0)	18
Enterobacter spp.	4 (80.0)	1 (20.0)	5
Citrobacter spp.	2 (66.7)	1 (33.3)	3
Total	81 (67.5)	39 (32.5)	120

Overall sensitivity of Gram-negative isolates to ceftriaxone–sulbactam was 67.5%. The highest sensitivity was observed among Escherichia coli (80.0%) and Enterobacter spp. (80.0%), whereas Acinetobacter baumannii showed the lowest sensitivity (50.0%).

Table 7: Comparative Antibiotic Sensitivity Pattern of Gram-Negative Isolates (n = 120)

Antibiotic	Sensitive n (%)	Resistant n (%)	p -Value
Ceftriaxone–Sulbactam	81 (67.5)	39 (32.5)	
Piperacillin–Tazobactam	92 (76.7)	28 (23.3)	<0.05*
Cefoperazone–Sulbactam	88 (73.3)	32 (26.7)	<0.05*
Amikacin	96 (80.0)	24 (20.0)	<0.01*
Meropenem	102 (85.0)	18 (15.0)	<0.01*
Imipenem	100 (83.3)	20 (16.7)	<0.01*
Ciprofloxacin	58 (48.3)	62 (51.7)	<0.001*

The comparative antibiotic sensitivity pattern showed that carbapenems (meropenem and imipenem) demonstrated the highest effectiveness with statistically significant higher sensitivity ($p < 0.01$), followed by amikacin. B-lactam/β-lactamase inhibitor combinations such as piperacillin–tazobactam and Cefoperazone–sulbactam also showed significantly better activity compared to ceftriaxone–sulbactam ($p < 0.05$). In contrast, ciprofloxacin exhibited the lowest sensitivity with the highest resistance rate, showing a highly significant difference ($p < 0.001$). Overall, ceftriaxone–sulbactam demonstrated moderate efficacy among Gram-negative ICU isolates.

Discussion:

The present study demonstrates a high burden of antimicrobial resistance among Gram-negative ICU pathogens, with Klebsiella pneumoniae and Escherichia coli being the most common isolates. Ceftriaxone–sulbactam showed moderate effectiveness with 67.5% sensitivity, indicating its limited but potential role as a carbapenem-sparing agent. Carbapenems (meropenem and imipenem) and amikacin exhibited the highest sensitivity rates, confirming their continued reliability for severe ICU infections, although emerging resistance remains a concern. Ciprofloxacin showed the lowest sensitivity with high resistance, making it less suitable for empirical therapy.

These findings are consistent with recent studies from Indian ICUs reporting increasing resistance to fluoroquinolones and variable response to β-lactam/β-lactamase inhibitor combinations. Overall, the study emphasizes the importance of continuous antimicrobial surveillance and strict antibiotic stewardship to optimize empirical therapy and preserve the effectiveness of existing antibiotics.

Conclusion:

Gram-negative bacterial pathogens in ICU settings show a high level of antimicrobial resistance, with Klebsiella pneumoniae and Escherichia coli being the predominant isolates. Ceftriaxone–sulbactam demonstrated moderate in-vitro activity (67.5% sensitivity), indicating its potential as a carbapenem-sparing option in selected cases. However, carbapenems and amikacin remain the most effective agents against these organisms, while ciprofloxacin shows poor efficacy due to high resistance. The study highlights the necessity of regular antimicrobial surveillance, strict infection control practices, and rational antibiotic stewardship to curb the emergence and spread of multidrug-resistant organisms in ICU settings.

Limitations:

- The study was conducted in a single tertiary care hospital, which may limit the generalizability of the results.
- The sample size was relatively small.
- The study was based only on in-vitro antimicrobial susceptibility testing, which may not fully correlate with clinical outcomes.
- Molecular characterization of resistance mechanisms (ESBL, carbapenemase, MBL) was not performed.
- Important patient-related factors such as prior antibiotic use, comorbidities, and duration of ICU stay were not analyzed in detail.
- Pharmacokinetic and pharmacodynamic properties of ceftriaxone–sulbactam were not assessed.
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Conflict of Interest: The authors declare that there is no conflict of interest regarding the publication of this study.

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