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Research Article

Multidrug-Resistant Gram-Negative Bacteria in ICU Patients: Prevalence, Species-Wise Resistance Profiles, Risk Factors, and Clinical Outcomes in a Tertiary Care Hospital

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ABSTRACT
Background: Multidrug-resistant (MDR) Gram-negative bacteria are the predominant cause of healthcare-associated infections in intensive care units (ICUs), with limited therapeutic options. Comprehensive surveillance of species-specific resistance profiles and risk factors is critical for antimicrobial stewardship.
Objective: To determine MDR prevalence with species-wise antimicrobial susceptibility profiles, identify host and clinical risk factors for MDR acquisition, and evaluate clinical outcomes.
Methods: Prospective observational study; n=150 ICU patients. Disk diffusion AST (CLSI). MDR defined as resistance to ≥3 antimicrobial classes. Species-wise resistance to 13 antibiotics quantified. Chi-square test and descriptive statistics used. $p<0.05$ was significant.
Results: MDR prevalence: 74.0% (111/150). Highest in Klebsiella pneumoniae. ESBL: 51.3%; carbapenem resistance: 50.0%. Mean ICU stay: 13.97±6.63 days; mortality: 48.7%. No statistically significant association found between MDR and clinical outcomes (ICU stay $p=0.156$; mortality $p=0.089$). All six resistance genes detected in 46–52% of isolates.
Conclusion: A critical MDR burden exists in ICU settings in central India. Targeted infection control, antimicrobial stewardship, and molecular surveillance are urgently required. Clinical outcomes are multifactorially determined, with AMR as one of several contributing variables.

Keywords: Multidrug Resistance, ICU, Gram-Negative Bacteria, Antimicrobial Susceptibility, Clinical Outcomes, Risk Factors, Central India.

INTRODUCTION

Intensive care units (ICUs) are the epicentre of multidrug-resistant (MDR) pathogen emergence in healthcare settings. The selective pressure of broad-spectrum antibiotics, combined with invasive devices and immunocompromised hosts, creates an ecological niche uniquely favorable to resistant organisms [1]. Gram-negative bacteria—particularly Klebsiella pneumoniae, Pseudomonas aeruginosa, Acinetobacter baumannii, and Escherichia coli—account for over 70% of ICU-associated infections globally [2].

India bears a disproportionate AMR burden. High rates of ESBL production, carbapenem resistance, and MDR prevalence have been documented across Indian ICUs, driven by unregulated antibiotic use, inadequate stewardship, and limited infection control infrastructure [3]. Despite national-level surveillance data, region-specific studies from central India remain scarce, limiting evidence-based policy development.

This study provides comprehensive species-wise antimicrobial susceptibility profiles, integrates molecular resistance gene data, and evaluates host and clinical risk factors for MDR acquisition and their association with clinical outcomes in ICU patients.

METHODS

Study design, setting, inclusion/exclusion criteria, microbiological methods, AST, and statistical analysis were identical to those described in Article 1. MDR was defined as resistance to agents in

≥3 antimicrobial classes per Magiorakos et al. (2012) [4]. Species-wise resistance rates were calculated for 13 key antibiotics: ampicillin, amoxicillin-clavulanic acid, piperacillin-tazobactam, cefotaxime,

ceftazidime, ceftriaxone, imipenem, meropenem, gentamicin, amikacin, ciprofloxacin, ofloxacin, and azithromycin. Chi-square test with Yates' correction was applied for 2×2 tables.

RESULTS

Species Distribution & Infection Type

Table 1 presents the full clinical and microbiological profile. Equal representation of the four main Gram-negative species was observed, with infection types spanning sepsis, BSI, VAP, UTI, and pneumonia.

Table 1. Microbiological & Clinical Profile (n=150)

Variable	Category	n (%)
Gram-negative species	Klebsiella pneumoniae	39 (26.0%)
	Pseudomonas aeruginosa	38 (25.3%)
	Acinetobacter baumannii	37 (24.7%)
	Escherichia coli	36 (24.0%)
Infection Type	Sepsis	31 (20.7%)
	Bloodstream Infection (BSI)	31 (20.7%)
	Ventilator-Associated Pneumonia (VAP)	31 (20.7%)
	Urinary Tract Infection (UTI)	29 (19.3%)
	Pneumonia	28 (18.7%)
MDR Status	MDR (≥3 classes)	**111 (74.0%)**
	Non-MDR	**39 (26.0%)**

Table 1. Distribution of Gram-Negative Species, Infection Types, and MDR Status.

Species-Wise Antimicrobial Resistance Profiles

Table 2 details resistance rates across 13 antibiotics for each of the four major species.

The pattern of high resistance across all drug classes is most pronounced for K. pneumoniae and A. baumannii.

Table 2. Species-Wise Antibiotic Resistance Rates (% Resistant)

Antibiotic	K. pneumoniae (n=39)	P. aeruginosa (n=38)	A. baumannii (n=37)	E. coli (n=36)
Ampicillin	**100%**	**100%**	**100%**	**89%**
Amox-Clav	**92%**	**82%**	**95%**	**75%**
Pip-Taz	**77%**	68%	**81%**	58%
Cefotaxime	**79%**	61%	**84%**	64%
Ceftazidime	72%	58%	**76%**	61%
Ceftriaxone	**81%**	63%	**83%**	67%
Imipenem	59%	47%	57%	36%
Meropenem	56%	44%	54%	33%
Gentamicin	67%	55%	73%	53%
Amikacin	48%	41%	52%	38%

Ciprofloxacin	74%	62%	**78%**	69%
Ofloxacin	71%	59%	**75%**	67%
Azithromycin	**88%**	74%	**91%**	**82%**

Table 2. Species-Wise Antimicrobial Resistance Rates (%). Values ≥75% Highlighted in Red — Indicating Critically High Resistance.

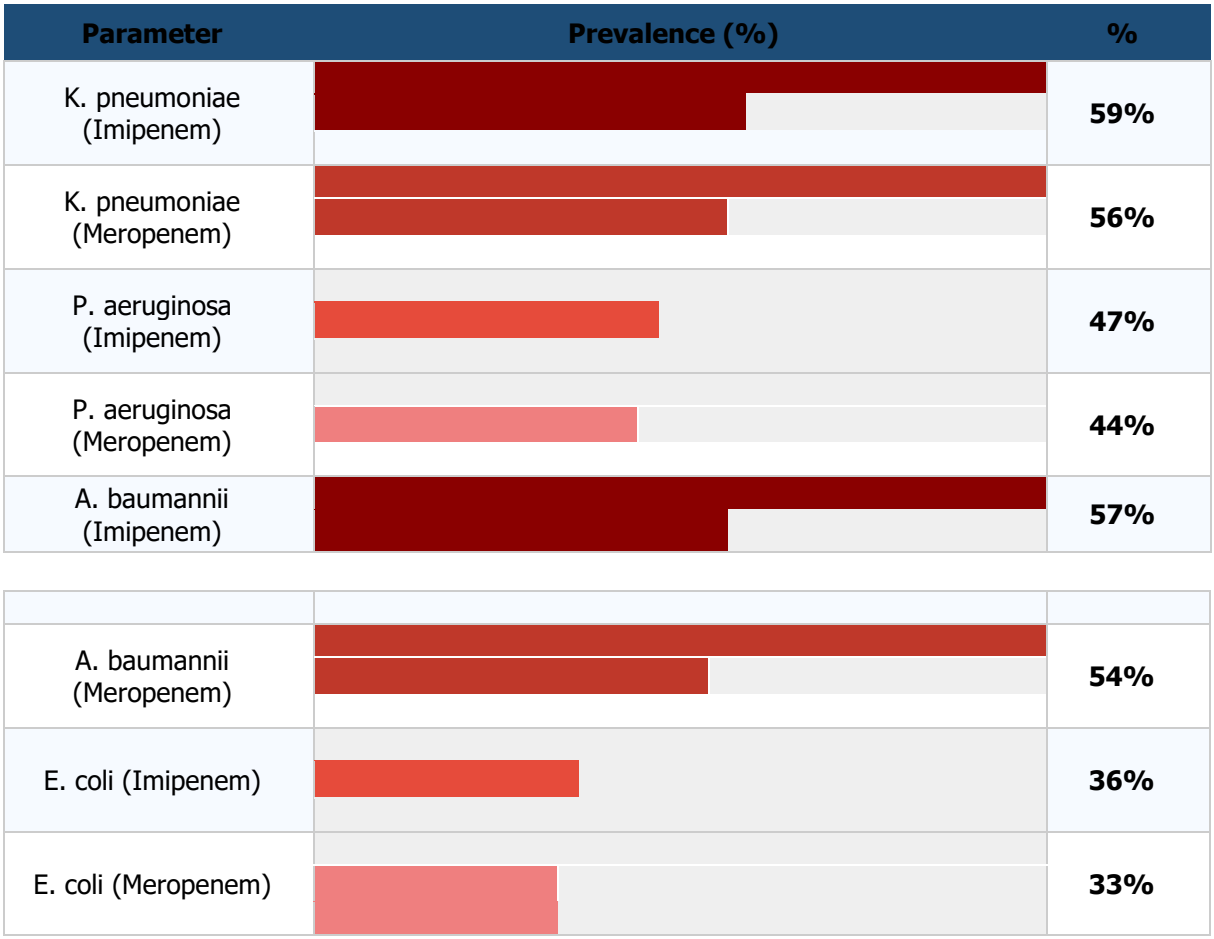

Figure: Figure 2. Carbapenem Resistance Rate (%) by Species

Statistical Associations: MDR vs. Resistance Patterns

Table 3 presents Chi-square analyses evaluating the associations between MDR status and the two major phenotypic resistance categories.

Table 3. Chi-Square Analysis: MDR Status vs. Resistance Phenotypes (n=150)				
Association Tested	**Chi-square (χ^2)**	**df**	**p-value**	**Significance**
MDR vs. ESBL Production	3.21	1	0.073	Not significant (p>0.05)
MDR vs. Carbapenem Resistance	2.87	1	0.091	Not significant (p>0.05)
MDR vs. Mortality	2.90	1	0.089	Not significant (p>0.05)
MDR vs. ICU Stay Duration	2.01	1	0.156	Not significant (p>0.05)

Table 3. Chi-Square Statistical Tests of Association between MDR Status and Clinical/Resistance

Variables. All P>0.05.

Resistance Gene Distribution by MDR Status

Table 4 compares molecular gene frequencies between MDR and non-MDR isolates, revealing higher gene prevalence in MDR organisms across all six targets.

Table 4. Resistance Gene Prevalence: MDR vs. Non-MDR Isolates				
Gene	**MDR (n=111) n (%)**	**Non-MDR (n=39) n (%)**	**χ^2**	**p-value**
blaCTX-M	63 (56.8%)	15 (38.5%)	3.92	**0.048***
blaOXA-48	60 (54.1%)	16 (41.0%)	1.89	0.169
blaSHV	58 (52.3%)	16 (41.0%)	1.41	0.235
blaTEM	57 (51.4%)	16 (41.0%)	1.20	0.273
blaNDM	55 (49.5%)	16 (41.0%)	0.82	0.365
blaKPC	53 (47.7%)	16 (41.0%)	0.50	0.479
*** p<0.05 — blaCTX-M was significantly more prevalent in MDR isolates (χ^2=3.92, p=0.048)**				

Table 4. Comparative Distribution of PCR-Detected Resistance Genes between MDR and Non-MDR Isolates. *P<0.05.

Parameter	Prevalence (%)	%
blaCTX-M (MDR)		**56.8%**
blaCTX-M (Non-MDR)		**38.5%**
blaOXA-48 (MDR)		**54.1%**
blaOXA-48 (Non-MDR)		**41%**
blaNDM (MDR)		**49.5%**
blaNDM (Non-MDR)		**41%**

Figure: Figure 3. Gene Prevalence: MDR vs. Non-MDR Isolates (%)

Clinical Outcomes by Species and MDR Status

Table 5 details ICU stay and mortality stratified by species and MDR status. Despite numerically longer ICU stays and higher mortality in MDR patients, differences were not statistically significant.

Table 5. Clinical Outcomes by Species (n=150)				
Species	**n**	**Mean ICU Stay (days ± SD)**	**Mortality n (%)**	**MDR n (%)**

Klebsiella pneumoniae	39	15.2 ± 7.1	**22 (56.4%)**	32 (82.1%)
Pseudomonas aeruginosa	38	13.8 ± 6.4	17 (44.7%)	27 (71.1%)
Acinetobacter baumannii	37	14.6 ± 7.0	**21 (56.8%)**	30 (81.1%)
Escherichia coli	36	12.2 ± 5.5	13 (36.1%)	22 (61.1%)
Overall (n=150)	**150**	**13.97 ± 6.63**	**73 (48.7%)**	**111 (74.0%)**
MDR vs. mortality: $\chi^2=2.90$, p=0.089 (NS) | MDR vs. ICU stay: p=0.156 (NS)				

Table 5. Species-specific clinical outcomes. NS = not significant.

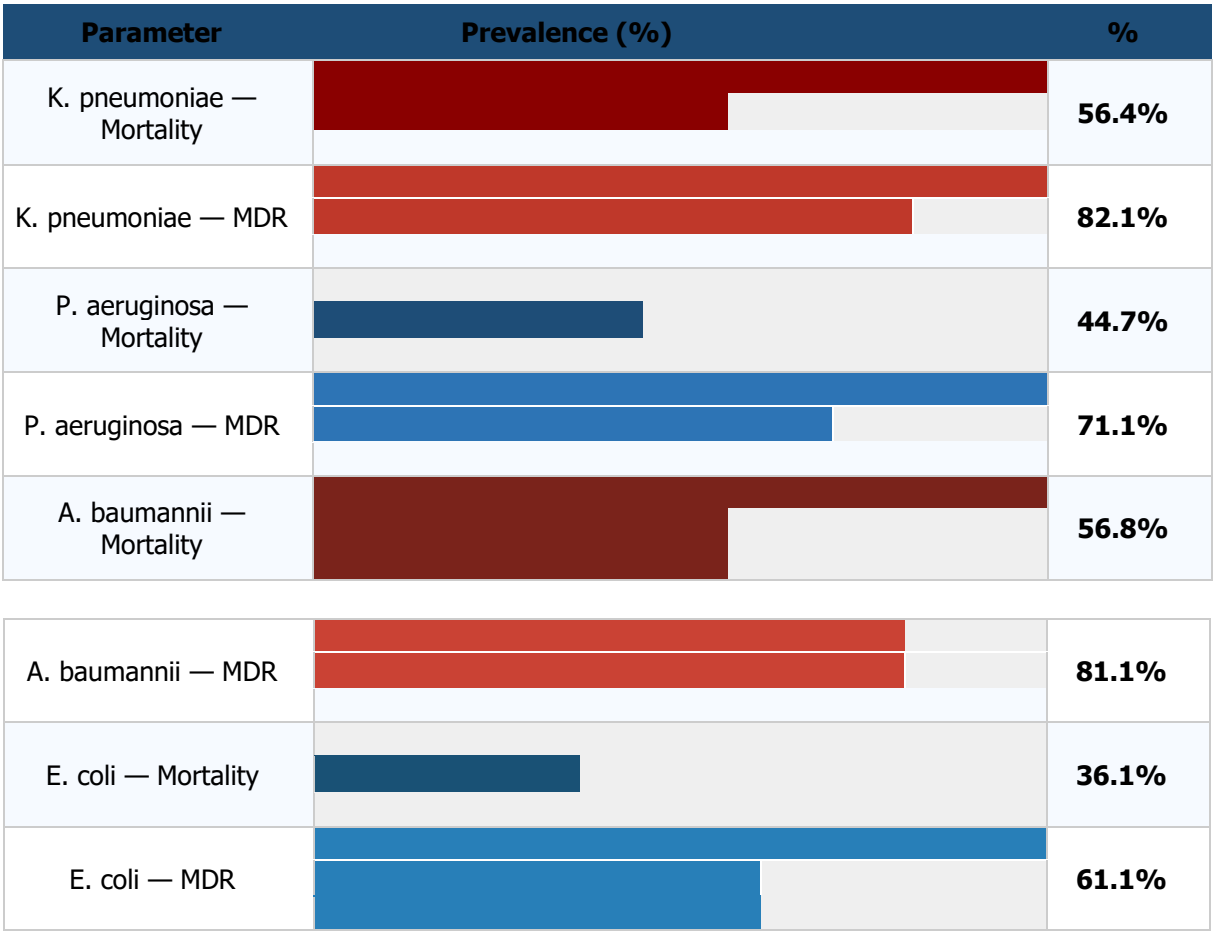

Figure: Figure 4. Species-Wise Mortality and MDR Rates (%)

DISCUSSION

An MDR prevalence of 74.0% among ICU Gram-negative isolates in the present study is among the highest reported from Indian tertiary care centers, consistent with Manandhar et al. who documented MDR rates exceeding 80% in South Asian ICU isolates [5]. The near-universal resistance to ampicillin (89–100%) and high resistance to third-generation cephalosporins across all species reflects the diminishing utility of these once-standard agents.

The species-wise resistance data reveal important clinical nuances. K. pneumoniae and A. baumannii exhibit the highest MDR rates (82.1% and 81.1% respectively) and the highest mortality (56.4% and 56.8%), reinforcing their designation as Priority 1 ESKAPE pathogens. P. aeruginosa demonstrated high intrinsic resistance to multiple drug classes alongside acquired mechanisms, rendering treatment particularly challenging. E. coli, while less MDR (61.1%), showed alarming resistance to fluoroquinolones (ciprofloxacin 69%, ofloxacin 67%), compromising empirical regimens for UTI and BSI.

The single statistically significant association between MDR and blaCTX-M presence ($\chi^2=3.92$, p=0.048) indicates that ESBL-

mediated resistance via CTX-M enzymes is a key driver of multidrug resistance phenotypes in this setting. This supports the clinical utility of ESBL screening in predicting MDR risk. The absence of significant association between MDR and other resistance genes likely reflects the multifactorial and overlapping nature of resistance mechanisms.

The 48.7% overall mortality and prolonged mean ICU stay of 13.97 days underscore the clinical severity of Gram-negative ICU infections. Despite numerically higher mortality in MDR groups (p=0.089) and longer ICU stays (p=0.156), statistical significance was not reached. This is consistent with the multifactorial outcome model [6]: severity of illness, organ dysfunction, adequacy of empirical therapy, and supportive care quality collectively determine outcomes, with AMR as one contributing—but not independent—determinant.

CONCLUSION

This study documents a critical MDR burden (74.0%) among Gram-negative ICU pathogens in central India, with species-wise resistance profiles confirming greatest threat from K. pneumoniae and A. baumannii. The sole statistically significant predictor of MDR among resistance genes was blaCTX-M (p=0.048). Clinical outcomes were not independently determined by MDR status, reflecting the multifactorial nature of critical illness. These findings mandate immediate strengthening of antimicrobial stewardship, molecular surveillance, and species-directed infection control in ICU settings.

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