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Carbapenem-Resistant *Pseudomonas aeruginosa* in Intensive Care Unit Patients: Prevalence, Antimicrobial Susceptibility, Risk Factors, and Clinical Outcomes at a Tertiary Care Centre in Western Rajasthan, India

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ABSTRACT

Carbapenem-resistant *Pseudomonas aeruginosa* (CRPA) represents a critical clinical challenge in intensive care units (ICUs), limiting therapeutic options and contributing to increased morbidity and mortality. Characterizing its epidemiology and resistance determinants is essential to guide antimicrobial stewardship and infection control strategies. To determine the prevalence of CRPA among ICU patients, and to analyze antimicrobial susceptibility patterns, identify independent risk factors for resistance acquisition, and compare clinical outcomes between CRPA and carbapenem-sensitive *P. aeruginosa* (CSPA) infections. A prospective observational study was conducted from January 2024 to July 2024 at a tertiary care teaching hospital in Western Rajasthan, India. A total of 1,121 respiratory specimens were processed. Isolates were identified using standard biochemical methods and Matrix-Assisted Laser Desorption/Ionization Time-of-Flight Mass Spectrometry (MALDI-TOF MS). Antimicrobial susceptibility testing was performed using the Kirby–Bauer disc diffusion method per CLSI 2024 guidelines; colistin susceptibility was confirmed by broth microdilution (BMD). Multivariate logistic regression was used to identify independent risk factors. Among 138 *P. aeruginosa* isolates, 39 (28.3%) were CRPA. Patients with CRPA were significantly older (mean age 64.2 ± 11.4 vs. 54.9 ± 12.1 years; $p = 0.032$) and had higher rates of hypertension (66.7% vs. 44.4%; $p = 0.024$). Independent risk factors for CRPA included prior antibiotic exposure (odds ratio (OR) 5.6; 95% CI: 2.1–14.8; $p = 0.001$), prolonged mechanical ventilation (OR 10.8; 95% CI: 2.4–48.3; $p = 0.001$), and ICU stay >7 days (OR 10.1; 95% CI: 3.5–29.2; $p < 0.001$). CRPA isolates showed high resistance to β -lactams (87.2%) and fluoroquinolones (82.1%), but retained 100% susceptibility to colistin and 74% susceptibility to tigecycline by disc diffusion. CRPA infections were associated with significantly higher mortality (51.3% vs. 22.2%; $p = 0.004$) and longer hospitalization (25.8 ± 9.8 vs. 14.9 ± 5.2 days; $p < 0.001$). CRPA infections in ICU settings present with limited therapeutic options and poor clinical outcomes. Strengthening antimicrobial stewardship, infection control practices, and ventilator care bundles is essential to curb CRPA spread. Multicenter studies with molecular resistance characterization are warranted.

Keywords

Pseudomonas aeruginosa, carbapenem resistance, intensive care unit, antimicrobial susceptibility, colistin, odds ratio, infection control

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Introduction

Pseudomonas aeruginosa is a non-fermenting, aerobic, Gram-negative bacillus widely recognized as one of the most important opportunistic pathogens responsible for healthcare-associated infections (HAIs), particularly in critically ill and immunocompromised patients (1). It possesses remarkable adaptability and intrinsic resistance mechanisms that enable survival in hostile hospital environments, especially ICUs. The organism commonly causes ventilator-associated pneumonia (VAP), bloodstream infections, urinary tract infections, surgical site infections, and sepsis among hospitalized patients (2). ICU patients are particularly vulnerable because of prolonged hospitalization, invasive procedures, mechanical ventilation, immunosuppression, and repeated exposure to broad-spectrum antibiotics (3).

Over the past decade (2014–2024), carbapenem-resistant *Pseudomonas aeruginosa* (CRPA) has emerged as a major global public health priority. Carbapenems such as meropenem and imipenem were previously considered highly effective therapeutic options against multidrug-resistant (MDR) Gram-negative bacilli. However, increasing resistance to carbapenems has significantly reduced available treatment options and has been associated with higher morbidity, mortality, prolonged hospital stay, and increased healthcare costs (4, 5).

The resistance mechanisms of *P. aeruginosa* are complex and multifactorial. These include production of carbapenemases such as metallo- β -lactamases (MBLs), loss or alteration of outer membrane porins (particularly OprD), overexpression of efflux pumps (MexAB-OprM, MexXY-OprM), AmpC β -lactamase hyperproduction, and biofilm formation (6, 7, 8, 9). These mechanisms collectively contribute to MDR and treatment failure.

Several studies worldwide have reported increasing prevalence of CRPA in ICU settings, especially among patients requiring prolonged mechanical ventilation and invasive procedures (10, 11). Prior exposure to broad-spectrum antibiotics, extended ICU stay, indwelling medical devices, and underlying comorbid conditions have been identified as important risk factors associated with acquisition of CRPA infections (3, 12).

In India, antimicrobial resistance among Gram-negative pathogens has become a major challenge due to widespread antibiotic use, inadequate infection control practices, and limited antimicrobial stewardship

implementation (13). Data regarding CRPA epidemiology and clinical outcomes from Western Rajasthan remain limited; to our knowledge, no published study has specifically examined CRPA epidemiology from this region.

Understanding the prevalence, antimicrobial susceptibility profile, risk factors, and clinical outcomes associated with CRPA infections is essential for guiding appropriate empirical therapy, optimizing infection control strategies, and strengthening antimicrobial stewardship programs.

Therefore, the present study was undertaken with the following objectives: (a) to determine the prevalence of CRPA among ICU patients; (b) to analyze antimicrobial susceptibility patterns; (c) to identify independent risk factors associated with carbapenem resistance; and (d) to compare clinical outcomes between CRPA and CSPA infections in a tertiary care hospital in Western Rajasthan.

Materials and Methods

Study Design and Setting

A prospective observational study was conducted from January 2024 to July 2024 in the Department of Microbiology at a tertiary care teaching hospital in Western Rajasthan, India. The study included respiratory samples received from medical ICU, surgical ICU, respiratory ICU, and trauma ICU.

Study Population

All ICU patients clinically suspected of lower respiratory tract infections whose respiratory samples yielded *Pseudomonas aeruginosa* during the study period were included.

Inclusion and Exclusion Criteria

Inclusion criteria:

- Patients admitted to the ICU for more than 48 hours.
- Patients with clinically suspected respiratory tract infections.
- Respiratory samples positive for *Pseudomonas aeruginosa*.
- Patients of all age groups and both genders.

Exclusion criteria:

- Duplicate isolates from the same patient.
- Contaminated or improperly collected samples.
- Patients with incomplete clinical records.
- Non-ICU patients.

Sample Collection

A total of 1,121 respiratory specimens including sputum samples and endotracheal aspirates (ETAs) were collected aseptically from ICU patients during the study period. Samples were transported immediately to the microbiology laboratory and processed without delay according to standard microbiological procedures.

Microbiological Processing

Samples were inoculated on Blood agar and MacConkey agar plates and incubated aerobically at 37°C for 18–24 hours. Preliminary identification was performed using colony morphology, pigment production, oxidase test, Gram staining, and conventional biochemical tests. Definitive identification of isolates was performed using Matrix-Assisted Laser Desorption/Ionization Time-of-Flight Mass Spectrometry (MALDI-TOF MS).

Antimicrobial Susceptibility Testing

Antimicrobial susceptibility testing was performed using the Kirby–Bauer disc diffusion method on Mueller–Hinton agar according to Clinical and Laboratory Standards Institute (CLSI) 2024 guidelines (8).

The following antimicrobial agents were tested: piperacillin-tazobactam, cefepime, ceftazidime, meropenem, imipenem, levofloxacin, gentamicin, amikacin, tigecycline, and colistin.

Carbapenem resistance was determined based on CLSI zone diameter criteria for meropenem and imipenem. Colistin susceptibility was confirmed using BMD as recommended by CLSI (8). Quality control strains used included *Pseudomonas aeruginosa* ATCC 27853 and *Escherichia coli* ATCC 25922.

Definitions

CRPA: Isolates resistant to either meropenem or imipenem according to CLSI 2024 criteria.

CSPA: Isolates susceptible to carbapenems.

MDR: Non-susceptibility to at least one agent in three or more antimicrobial categories, as per Magiorakos *et al.*, criteria (13).

Data Collection

Clinical and demographic details were collected from hospital records using a pre-structured data collection form. Variables analyzed included: age, gender, comorbidities, prior antibiotic exposure, mechanical ventilation, ICU stay duration, length of hospital stay, and mortality outcome.

Statistical Analysis

Data were entered and analyzed using Statistical Package for Social Sciences (SPSS) software version 26.0. Categorical variables were expressed as percentages and compared using Chi-square test or Fisher’s exact test where appropriate. Continuous variables were expressed as mean \pm standard deviation (SD). Multivariate logistic regression analysis was performed to identify independent risk factors for CRPA infection; odds ratios (OR) with 95% confidence intervals (CI) were calculated. A *p*-value <0.05 was considered statistically significant.

Ethical Considerations

The study was conducted after approval from the Institutional Ethics Committee (IEC/SNMC/2023/08, approved December 2023). Written informed consent was obtained from all patients or their legal guardians prior to enrollment. Patient confidentiality was maintained throughout the study.

Results and Discussion

During the study period, 1,121 respiratory specimens were processed from ICU patients. Among these, 138 isolates of *Pseudomonas aeruginosa* were identified (isolation rate 12.3%). Of these, 39 (28.3%) were CRPA and 99 (71.7%) were CSPA.

Demographic and Clinical Characteristics

Patients with CRPA infection were significantly older than those with CSPA infection (64.2 ± 11.4 vs. 54.9 ± 12.1 years; *p* = 0.032). Among CRPA patients, males constituted 61.5% and females 38.5%; the gender

distribution between groups was not statistically significant ($p = 0.61$). Hypertension was the most common comorbidity in CRPA patients, significantly more frequent than in CSPA patients (66.7% vs. 44.4%; $p = 0.024$). Diabetes mellitus (38.5% vs. 29.3%; $p = 0.31$) and chronic respiratory disease (30.8% vs. 24.2%; $p = 0.43$) were also more common among CRPA patients, though differences were not statistically significant. Detailed demographic characteristics are summarized in Table 1.

Distribution of Clinical Samples

Among CRPA isolates, 24 (61.5%) were recovered from sputum and 15 (38.5%) from endotracheal aspirates. Among CSPA isolates, 70 (70.7%) were from sputum and 29 (29.3%) from ETAs. The difference in sample distribution between groups was not statistically significant ($p = 0.31$).

Antimicrobial Susceptibility Pattern

CRPA isolates demonstrated extensive resistance to multiple antimicrobial agents. Table 2 presents the complete susceptibility profile for both CRPA and CSPA isolates.

Risk Factors Associated with CRPA Infection

Multivariate logistic regression identified several independent risk factors for CRPA infection (Table 3). Prior antibiotic exposure (OR 5.6; 95% CI: 2.1–14.8; $p = 0.001$), prolonged mechanical ventilation (OR 10.8; 95% CI: 2.4–48.3; $p = 0.001$), and ICU stay exceeding seven days (OR 10.1; 95% CI: 3.5–29.2; $p < 0.001$) were the strongest independent predictors of CRPA acquisition.

Clinical Outcomes

CRPA infections were associated with significantly inferior clinical outcomes compared to CSPA infections. Mortality among CRPA patients was 51.3% versus 22.2% in CSPA patients ($p = 0.004$; OR 3.7; 95% CI: 1.6–8.6).

Mean hospital stay was significantly longer in the CRPA group (25.8 ± 9.8 days vs. 14.9 ± 5.2 days; $p < 0.001$). ICU readmission was more frequent among CRPA patients (20.5% vs. 11.1%; $p = 0.17$), though this did not reach statistical significance.

Carbapenem-resistant *Pseudomonas aeruginosa* has emerged as a serious therapeutic and epidemiological challenge in ICUs worldwide (12). The increasing prevalence of MDR Gram-negative organisms has significantly complicated management of critically ill patients and contributed to adverse clinical outcomes (4, 5).

In the present study, the prevalence of CRPA among *P. aeruginosa* isolates was 28.3%, which is comparable to findings reported in national and international studies (1, 10, 20). Similar prevalence rates have been documented in Indian tertiary care hospitals where prolonged antibiotic exposure and extensive ICU utilization contribute significantly to antimicrobial resistance (13). The overall isolation rate of *P. aeruginosa* from respiratory specimens was 12.3%, consistent with previously published data on ICU-associated respiratory infections (11). Patients with CRPA infections were significantly older than those with CSPA. Elderly patients are more vulnerable due to immunosenescence, multiple comorbidities, repeated healthcare exposure, and frequent antibiotic administration (8). This observation aligns with findings from multiple prior studies (3, 10).

Hypertension was significantly associated with CRPA infection in the present study. Cardiovascular comorbidities have been linked with increased susceptibility to MDR infections in previous reports, likely due to frequent healthcare utilization and antibiotic exposure in this population (10, 12).

Prior antibiotic exposure emerged as a major independent risk factor for CRPA acquisition (OR 5.6; $p = 0.001$). Excessive and inappropriate use of broad-spectrum antibiotics creates selective pressure favoring emergence and persistence of resistant strains (6,19). Similar observations have been consistently reported in ICU-based studies worldwide (1, 3, 7).

Prolonged mechanical ventilation was one of the strongest predictors of CRPA infection (OR 10.8). Mechanical ventilation compromises natural respiratory defenses and facilitates colonization of the lower respiratory tract by resistant pathogens. Biofilm formation on endotracheal tubes further contributes to persistence and antimicrobial resistance (9).

Table.1 Demographic and Clinical Characteristics of CRPA vs. CSPA Patients

Characteristic	CRPA (n=39)	CSPA (n=99)	p-value
Mean age (years ± SD)	64.2 ± 11.4	54.9 ± 12.1	0.032*
Male gender (%)	61.5%	58.6%	0.61
Hypertension (%)	66.7%	44.4%	0.024*
Diabetes mellitus (%)	38.5%	29.3%	0.31
Chronic respiratory disease (%)	30.8%	24.2%	0.43
Prior antibiotic exposure (%)	79.5%	36.4%	<0.001*
Mechanical ventilation >7 days (%)	74.4%	28.3%	<0.001*
ICU stay >7 days (%)	82.1%	37.4%	<0.001*

Note: CRPA = Carbapenem-Resistant *P. aeruginosa*; CSPA = Carbapenem-Sensitive *P. aeruginosa*; SD = Standard Deviation. *Statistically significant (p < 0.05).

Table.2 Antimicrobial Susceptibility of CRPA vs. CSPA Isolates

Antimicrobial Agent	CRPA Susceptible (%)	CSPA Susceptible (%)	p-value
Piperacillin-tazobactam	12.8%	79.8%	<0.001*
Cefepime	10.3%	74.7%	<0.001*
Ceftazidime	15.4%	76.8%	<0.001*
Meropenem	0%	100%	<0.001*
Imipenem	0%	100%	<0.001*
Levofloxacin	17.9%	68.7%	<0.001*
Gentamicin	41.0%	77.8%	<0.001*
Amikacin	48.7%	83.8%	<0.001*
Tigecycline	74.4%	91.9%	0.02*
Colistin (BMD)	100%	100%	NS

Note: BMD = Broth Microdilution; NS = Not Significant. *Statistically significant (p < 0.05). Tigecycline susceptibility determined by disc diffusion using interpretive criteria only; CLSI has not established validated breakpoints for *P. aeruginosa* — results should be interpreted with caution and not used as sole basis for clinical decision-making. All other agents tested by Kirby-Bauer disc diffusion per CLSI M100 2024. Colistin confirmed by BMD.

Table.3 Multivariate Logistic Regression: Independent Risk Factors for CRPA Infection

Risk Factor	OR	95% CI	p-value
Prior antibiotic exposure	5.6	2.1 – 14.8	0.001*
Prolonged mechanical ventilation (>7 days)	10.8	2.4 – 48.3	0.001*
ICU stay >7 days	10.1	3.5 – 29.2	<0.001*
Comorbid hypertension	2.5	1.1 – 5.8	0.033*
Age >60 years	2.1	0.9 – 4.9	0.08
Diabetes mellitus	1.6	0.7 – 3.7	0.27

Note: OR = Odds Ratio; CI = Confidence Interval. *Statistically significant (p < 0.05). Variables adjusted for all others in the model.

Extended ICU stay (>7 days) was another important predictor of CRPA infection (OR 10.1). Longer ICU stays increase exposure to invasive procedures, contaminated hospital environments, and resistant

bacterial flora (3, 12). The antimicrobial susceptibility pattern demonstrated extensive resistance among CRPA isolates to commonly used antipseudomonal agents. Piperacillin-tazobactam susceptibility was only 12.8% in

CRPA versus 79.8% in CSPA isolates. These findings reflect the growing therapeutic challenge posed by MDR *Pseudomonas aeruginosa* (1, 14).

Colistin retained excellent activity against CRPA isolates (100% susceptibility by BMD). Similar findings have been reported in Indian and international studies (7, 15). However, colistin carries significant nephrotoxicity and should be used judiciously, with dose optimization guided by therapeutic drug monitoring as recommended by the IDSA guidelines (7). Increasing reports of emerging colistin resistance worldwide are concerning and reinforce the importance of rational antibiotic use (15).

The significantly higher mortality observed among CRPA patients (51.3% vs. 22.2%) underscores the severe clinical impact of carbapenem resistance. Delayed initiation of effective antimicrobial therapy, limited treatment options, severe underlying illness, and prolonged ICU stay may all contribute to increased mortality (4, 17).

Similarly, prolonged hospitalization (25.8 vs. 14.9 days) among CRPA patients reflects increased disease severity and healthcare burden (10, 12).

The present study emphasizes the urgent need for robust infection prevention and control measures in ICU settings, including strict hand hygiene, environmental cleaning, surveillance cultures, ventilator care bundles, and antimicrobial stewardship programs (13). Continuous microbiological surveillance, institutional antibiograms, and rational antibiotic prescribing are essential tools to limit the spread of CRPA.

Limitations

The study was conducted over a six-month period (January–July 2024), which may introduce seasonal bias and limits generalizability of findings. The relatively small CRPA cohort (n = 39) may affect the statistical power of the multivariate regression model. Molecular characterization of carbapenem resistance mechanisms — including metallo- β -lactamase genes (NDM, VIM, IMP) and OprD mutations — was not performed, limiting mechanistic insights. As a single-centre study, results may not be representative of all healthcare settings in the region. Larger multicenter studies with molecular analysis and extended follow-up are recommended to validate these findings.

In conclusion, Carbapenem-resistant *Pseudomonas aeruginosa* represents a significant healthcare-associated pathogen in ICU settings and is associated with considerable morbidity, mortality, and prolonged hospitalization. The present study demonstrated that 28.3% of *Pseudomonas aeruginosa* isolates from ICU respiratory specimens were carbapenem-resistant. Prior antibiotic exposure, prolonged mechanical ventilation, extended ICU stay, and comorbid hypertension were identified as major independent risk factors for CRPA acquisition.

CRPA isolates exhibited extensive resistance to multiple antimicrobial agents. Colistin remained the most effective antimicrobial agent, retaining 100% susceptibility. The significantly higher mortality and prolonged hospitalization associated with CRPA infections emphasize the urgent need for early detection, strict infection control, optimized ventilator care, and strengthened antimicrobial stewardship programs. Integration of CRPA surveillance data into institutional antibiograms should be mandated to guide empirical therapy in ICU settings. Multicenter studies incorporating molecular resistance mechanisms are required to better understand the evolving epidemiology and resistance patterns of CRPA in India.

Author Contributions

Deepak Kanjani: Investigation, formal analysis, writing—original draft. Seema Bhamu: Validation, methodology, writing—reviewing. Varsha Kanjani:— Formal analysis, writing—review and editing. Amrin Khan: Investigation, writing—reviewing.

Data Availability

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

Declarations

Ethical Approval Not applicable.

Consent to Participate Not applicable.

Consent to Publish Not applicable.

Conflict of Interest The authors declare no competing interests.

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