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Research Article

Incidence and Clinical Outcomes of Ventilator-Associated Pneumonia Caused by Carbapenem-Resistant Gram-Negative bacteria in a Tertiary Care Centre: An Ambispective Observational Study

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Abstract

Background: Over the past few decades, there has been an increasing prevalence of Carbapenem-resistant Gram-negative pathogens associated Ventilator Associated Pneumonia (VAP), contributing to higher morbidity and mortality.

Objective: The present study was conducted to evaluate the clinical characteristics, risk factors, and outcomes associated with carbapenem-resistant Gram-negative infections in patients with Ventilator-Associated Pneumonia (VAP).

Materials and Methodology: This ambispective observational study, included 96 diagnosed cases of VAP. Study was conducted over a period of 1.5 years. Demographic details, relevant medical and surgical history, duration of mechanical ventilation, ICU stay, and biochemical parameters were recorded. Microbiological analysis was performed using Kirby–Bauer disc diffusion method and broth microdilution technique for organism identification and microbiological susceptibility testing. Patients were categorized into carbapenem-resistant and carbapenem-sensitive groups for comparative statistical analysis. All relevant parameter were compared between the two groups. Data analysis was performed using Microsoft Excel, IBM SPSS version 21 applying appropriate statistical tests.

Results: Among the isolated, 38 (39.6%) exhibited carbapenem resistance, while 58 (60.4%) were carbapenem-sensitive. Overall, a male predominance was observed accounting for 75% of the study population. No significant associations were found between carbapenem resistance and comorbidities, ICU parameters, or severity scores. The overall mortality rate was 43.8 %, with no significant difference between the two groups.

Conclusion: Carbapenem resistance was common among patients with VAP and was not significantly associated with most demographic or clinical variables. Immunosuppression, particularly malignancy, was significantly associated with resistance. This observation warrants further investigation into influencing clinical outcomes and underscores the need for future research.

Keywords: Ventilator-Associated Pneumonia (VAP), Carbapenem resistance, ICU infections, Gram-negative bacteria, Antimicrobial resistance, Mortality

Introduction

Ventilator-Associated Pneumonia (VAP) is defined as pneumonia that develops in patients receiving mechanical ventilation for more than 48 hrs. It is one of the most common healthcare-associated infections in Intensive Care Units (ICUs) and remains a major cause of morbidity, mortality, prolonged hospitalization, and increased healthcare costs. [1,2] The incidence of VAP ranges from 13 to 51 episodes per 1,000 ventilator-days, with higher rates reported in developing countries and Asian ICUS [3,4]. VAP frequently leads to prolonged mechanical ventilation, difficulty in weaning, and extended ICU stay, thereby increasing resource utilization. Delayed or inappropriate antimicrobial therapy is associated with worse clinical outcomes and increased mortality, emphasizing the need for early diagnosis and targeted treatment [5].

The most common causative organisms include Staphylococcus aureus, Pseudomonas aeruginosa, Escherichia coli, Klebsiella pneumoniae, and Acinetobacter baumannii [6,7]. Among these, carbapenem-resistant Gram-negative bacteria have emerged as a major global concern. Carbapenems are last-resort antibiotics used for severe multidrug-resistant infections; however, increasing carbapenems production has led to rising resistance among Enterobacteriaceae, P. aeruginosa, and A. baumannii [7-9]. Indian data report carbapenem resistance rates of 12-15% among Enterobacteriaceae and 40-60% among A. baumanni and P aeruginosa [10]. VAP diagnosis remains challenging due to nonspecific clinical features. IDSA/ATS guidelines recommend diagnosis based on a new pulmonary infiltrate with clinical evidence of infection such as fever, purulent secretions, leucocytosis, and worsening oxygenation [11]. The burden of carbapenem-resistant Gram-negative VAP varies geographically and has increased globally, complicating treatment and infection control [12,13]. Therefore, this study was undertaken to evaluate the incidence and clinical outcomes of VAP caused by carbapenem-resistant Gram-negative bacteria.

Materials and Methodology

The present study was an ambispective, observational, single-centre study conducted in a tertiary care hospital. It included patients admitted to the Intensive Care Unit (ICU) who were on mechanical ventilation and diagnosed with Ventilator-Associated Pneumonia (VAP). The study was conducted over a period of 1.5 years from the date of ethical approval, and a total of 96 patients were included.

Sample Size Estimation

To estimate the incidence of Ventilator-Associated Pneumonia (VAP) caused by carbapenem- resistance Gram-negative bacteria among VAP isolates with a 95% confidence level and 15 % relative precision, assuming a documented incidence of 38%, the minimum required sample size was calculated to be 96 VAP patient admitted to the tertiary care hospital.

Inclusion Criteria

a) All the patients fulfilling the criteria of VAP as per IDSA guidelines were included in the study.

b) VAP was defined as: the presence of new or modifying chest x-ray infiltrates occurring more than 48 h after initiation of invasive mechanical ventilation with at least one of the following:

i. Body temperature ≥38°C.

ii. Total peripheral white blood cell count ≥12,000 cells/µl or ≤4000 cells/µl and at least two of the following.

a. New onset of purulent sputum or change in the character of sputum or increased respiratory secretions or increased suctioning requirements.

b. New-onset or worsening cough or dyspnoea or tachypnoea.

c. Rales or bronchial breath sounds.

d. Worsening gas exchange, increased oxygen requirements or increased ventilator demand.

Exclusion Criteria

a) Not fulfilling VAP criteria like colonizers and onset of pneumonia less than 48 hours.

b) Non-infectious mimics such as pulmonary edema.

c) Inability or unwillingness of research participant caretaker to give written informed consent.

d) Age<18 years.

Methodology

After enrolment, patients were subjected to thorough history taking for as per proforma attached in Appendix. Blood investigations, radiological assessment, respiratory secretions for gram stain, culture were taken after taking written informed consent from NOK of patients. All findings were endorsed in tabulated format and subjected to statistical analysis for results.

Classifying Vap

Clinical evidence mandated at least two of the following: fever (>38 °C) or hypothermia (<36 °C), leucocytosis (>12,000/µL) or leukopenia (<4000/µL), purulent respiratory secretions, paired with significant bacterial isolation from sterile sites (blood, bronchoalveolar lavage) or quantitative cultures from non-sterile sites (tracheal aspirates ≥105 CFU/mL). Pulmonary infections were classified as Hospital-Associated Pneumonia (HAP) when manifesting ≥48 h after admission without evidence of incubation at admission, or Ventilator-Associated Pneumonia (VAP) when occurring >48 h post-intubation with new radiographic infiltrates. All cases underwent independent validation by two intensivists, with discrepancies resolved through infectious disease consultation, ensuring rigorous diagnostic accuracy throughout the study cohort.

Antimicrobial Sensitivity

Initial screening for carbapenem resistance for gram negative cultures grown was performed using the Kirby–Bauer disc diffusion method with imipenem (10 µg) and meropenem (10 µg) discs. Minimum Inhibitory Concentrations (MICs) were determined by broth microdilution, and results were interpreted according to Clinical and Laboratory Standards Institute (CLSI) 2024 guidelines. Isolates resistant to either imipenem or meropenem were classified as carbapenem-resistant.

Statistical Tests

Data is analysed using SPSS software version 21 and Excel. Categorical variables are given in the form of frequency table. Continuous variables are given in Mean ± SD/ Median (Min, Max) form. Chi square test is used to check the association of categorical variables with groups. Normality of variable is checked by Shapiro Wilk test and QQ plot. If data follows normal distribution, parametric tests like independent t test will be used, if not non-parametric test like Mann Whitney U test. p-value less than or equal to 0.05 indicates statistical significance.

Results

Out of 96 patients, we included in the study, 58 (60.41%) patients tested to be carbapenem sensitive and the rest 38 (39.59%) were found to be having resistance towards carbapenem antimicrobials. All the noted parameters were compared between the resistant and sensitive group using the above-mentioned statistical tests, to meet our objectives. The obtained results are represented as tables and graphs (Table 1). Patients in the carbapenem-resistant group had a slightly lower mean age compared to the sensitive group (56.13 ± 18.12 years versus 61.15 ± 16.26 years) with no statistically significant difference (p=0.170). Gender distribution reflected male predominance but had no statistical significance (p=0.092) (Table 2). Among comorbidities, diabetes and hypertension were most common in both groups. The proportion of malignancy in resistant group was significantly higher than in sensitive group. Immune surveillance was noted in only 3.1% of the total population, with 2.6% in the resistant group and 3.4% in the sensitive group (p=0.822) (Table 3). Acinetobacter baumannii and Klebsiella pneumonia were the most common organisms isolated across both carbapenem resistant and sensitive groups with the prevalence of 42.1% and 37.9%, respectively (Table 4).

Table 1: Distribution of demographic details across the carbapenem resistance pattern.

Subcategory	Carbapenem resistance		Total	p-value
	Resistance (N=38)	Sensitive (N=58)		
Age				
Mean ± SD	56.13 ± 18.12	61.15 ± 16.26	59.2 ± 17.1	0.170MW
Median (Q1, Q3)	56 (42, 73)	67 (51, 75)	63 (47, 73)	
Gender				
Female	6 (15.8%)	18 (31%)	24 (25%)	0.092C
Male	32 (84.2%)	40 (69%)	72 (75%)	

Table 2: Distribution of comorbid conditions and cause of ICU admission across the carbapenem resistance pattern.

Associated comorbidities	Carbapenem Resistance		Total	P value
	Resistance (N=38)	Sensitive (N=58)		
Diabetes	5 (13.2%)	13 (22.4%)	18 (18.8%)	0.256[C]
Hypertension	7 (18.4%)	17 (29.3%)	24 (25%)	0.228[C]
CKD	5 (13.2%)	4 (6.9%)	9 (9.4%)	0.303[C]
Stroke	9 (23.7%)	19 (32.8%)	28 (29.2%)	0.339[C]
Sepsis	6 (15.8%)	15 (25.9%)	21 (21.9%)	0.243[C]
Surgical	3 (7.9%)	3 (5.2%)	6 (6.3%)	0.590[C]
RTA	10 (26.3%)	9 (15.5%)	19 (19.8%)	0.194[C]
Malignancy	5 (13.2%)	0	5 (5.2%)	**0.005*[C]**
CAD	6 (15.8%)	9 (15.5%)	15 (15.6%)	0.971[C]
Respiratory	2 (5.3%)	6 (10.3%)	8 (8.3%)	0.378[C]
CLD	0	4 (6.9%)	4 (4.2%)	0.098[C]
Immune surveillance	1 (2.6%)	2 (3.4%)	3 (3.1%)	0.822[C]

Table 3: Distribution of isolated organisms across carbapenem resistance pattern.

Microorganism	Carbapenem Resistant (N=38)	Carbapenem Sensitive (N=58)	Total (N=96)	p-value
Acinetobacter baumannii	16 (42.1%)	22 (37.9%)	38 (39.6%)	0.682[c]
Klebsiella pneumoniae	14 (36.8%)	18 (31.0%)	32 (33.3%)	0.553[C]
Pseudomonas aeruginosa	4 (10.5%)	12 (20.7%)	16 (16.7%)	0.194[C]
Klebsiella oxytoca	0 (0%)	2 (3.4%)	2 (2.1%)	0.518[F]
Enterococcus spp.	1 (2.6%)	0 (0%)	1 (1.0%)	0.396[F]
Burkholderia cepacia	0 (0%)	1 (1.7%)	1 (1.0%)	1.000[F]
Candida albicans	0 (0%)	1 (1.7%)	1 (1.0%)	1.000[F]
Streptococcus pneumoniae	0 (0%)	1 (1.7%)	1 (1.0%)	1.000[F]
MRSA	1 (2.6%)	1 (1.7%)	2 (2.1%)	1.000[F]
MSSA	0 (0%)	1 (1.7%)	1 (1.0%)	1.000[F]
Polymicrobial isolates	2 (5.3%)	1 (1.7%)	3 (3.1%)	0.560[F]

Table 4: Distribution of study population based on Ventilatory support and ICU admission.

Variable	Subcategory	Carbapenem resistance		Total	p-value
		Resistance (N=38)	Sensitive (N=58)		
No of days of VAP onset post ICU admission	Mean ± SD Median (min, max)	9 ± 2.7 9 (7, 11)	8.91 ± 2.21 9 (7, 11)	8.94 ± 2.4 9 (7, 11)	0.881[MW]
Mechanical ventilation days prior to VAP	Mean ± SD Median (min, max)	5.13 ± 1.83 5 (4, 7)	5.19 ± 1.68 5 (4, 6)	5.16 ± 1.73 5 (4, 6)	0.661[MW]
Chest Radiological involvement	Bilateral	16 (42.1%)	36 (62.1%)	52 (54.2%)	0.055[C]
	Unilateral	22 (57.9%)	22 (37.9%)	44 (45.8%)	

The mean duration for onset of VAP post ICU admission was comparable between groups, while the radiological involvement showed a higher proportion of bilateral involvement in the sensitive group (62.1%) compared to resistant (42.1%), approaching statistical significance (p=0.055) (Figure 1) (Figure 2) (Table 5). Severity scores were similar between groups. The mean SAPS II score was 52.99 ± 15.8 overall, with slightly lower values in resistant patients (51.76 ± 17.6) compared to sensitive patients (53.78 ± 14.6), without statistical significance (p=0.310). SOFA scores also showed no significant difference (resistant: 8.31 ± 3.95; sensitive: 9.77 ± 7.4; p=0.792) (Figure 3). Out of 42 patients died, 15 (39.5%) had carbapenem resistance and 27 (46.6%) were noted be infected with carbapenem sensitive organisms. There was no significant mortality difference between the two groups (Table 6). The mean age among deceased patients was higher (61.6 ± 16.63 years; median: 68 [50–75]) compared to survivors

(57.3 ± 17.4 years; median: 57 [46–70.75]), though not statistically significant (p=0.219). Gender distribution was similar across outcomes (p=0.812). Among comorbidities, CKD showed a strong association with mortality, present in 21.4% of deaths and absent among survivors (p<0.001). CLD was also significantly associated with mortality (9.5% in deaths vs 0% in survivors; p=0.021). Sepsis (31% vs 14.8%; p=0.058) and RTA (11.9% vs 25.9%; p=0.087) showed trends but did not reach statistical significance. Immune surveillance status remained comparable (p=0.416) (Table 7). ICU variables showed that the timing of VAP onset and duration of ventilation were similar between deceased and surviving patients (p=0.988 and p=0.778, respectively).

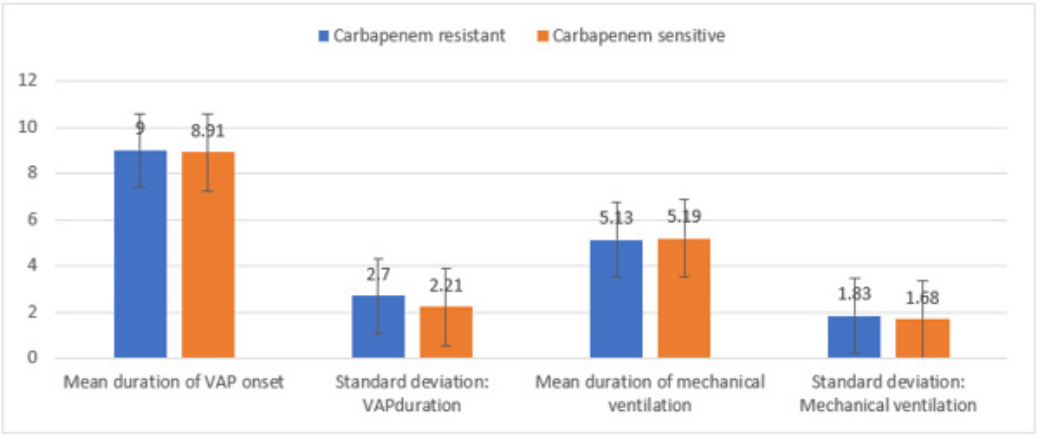

Figure 1: Distribution of mean and standard duration of VAP onset and duration of ventilation.

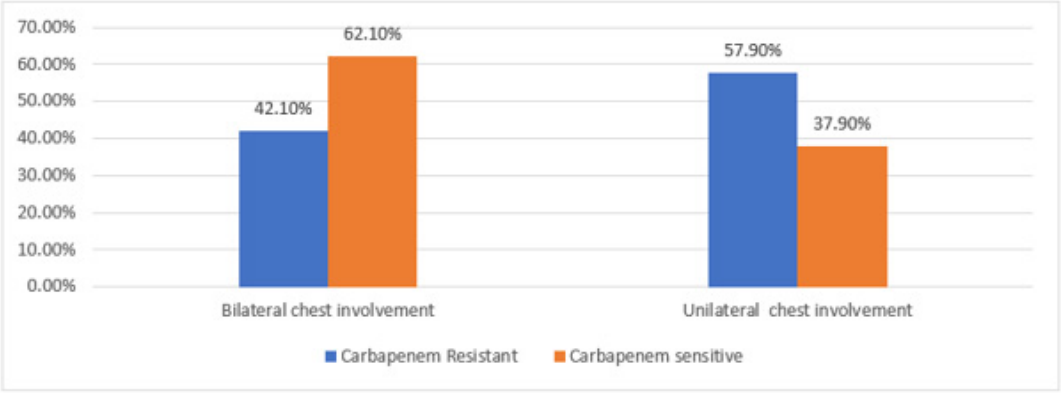

Figure 2: Distribution of study population based on the chest radiography lung field involvement.

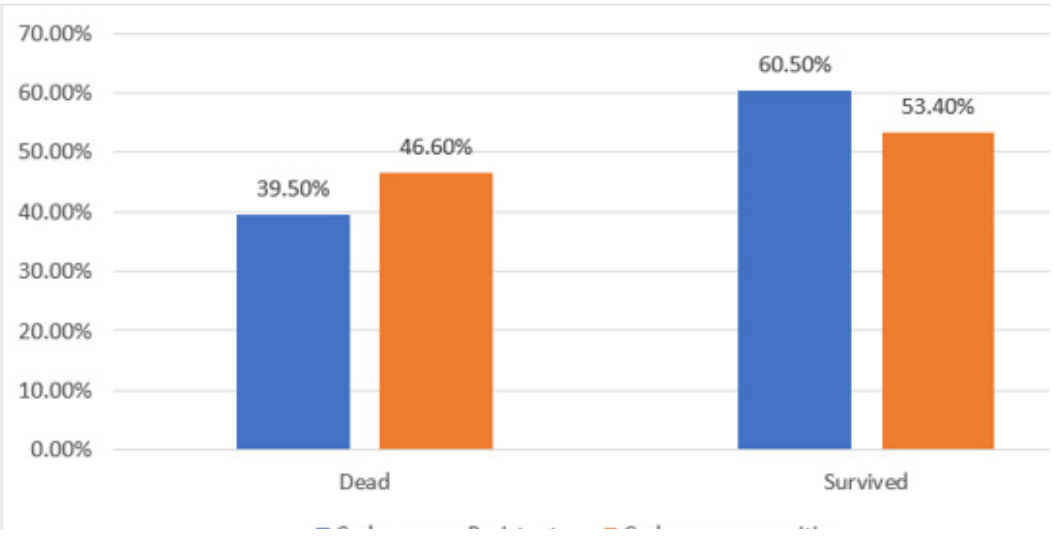

Figure 3: Distribution of mortality across the carbapenem resistance status.

Table 5: Distribution of average ICU severity score across resistance pattern.

Parameter	Resistance (N=38)	Sensitive (N=58)	Total	P value
Severity Score - SAPS II	51.76 ± 17.6 46.5 (39.5, 64)	53.78 ± 14.6 52 (42.75, 65)	52.99 ± 15.8 52 (40, 64)	0.310[MW]
Severity Score - SOFA	8.31 ± 3.95 7 (5, 10.25)	9.77 ± 7.4 7 (4, 16)	9.2 ± 6.3 7 (5, 12)	0.792[MW]

Table 6: Distribution of parameter across the outcome.

Parameter	Outcome		Total	p-value
	Death (n=42)	Survived (n=54)		
Age: Mean ± SD	61.6 ± 16.63	57.3 ± 17.4	59.2 ± 17.1	0.219[MW]
Median (Q1, Q3)	68 (50, 75)	57 (46, 70.75)	63 (47, 73)	
Female	11 (26.2%)	13 (24.1%)	24 (25%)	0.812[C]
Male	31 (73.8%)	41 (75.9%)	72 (75%)	
Diabetes Mellitus	7 (16.7%)	11 (20.4%)	18 (18.8%)	0.645[C]
Hypertension	9 (21.4%)	15 (27.8%)	24 (25%)	0.476[C]
CKD	9 (21.4%)	0	9 (9.4%)	**<0.001*C**
Stroke	9 (21.4%)	19 (35.2%)	28 (29.2%)	0.141[C]
Sepsis	13 (31%)	8 (14.8%)	21 (21.9%)	0.058[C]
Surgical management	2 (4.8%)	4 (7.4%)	6 (6.3%)	0.595[C]
RTA	5 (11.9%)	14 (25.9%)	19 (19.8%)	0.087[C]
Malignancy	3 (7.1%)	2 (3.7%)	5 (5.2%)	0.452[C]
CAD	5 (11.9%)	10 (18.5%)	15 (15.6%)	0.376[C]
Respiratory	5 (11.9%)	3 (5.6%)	8 (8.3%)	0.264[C]
CLD	4 (9.5%)	0	4 (4.2%)	**0.021*C**
Immune surveillance	2 (4.8%)	1 (1.9%)	3 (3.1%)	0.416[C]

Table 7: Distribution of ICU variables across mortality.

Parameter	Death (n=42)	Survived (n=54)	Total	P value
No of days of VAP onset post ICU admission	9 ± 2.35 9 (7, 10.25)	8.9 ± 2.46 9 (7, 11)	8.94 ± 2.4 9 (7, 11)	0.988[MW]
Mechanical ventilation days prior to VAP	5.04 ± 1.46 5 (4, 6)	5.25 ± 1.92 5 (4, 7)	5.16 ± 1.73 5 (4, 6)	0.778[MW]
Bilateral lung involvement	36 (85.7%)	16 (29.6%)	52 (54.2%)	**<0.001*C**
Unilateral lung involvement	6 (14.3%)	38 (70.4%)	44 (45.8%)	
Severity Score - SAPS II	64.83 ± 13.98 65 (25, 94)	43.77 ± 9.93 41.5 (26, 72)	52.99 ± 15.8 52 (25, 94)	**<0.001*t**
Severity Score - SOFA	11.81 ± 7.79 10 (5, 17.25)	7.16 ± 3.77 6 (5, 10)	9.19 ± 6.28 7 (5, 12)	**0.004*MW**

However, bilateral lung involvement was significantly associated with mortality, seen in 85.7% of deaths compared to only 29.6% of survivors (p<0.001). Severity scores were markedly higher among deceased patients, with SAPS II scores averaging 64.83 ± 13.98 compared to 43.77 ± 9.93 in survivors (p<0.001). Similarly, SOFA scores were significantly elevated in deaths (11.81 ± 7.79 vs 7.16 ± 3.77; p=0.004) (Table 8). Binary logistic regression analysis was performed to evaluate the association between carbapenem resistance and various demographic, clinical, and ICU-related parameters. No variables had the significant values to be considered as independent variables (Table 9). Binary logistic regression analysis identified several key predictors of mortality among the study population. CKD, CLD, bilateral radiological involvement, SAPS II and SOFA were observed to have significant positive association.

Table 8: Logistical regression for association between various parameters and the carbapenem resistance.

Variable	Crude OR (95% CI)	Adjusted OR (95% CI)	P value
Age	0.98 (0.95–1.01)	0.97 (0.94–1.01)	0.168
Gender	2.40 (0.85–6.78)	2.10 (0.71–6.21)	0.182
Diabetes	0.52 (0.17–1.57)	0.60 (0.18–1.94)	0.397
Hypertension	0.55 (0.21–1.42)	0.62 (0.22–1.71)	0.356
CKD	2.05 (0.49–8.56)	1.88 (0.41–8.62)	0.418
Stroke	0.64 (0.26–1.56)	0.71 (0.28–1.81)	0.476
Sepsis	0.54 (0.20–1.43)	0.60 (0.22–1.64)	0.321
RTA	1.92 (0.73–5.06)	1.78 (0.64–4.94)	0.269
CAD	1.02 (0.34–3.02)	0.98 (0.32–3.01)	0.971
Respiratory disease	0.48 (0.09–2.41)	0.52 (0.10–2.75)	0.449
Days to VAP onset	1.01 (0.87–1.17)	1.00 (0.85–1.18)	0.881
MV days before VAP	0.99 (0.78–1.25)	1.02 (0.80–1.30)	0.661
Bilateral involvement	0.45 (0.19–1.04)	0.50 (0.20–1.21)	0.055
SAPS II score	0.99 (0.96–1.02)	0.98 (0.95–1.02)	0.31
SOFA score	0.96 (0.87–1.05)	0.97 (0.88–1.06)	0.792

Table 9: Logistic regression model for association between mortality with other clinical variables.

Variable	Death (%)	Survived (%)	P value
Age	61.6 ± 16.63	57.3 ± 17.4	0.219
Male gender	73.80%	75.90%	0.812
Diabetes	16.70%	20.40%	0.645
Hypertension	21.40%	27.80%	0.476
CKD	21.40%	0%	<0.001*
Stroke	21.40%	35.20%	0.141
Sepsis	31%	14.80%	0.058
RTA	11.90%	25.90%	0.087
Malignancy	7.10%	3.70%	0.452
CAD	11.90%	18.50%	0.376
Respiratory	11.90%	5.60%	0.264
CLD	9.50%	0%	**0.021***
Bilateral involvement	85.70%	29.60%	**<0.001***
SAPS II	64.83 ± 13.98	43.77 ± 9.93	**<0.001***
SOFA	11.81 ± 7.79	7.16 ± 3.77	**0.004***

Discussion

The occurrence of Ventilator-Associated Pneumonia (VAP) due to Carbapenem-Resistant Gram-Negative Bacteria (CR-GNB) represents a major challenge in intensive care units worldwide. The rising prevalence of antimicrobial resistance has not only limited therapeutic options but also complicated clinical management and outcome prediction in critically ill patients. [7,10] The present study was conducted to estimate the prevalence of carbapenem resistance among patients admitted diagnosed with VAP in a tertiary care centre within our epidemiological setting and to analyse the associated factors influencing clinical outcomes.

Prevalence of Carbapenem Resistance in Ventilator Associated Pneumonia

In the present study, carbapenem resistance was observed in 38

(39.6%) among the patients diagnosed with VAP. A diverse spectrum of microorganisms was identified with Acinetobacter baumannii being the most frequently isolated pathogen (39.6%) isolates, followed by Klebsiella pneumoniae (33.3%) and Pseudomonas aeruginosa (16.7%). Together, these organisms accounted for nearly 90% of all isolates, highlighting the dominance of non-fermenting Gram-negative bacilli and Enterobacterales in ICU-acquired respiratory illness. Although intergroup differences were not statistically significant, the distribution underscores the high burden of multidrug-resistant organism in critically ill patients. Our findings are comparable with Mohamed A et al. who reported 76% of VAP cases were caused by Gram negative organisms, with Klebsiella pneumoniae, Pseudomonas aeruginosa and E. coli being predominant. Notably, 94.7% of the isolates in their study were carbapenemase resistant [14] Similarly, Hegazy EE et al. identified Klebsiella pneumoniae, Acinetobacter baumannii and Pseudomonas aeruginosa as the leading pathogens, accounting for 34.9%, 20.5% and 18.1% respectively [15]. Saleem M et al. also reported prevalence a VAP prevalence of 43% with Klebsiella pneumoniae being the most frequently resistant isolate [16].

The sporadic isolation of Gram-positive organisms including MRSA (2.1%), MSSA, Enterococcus species and Streptococcus pneumoniae (1% each) of our patients, reflects the predominant Gram-negative etiology in late-onset VAP, with limited polymicrobial infections. However, the presence of MRSA across both resistant and sensitive groups emphasizes the need of continued surveillance, as Staphylococcal VAP is associated with significant morbidity and often requires glycopeptide or lipopeptide therapy [17]. Gong Y et al. reported carbapenem resistance rated ranging from 16 to 51.4% among immunocompromised ICU patients, which are comparable yet slightly higher than our finfings [18]. Abedi H et al. observed CR-GNB being the most common pathogen among elderly ICY patients (mean age 67.5 ± 16.9 years), with a mortality rate of 71.4%, highlighting the severity of infection in high-risk population. [19] *Gurjar M,* et al. demonstrated a high burden of Acinetobacter baumannii -associated VAP in Indian ICUs, reinforcing the endemic nature of the pathogen. Across studies, carbapenem resistance in VAP ranges between 31% and 61%, reflecting variability due to institutional practices, patient populations, and diagnostic methodologies [16-21].

Demographic Details and Resistance Pattern

In our study, patients with carbapenem-resistant infections had a slightly lower mean age (56.13 ± 18.12 years) compared to those with sensitive isolates (61.15 ± 16.26 years), though this difference was not statistically significant (p=0.170). This is consistent with Mohamed A et al., who reported a similar mean age of 56 ± 17.5 years. Hegazy et al. also observed comparable findings with comparable mean age 59 ± 17.3 years, with no significant difference between resistant and sensitive groups. [15] *Gurja,* et al. reported a lower mean age (IQR 32-63 years), although resistance association was not analysed [20]. Male predominance was observed in our study (75%), consistent across both resistant (84.2%) and sensitive (69%) groups, though not statistically significant (p=0.092). Similar trend has been widely reported in ICU studies. Saleem M et al documented that 72.4% of ICU infections occurred in males [16]. This may reflect higher exposure to risk factors such as smoking, chronic respiratory disease, occupational hazards, and increased ICU admissions among male in our population.

Comorbidities and Risk Factors

Diabetes mellitus (18.8%), hypertension (25%), and stroke (29.2%) were the most common comorbidities in our cohort. However, no significant association was observed between these conditions and carbapenem resistance, except for malignancy, which was significantly more frequent in resistant cases (13.2 % vs 0%), p= 0.005). Gong et al. similarly identified malignancy an independent predictor of CR_GNB resistance (OR=2.38; p=0.036). Hegazy EE et al. reported higher rates of trauma, ischemic injury, and diabetes reflecting variability in ICU population [15]. In contrast, Abedi H et al. and Mohamed A et al. did not find a significant association between malignancy and resistance [14,19]. These differences likely reflect heterogeneity in the study design and patient selection.

Ventilatory Parameters and Status of Resistance

The mean time to VAP onset was similar between carbapenem-resistant (9 ± 2.7 days) and (8.91 ± 2.21 days), with no significant difference (p=0.881). Duration of mechanical ventilation prior to VAP was also comparable (5.13 ± 1.83 vs 5.19 ± 1.68 days; p=0.661). These findings align with Hegazy EE et al., who reported a mean VAP onset of approximately 10 days. [15] *Patel SK,* et al. demonstrated longer ICU stay and ventilation duration in resistant cases, although their findings were specific to Pseudomonas aeruginosa VAP [21]. Gurjar M et al. also reported prolonged ICU stays in CR cases [20]. The similarity in timing between groups in our study suggest that resistance is more closely related to microbial ecology and prior antibiotic exposure rather than ventilation duration alone. Prolonged mechanical ventilation remains a universal risk factor for VAP, typically beyond 5-7 days, regardless of resistance status.

Radiological Observations and the Association with Status of Carbapenem Resistance

Bilateral pulmonary infiltrates were more frequent in sensitive cases (62.1%) compared to resistant cases (42.1%), though these differences approached statistical significance (p=0.055). Conversely, unilateral involvement was more common in resistant infections. Bilateral involvement was associated with higher mortality, indicating that radiological severity plays a crucial role in prognosis.

ICU Indicators and Association with Carbapenem Resistance

SAPS II and SOFA scores were comparable between groups, though slightly higher in the sensitive group. This may explain the paradoxically higher mortality observed in this group. Abedi H et al.

did not utilize severity scoring system for correlation, while Gong Y et al. reported no significant association between clinical severity markers and resistance. [18,19] Differences may reflect variations in ICU protocols and early intervention strategies.

Clinical Outcome and Associated Indicators

Overall mortality in the current study was 43.8%, with higher mortality observed in the carbapenem-sensitive group. This contrasts with several studies linking resistance with worse outcomes, but aligns with emerging evidence suggesting that host severity at infection onset may be more important than resistance alone. Mohamed A et al. reported higher mortality in CR-GNB infections (57.9% vs 36.4%)14 Gurjar M et al. also reported mortality around 46% in CR VAP cases [20]. Lower SAPS II and SOFA scores in the resistant group in our study may explain improved survival, suggesting that baseline physiological status influences outcomes more than antimicrobial susceptibility alone. Regression analysis identified bilateral lung involvement, CKD, CLD, SAPS II score, and SOFA score as independent predictors of mortality. Bilateral infiltrates were strongly associated with death (85.7% vs 29.6%, p<0.001), with an adjusted odds ratio of 12.8. Similar findings have been reported by Gurjar M et al. where disease severity significantly influenced mortality. [20] Patel SK et al. reported higher APACHE II scores in resistant infections, indicating worse physiological status.20 Gong Y et al reported median SOFA of 8 but did not correlate them with resistance patterns [18]. CKD (p<0.001) and CLD (p 0.021) were significant predictors of mortality, highlighting the role of pre-existing organ dysfunction on poor outcomes. Abedi H et al similarly identified malignancy and prolonged hospitalization as predictors of adverse outcomes [19].

Strength of the Study

a) As a prospective observational study, ensures systematic and real-time data collection, thereby minimizing recall bias and improving the accuracy of clinical and microbiological parameters.

b) Following IDSA guidelines, incorporating clinical, radiological, and microbiological evidence, along with independent validation by intensivists. This reduced the misclassification bias and strengthened the internal validity.

c) Comparative analysis between carbapenem-resistant and carbapenem-sensitive groups within the same cohort minimized the confounding variables related to institutional practices, antibiotic policies, and ICU environment, which are often limitations in multi-centre studies.

Limitations of the Study

a) Relatively small sample size, single centric considering the geographical distribution of the considered epidemiological population, which limited the power of analysing variables.

b) Molecular characterization of resistance mechanisms, limited the understanding of the underlying genetic drivers of resistance, which is relevant parameter.

c) Data on prior antibiotic exposure, would have improved the outcome.

d) The higher mortality in the carbapenem-sensitive group might have been due to the unmeasured confounders.

Conclusion

Carbapenem-resistant Gram-negative bacteria constitute a substantial proportion of pathogens causing Ventilator-Associated Pneumonia (VAP), with Acinetobacter baumannii remaining the predominant organism, followed by klebsiella pneumoniae and Pseudomonas aeruginosa. Chronic Kidney disease and malignancy were significantly associated with carbapenem resistance, whereas ICU-related variables did not demonstrate a significant relationship. The unexpectedly higher mortality observed among the patients with carbapenem-sensitive infections suggests that clinical outcomes in VPA are determined not only by antimicrobial resistance but also by underlying host factors and the severity of illness. These findings underscore the multifactorial nature of ICU mortality and highlight the importance of early risk stratification, judicious antimicrobial stewardship, and comprehensive patient management. Further multicentre studies with larger sample sizes are warranted to better delineate the determinants of mortality and to optimize management strategies for patients with VAP.

Human Ethics

All procedures performed in studies involving human participants were in accordance with the institutional review committee and with the 1964 Helsinki declaration and its later amendments.

Ethical Approval

Ethical approval for the study was obtained from Institutional Review Committee.

Consent to Participate

Written informed consent was obtained from each participant.

Clinical Trial Number

Not applicable.

Availability of Data and Materials

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

Conflict Of Interest

The authors declare that they have no competing interests.

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