

Clinical Characteristics and Outcomes of Carbapenem-Resistant Gram-Negative Bacteria Pneumonia in Immunocompromised ICU Patients: A Retrospective Study

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Background: Immunocompromised patients are increasingly admitted to intensive care units (ICUs), where carbapenem-resistant Gram-negative bacteria (CRGNB) pneumonia poses a growing threat due to limited treatment options and high mortality. This study aimed to compare the characteristics and outcomes of immunocompromised and immunocompetent ICU patients with CRGNB pneumonia and identify risk factors for ICU mortality.

Methods: We retrospectively analyzed the clinical characteristics, laboratory findings, and outcomes of patients with laboratory-confirmed CRGNB pneumonia admitted to Third Affiliated Hospital of Sun Yat-sen University from January 2021 to April 2025.

Results: Among 185 patients, 83 (44.9%) were immunocompromised, most often due to corticosteroid use (33.7%) or cancer chemotherapy (27.7%). Compared with immunocompetent patients, immunocompromised patients had higher rates of viral co-infection (36.1% vs 20.6%, $p = 0.029$), bacteremia (39.8% vs 15.7%, $p < 0.001$), and ICU mortality (65.1% vs 26.5%, $p < 0.001$). Escalation therapy was observed more commonly in immunocompromised patients (79.5% vs 61.8%, $p = 0.014$). In multivariate analysis, ICU mortality among immunocompromised patients was independently associated with vasopressor therapy (OR = 4.53, 95% CI: 1.35–16.85, $p = 0.01$), the ratio of invasive mechanical ventilation time to ICU length of stay (IMV time/ICU LOS) (OR = 1.18, 95% CI: 1.01–1.40, $p = 0.04$), age > 65 years (OR = 3.59, 95% CI: 1.20–12.14, $p = 0.02$), and platelet count $< 100 \times 10^9/L$ (OR = 3.26, 95% CI: 1.02–12.12, $p = 0.04$). Among immunocompetent patients, vasopressor therapy (OR = 37.76, $p < 0.001$), CRRT (OR = 16.60, $p = 0.001$), pre-existing heart failure (OR = 3.26, $p = 0.049$), and IMV time/ICU LOS (OR = 1.48, $p < 0.001$) were independent mortality predictors, while tracheostomy was protective (OR = 0.13, $p = 0.016$).

Conclusion: Immunocompromised ICU patients with CRGNB pneumonia have distinct clinical characteristics, higher mortality, and risk factors that should be incorporated into prognostic evaluation and management.

Keywords: intensive care unit, immunocompromised, carbapenem-resistant gram-negative bacteria, pneumonia, retrospective study

Introduction

Carbapenem-resistant Gram-negative bacteria (CRGNB), including *CR-Acinetobacter baumannii* (CRAB), *CR-Pseudomonas aeruginosa* (CRPA), *CR-Klebsiella pneumoniae* (CRKP), and *CR-Escherichia coli* (CRECO), pose a growing global public health threat, characterized by limited therapeutic options and high mortality rates.^{1–4} CRGNB have increasingly been recognized as a leading cause of hospital-acquired infections (HAIs) in intensive care units (ICUs), particularly in cases of pneumonia.^{5–7} CRGNB infections present a significant challenge for ICUs in both developed and developing countries. In resource-limited settings, restricted access to effective antimicrobials and inadequate infection control result in a higher incidence of these infections.⁸ Moreover, CRGNB infections occur in both adults and children, with severe pneumonia and high mortality rates often reported in pediatric ICUs.⁹ The progress

of effective therapeutic interventions for a range of diseases, including cancer, hematologic malignancies, and autoimmune diseases, has contributed to a steady increase in the population of immunocompromised patients.^{10,11} These individuals represent a substantial proportion of ICU admissions, with approximately one-third of ICU patients having at least one risk factor for immunosuppression.^{12,13} Baseline immune deficiencies, exposure to broad-spectrum antibiotics, and the need for invasive interventions led these patients to be particularly vulnerable to infection during their ICU stay, especially from multidrug-resistant (MDR) pathogens, including CRGNB.^{12,14,15}

Compared to immunocompetent individuals, immunocompromised patients often present with atypical clinical manifestations, experience more aggressive disease progression, and have poorer prognoses.^{6,16} Therefore, characterizing the clinical features and identifying independent mortality risk factors in this distinct population is crucial. However, research focused on immunocompromised ICU patients with CRGNB pneumonia remains limited. Most existing studies concentrate on single pathogens (e.g., *Klebsiella pneumoniae* or *Pseudomonas aeruginosa*) or specific immunocompromised subgroups, such as those with cancers, transplantation, or hematological diseases, thereby limiting the generalizability of their conclusions.^{17–21} To address this gap, we evaluated the risk factors for mortality in immunocompromised ICU patients with CRGNB pneumonia. In addition, we investigated the clinical characteristics, therapeutic management strategies, and clinical outcomes. Our findings aim to provide valuable insights into the stratified management of CRGNB pneumonia in ICUs, particularly for optimizing personalized treatment strategies for immunocompromised individuals.

Methods

Design and Population

A retrospective study was conducted at the Medical Intensive Care Unit (MICU) of the Third Affiliated Hospital of Sun Yat-sen University, Guangzhou, China, from January 1, 2021, to April 30, 2025. Adult patients (≥ 18 years) admitted to the MICU for ≥ 48 hours with microbiologically confirmed pneumonia caused by CRGNB were recruited. All patients, irrespective of their immune status, were enrolled, with only the initial infectious episode included in the final analysis. Exclusion criteria included: (1) clinically suspected community-acquired pneumonia (CAP); (2) cases reflecting bacterial colonization; (3) pneumonia caused by carbapenem-susceptible Gram-negative pathogens; and (4) incomplete clinical data or missing antimicrobial susceptibility data (Figure 1).

Study Definitions

Immunosuppression was defined based on established consensus, determined by meeting one of the following criteria: solid cancer (active or in remission for less than 5 years), active hematologic malignancy, solid-organ transplant, receiving corticosteroid therapy with a prednisone dose of 20 mg or equivalent daily for ≥ 14 days or a cumulative dose > 700 mg, receiving cancer chemotherapy, use of biologic immune modulators, receiving disease-modifying antirheumatic or other immunosuppressive drugs, human immunodeficiency virus infection, and genetic immunodeficiency.^{22–24} Immune status was recorded at the end of the hospitalization to accurately classify patients in whom a diagnosis associated with immunosuppression was established during ICU stay.

Pneumonia was diagnosed based on the presence of both clinical symptoms/signs of infection, together with infiltrate(s) on chest X-rays at ICU admission. Hospital-acquired pneumonia (HAP) was defined as pneumonia developing ≥ 48 hours after hospital admission. Hospital acquisition was considered if the patient resided in a long-term care facility or was directly transferred from another hospital.²⁵ Although ventilator-associated pneumonia (VAP) was defined as HAP developing ≥ 48 hours after endotracheal intubation,^{26,27} VAP cases were not separately recorded or analyzed, as the study primarily focused on HAP and excluded clinically suspected CAP. CRGNB were defined as *Acinetobacter baumannii*, *Pseudomonas aeruginosa*, or *Enterobacterales* with resistance to any carbapenem (susceptible results were reported as resistant). Microbiological cultures were obtained from specimens of the lower respiratory tract (e.g., bronchoalveolar lavage, endotracheal aspirate, or qualified sputum), and all cases included had pathogens isolated from a respiratory source. All isolates were identified and tested using the Beckman MicroScan Walkaway 96 Plus, a fully automated microbiological drug susceptibility analyzer. Bacterial isolation and identification, and drug susceptibility testing were performed per relevant

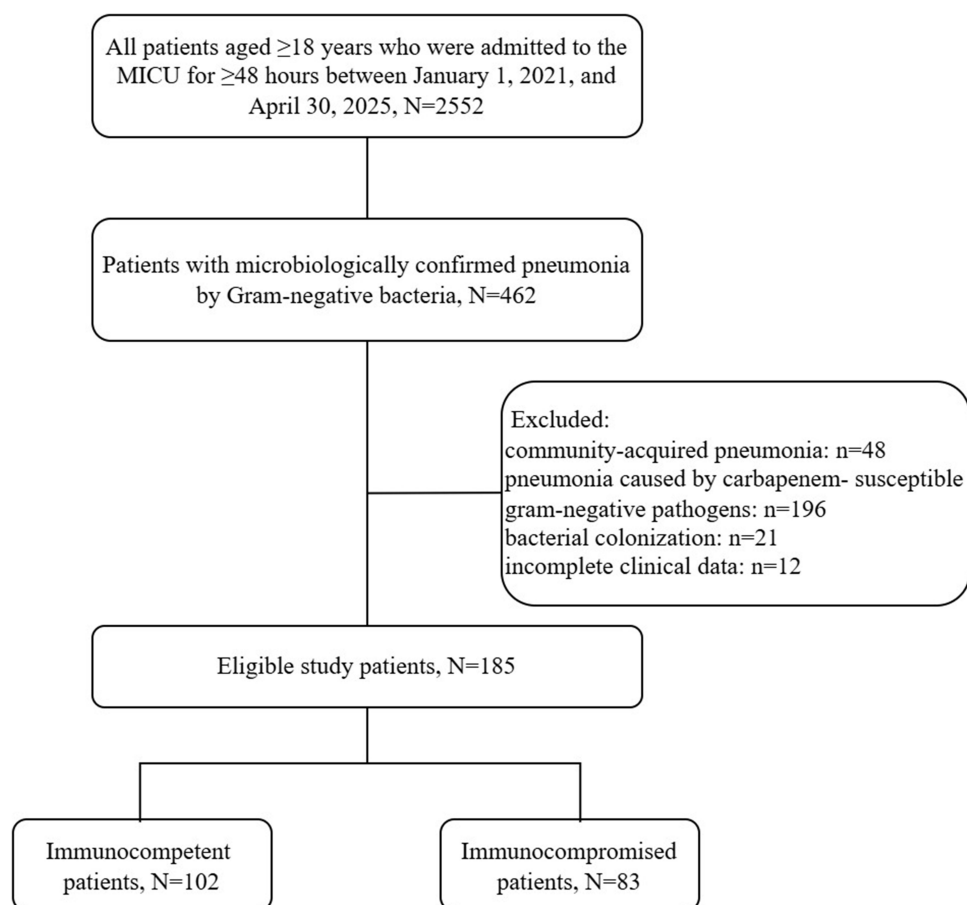


Figure 1 Study flow chart.

national industry standards for clinical microbiology. All cases were reviewed by a senior Infectious Diseases specialist to determine the presence of true clinical infection and source. Patients were classified as having a CRGNB infection if they had a positive culture from a significant clinical sample and clinical signs of infection. Polymicrobial pneumonia was defined as having more than 1 potentially pathogenic microorganism identified.²⁸

The ratio of invasive mechanical ventilation time to ICU length of stay (IMV time /ICU LOS ratio) was defined as the total duration of invasive mechanical ventilation (in days) divided by the total ICU length of stay (in days). Escalation of therapy was defined as a switch to or addition of any antimicrobial agent with additional coverage after definitive identification of CRGNB. Combination therapy was defined as the concomitant use of at least two antibiotics for more than 48 hours.

Data Collection and Outcome Measures

All relevant data were collected from the electronic medical record system, encompassing demographic characteristics, comorbidities, immune status, recent hospitalization or antibiotic exposure, ICU severity scores on admission, laboratory results on ICU admission, pathogenic bacteria, treatment-related data (vasopressors, corticosteroids, cardiopulmonary resuscitation, tracheostomy, continuous renal replacement therapy (CRRT), invasive mechanical ventilation), antibiotic regimens, and outcomes including co-infections, ICU mortality, and post-ICU disposition. The main outcome variable was all-cause ICU mortality.

Ethical Considerations

The study was conducted in accordance with the Declaration of Helsinki and approved by the Medical Ethics Committee of the Third Affiliated Hospital of Sun Yat-sen University on January 23, 2025 (II2025-031-01). The requirement for

informed consent was waived due to the non-interventional nature of the study, which involved the analysis of data from previous electronic medical records and did not involve personal privacy or commercial interests.

Statistical Analyses

Categorical variables were analyzed using the Chi-square test or Fisher's exact test. The *t*-test was used for normally distributed continuous variables, whereas the Wilcoxon rank-sum test was applied to those with a non-normal distribution. The categorical and continuous variables are presented as percentages and means $\pm$ SDs, respectively. *P* values < 0.05 were considered statistically significant. To identify the risk factors of ICU mortality, multivariable logistic regression analysis was performed using Firth's penalized likelihood approach to mitigate sparse-data bias, particularly within small sample subgroups. Variables with a univariate *p*-value < 0.1 were considered for inclusion in multivariate logistic regression analysis using stepwise forward selection based on the likelihood ratio. A value of *p* < 0.05 was considered statistically significant. Despite these adjustments, the possibility of residual confounding due to unmeasured variables cannot be entirely excluded. All statistical analyses were performed using R software, version 4.4.1, and SPSS 27.0 statistical software.

Results

Study Population and Clinical Characteristics

Based on the exclusion criteria, a total of 185 patients were identified during the study period, including 102 (55.1%) immunocompetent and 83 (44.9%) immunocompromised individuals. The five most common immunocompromising conditions were corticosteroid therapy (28/83, 33.7%), cancer chemotherapy (23/83, 27.7%), immunosuppressive therapy (17/83, 20.5%), and solid cancer (10/83, 12.1%) (Figure 2). Immunocompromised patients were characterized by a significantly lower median age compared to immunocompetent patients (66 vs 69 years, *p* = 0.033). Underlying conditions that were significant included hypertension (57.8% vs 50.6%), cerebral vascular disease (47.1% vs 12.0%), and diabetes mellitus (32.4% vs 24.1%) in the immunocompetent and immunocompromised groups.

Laboratory evaluations on ICU admission demonstrated that immunocompromised patients exhibited markedly lymphocyte counts (0.53 vs $0.80 \times 10^9/L$, *p* < 0.001 ; $\leq 0.8 \times 10^9/L$: 69.9% vs 53.9%, *p* = 0.039), and reduced platelet counts (137.00 vs $194.50 \times 10^9/L$, *p* = 0.001), with 33.7% having thrombocytopenia ($< 100 \times 10^9/L$, *p* = 0.002). Leukopenia (10.8% vs 2%, *p* = 0.034) and hypoalbuminemia (≤ 30 g/L; 65.1% vs 49.0%, *p* = 0.042) were more prevalent in immunocompromised cohorts, alongside lower serum potassium levels (3.76 vs 3.99 mmol/L, *p* = 0.013). The highest value of procalcitonin (*p* = 0.024) and interleukin-6 (*p* < 0.001) during hospitalization was significantly higher in the immunocompromised group, whereas no clear differences in admission were found. No statistically significant differences were identified in the prevalence of most comorbidities or pre-hospital clinical statuses, severity of illness scores (APACHE-II, SOFA, GCS), other infection-related biomarkers (e.g., C-reactive protein), renal function markers, or other baseline laboratory parameters (all *P* > 0.05) (Table 1).

Treatments and Clinical Outcomes

Received vasopressor therapy (75.9% vs 60.8%, *p* = 0.043), corticosteroids (80.7% vs 35.3%, *p* < 0.001), and cardiopulmonary resuscitation (15.7% vs 4.9%, *p* = 0.027) were administered more commonly in immunocompromised patients. However, tracheostomy rates were lower in the immunocompromised group (27.7% vs 44.1%, *p* = 0.032). Viral co-infection (36.1% vs 20.6%, *p* = 0.029) and bacteremia (39.8% vs 15.7%, *p* < 0.001) were significantly higher in immunocompromised patients, while fungal colonization/infection and polymicrobial infection rates were comparable. Although most patients required invasive mechanical ventilation (82.7%), immunocompromised patients received IMV more frequently (92.8% vs 74.5%, *p* = 0.002), with longer IMV duration (11.0 vs 8.0 days, *p* = 0.001) and a higher IMV time /ICU LOS ratio (0.82 vs 0.53, *p* = 0.001). Critically, the rates of ICU mortality (65.1% vs 26.5%, *p* < 0.001) were higher in immunocompromised patients. Survivors in the immunocompetent group were more likely to be transferred to secondary or rehabilitation hospitals (43.1% vs 22.9%, *p* = 0.006). Although ICU length of stay trended longer in

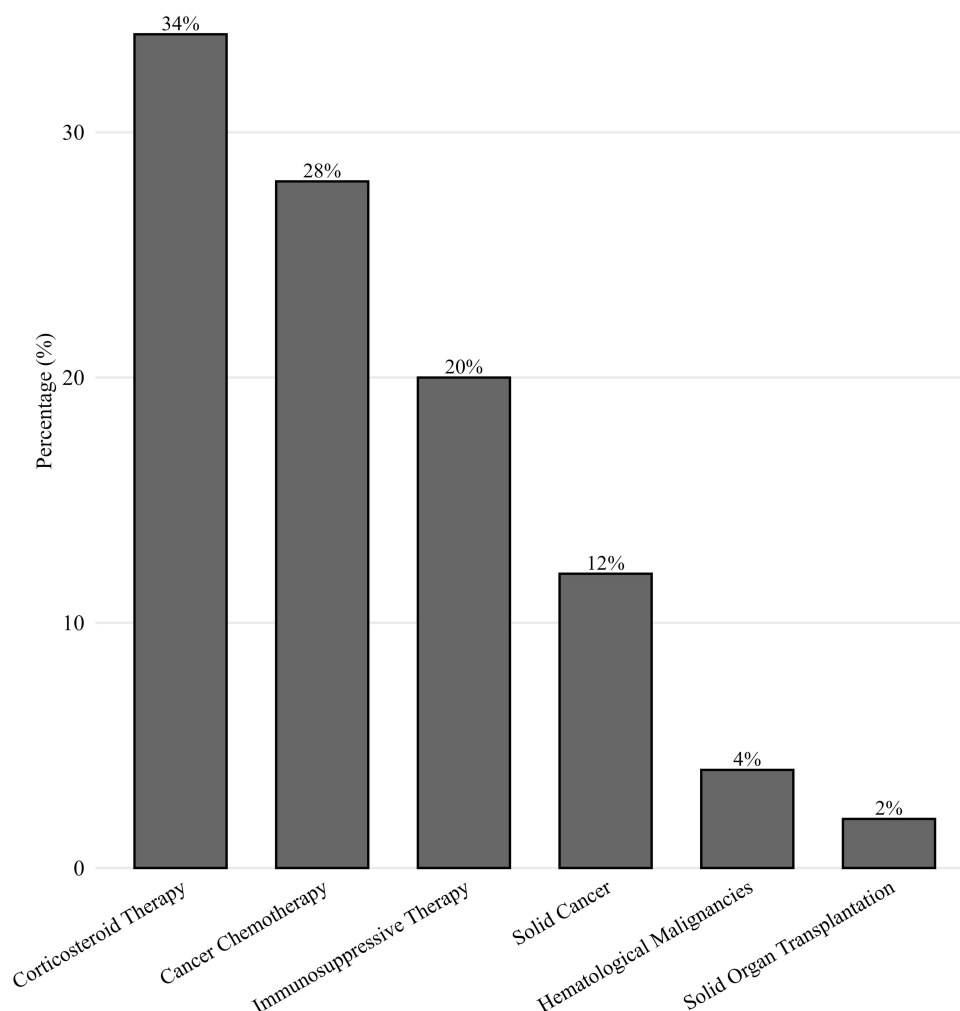


Figure 2 Composition of immunocompromised patients.

immunocompromised patients (16.0 vs 14.0 days, $p = 0.051$), hospital length of stay did not differ between groups (Table 2).

Microbiological Characteristics and Antibiotic Therapy

CRAB was the most frequently isolated pathogen among all patients ($n = 95$, 51.4%), with a comparable prevalence between the immunocompetent and immunocompromised subgroups (48.0% vs 55.4%). No significant difference in distribution for pathogens was observed for other CRGNB: CRKP (33.3% vs 26.5%), CRPA (17.6% vs 14.5%), and CRECO (1.1% vs 3.6%). Among 185 ICU patients with CRGNB pneumonia, a wide range of antibiotics was used for antibiotic therapy among the patients, with tigecycline (47.0%), cefoperazone-sulbactam (27.6%), and ceftazidime-avibactam (27.6%) being the most used. Combination antibiotic therapy was administered in 46.5% ($n = 86$), including colistin-based (18.9%) and tigecycline-based (38.9%) combinations, and did not differ between the two groups. However, escalation therapy was observed more commonly in immunocompromised patients (79.5% vs 61.8%, $p = 0.014$). The details of the pathogens and antibiotics identified are shown in Table 3.

Risk Factors for ICU Mortality in Immunocompromised Patients

The overall ICU mortality was 65.1% in immunocompromised patients. When compared with surviving patients, the deceased had a higher incidence of vasopressor therapy (87% vs 55.2%, $p = 0.003$) and IMV (98% vs 82.8%, $p = 0.033$), higher level of blood urea nitrogen ($p = 0.04$), procalcitonin ($p = 0.039$), interleukin-6 ($p = 0.008$) and IMV time/ICU LOS ratio ($p = 0.004$),

Table I Demographic and Laboratory Values of the Immunocompromised and Immunocompetent Patients

Variable	Overall (N=185)	Immunocompetent (N=102)	Immunocompromised (N=83)	P-value
Age (median, IQR)	69.00 [57.00, 80.00]	69.00 [60.25, 81.75]	66.00 [54.50, 76.50]	0.033
≤45	23 (12.4%)	9 (8.8%)	14 (16.9%)	0.178
45<x≤65	55 (29.7%)	29 (28.4%)	26 (31.3%)	
>65	107 (57.8%)	64 (62.7%)	43 (51.8%)	
Female (n, %)	57 (30.8%)	26 (25.5%)	31 (37.3%)	0.115
Male (n, %)	128 (69.2%)	76 (74.5%)	52 (62.7%)	
Comorbidities				
Hypertensive (n, %)	101 (54.6%)	59 (57.8%)	42 (50.6%)	0.404
Diabetes Mellitus (n, %)	53 (28.6%)	33 (32.4%)	20 (24.1%)	0.284
COPD (n, %)	10 (5.4%)	7 (6.9%)	3 (3.6%)	0.519
Cerebral Vascular Disease (n, %)	58 (31.4%)	48 (47.1%)	10 (12.0%)	<0.001
Coronary Heart Disease (n, %)	26 (14.1%)	16 (15.7%)	10 (12.0%)	0.620
Heart Failure (n, %)	44 (23.8%)	24 (23.5%)	20 (24.1%)	1.000
Chronic kidney disease (n, %)	22 (11.9%)	14 (13.7%)	8 (9.6%)	0.531
Liver Cirrhosis (n, %)	14 (7.6%)	6 (5.9%)	8 (9.6%)	0.496
Recent (< 1 months) antibiotics (n, %)	130 (70.3%)	77 (75.5%)	53 (63.9%)	0.119
Recent (< 3 months) hospitalization > 48 h (n, %)	139 (75.1%)	79 (77.5%)	60 (72.3%)	0.524
Recent (< 1 month) ICU admission (n, %)	79 (42.7%)	45 (44.1%)	34 (41.0%)	0.778
APACHE-II scores (mean ± SD)	22.82 ± 7.08	23.21 ± 6.62	22.34 ± 7.63	0.408
SOFA score (median, IQR)	8.00 [6.00, 10.00]	8.00 [5.25, 10.00]	7.00 [6.00, 10.00]	0.951
GCS score (median, IQR)	6.00 [4.00, 13.00]	6.50 [4.00, 12.00]	6.00 [4.50, 13.50]	0.385
Pauda score (median, IQR)	6.00 [5.00, 7.00]	6.00 [5.00, 7.00]	6.00 [5.00, 8.00]	0.798
Lactate (mmol/L, median, IQR)	1.40 [0.90, 2.20]	1.30 [0.83, 2.08]	1.50 [0.95, 2.40]	0.218
K ⁺ (mmol/L)	3.89 ± 0.65	3.99 ± 0.65	3.76 ± 0.6	0.013
PCO ₂ (mmHg, median, IQR)	39.80 [32.70, 46.40]	40.00 [32.90, 46.88]	39.60 [32.05, 45.35]	0.339
PaO ₂ /FiO ₂ (mmHg, median, IQR)	216.20 [133.00, 313.90]	230.00 [137.12, 338.50]	198.30 [130.75, 272.00]	0.150
White blood cell (×10 ⁹ /L, median, IQR)	11.36 [7.64, 15.68]	11.78 [8.45, 15.30]	10.48 [6.64, 16.48]	0.131
≤4	11 (5.9%)	2 (2.0%)	9 (10.8%)	0.034
>4 to ≤10	64 (34.6%)	35 (34.3%)	29 (34.9%)	
>10	110 (59.5%)	65 (63.7%)	45 (54.2%)	
Neutrophil (×10 ⁹ /L, median, IQR)	9.52 [6.28, 13.83]	10.02 [7.06, 13.63]	9.21 [5.17, 14.87]	0.289
Lymphocyte (×10 ⁹ /L, median, IQR)	0.66 [0.42, 0.97]	0.80 [0.51, 1.11]	0.53 [0.34, 0.86]	<0.001
≤0.8	113 (61.1%)	55 (53.9%)	58 (69.9%)	0.039
NLR	14.11 [8.41, 25.76]	13.47 [7.57, 20.69]	15.32 [9.66, 31.79]	0.086
Hemoglobin (g/L, median, IQR)	90.00 [73.00, 111.00]	91.50 [75.00, 111.00]	88.00 [72.50, 110.00]	0.52
Platelet (×10 ⁹ /L, median, IQR)	173.00 [104.00, 255.00]	194.50 [130.50, 271.00]	137.00 [76.50, 239.50]	0.001

≤100	42 (22.7%)	14 (13.7%)	28 (33.7%)	0.002
BUN (mg/dL, median, IQR)	9.85 [6.66, 16.80]	9.66 [7.19, 17.94]	9.90 [6.27, 15.46]	0.519
Creatinine (μmol/L, median, IQR)	81.00 [49.00, 151.30]	89.50 [54.50, 156.50]	66.00 [45.20, 148.50]	0.104
Albumin (g/L, median, IQR)	29.00 [25.80, 32.90]	30.60 [26.70, 33.68]	28.30 [25.10, 31.65]	0.033
≤30	104 (56.2%)	50 (49%)	54 (65.1%)	0.042
C-reactive protein (mg/L, median, IQR)	61.90 [32.10, 141.20]	58.45 [39.50, 121.02]	71.90 [19.77, 153.65]	0.793
Procalcitonin (ng/mL, median, IQR)	1.09 [0.29, 3.85]	0.99 [0.27, 3.71]	1.18 [0.34, 4.06]	0.546
Interleukin-6 (pg/mL, median, IQR)	51.73 [23.65, 150.70]	55.36 [25.06, 115.87]	46.47 [21.16, 219.10]	0.702
PT (sec, median, IQR)	14.90 [13.90, 16.60]	14.90 [13.83, 16.00]	14.90 [13.90, 16.90]	0.747
APTT (sec, median, IQR)	41.70 [37.00, 48.80]	41.55 [38.12, 47.48]	42.00 [36.35, 49.00]	0.615
D dimer (mg/L, median, IQR)	2.63 [1.67, 5.67]	2.48 [1.5, 5.05]	2.71 [1.84, 6.33]	0.171
Fibrinogen (g/L, median, IQR)	4.24 [2.93, 5.57]	4.24 [3.09, 5.45]	3.97 [2.82, 5.78]	0.975
The highest value during hospitalization				
BUN (mg/dL, median, IQR)	17.58 [9.16, 31.72]	16.22 [8.45, 31.29]	17.72 [9.78, 32.36]	0.425
Creatinine (μmol/L, median, IQR)	126.00 [66.00, 288.00]	128.50 [66.75, 290.92]	122.09 [65.50, 276.50]	0.814
C-reactive protein (mg/L, median, IQR)	140.50 [89.90, 215.60]	138.25 [77.90, 184.45]	146.30 [94.85, 244.80]	0.216
Procalcitonin (ng/mL, median, IQR)	3.85 [0.74, 18.00]	2.75 [0.62, 9.90]	6.00 [1.06, 27.40]	0.024
Interleukin-6 (pg/mL, median, IQR)	156.10 [62.39, 799.50]	115.65 [53.59, 311.90]	399.60 [88.82, 1271.00]	<0.001

Abbreviations: IQR, interquartile range; SD, standard deviation; COPD, chronic obstructive pulmonary disease; APACHE-II, acute physiology and chronic health evaluation scoring system II; SOFA, sequential organ failure assessment; GCS, glasgow coma scale; PaO₂/FiO₂, the ratio of arterial oxygen partial pressure to fractional inspired oxygen; ICU, intensive care unit; NLR, the ratio of neutrophil to lymphocyte count; BUN, blood urea Nitrogen; CPR, cardiopulmonary resuscitation; PT, prothrombin time; APTT, activated partial thromboplastin clotting time.

Table 2 Clinical Characteristics and Outcomes of the Immunocompromised and Immunocompetent Patients

Variable	Overall (N=185)	Immunocompetent (N=102)	Immunocompromised (N=83)	P-value
Vasopressor therapy (n, %)	125 (67.6%)	62 (60.8%)	63 (75.9%)	0.043
Corticosteroid therapy (n, %)	103 (55.7%)	36 (35.3%)	67 (80.7%)	<0.001
Cardiopulmonary Resuscitation (n, %)	18 (9.7%)	5 (4.9%)	13 (15.7%)	0.027
Tracheostomy (n, %)	68 (36.8%)	45 (44.1%)	23 (27.7%)	0.032
CRRT (n, %)	57 (30.8%)	30 (29.4%)	27 (32.5%)	0.767
Bacteremia (n, %)	49 (26.5%)	16 (15.7%)	33 (39.8%)	<0.001
Fungal colonization or infection (n, %)	90 (48.6%)	56 (46.7%)	34 (52.3%)	0.563
Viral co-infection (n, %)	51 (27.6%)	21 (20.6%)	30 (36.1%)	0.029
Polymicrobial infections (n, %)	125 (67.6)	70 (68.6)	55 (66.3)	0.854
Hospital length of stay (d, median, IQR)	24.00 [16.00, 31.00]	24.00 [17.00, 29.75]	24.00 [15.00, 34.00]	0.536
ICU length of stay (d, median, IQR)	15.00 [11.00, 24.00]	14.00 [10.00, 21.75]	16.00 [12.50, 25.00]	0.051
Using IMV during ICU (n, %)	153 (82.7%)	76 (74.5%)	77 (92.8%)	0.002
Reintubation (n, %)	25 (13.5%)	11 (10.8%)	14 (16.9%)	0.323
IMV time (d, median, IQR)	10.00 [3.00, 17.00]	8.00 [0.50, 14.00]	11.00 [6.50, 20.00]	0.001
IMV time/ICU LOS	0.71 [0.23, 1.00]	0.53 [0.02, 0.94]	0.82 [0.46, 1.00]	0.001
ICU mortality (n, %)	81 (43.8%)	27 (26.5%)	54 (65.1%)	<0.001
Transfer to secondary hospitals (n, %)	63 (34.1%)	44 (43.1%)	19 (22.9%)	0.006

Abbreviations: ICU, intensive care unit; CRRT, continuous renal replacement therapy; IMV, invasive mechanical ventilation; IMV/ICU LOS, the ratio of invasive mechanical ventilation time to ICU length of stay.

Table 3 Characteristics of Pathogens and Antibiotics

Variable	Overall (N=185)	Immunocompetent (N=102)	Immunocompromised (N=83)	P-value
Pathogens				
CRKP (n, %)	56 (30.3%)	34 (33.3%)	22 (26.5%)	0.398
CRAB (n, %)	95 (51.4%)	49 (48.0%)	46 (55.4%)	0.395
CRPA (n, %)	30 (16.2%)	18 (17.6%)	12 (14.5%)	0.700
CRECO (n, %)	4 (2.1%)	1 (1.1%)	3 (3.6%)	0.473
Therapy				
Combination therapy (n, %)	86 (46.5%)	48 (47.1%)	38 (45.8%)	0.980
Escalation therapy (n, %)	129 (69.7%)	63 (61.8%)	66 (79.5%)	0.014
Tigecycline-based combinations (n, %)	72 (38.9%)	39 (38.2%)	33 (39.8%)	0.952
Colistin-based combinations (n, %)	35 (18.9%)	18 (17.6%)	17 (20.5%)	0.763
Colistin Intravenous (n, %)	9 (4.9%)	3 (2.9%)	6 (7.2%)	0.315
Colistin Inhaled (n, %)	30 (16.2%)	16 (15.7%)	14 (16.9%)	0.987
Antibacterial therapy				
Tigecycline	87 (47.0%)	44 (43.1%)	43 (51.8%)	0.304
Cefoperazone-sulbactam	51 (27.6%)	27 (26.5%)	24 (28.9%)	0.838
Meropenem	43 (23.2%)	23 (22.5%)	20 (24.1%)	0.942
Imipenem	18 (9.7%)	12 (11.8%)	6 (7.2%)	0.432
Piperacillin-tazobactam	22 (11.9%)	13 (12.7%)	9 (10.8%)	0.866
Ceftazidime-avibactam	51 (27.6%)	29 (28.4%)	22 (26.5%)	0.900
Amikacin	19 (10.3%)	13 (12.7%)	6 (7.2%)	0.324
Omadacycline	6 (3.2%)	4 (3.9%)	2 (2.4%)	0.873

Abbreviations: CRKP, carbapenem-resistant *Klebsiella pneumoniae*; CRAB, carbapenem-resistant *Acinetobacter baumannii*; CRPA, carbapenem-resistant *Pseudomonas aeruginosa*; CRECO, carbapenem-resistant *Escherichia coli*.

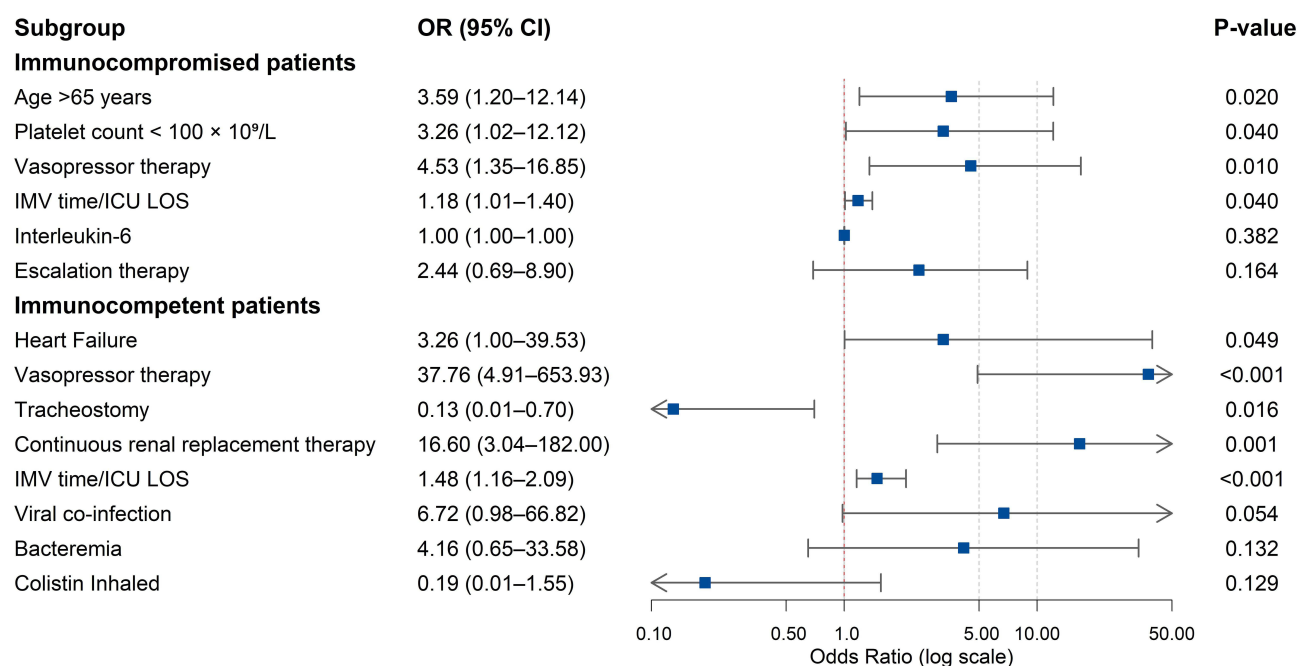


Figure 3 Forest plot of independent predictors of ICU mortality in immunocompromised and immunocompetent patients.

Abbreviations: IMV time/ICU LOS, the ratio of invasive mechanical ventilation time to ICU length of stay; OR, odds ratio; CI, confidence interval.

longer prothrombin time ($p = 0.02$) and IMV time (13 days vs 8 days, $p = 0.026$), and reduced platelet counts ($p = 0.014$). The details are shown in [Supplementary Table S1–3](#).

Univariate logistic regression analysis showed that age >65 years (OR = 2.99, 95% confidence interval (CI): 1.19–7.89), platelet count < 100 × 10⁹/L (OR = 3.56, 95% CI: 1.25–11.84), vasopressor therapy (OR = 5.45, 95% CI: 1.90–16.88), IMV (OR = 11.04, 95% CI: 1.66–217.73), and higher IMV time/ICU LOS ratio (OR = 1.24, 95% CI: 1.08–1.44) were significantly associated with ICU mortality in immunocompromised patients with CRGNB pneumonia ($p < 0.05$) ([Supplementary Table S4](#)). Variables with $p < 0.1$ were entered into the multivariable Firth-penalized logistic regression model that showed vasopressor therapy (OR = 4.53, 95% CI: 1.35–16.85, $p = 0.01$), age > 65 years (OR = 3.59, 95% CI: 1.20–12.14, $p = 0.02$), IMV time/ICU LOS ratio (OR = 1.18, 95% CI: 1.01–1.40, $p = 0.04$), and platelet count < 100 × 10⁹/L (OR = 3.26, 95% CI: 1.02–12.12, $p = 0.04$) were considered as significant factors for ICU mortality ([Figure 3](#) and [Supplementary Table S6](#)).

Risk Factors for ICU Mortality in Immunocompetent Patients

Among immunocompetent patients, the variables with $p < 0.05$ in the univariate analysis included combined diseases (coronary heart disease, heart failure), vasopressor therapy, corticosteroid therapy, cardiopulmonary resuscitation, tracheostomy, CRRT, Bacteremia, reintubation, viral co-infection, procalcitonin, D-dimer, hospital LOS, IMV time/ICU LOS ratio, and prolonged prothrombin time (PT > 16 sec) were correlated to ICU mortality ($p < 0.05$) ([Supplementary Table S5](#)). The multivariate logistic regression analysis was performed to include single factors with $p < 0.1$ into the formula. The result showed that vasopressor therapy (OR = 37.76, 95% CI: 4.91–653.93, $p < 0.001$), CRRT (OR = 16.60, 95% CI: 3.04–182.0, $p = 0.001$), heart failure (OR = 3.26, 95% CI: 1.005–39.53, $p = 0.049$), and IMV time /ICU LOS ratio (OR = 1.48, 95% CI: 1.16–2.09, $p < 0.001$) were identified as independent predictors of mortality, while tracheostomy (OR = 0.13, 95% CI: 0.01–0.70, $p = 0.016$) showed a protective effect ([Figure 3](#) and [Supplementary Table S6](#)).

Discussion

Healthcare-associated infections and antimicrobial resistance present persistent clinical challenges, associated with high morbidity, mortality, and raised healthcare costs.^{29,30} The incidence of MDR bacteria, particularly CRGNB, is rising among immunocompromised ICU patients, a condition that is often associated with a worse prognosis.³¹ However, few studies have specifically examined the clinical characteristics and outcomes of CRGNB pneumonia in this vulnerable population.^{19,32,33} This study revealed differences between immunocompetent and immunocompromised patients in terms of baseline host conditions, laboratory characteristics, and therapeutic management. Immunocompromised patients with CRGNB pneumonia had higher ICU mortality than immunocompetent individuals. Across both groups, vasopressor therapy and higher IMV time/ICU LOS ratio predicted mortality. Age > 65 years and a platelet count < $100 \times 10^9/L$ were prognostic factors in immunocompromised patients, whereas pre-existing heart failure and the need for CRRT were associated with mortality among immunocompetent patients, while tracheostomy showed a potential protective effect. These findings emphasize the importance of immune status in CRGNB pneumonia and highlight the need for individualized assessment in high-risk ICU patients.

CRAB and CRKP were the predominant pathogens in both groups, aligning with prior reports.^{15,34} There was no significant difference in the distribution of these pathogens between immune-status groups or between survivors and non-survivors, suggesting that prognosis may be driven primarily by host-related factors or therapeutic variables. Immunocompromised patients exhibited poorer hematological and nutritional conditions with lower lymphocyte and platelet counts, hypoalbuminemia, and hypokalemia, which are similar to findings in a study of immunosuppressed patients with CRGNB bloodstream infection.³⁵ Reduced serum albumin and potassium levels have been linked to greater severity of pneumonia, reflecting the physiologic vulnerability of this population.^{36–38} They were also more likely to develop bacteremia and viral co-infection, consistent with impaired immune clearance.¹⁶ Moreover, they had higher requirements for mechanical ventilation, vasopressor support, and corticosteroid therapy.³⁹ Although antimicrobial regimens were similar between groups, escalation therapy was more frequent among immunocompromised patients.⁴⁰ Immunocompromised patients are more susceptible to rapidly progressing infections due to immunodeficiency, and when the initial empiric coverage is inadequate or clinical deterioration occurs, clinicians tend to escalate aggressively.⁴¹

Our findings revealed a significantly higher ICU mortality rate among immunocompromised patients (65.1% vs 26.5%), which is consistent with previous reports.^{15,42} Vasopressor therapy and a higher IMV time/ICU LOS ratio were independent predictors for mortality in both subgroups. Additionally, age > 65 years and platelet count < $100 \times 10^9/L$ were unique risk factors in the immunocompromised group. Although our multivariable models took major clinical variables into account, factors such as treatment variability and baseline frailty may partly explain the remaining mortality difference between groups. Prior research has shown that immunocompromised patients with *Klebsiella pneumoniae* infection using mechanical ventilation have higher 30-day mortality.¹⁹ Similarly, tracheal intubation has been identified as a risk factor for death in ICU patients with gram-negative bacillary pneumonia.⁴³ In contrast, while IMV was associated with ICU mortality in univariate analysis in our cohort, it did not retain statistical significance in multivariable models, suggesting sustained ventilator dependence may have greater prognostic value than IMV use alone. Mechanical ventilation is a well-established risk factor for CRGNB infections,^{44,45} with a greater need in patients with these infections compared to those with carbapenem-sensitive infections.⁴⁶ This may create a vicious cycle in which IMV facilitates CRGNB acquisition by compromising the innate respiratory tract barriers and airway defenses through intubation or tracheostomy, whereas lung injury induced by CRGNB often prolongs ventilatory duration.^{47,48} In immunocompromised patients, impaired host defenses and limited therapeutic options further intensify this cycle,^{49,50} which may contribute to prolonged hospitalization, delayed microbial clearance, and poorer outcome.^{46,51,52} Therefore, this ratio provides a more nuanced indicator of ventilator dependency than isolated temporal metrics, and a higher ratio prompts careful monitoring for disease progression and timely optimization of respiratory management.

Consistent with previous investigations of CRGNB pneumonia in the critically ill population, vasopressor therapy was associated with ICU mortality in our immunocompromised cohort.³⁹ The need for vasopressor support likely reflects progression to critical stages, such as septic shock or multiorgan failure, both of which are common and life-threatening complications of severe pneumonia. Platelet count < $100 \times 10^9/L$ also emerged as a critical predictor of ICU mortality.

Although direct evidence supporting this association is limited, the association between thrombocytopenia and increased mortality in critically ill populations is well established.⁵³ Platelet depletion may indicate disease severity and the presence of dysregulated coagulation caused by bacterial endotoxins.^{54–56} Thus, close platelet monitoring in immunocompromised ICU patients is important, where a declining trend should prompt a comprehensive evaluation and timely therapeutic interventions. Furthermore, our results found that older age is significantly associated with poor outcomes, which is largely consistent with previous findings.^{15,57}

Among immunocompetent patients, pre-existing heart failure and the need for continuous renal replacement therapy (CRRT) were associated with ICU mortality. Heart failure is often accompanied by systemic consequences, including impaired intestinal barrier integrity and bacterial translocation, which may increase the risk of developing sepsis, leading to higher mortality.^{58,59} Likewise, the requirement for CRRT may reflect underlying renal compromise, which has been linked to adverse outcomes.⁶⁰ Interestingly, tracheostomy was the only protective factor in our study, potentially due to improved airway management and reduced incidence of ventilator-associated complications.⁶¹ While vasopressor therapy and IMV time/ICU LOS affect both groups, immunocompetent patients may be more vulnerable to the cumulative burden of chronic organ dysfunction. This emphasizes the importance of optimizing long-term comorbidity management in this subgroup.

Our study emphasizes the importance of assessing immune status and the clinical utility of stratifying patients with CRGNB pneumonia in ICUs according to immune competence when evaluating prognosis and personalizing management strategies. For immunocompromised patients, especially the elderly, additional attention should be paid to this subgroup when assessing prognosis. Moreover, due to their vulnerability to co-infections, early and comprehensive diagnostic strategies such as next-generation sequencing and proactive management of thrombocytopenia may improve outcomes. Additionally, monitoring the IMV time/ICU LOS ratio may help identify patients with persistent ventilator dependence and prompt early respiratory optimization. To our knowledge, this is among the first studies to examine mortality-associated risk factors in ICU patients with CRGNB pneumonia stratified by immune status, thereby providing novel insights into risk stratification and tailored management in this high-risk population.

Nevertheless, several limitations should be acknowledged. First, this was a retrospective, single-center study that may introduce selection bias and limit the generalizability of our findings. Second, the limited sample size contributed to wide confidence intervals for certain odds ratios. Third, there is a possibility that unmeasured confounding factors influenced both patient outcomes and the associations identified in our analyses. Additionally, as this study was not designed to evaluate immune function, relevant immunological indicators were not included. Finally, our study did not specifically evaluate the influence of antibiotic therapy on clinical outcomes, which could affect mortality. Therefore, future prospective multicenter investigations are needed to validate these findings and further elucidate pathophysiological mechanisms. Additionally, integration of immune status into risk prediction models may facilitate early identification of high-risk patients and guide targeted treatment strategies.

Conclusion

Immunocompromised patients with CRGNB pneumonia have distinct clinical characteristics and higher ICU mortality. Age > 65 years, platelet count < $100 \times 10^9/L$, vasopressor requirement, and higher IMV time/ICU LOS ratio were independent prognostic factors for ICU mortality. These findings underscore the importance of immune-status-based stratification to guide prognostic assessment and therapeutic strategies in the ICU setting.

Abbreviations

CRGNB, carbapenem-resistant gram-negative bacteria; CRKP, carbapenem-resistant *Klebsiella pneumoniae*; CRAB, carbapenem-resistant *Acinetobacter baumannii*; CRPA, carbapenem-resistant *Pseudomonas aeruginosa*; CRECO, carbapenem-resistant *Escherichia coli*; ICU, intensive care unit; MDR, multidrug-resistant; IMV, invasive mechanical ventilation; LOS, length of stay; CRRT, continuous renal replacement therapy; OR, odds ratio; CI, confidence interval.

Data Sharing Statement

The datasets used and/or analyzed during the current study are available from the corresponding author (Benquan Wu) on reasonable request.

Ethics Approval and Consent to Participate

The study was conducted in accordance with the Declaration of Helsinki and approved by the Medical Ethics Committee of the Third Affiliated Hospital of Sun Yat-sen University on January 23, 2025 (II2025-031-01). The requirement for written informed consent was waived by the Ethics Committee of the Third Affiliated Hospital of Sun Yat-sen University because of the retrospective analysis of anonymized data.

Acknowledgments

The authors thank those who have contributed significantly to this study, including nurses, doctors, statisticians, reviewers, and editors.

Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

Funding

This work was supported by the Science and Technology Planning Project of Guangdong Province of China (2017A020215177).

Disclosure

The authors report no conflicts of interest in this work.

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