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Original Article

Clinical and molecular predictors of mortality in patients with carbapenem-resistant *Acinetobacter baumannii* bacteremia: A retrospective cohort study

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KEYWORDS
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Bacteremia;
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Risk factors

Abstract *Background/Purpose:* To investigate the virulence profiles and identify clinical and microbiological predictors of mortality in patients with carbapenem-resistant *Acinetobacter baumannii* (*A. baumannii*) bacteremia.
Methods: This retrospective cohort study enrolled adult patients with carbapenem-resistant *A. baumannii* (CRAB). Multivariate logistic regression was used to identify the predictors of 30-day mortality. All isolates were subjected to real-time polymerase chain reaction for virulence factors and genotyped using multilocus sequence typing.
Results: Among the 153 patients with CRAB bacteremia, 66 % received appropriate definitive antibiotic therapy. The in-hospital and 30-day mortality rates were 58.3 and 23.5 %, respectively. Ultimately, we enrolled 125 patients with CRAB bacteremia in the analysis, excluding early mortality cases. All CRAB isolates carried bla_{OXA-23} and bla_{OXA-51}. The clinical strains belonged to 10 sequence types (STs), and the major genotypes were ST191, ST195, ST451, and ST784. The distribution of virulence factors included surface adhesion (Ata, 84.8 %; ChoP, 7.2 %), biofilm formation (OmpA, 76.8 %), killing of host cells (AbeD, 99.2 %), toxins (LipA, 99.2 %), and conjugation (BfmR, 90.4 %). In multivariate logistic regression analysis, hemodialysis due to acute kidney injury and moderate to severe thrombocytopenia were significant risk factors associated with 30-day mortality. However, microbiological factors were not significant predictors.

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Conclusions: Clinical factors such as hemodialysis due to acute renal injury and moderate to severe thrombocytopenia have a greater influence on mortality in CRAB bacteremia compared with microbiological factors.

Introduction

Acinetobacter baumannii (*A. baumannii*) is a significant nosocomial pathogen that has become a growing global concern.[1] This bacterium primarily manifests as bacteremia and pneumonia. According to the 2019 Centers for Disease Control and Prevention Antibiotic Resistance Threats Report, carbapenem-resistant *A. baumannii* (CRAB) is classified as an urgent pathogenic threat.[2] The prevalence of nosocomial infections caused by CRAB is increasing exponentially, imposing significant economic and societal burdens.[3] Notably, in a report from the Korean sector of the Global Antimicrobial Resistance Surveillance System, 92.1 % of *A. baumannii* strains exhibited resistance to both imipenem and meropenem.[4,5]

CRAB bacteremia demonstrates a high 30-d mortality rate of 55—79.8 % in the Republic of Korea (ROK), due to its formidable antibiotic resistance level and limited treatment options in the region.[6,7] However, whether the microbiological features of CRAB itself contribute to higher mortality remains a subject of controversy. Moreover, insights into the virulence of CRAB and the epidemiological data on its microbiological factors in ROK are limited. Furthermore, microbiological factors, optimal antibiotic treatment, and clinical factors such as comorbidities or disease severity should be considered when establishing a strategy to increase survival rates.

Understanding the molecular mechanisms of carbapenem resistance and their local epidemiology is critical in determining the optimal antibiotic treatment.[8] Specifically, identifying the characteristics of pathogens and host—pathogen interactions at the molecular and genetic levels can serve as a guiding principle in the realm of precision medicine for treating infectious diseases. Therefore, the clinical implications of the microbiological properties of CRAB isolates must be characterized. This study aimed to investigate the virulence profile and identify clinical and microbiological factors associated with mortality in patients with CRAB bacteremia.

Methods

Hospital setting and study design

This retrospective cohort study was conducted at a 1048-bed university-affiliated hospital in Seoul, South Korea, from July 2015 to July 2021. The study included adult patients (≥18 years old) diagnosed with CRAB bacteremia, excluding those with polymicrobial bacteremia. Patients, who were discharged before antimicrobial susceptibility results became available after blood cultures, were also excluded. In patients with multiple episodes of CRAB bacteremia, only the first episode was analyzed.

Definitions and data collection

The following potential predictive variables for mortality associated with CRAB bacteremia were collected from the electronic medical records of each patient: age, sex, comorbidities, source of CRAB bacteremia, laboratory findings, Pitt bacteremia score at the time of bacteremia, history of operations or procedures within the last month, exposure to a medical environment, immunosuppressant use, and administration of antibiotics for >3 days within the last month.

CRAB bacteremia was defined as at least one blood culture positive for *A. baumannii* obtained from a patient. Neutropenia and thrombocytopenia were defined as an absolute neutrophil count of <500 cells/mm^3 and a platelet count of <150,000/μL, respectively. Thrombocytopenia grade was classified as mild (100,000—150,000/μL), moderate (50,000—99,000/μL), or severe (<50,000/μL). Definitive therapy was defined as treatment that was continued or initiated on the day the antibiotic susceptibility results were reported to the clinicians. Appropriate definitive antibiotic therapy was considered if a patient received at least one antimicrobial agent with *in vitro* activity against CRAB isolated from blood cultures, consistent with the recommended dosage.[9,10] A diagnosis of septic shock was adapted from the International Guidelines for Management of Sepsis and Septic shock.[11] The source of bacteremia was classified according to the Centers for Disease Control and Prevention criteria by the attending physician.[12] Early mortality was defined as patients who died within 72 h of blood cultures, prior to the availability of antimicrobial susceptibility results.

Microbiological methods

Consecutive blood isolates obtained on the first day of CRAB bacteremia diagnosis were collected for further microbiological analysis. The identity and antibiotic susceptibility of *A. baumannii* isolates from blood cultures were determined using a MicroScan WalkAway-96 Plus system (Beckman Coulter, Inc., CA, USA). Carbapenem resistance was defined as a minimum inhibitory concentrations of ≥8 μg/mL for imipenem or meropenem. The susceptibility test results were interpreted in accordance with the Clinical Laboratory Standards Institute guidelines.[13] A susceptibility breakpoint of ≤2 mg/L for colistin was used to evaluate the susceptibility of *A. baumannii*

based on the European Committee on Antimicrobial Susceptibility Testing (EUCAST) breakpoints.

The genomic species of CRAB were identified by a multiplex polymerase chain reaction (PCR) method.[14] Six virulence factor genes (*ompA, bfmR, Ata, lipA, abeD,* and *choP*) and carbapenem-resistant genes ($bla_{oxa\text{-}23}$ and $bla_{oxa\text{-}51}$) were detected using specific primers (Supplementary Table 1). Amplification cycles comprised the following steps: denaturation at 95 °C for 5 min, annealing between 50 and 61 °C for 30–45 s, and extension at 72 °C for 1 min, repeated for 34 cycles. Amplified PCR products were assessed through electrophoretic separation on a 2 % agarose gel and visualization using a transilluminator. For multilocus sequence typing (MLST), seven housekeeping genes (*gltA, gyrB, gdhB, recA, cpn60, gpi,* and *rpoD*) were amplified and sequenced for *A. baumannii* using specific primers (Supplementary Table 2). Isolates were assigned sequence types (STs) using tools available in the *A. baumannii* MLST database (https://pubmlst.org/organisms/acinetobacter-baumannii).

Statistical analyses

Categorical variables were analyzed using the Pearson χ^2 test or Fisher's exact test and are presented as frequencies. Continuous variables were analyzed using the Wilcoxon rank-sum test and expressed as medians with interquartile ranges (IQRs). Variables with $P < 0.1$ in the comparison analysis were included in a multivariate logistic regression analysis with stepwise variable selection based on the Wald statistical criterion to determine the risk factors associated with 30-day mortality in patients with CRAB bacteremia. Statistical significance was set at $P < 0.05$. The final selected model was evaluated using the Hosmer–Lemeshow goodness-of-fit test.

Receiver operating characteristic (ROC) curve analysis was performed using the final models to generate a risk index for identifying patients with 30-day mortality. The discriminative ability of the final models to predict the probability of mortality was evaluated using the area under the ROC curve (AUC) analysis. The cutoff value of the optimal ROC curve was deduced from the Youden's index. Furthermore, the performance of the final multivariate logistic regression model was confirmed by evaluating its predictive accuracy using the leave-one-out cross-validation (LOOCV) method and the test dataset. SPSS for Windows software package (version 23.0; SPSS Inc., Chicago, IL., USA), IBM SPSS Statistics (version 20.0; IBM, Armonk, NY, USA), and SAS 9.4 (SAS Institute Inc., Cary, NC, USA) were used for statistical analyses.

Results

Patients with CRAB bacteremia and antibiotic treatment

During the study period, we collected CRAB isolates from 153 patients. The mean age of the patients was 67 years (IQR, 56–77 years), and 60.1 % were male. Cardiovascular (51.6 %), neurological (32.0 %), and metabolic (35.9 %) diseases were the most common comorbidities. Furthermore, catheter-related bloodstream infection (52.9 %) was the predominant source of CRAB bacteremia, followed by primary bloodstream (22.2 %) and intra-abdominal infections (15.0 %). Septic shock occurred in 72 (47.1 %) patients. The in-hospital and 30-day mortality rates were 58.3 and 23.5 %, respectively. Among the 153 patients, 28 patients died within 72 h after blood cultures without receiving appropriate definitive antibiotic therapy, resulting in an early mortality rate of 18.3 %. Finally, we included 125 patients with CRAB bacteremia, excluding early mortality, in the analysis (Table 1). Table 1 presents the details of antibiotic treatment for CRAB bacteremia. Only 83 (66.4 %) of the 125 patients received appropriate definitive antibiotic therapy even after CRAB was isolated from blood cultures. The most common regimen for appropriate definitive antibiotic treatment was a combination of carbapenem and colistin (n = 62/83; 74.7 %), followed by a combination of carbapenem and tigecycline (n = 14/83, 16.9 %) (Table 1).

Microbiologic characteristics

All CRAB isolates were susceptible to colistin and harbored $bla_{OXA\text{-}23}$ and $bla_{OXA\text{-}51}$. No significant differences in antimicrobial susceptibility were observed between the survivors and non-survivors (Table 2). The clinical strains belonged to 10 STs, and the major genotypes were ST191 (27.2 %), ST195 (17.6 %), ST451 (16.0 %), and ST784 (14.4 %). The distribution of virulence factors was as follows: surface adhesion (*ata*, 84.8 %; *choP*, 7.2 %), biofilm formation (*ompA*, 76.8 %), killing of host cells (*abeD*, 99.2 %), toxins (*lipA*, 99.2 %), and conjugation (*bfmR*, 90.4 %). No significant differences in mortality according to STs or virulence factors were observed between the two groups (Table 2).

Risk factors for 30-day mortality

No significant differences in age, sex, or underlying diseases were observed between the survivors and non-survivors (Table 1). The sources of CRAB bacteremia did not significantly differ between the two groups (Table 1). However, non-survivors had a higher Pitt bacteremia score than survivors (Table 1). The mortality rate was higher in patients receiving hemodialysis than in those who did not (Table 1). In terms of laboratory findings at the time of CRAB bacteremia diagnosis, non-survivors had significantly higher lactic acid levels than survivors (Table 1). Moderate-to-severe thrombocytopenia was more common in non-survivors than in survivors. However, there were no significant differences in prior exposure to antibiotics and risk factors within 30 days between the two groups. Furthermore, appropriate definitive antibiotic treatment and antibiotic treatment regimens showed no significant differences between the two groups (Table 1).

Multivariate logistic regression analysis included significant variables ($P < 0.1$) in the univariate analysis to identify the independent risk factors for 30-day mortality in patients with CRAB bacteremia. Upon examining multicollinearity among the variables, no correlation was identified. In the multivariate logistic regression analysis, hemodialysis due to acute kidney injury (odds ratio (OR) = 5.675, 95 %

Table 1 Comparison of demographic and clinical characteristics between survivors and non-survivors among patients with CRAB bacteremia.

	Total (n = 125)	Survivors (n = 105)	Non-survivors (n = 20)	*P*-value
Age, (years) median (IQR)	69 (56–76)	69 (56–77)	65 (61–74)	0.959
Male, n (%)	78 (62.4)	65 (61.9)	13 (65.0)	0.793
Comorbidities, n (%)				
Cardiovascular diseases	68 (54.4)	54 (51.4)	14 (70.0)	0.126
Neurologic diseases	42 (33.6)	34 (32.4)	8 (40.0)	0.509
Hematologic malignancy	9 (7.2)	6 (5.7)	3 (15.0)	0.141
Solid organ malignancy	37 (29.6)	32 (30.5)	5 (25.0)	0.623
Chronic renal diseases	26 (20.8)	22 (21.0)	4 (20.0)	0.923
Chronic liver diseases	17 (13.6)	13 (12.4)	4 (20.0)	0.362
Chronic pulmonary diseases	12 (9.6)	10 (9.5)	2 (10.0)	0.947
Transplantation	7 (5.6)	5 (4.8)	2 (10.0)	0.350
Metabolic diseases	46 (36.8)	39 (37.1)	7 (35.0)	0.855
Hematologic diseases	6 (4.8)	5 (4.8)	1 (5.0)	0.964
Charlsons comorbidity index, median (IQR)	3 (1–5)	3 (1–5)	3 (2–5)	0.708
Infection sources of CRAB bacteremia, n (%)				
Primary BSI	27 (21.6)	23 (21.9)	4 (20.0)	0.850
Catheter-related BSI	68 (54.4)	55 (52.4)	13 (65.0)	0.299
Pneumonia	12 (9.6)	11 (10.5)	1 (5.0)	0.446
Intra-abdominal infections	19 (15.2)	17 (16.2)	2 (10.0)	0.480
Clinical severity of CRAB bacteremia				
Pitt bacteremia score, median (IQR)	3 (2–4)	3 (2–4)	4 (2–5)	0.049
Septic shock, n (%)	56 (44.8)	44 (41.9)	12 (60.0)	0.136
Mechanical ventilator, n (%)	88 (70.4)	71 (67.6)	17 (85.0)	0.119
Hemodialysis	39 (31.2)	28 (26.7)	11 (55.0)	0.012
ESRD, n (%)	14 (11.2)	12 (11.4)	2 (10.0)	0.853
Acute kidney injury, n (%)	10 (8.0)	5 (4.8)	5 (25.0)	0.002
ECMO, n (%)	7 (5.6)	5 (4.8)	2 (10.0)	0.350
Risk factors				
Length of stay before CRAB bacteremia (days), median (IQR)	29 (18–49)	36 (23–61)	17 (12–24)	<0.001
Recent ICU admission, n (%)	107 (85.6)	88 (83.8)	19 (95.0)	0.191
Prior to operation within 30 days, n (%)	37 (29.6)	30 (28.6)	7 (35.0)	0.564
Neutropenia, n (%)	8 (6.4)	5 (4.8)	3 (15.0)	0.086
Immunosuppressive agents within 30 days, n (%)	20 (16.0)	15 (14.3)	5 (25.0)	0.231
Prior antibiotic exposure				
3rd generation cephalosporin, n (%)	46 (36.8)	37 (35.2)	9 (45.0)	0.407
4th generation cephalosporin, n (%)	12 (9.6)	11 (10.5)	1 (5.0)	0.446
Quinolones, n (%)	27 (21.6)	24 (22.9)	3 (15.0)	0.434
Carbapenems, n (%)	15 (12.0)	14 (13.3)	1 (5.0)	0.293
β-lactam/β-lactamase inhibitors, n (%)	44 (35.2)	37 (35.2)	7 (35.0)	0.984
Laboratory findings, median (IQR)				
WBC ($\times 10^3/\mu L$)	11.6 (6.87–17.25)	11.6 (6.79–17.25)	11.9 (1.08–19.55)	0.622
CRP (mg/L)	124.5 (66.7–183.4)	119 (63.7–170.8)	185.8 (119.7–242.6)	0.014
Procalcitonin (ng/mL)	1.9 (0.34–6.2)	1.4 (0.3–4.6)	8.7 (2.1–17.7)	0.055
Albumin (g/dL)	2.6 (2.3–2.9)	2.6 (2.3–2.9)	2.5 (2.2–3.1)	0.938
LDH (IU/L)	649 (414–891)	617 (404–882)	736 (498–1049)	0.287
Lactic acid (mmol/L)	1.7 (1.2–2.2)	1.6 (1.2–2.1)	2.5 (1.2–6.2)	0.039
Platelet/lymphocyte ratio	152.9 (72.7–259.8)	166.7 (74.9–259.8)	88.6 (49.3–343.5)	0.852
Thrombocytopenia, n (%)	71 (56.8)	54 (51.4)	17 (56.8)	0.005
Moderate-to-severe thrombocytopenia, n (%)	54 (43.2)	38 (36.2)	16 (80.0)	<0.001
Antibiotic treatment, n (%)				
Appropriate definitive antibiotic	83 (66.4)	70 (66.7)	13 (65.0)	0.885

(*continued on next page*)

Table 1 (*continued*)

	Total (n = 125)	Survivors (n = 105)	Non-survivors (n = 20)	*P*-value
treatment for CRAB bacteremia				
Carbapenem + Tigecycline	14 (16.9)	13 (18.6)	1 (7.7)	0.336
Carbapenem + colistin	62 (74.7)	53 (75.7)	9 (69.2)	0.621
Others[b]	7 (8.4)	6 (8.6)	1 (7.7)	0.917
Outcomes, median (IQR)				
Length of hospital stay, (days)	62 (34—103)	69 (42—114)	19 (17—25)	<0.001
Length of stay after CRAB bacteremia, (days)	21 (6—57)	28 (9—61)	2 (1—6)	<0.001

[a] The antibiotics were prescribed within 48 h after diagnosis of CRAB bacteremia.
[b] Colistin, tigecycline, carbapenem, minocycline and minocycline + carbapenem were included.
Abbreviations: ICU, intensive care unit; BSI, bloodstream infection; CRAB, carbapenem-resistant *A. baumannii*; CRP, C-reactive protein; ECMO, extracorporeal membrane oxygenation; ESRD, end-stage renal disease; IQR, interquartile range; LDH, lactate dehydrogenase; WBC, white blood cells.

Table 2 Comparison of microbiologic characteristics between survivors and non-survivors among patients with CRAB bacteremia.

Virulence factors	Total (n = 125)	Survivors (n = 105)	Non-survivors (n = 20)	*P*-value
Antibiotic susceptibility, n (%)				
Sulbactam (R)	121 (96.8)	102 (97.1)	19 (95.0)	0.618
Tigecycline (R)	16 (16.5)	13 (15.9)	3 (20.0)	0.691
Minocycline (R)	12 (9.7)	10 (9.5)	2 (10.5)	0.892
Type of carbapenemase, n (%)				
OXA-23	125 (100)	105 (100)	20 (100)	—
OXA-51	125 (100)	105 (100)	20 (100)	—
Virulence factors, n (%)				
Surface adhesion				
Ata	106 (84.8)	91 (86.7)	15 (75.0)	0.183
ChoP	9 (7.2)	6 (5.7)	3 (15.0)	0.141
Biofilm formation				
OmpA	96 (76.8)	79 (75.2)	17 (85.0)	0.343
Killing host cell				
AbeD	124 (99.2)	104 (99.0)	20 (100)	0.661
Toxin				
LipA	124 (99.2)	104 (99.0)	20 (100)	0.661
Conjugation				
BfmR	113 (90.4)	93 (88.6)	20 (100)	0.112
Sequence types (allelic profile[a]), n (%)				
ST 191 (1-3-3-2-2-94-3)	34 (27.2)	29 (27.6)	5 (25.0)	0.809
ST 195 (1-3-3-2-2-96-3)	22 (17.6)	18 (17.1)	4 (20.0)	0.758
ST 208 (1-3-3-2-2-97-3)	7 (5.6)	7 (6.7)	0 (0)	0.235
ST 369 (1-3-3-2-2-106-3)	6 (4.8)	3 (2.9)	3 (15.0)	0.020
ST 451 (1-3-3-2-2-142-3)	20 (16.0)	18 (17.1)	2 (10.0)	0.425
ST 469 (1-12-3-2-2-103-3)	2 (1.6)	1 (1.0)	1 (5.0)	0.186
ST 491 (10-53-4-11-4-98-5)	2 (1.6)	2 (1.9)	0 (0)	0.534
ST 784 (1-3-3-2-2-107-3)	18 (14.4)	15 (14.3)	3 (15.0)	0.934
ST 1599 (1-12-3-2-2-98-3)	5 (4.0)	5 (4.8)	0 (0)	0.319
ST 1653 (1-3-3-2-59-96-3)	1 (0.8)	1 (1.0)	0 (0)	0.661
Non-typable strains	8 (6.4)	6 (5.7)	2 (10.0)	0.473

[a] Allelic profile: *gltA — gyrB — gdhB — recA - cpn60 — gpi — rpoD*.
Abbreviations: R, resistant; ST, sequence type.

Table 3 Multivariable logistic regression analysis of the risk factors associated with 30-day mortality in patients with CRAB bacteremia.

Risk factors	β-coefficient	Standard error	Odds ratio	95 % confidence interval	*P*-value
Acute kidney injury	1.736	0.780	5.675	1.230–26.183	0.026
Moderate to severe thrombocytopenia	1.947	0.826	7.006	1.388–35.369	0.018

In the multivariate logistic regression model, a backward selection approach was adopted with variables including the Pitt bacteremia score, moderate-to-severe thrombocytopenia, acute kidney injury, CRP, procalcitonin, lactic acid, neutropenia, and ST 369 ($P < 0.1$, univariate analysis).

confidence interval (CI) = 1.230–26.183, $P = 0.026$), and moderate to severe thrombocytopenia (OR = 7.006, 95 % CI = 1.388–35.369, $P = 0.018$) were significant risk factors associated with 30-day mortality in the patients with CRAB bacteremia (Table 3). However, microbiological factors were not significant predictors. The Hosmer–Lemeshow goodness-of-fit test yielded a *P*-value <0.001, indicating no significant evidence for lack of fit in the final models. The LOOCV was used to assess the predictive accuracy of the final model. When the cutoff values of >0.141 and >0.086 were applied to the model, the AUC values for the model were 0.841 (95 % CI 0.749–0.909) and 0.740 (95 % CI 0.637–0.827), respectively, for both raw data and LOOCV. The sensitivity, specificity, positive predictive value, and negative predictive value of this prediction rule were 83.3 (95 % CI, 51.6–97.9), 83.3 (95 % CI, 73.2–90.8), 43.5 (95 % CI, 30.6–57.3), and 97.0 % (95 % CI, 90.1–99.1), respectively.

Discussion

This study identified hemodialysis for acute kidney injury and moderate to severe thrombocytopenia as predictors of mortality in patients with CRAB bacteremia. Although no significant association was identified between microbiological factors and mortality, the major strain was ST191 carrying $bla_{\text{OXA-23}}$.

In our study, hemodialysis due to acute kidney injury during treatment for CRAB bacteremia was a risk factor for 30-day mortality. Notably, using a central venous catheter for hemodialysis is the most important risk factor for developing CRAB bacteremia in patients receiving hemodialysis.[15] In a recent systematic review, acute renal failure was a risk factor for mortality in CRAB bacteremia.[16] Meanwhile, considering the concerns regarding reduced antibiotic dosing regimens in patients undergoing hemodialysis, dialysis may have compromised adequate antibiotic therapy.[17]

Our findings suggest that the presence of thrombocytopenia at the onset of CRAB bacteremia is associated with unfavorable outcomes. Severe or sustained thrombocytopenia is closely associated with microvascular thrombosis, organ failure, and higher mortality in septic conditions.[18] A previous study also reported that thrombocytopenia during bacteremia was associated with an increased risk of mortality.[19]

In our study, only 66.4 % of patients with CRAB bacteremia received appropriate definitive antibiotics. These findings underscore the importance of antibiotic stewardship and early diagnosis to improve treatment outcomes in patients with CRAB bacteremia. In the ROK, novel antibiotics such as cefiderocol, which are effective against CRAB infection, are not available; therefore, the rapid introduction of these antibiotics is urgent.

Our study revealed that $bla_{\text{OXA-23}}$ and $bla_{\text{OXA-51}}$ were present in all the CRAB isolates. Overexpression of $bla_{\text{OXA-51}}$ is known to cause intrinsic resistance to carbapenems,[20] and in Asian countries, $bla_{\text{OXA-23}}$ is the most frequently identified carbapenemase among CRAB isolates.[21,22] In our hospital, collecting CRAB isolates producing non-$bla_{\text{OXA-23}}$ carbapenemases was challenging, preventing the evaluation of clinical features according to carbapenem-resistant genes.

The detection rate of OmpA, which is associated with biofilm formation, was 76.8 %. Compared with that of the other five virulence factors (OmpA, Ate, AbeD, LipA, and BfmR), the detection rate of ChoP was relatively low at 7.2 %. Furthermore, each CRAB isolate often harbors multiple virulence genes. In theory, microbiological factors such as complex antibiotic resistance and pathogen virulence can contribute to serious conditions and death in patients.[23] A recent study reported that 56.0 % of 30-day mortality cases with CRAB bacteremia occurred within 3 days, similar to 53.3 % in our study.[24] Considering that the effect of antibiotics is evaluated 3 days after administration, the virulence and clinical severity of the patients can be important factors in determining the patient's prognosis. Currently, the virulence determinants of CRAB have not been completely elucidated; however, the acquisition or expression of virulence-associated genes determines their pathogenicity under different regulations for each unique condition. However, no virulence factors were associated with 30-day mortality in the patients with CRAB bacteremia in this study. Therefore, further studies are needed to evaluate whether other unanalyzed virulence factors are associated with the prognosis of CRAB bacteremia.

ST191 was the predominant strain in our study, known to express $bla_{\text{OXA-23}}$ associated with a high rate of carbapenem resistance, consistent with previous findings.[24] ST191 accounted for 27.2 % of the total CRAB isolates, and other clones, such as ST195, ST451, and ST784, accounted for 48.0 % of the representative CRAB isolates. Previous studies have suggested differences in the occurrence of septic shock or death among diverse clones.[25,26] In particular, the ST218 strain harboring $bla_{\text{OXA-72}}$ was associated with high mortality.[27] However, the STs were not significantly associated with 30-day mortality of CRAB bacteremia in this study. The heterogeneity among these study findings highlights the need for well-designed research on the clinical outcomes of patients with CRAB bacteremia according to the genotypes of the CRAB isolates.

Our study has several limitations. First, it was a retrospective, single-center study involving a relatively small number of participants. Second, although hemodialysis during the treatment of CRAB bacteremia was significantly associated with mortality, distinguishing whether the cause of acute kidney injury was organ dysfunction caused by bacteremia or adverse events related to drugs such as colistin was difficult.

Conclusions

Our study revealed that hemodialysis due to acute kidney injury during the treatment of CRAB bacteremia and moderate to severe thrombocytopenia were significantly associated with mortality in patients with CRAB bacteremia. These clinical factors had a more pronounced impact on the clinical course of CRAB bacteremia compared to microbiological factors. Nonetheless, comprehensive microbiological data remains crucial for infection control and the development of patient-specific treatment strategies.

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Availability of data and materials

Data supporting the findings of this study are available upon request from the corresponding author.

Conflicts of interest

The authors declare no competing interests.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jmii.2023.11.001.