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ORIGINAL RESEARCH

Epidemiology, Clinical Characteristics and Treatment Outcomes of *Acinetobacter baumannii* Infection at a Regional Hospital in Thailand

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Objective: This retrospective cohort study evaluated the treatment outcome of *Acinetobacter baumannii* infection.

Methods: In this retrospective cohort study, 476 patients with *Acinetobacter baumannii* (*A. baumannii*) infection who were admitted to the internal medicine ward at Lampang Hospital, Lampang, Thailand, from 1 January 2020 to 31 December 2020 were enrolled. Medical records were reviewed.

Results: A total of 476 patients with *A. baumannii* infection were enrolled. Of these, 204 (43%) survived, while 272 (57%) died. Extensively drug-resistant (XDR) *A. baumannii* with hospital-acquired pneumonia was the most common presentation. Risk factors for acquiring multidrug-resistant (MDR) pathogens included previous hospitalization or antibiotic use and the presence of an indwelling urinary catheter, which was common in both survived and deceased groups. The survival group was significantly more likely to have received appropriate antibiotic therapy compared to the deceased group (71% vs 51%; *p*<0.001), particularly with colistin mono-therapy (34% vs 18%; *p*<0.001). Additionally, multivariate analysis showed that predictors of unfavorable outcomes, such as multiorgan failure, hypoalbuminemia, hematologic malignancy, and healthcare-associated pneumonia. The survival group had a significantly longer hospital stay compared to the deceased group (15 days vs 7 days; *p*<0.001) and also showed an increased microbiological cure rate (49% vs 26%; *p*<0.001).

Conclusion: XDR *A. baumannii* leads to serious nosocomial infections. Understanding the risk factors for XDR *A. baumannii* infections could enhance colistin prescription prior to the antimicrobial susceptibility testing results.

Keywords: *Acinetobacter baumannii* infection, multidrug-resistant pathogens, clinical outcomes, microbiological outcomes

Introduction

Acinetobacter baumannii has become an important nosocomial pathogen that is responsible for a broad range of severe infections with significant contact with the health care system.[1] Carbapenem-resistant *A. baumannii* has been prioritized as critical of the need for new antibiotics in recent years.[2] Approximately 45% of global isolates are MDR *A. baumannii*, with more than 60% in the United States,[3] while Turkey and Greece reported MDR exceeding 90%.[4] XDR strains had a significantly higher mortality rate compared with susceptible strains (70% vs 25%)[5] Predisposing factors for *Acinetobacter* infections are the length of stay, invasive procedures, previous antibiotic exposure, and severe illness.[6] Antibiotic therapy is complicated by antibiotic resistance, including carbapenem resistance. Receiving appropriate antibiotic therapy decreases in 30-day mortality (39.5% appropriate therapy vs 65% inappropriate therapy; *p*=0.011).[7] Colistin is an important antibiotic for the treatment of CRAB infections.[8] A previous study reported a cure rate for colistin 57–77% among severely ill patients with MDR *A. baumannii*.[9] Numerous studies have described outcome of patients with *A. baumannii* infection who were treated with nebulized polymyxins. In one study, use of inhaled colistin increased microbial eradication in ventilated patients compared to systemic therapy.[10] Another study reported no difference in mortality between systemic colistin and combination of systemic and inhaled colistin therapy.[11] In addition,

combination therapy had no benefit to prevent emergence of resistance and could not conclude impact on treatment outcome due to the difference of clinical characteristics[12] A recent study showed no difference in clinical outcome and microbiological cure between colistin monotherapy and combination therapy with colistin and meropenem.[13–15] The current guideline recommends ampicillin-sulbactam for sulbactam susceptible CRAB infection. For severe, high-risk sulbactam-resistant CRAB infection, a combination of in vitro active antibiotics including polymyxin, high-dose tigecycline, ampicillin-sulbactam, aminoglycoside and high-dose extended-infusion meropenem may be considered if a meropenem MIC < 8 µg/mL, and avoid colistin-meropenem or colistin–rifampicin combination therapy.[16] In addition, colistin–meropenem combination or other regimens did not result in better outcomes compared with colistin mono-therapy because CRAB isolates are almost significantly higher MICs of meropenem (higher than 8 µg/mL), so it is unlikely to offer the advantage of colistin–meropenem combination therapy.[17] Difficulties in treating CRAB infections still challenge physicians in optimizing antibiotic therapy in the setting of highly resistant pathogens. To provide timely and proper antibiotic therapy, it is important to know the risk factors for carbapenem-resistant *A. baumannii* acquisition and the characteristics of *A. baumannii* infection. Therefore, this study was to investigate treatment outcomes by comparing the appropriateness of antibiotic therapy between the survived and deceased groups. Secondary outcomes included the comparison of 4-week all-cause mortality, length of hospital stay, and microbiological outcome.

Material and Methods

Study Design

The study was conducted at Lampang Hospital. Data were collected from patients with *A. baumannii* infections who were admitted internal medicine ward between January 1, 2020, and December 31, 2020. Antibiotic susceptibility tests were performed by broth microdilution method, BD Phoenix M50, according to the Clinical and Laboratory Standard Institutes (CLSI) 2019–2020.[18] The study protocol was approved by the Lampang Ethics Committees (code 008/66).

The primary outcome is the treatment outcome of *A. baumannii* infection. The secondary outcomes are the length of hospital stay, microbiological outcomes, and 4-week all-cause mortality.

Definition

Infection was defined as a clinically suspected infection in a patient with a documented source, assessed based on available clinical data and microbiological results, along with the administration of antibiotics by an attending physician. Community-acquired infection was defined as a clinically suspected infection with a positive *A. baumannii* culture from any site obtained within ≤48 hours of hospitalization.[19] Nosocomial infection was defined as a clinically suspected infection with a positive *A. baumannii* culture obtained >48 hours after hospitalization or within 2 days of hospital discharge.[20] Healthcare-associated infection was defined as a clinically suspected infection with a positive *A. baumannii* culture obtained within ≤48 hours of hospitalization and significant recent exposure to the healthcare system.[19–21] MDR *A. baumannii* was defined as non-susceptibility to at least one agent in three classes of antibiotics approved for the treatment of *A. baumannii* infection: aminoglycosides, antipseudomonal penicillin-β-lactamase inhibitors, antipseudo-monal carbapenems, antipseudomonal fluoroquinolones, trimethoprim-sulfamethoxazole, cephalosporins, ampicillin-sulbactam, polymyxins, or tetracyclines. XDR *A. baumannii* was defined as susceptibility only to polymyxins and tigecycline.[22]

Microbiological eradication was defined as the time of negative culture after starting treatment with antibiotics (as most recent cultures on or close to the end of antibiotic treatment from any site of baseline infection were negative).[23] Persistence was defined as the same causative organism as in the initial episode was still detected in culture from any site of baseline infection at the end of treatment.[23]

Superinfection was defined as clinical failure or improvement and isolation of a pathogen not present at baseline was assessed based on available clinical data and microbiological results, and the physician agreed that the patient requires antibiotic therapy.[24]

Appropriate specific antibiotic therapy was considered based on susceptibility results according to CLSI 2019–2020 and compatible with the clinical course.

Previous antibiotic was defined as antibiotic treatment within 90 days before admission without concern about antibiotic duration.

Previous hospitalization was defined as hospitalization without regard to the cause of admission within 90 days before admission.

Time of presentation was defined as time of suspected infection with any site cultures were taken, which is the index date (day 0).

Time to appropriate antibiotic therapy was defined as the time of any site culture collection to time of the most specific antibiotic therapy in consideration of AST results. If a patient was already on antibiotics at the time of culture collection, the time to receipt of antibiotics was zero.

Statistical Analyses

Continuous variables were presented as mean ± standard deviation (SD) or median and interquartile range (IQR), categorical variables were presented as number (percentage). Student's t-test was used to examine continuous variables, and Chi-square test or Fisher exact was used to examine categorical variables. Comparison of time to appropriate antibiotic therapy between groups was performed using paired sample t-test. Nelson-Aalen estimator of the cumulative hazard function to evaluate antibiotic therapy. Kaplan–Meier survival curve estimation and Log rank testing was used to compare survival between colistin monotherapy and colistin–meropenem combination therapy. Univariable generalized linear mixed regression analysis was included in the multivariable analysis for risk factors associated with 4 weeks of All-cause Mortality. Stepwise backward elimination was performed until risk factors in the multivariate generalized linear mixed regression model had a p-value <0.05. Statistical analysis was carried out using Stata version 16.0, with a significance p <0.001.

Results

Demographics and Clinical Characteristics

A total of 476 patients were included, 204 (43%) patients were in the survival group and 272 (57%) patients were in the deceased group. Baseline characteristics, medical history and severity of illness are presented in Table 1. Almost

Table 1 Characteristics of Patients With *A. baumannii* Infection

Characteristic	Survive (N=204)	Decease (N=272)	p- value
Age, median (IQR) – yr	68 (24–92)	68 (18–96)	0.406
Male sex - no (%)	129 (63.24)	144 (52.94)	0.025
MDR pathogen			0.676
- Non MDR	12 (5.88)	12 (4.41)	
- MDR	7 (3.43)	12 (4.41)	
- XDR	185 (90.69)	248 (91.18)	
Charlson Comorbidity Index	2.43±2.06	2.67±2.13	0.207
Comorbidity -no (%)			
- Malignancy	15 (7.35)	33 (12.18)	0.084
- Diabetes mellitus	30 (14.71)	34 (12.50)	0.485
- Chronic kidney disease	56 (27.45)	66 (24.26)	0.431
- Stroke	45 (22.06)	57 (20.96)	0.772
- Pulmonary disease	37 (18.14)	40 (14.71)	0.314
- Cardiovascular disease	37 (18.14)	53 (19.49)	0.710
- AIDS	1 (0.49)	10 (3.68)	0.022

(*Continued*)

Table 1 (Continued).

Characteristic	Survive (N=204)	Decease (N=272)	p- value
Immunosuppression			
- Chronic systemic steroid[a]	2 (0.98)	2 (0.74)	0.772
- Immunosuppressive therapy[b]	3 (1.47)	9 (3.31)	0.205
- Chemotherapy and radiotherapy within 30 days	2 (0.98)	4 (1.47)	0.635
Risk factors of MDR pathogen acquisition			
- Past Hospitalization in 90 days - no (%)	194 (95.10)	261 (95.96)	0.652
- Past Antibiotic used in 90 days - no (%)	194 (95.10)	262 (96.32)	0.510
- Prior MDRO colonization or infection-no (%)	46 (22.55)	58 (21.32)	0.749
- Indwelling bladder catheter- no (%)	171 (83.82)	241 (88.60)	0.130
- Central catheter - no (%)	41 (20.10)	59 (21.69)	0.673
- Chronic dialysis	16 (7.84)	37 (13.60)	0.048
Severity of Illness			
Pitt Bacteremia Score, median (IQR)	2.79±1.98	3.73±2.10	< 0.001
SOFA Score, median (IQR)	4.05±2.80	5.88±3.86	< 0.001
Septic Shock - no (%)	21 (10.29)	75 (27.57)	< 0.001
Organ Dysfunction, median (IQR)	2.29±1.37	3.09±1.50	<0.001
- Metabolic dysfunction	7 (3.43)	22 (8.09)	0.036
- Renal failure	98 (48.04)	141 (51.84)	0.412
- Respiratory failure	178 (87.25)	253 (93.01)	0.034
- Cognitive impairment	62 (30.39)	114 (41.91)	0.010
- Shock	58(28.43)	161 (59.19)	<0.001
- Hematologic dysfunction	25 (12.25)	73 (26.84)	<0.001
Serum albumin	2.66±0.56	2.37±0.66	<0.001
Meropenem MIC distribution (µg/mL)			
- ≤ 2	17 (8.33)	21 (7.72)	0.659
- 4	0 (0)	2 (0.74)	
- >4	187 (91.67)	249 (91.54)	
Site of Acquisition - no (%)			
- Community-acquired	8 (3.92)	13 (4.78)	0.353
- Healthcare-associated	17 (8.33)	14 (5.15)	
- Hospital-acquired	179 (87.75)	245 (90.07)	
Source of Bloodstream Infection- no (%)			
- Primary bloodstream infection	4 (1.96)	2 (0.74)	0.236
- Respiratory tract infection	187 (91.67)	258 (94.58)	0.163
- Hospital-acquired pneumonia-Ventilator-associated pneumonia	32 (15.69)	51 (18.75)	0.380
- Ventilator-associated tracheobronchitis	100 (49.02)	170 (62.50)	0.003
- Genitourinary tract infection	38 (18.63)	13 (4.78)	<0.001
- Intraabdominal infection	8 (3.92)	13 (4.78)	0.652
- Skin and soft tissue infection	2 (0.98)	2 (0.74)	0.772
	9 (4.41)	7 (2.57)	0.271

Note: Chronic systemic steroid[a] defined as chronic use of corticosteroid (> 10 mg of prednisolone equivalent daily) greater than 3 months. Immunosuppressive therapy[b] defined as treatment with methotrexate, sulfasalazine, cyclophosphamide, azathioprine, cyclosporine.
Abbreviations: IQR, interquartile range. MDR, multidrug resistant pathogen, XDR, extensively drug resistant pathogen.

of the isolations were XDR *A. baumannii* strains, more than 90% were resistant to meropenem (MICs of meropenem >4 μg/mL), 185 (91%) in the survived group and 248 (91%) in the deceased group. Respiratory tract infections were the most common site of infections in both groups. Risk factors for MDR pathogens acquisition included previous hospitalization or antibiotic use within 3 months, indwelling Foley catheters were presented in most of the patients in both groups. The severity of illness included septic shock, high Pitt bacteremia score or SOFA Score and multiorgan failure were statistically significant in the deceased group ($p < 0.001$).

Antibiotic Therapy and Treatment Outcomes of Patients With *A. baumannii* Infection

Appropriate antibiotic therapy in the survived group was 71%, compared to 51% in the deceased group ($p < 0.001$) (Table 2). Figure 1 shows cumulative hazard of antibiotic therapy. A significantly longer length of hospital stay was shown in patients receiving appropriate antibiotic therapy, compared to patients receiving inappropriate antibiotic therapy (15 days vs 7 days; $p < 0.001$). Figure 2 shows survival probability among patients receiving colistin monotherapy and colistin-meropenem combination therapy. No survival benefit with colistin–meropenem combination therapy compared with colistin monotherapy but were underpowered to assess significant differences ($p = 0.064$). We found colistin monotherapy was used 34% in the survival group and 18% in the deceased group ($p < 0.001$). Microbiological eradication was presented 49% in the survival group and 26% in the deceased group; ($p < 0.001$), superinfections were also significantly demonstrated in the survival group compared to the deceased group (26.47% vs 16.54%; $p = 0.008$).

Table 2 Antibiotic Therapy and Treatment Outcomes of Patients With *A. baumannii* Infection

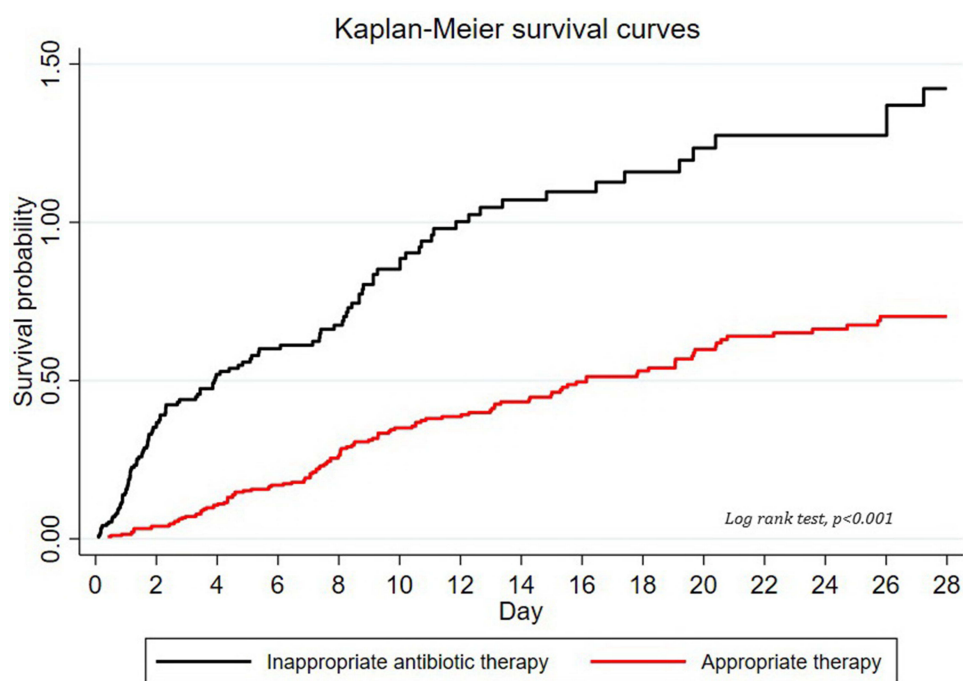| Variables	Survive N=204 (%)	Decease N=272 (%)	p- value
Appropriateness of Antibiotic Therapy - no (%)	144 (70.59)	138 (50.74)	<0.001
Time to Appropriate Antibiotic Therapy after Culture Taken			
Median Time – hr	84.37 (57,336)	55.35 (30,119)	<0.001
Antibiotic Regimen			
- Colistin monotherapy	69 (33.82)	49 (18.01)	<0.001
- Colistin-based therapy	67(32.84)	87 (31.99)	0.843
- Colistin and meropenem	55 (26.96)	82 (30.15)	
- Colistin and cefoperazone/sulbactam	4 (1.96)	1 (0.37)	
- Colistin and fosfomycin	0	1 (0.37)	
- Colistin and meropenem and fosfomycin	1 (0.49)	0	
- Other regimen	8 (3.92)	2 (0.74)	0.016
- No effective therapy	60 (29.41)	133 (48.90)	<0.001
Microbiological Outcome - no (%)			
- Microbiological eradication	99 (48.53)	72 (26.47)	<0.001
- Persistent	29 (14.22)	16 (5.88)	0.002
- Superinfection	54 (26.47)	45 (16.54)	0.008
Length of Hospital stay from Enrolment, median (IQR) – day	15 (21)	7 (11)	<0.001
Total Mortality in 4 weeks Distribution		238 (87.5)	
- 0 −7 days		134 (56.07)	<0.001
- 8–14 days		72 (30.13)	
- 15–21 days		25 (10.46)	
- 22–28 days		7 (2.93)	

Figure 1 Cumulative Hazard of Survival Probability among Patients with *A. baumannii* Infections Receiving Appropriate Antibiotic Therapy (red) and Inappropriate Antibiotic Therapy (black).
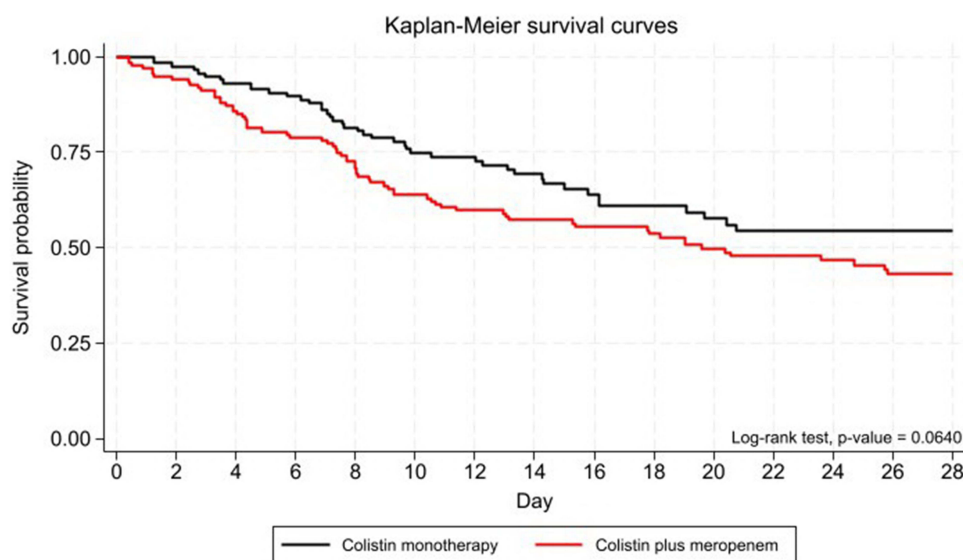

Figure 2 Cumulative Hazard of Survival Probability among Patients with *A. baumannii* Infections Receiving colistin monotherapy (black) and colistin plus meropenem (red).

Factor Associated With All-Cause Mortality

Multivariate analysis revealed independent risk factors for unfavorable outcomes, including hematologic malignancy (AHR = 4.33, 95% CI = 1.53–12.23), multiorgan failure (AHR = 2.58, 95% CI = 1.75–3.80), low serum albumin (AHR = 1.75, 95% CI = 1.23–2.50) and healthcare-associated pneumonia (HCAP) (AHR = 2.10, 95% CI = 1.11–3.96) were significantly demonstrated in deceased group (Table 3).

Table 3 Univariate and Multivariate Cox Regression Analyses of Variables Associated With 4 weeks All-Cause Mortality

Variables	Total	Died	Univariate analysis		Multivariate analysis Cox regression*		
	Cases	N (%)	HR (95% CI)	p-value	AHR	95% CI	p-value
Hematologic malignancy	7	6 (2)	3.28 (1.45, 7.39)	0.004	4.33	1.53, 12.23	0.006
VAT	51	13 (5)	0.39 (0.17, 0.91)	0.029	0.26	0.09, 0.71	0.008
HCAP	22	13 (5)	2.52 (1.17, 5.44)	0.019	2.10	1.11, 3.96	0.023
Multiorgan failure ≥4 organs	129	95 (35)	2.18 (1.68, 2.84)	<0.001	2.58	1.75, 3.80	<0.001
Septic shock	29	75 (28)	0.008 (0.001, 0.090)	<0.001	0.007	0.001, 0.08	<0.001
Serum Albumin <2.5 g/dL	107	78 (51)	1.49 (1.06, 2.09)	<0.021	1.75	1.23, 2.50	0.002
Microbiological eradication	171	72 (26)	0.26 (0.19, 0.35)	<0.001	0.18	0.12, 0.28	<0.001
Superinfection	99	45 (17)	0.28 (0.19, 0.41)	<0.001	0.20	0.12, 0.35	<0.001

Note: *Stratified by study group and site of infection.
Abbreviations: VAT, ventilator associated tracheobronchitis, HCAP. Healthcare-associated pneumonia; HR, Hazard ratio; AHR, Adjusted Hazard ratio.

Discussion

This study aimed to assess the treatment outcomes of *A. baumannii* infection. Most of the patients acquired XDR *A. baumannii* with hospital-acquired pneumonia. Our study identified similar risk factors for MDR pathogens as previous studies, including previous hospitalization or antibiotic use within 3 months and the presence of an indwelling Foley catheter.[6] Recognizing these factors could improve infection control practices and promote antibiotic stewardship according to local epidemiology to proper empirical antibiotics, which optimal infection control and appropriate antibiotic therapy may consequently lower rates of MDR pathogen transmission and optimize outcomes. We compared clinical outcomes between colistin monotherapy and colistin-based combination therapy (mostly with meropenem). Colistin–meropenem combination therapy did not demonstrate a greater survival benefit compared to colistin mono-therapy, consistent with previous studies that provided strong evidence against carbapenem-colistin use for the treatment of CRAB infections.[14,15] This suggests that there is no evidence of a synergistic effect between colistin and meropenem when the meropenem MIC exceeds 4 µg/mL. According to the IDSA 2024 guidance, most CRAB isolates exhibit highly elevated meropenem MICs, making it unlikely that colistin–meropenem combination therapy would offer any advantage.[17]

Thus, colistin remains an antibiotic option for XDR *A. baumannii* infection[8,9] and parenteral colistin therapy before AST results may be needed based on local epidemiological data. Additionally, clinical success in the survived group may be related to the lower severity of illness observed. Interestingly, significant clinical responses and microbiological cures were shown in the survived group, superinfections were also more common in the survival group compared to the deceased group. This may be due to the delay in appropriate antibiotic therapy, which impacted bacterial eradication and led to biofilm formation, making infections more difficult to treat.[25,26] Our findings showed a high 4-week mortality rate of 87.5%, which is similar to the mortality rate of XDR *A. baumannii* VAP reported in a previous study (85.3%).[27] Using multivariable analysis, HCAP, hematologic malignancy, and severe illness (organ dysfunction ≥4 and hypoalbuminemia) were identified as poor prognostic factors. This suggests that disease severity and malignancy[28] are associated with 4-week mortality. However, pathogen-specific factors (eg, *A. baumannii* resistance) and other clinical factors should also be considered, even though they were not found to be significant in this study. Therefore, early recognition of risk factors for MDR pathogen acquisition, along with measures to prevent the spread and acquisition of drug-resistant organisms, is essential. Additionally, local epidemiological data and rapid AST results are crucial to guide physicians in making decisions aligned with current practice guidelines, enabling the prescription of appropriate antibiotics and improving

clinical outcomes. Microbiological eradication should not be the goal of antibiotic treatment, but rather achieving a good clinical response should be prioritized.

This study has several limitations. The retrospective study design lacks randomization and involves a retrospective chart review, which limits data accessibility. Second, more data are needed on the pharmacokinetics, pharmacodynamics, and appropriate dosing of colistin. Third, treatment options are severely limited; to our knowledge, carbapenems and colistin remain the agents of choice for most MDR infections. The role of other agents and combination therapies remains unclear. Due to these limitations, further studies on other antibiotic regimens and the role of antibiotic combinations are essential.

In conclusion, XDR *A. baumannii* infections have become significant nosocomial pathogens. Colistin–meropenem combination therapy, even with highly elevated meropenem MICs, has not demonstrated a greater survival benefit compared to colistin monotherapy. Identifying risk factors for MDR pathogens, utilizing local epidemiological data, and obtaining rapid AST results are essential for appropriate antibiotic prescriptions and improved clinical outcomes.

Abbreviations
A. baumannii, Acinetobacter baumannii; CRAB, Carbapenem resistant *Acinetobacter baumannii;* AST, Antibiotic susceptibility testing; MIC: Minimum inhibitory concentration; MDR, Multidrug-resistant; XDR, Extensively drug-resistant; CLSI, Clinical Laboratory Standards Institute; HAP, Hospital-acquired pneumonia; VAP, Ventilator-associated pneumonia; VAT, Ventilator-associated tracheobronchitis; HCAP, Healthcare-associated pneumonia; BSI, Bloodstream infections.

Data Sharing Statement
The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

Ethics Approval
Lampang Clinical Research Ethics Committee. All data was handled confidentially.

Consent to Participate
Not applicable. Confidentially signifies the obligation to keep personal information private and secure following legal and ethical principles.

Consent Statement
The need for written informed consent was waived by the Clinical Research Ethics Committee due to the retrospective nature of the study.

Disclosure
The authors declare no competing interests in this work.

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