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RESEARCH ARTICLE

Clinical Characteristics, Antibiotic Resistance Profiles, and Factors Affecting Mortality in Patients Isolated *Acinetobacter Baumannii* in Intensive Care Unit: Retrospective Tertiary Center Analysis

Kadir Arslan, Ayça Sultan Şahin

Department of Anesthesiology and Reanimation, University of Health Sciences, Kanuni Sultan Süleyman Training and Research Hospital, İstanbul, Türkiye

ABSTRACT

Objective: *Acinetobacter baumannii* is an important opportunistic pathogen that can cause severe septicemia and mortality. This study aims to investigate the antibiotic resistance profiles of patients isolated from *A. baumannii* in the intensive care unit (ICU) and the factors affecting mortality.

Materials and Methods: Patients who were followed up in a tertiary ICU between January 2020 and January 2023 and who were found to have *A. baumannii* in various clinical samples were included in the study. The patients were divided into the mortality group (Group M) and the survival group (Group S). Their clinical features, antibiotic resistance profiles, and mortality factors were analyzed.

Results: A total of 228 patients, 110 (48.2%) in Group M and 118 (51.8%) in Group S, were included in the study. The median age of the entire population was 67.5 (18–96), and 60.1% were male. *A. baumannii* strains were most commonly (59.2%) isolated from tracheal aspirate and sputum cultures. Resistance to carbapenems was 94.2–96.8%, aminoglycosides 88.5–99.2%, tigecycline 54.6%, and colistin 8.1%. Group M had significantly higher Acute Physiology and Chronic Health Evaluation-2 (APACHE-2) scores, mechanical ventilation requirements, and multidrug-resistant *A. baumannii* count. Independent risk factors for mortality were determined by APACHE-2 scores and mechanical ventilator application at the time of admission to the ICU.

Conclusion: We think that in *A. baumannii* infections, which are highly resistant to many antibiotics and have high mortality rates, determining the risk factors indicating mortality and antibiotic resistance profiles and making treatment plans will contribute to the prognosis of the patients.

Keywords: *Acinetobacter baumannii*, antibiotic resistance, bacteremia, intensive care unit, mortality

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INTRODUCTION

Acinetobacter baumannii is a Gram-negative, non-fermentative coccobacillus bacterium and is an essential cause of hospital-acquired infections. It is an opportunistic pathogen that can cause respiratory tract infections such as pneumonia, urinary tract infections, surgical site infections, wound infections, and septicemia, especially in intensive care unit (ICU) patients.[1] Extended hospital stays of patients followed in ICUs, invasive procedures, use of broad-spectrum antibiotics, and previous operations have been reported as risk factors for the infection of this microorganism.[1–3]

A. baumannii can frequently cause nosocomial infections due to the increase in the number of patients followed in ICUs and can remain alive for a long time in the hospital environment due to their resistance to external environmental conditions.[4,5] The fact that *A. baumannii* strains are naturally resistant to many antibiotics and can develop resistance quickly can be a severe problem by limiting the antimicrobials to be used in the treatment against this infection, which can cause severe mortality.[6] In addition, *A. baumannii* infections in ICUs cause prolonged hospital stays, increasing ICU occupancy rates and hospital costs.

Address for Correspondence: Kadir Arslan, Department of Anesthesiology and Reanimation, University of Health Sciences, Kanuni Sultan Süleyman Training and Research Hospital, İstanbul, Türkiye
E-mail: kadir.arslan@sbu.edu.tr **ORCID ID:** 0000-0003-4061-0746

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The World Health Organization has made several recommendations to slow down and reduce the resistance developing against bacteria. It has been reported that the surveillance of antibiotic resistance should be carried out mainly in specialized units such as ICUs.[7] This study aims to investigate the clinical characteristics and antibiotic resistance of patients with *A. baumannii* strains found in their clinical samples in the tertiary center ICU and determine the risk factors for mortality.

MATERIALS and METHODS

For this retrospective cross-sectional study, approval was obtained from the Clinical Research Ethics Committee of the Kanuni Sultan Süleyman Training and Research Hospital (date: November 30, 2022, number: 230). The work was started following the principles of the Declaration of Helsinki. *A. baumannii* in blood, endotracheal aspirate, urine, wound, body fluid, and catheter tip samples were taken from patients who were followed up and treated between January 1, 2020, and January 1, 2023, at the Kanuni Sultan Süleyman Training and Research Hospital. All patients aged 18 years or older who stayed in the ICU for more than 72 h and had no deficiency in clinical and laboratory results were included in the study. Demographic data of patients with growth in clinical samples, antibiotic resistance profiles, comorbid diseases, Acute Physiology and Chronic Health Evaluation-2 (APACHE-2) scores at admission to the ICU, mechanical ventilation (Mv), and renal replacement therapy (RRT) requirements, ICU and MV, the duration of operation and tracheostomy, the presence of arterial and central venous catheters, and 28 and 90-day mortality were evaluated through the hospital information system. The factors affecting mortality were investigated by dividing the patients into Group M (mortality group) and Group S (survival group) according to their 28-day mortality status. In this retrospective cross-sectional study, the sample size was not determined, and all patients who met the inclusion criteria between the relevant dates were included.

Blood cultures in BACTEC Plus aerobic media bottles sent to the laboratory were incubated in the BACTEC-FX automated blood culture (Becton Dickinson, USA) device. All plates were incubated at 37°C for 18–24 h. All strains were identified at the species level using the VITEK 2 (bioMerieux, France) method. Antimicrobial susceptibility tests of the identified strains were performed in Phoenix 100 (Becton Dickinson Co., Sparks, Maryland, USA) device according to the manufacturer's operating procedures, according to the recommendations of the European Committee on Antimicrobial Susceptibility Testing (EUCAST). Amikacin, gentamicin, tobramycin, imipenem, meropenem, trimethoprim-sulfamethoxazole, ciprofloxacin, piperacillin-tazobactam, ceftazidime, tigecycline, and colistin resistance status of patients with *A. baumannii* growth were evaluated. Strains found to be moderately or less susceptible were considered resistant. The first isolate grown in the clinical sample of the same patient was included in the study.

Statistical Analysis

SPSS 26.0 (SPSS Inc., Chicago, USA) program was used to analyze the data. Descriptive data were expressed as the number of patients, percentage, median, and distribution range. The conformity of the variables to the normal distribution was evaluated analytically (Shapiro–Wilk test) and visually (histogram). Mann–Whitney U-test assessed the non-normally distributed quantitative data between groups. Pearson Chi-square and Fisher's exact test were used to evaluating categorical data. Multiple logistic regression analysis was applied to the significant variables in univariate analysis. The statistical significance limit was accepted as $p<0.05$.

RESULTS

Two hundred and twenty-eight patients followed in the ICU for 3 years and *A. baumannii* isolated in their clinical samples were included in the study. All populations' median age and distribution range was 67.5 (18–96), and 60.1% (n=137) were male. While Mv was administered to 93.4% (n=213) of the entire population, the median length of stay in the ICU was 21 (3–103) days. The median APACHE-2 score at admission to the ICU was 23 (6–54). Before admission to the ICU or during follow-up in the ICU, 39% of the entire population (n=89) underwent surgery. Arterial or central venous catheterization in 99.1% (n=226), blood transfusion in 78.9% (n=180), renal replacement therapy (RRT) in 61.1% (n=138), and 25.4% (n=58) of the patient's percutaneous tracheostomy were performed (Table 1). At least one comorbid disease was present in 81.1% (n=185) of the entire population. Hypertension (52.6%) and diabetes mellitus (30.7%) were the most common comorbid diseases. The presence of the comorbid illness did not differ significantly between the groups (Table 2). In the entire population, 28-day mortality was 48.2% (n=110), and 90-day mortality was 75% (n=171).

When the groups were compared, the length of stay in the ICU and percutaneous tracheostomy opening rates were significantly lower in Group M ($p<0.001$). Again in Group M, APACHE-2 scores, Mv application rates, and the number of multidrug-resistant (MDR) *A. baumannii* were significantly higher ($p=0.005$, $p<0.001$, and $p=0.034$, respective-

Table 1. Demographic data and some clinical characteristics of the patients

	All population (n=228)		Mortality group (n=110)		Survival group (n=118)		p
	n	%	n	%	n	%	
Age (years)	67.5 (18–96)		67.5 (18–95)		67.5 (20–96)		0.662
Gender							0.606
Male	137	60.1	68	61.8	69	58.5	
Female	91	39.9	42	38.2	49	41.5	
Comorbidity	185	81.1	94	85.5	91	77.1	0.108
APACHE-2 score	23 (6–54)		25 (11–54)		21 (6–38)		0.005
Duration of ICU (days)	21 (3–103)		16 (3–44)		34 (3–103)		<0.001
Mv	213	93.4	109	99.1	104	88.1	<0.001
Duration of Mv (days)	15 (0–100)		12 (0–35)		25 (0–100)		<0.001
Operation	89	39	42	38.2	47	39.8	0.799
Tracheostomy	58	25.4	13	11.8	45	38.1	<0.001
RRT	138	61.1	65	59.1	73	62.9	0.554
Blood transfusion	180	78.9	83	75.5	97	82.2	0.212
Arterial/venous catheter	226	99.1	109	99.1	117	99.2	0.960
MDR A.b	211	92.5	106	96.4	105	89	0.034
XDR A.b	140	61.4	62	56.4	78	66.1	0.131

Data are given as median (minimum-maximum), number of patients (n), and percentage. APACHE-2: Acute Physiology and Chronic Health Evaluation-2; ICU: Intensive care unit; Mv: Mechanical ventilation; RRT: Renal replacement therapy; MDR A.b: Multidrug-resistant *A. baumannii*; XDR A.b: *A. baumannii* resistant to all drugs except tigecycline and colistin

Table 2. Comorbid diseases of patients

	All population (n=228)		Mortality group (n=110)		Survival group (n=118)		p
	n	%	n	%	n	%	
Hypertension	111	48.7	58	52.7	53	44.9	0.238
Diabetes mellitus	61	26.8	31	28.2	30	25.4	0.638
Heart failure/CAD	52	22.8	27	24.5	25	21.2	0.546
Malignancy	27	11.8	14	12.7	13	11	0.690
Chronic renal failure	27	11.8	13	11.8	13	11.9	0.991
COPD	20	8.8	9	8.2	11	9.3	0.761
Cerebrovascular disease	19	8.3	10	9.1	9	7.6	0.689

Values are expressed as the number of patients (n) and percentage. CAD: Coronary artery disease; COPD: Chronic obstructive pulmonary disease

ly). In the multiple logistic regression analysis performed on the variables that differed significantly between the groups, APACHE-2 score and Mv application were determined as independent risk factors for mortality (p=0.001 and p=0.046, respectively) (Table 3).

A. baumannii strains were most commonly isolated from the patient's tracheal aspirate and sputum cultures of 59.2% (n=135). The number of *A. baumannii* strains isolated over the years has increased due to the number of beds and patients in our ICU (Table 4). The isolates' resistance rates

Table 3. Multiple logistic regression analysis of factors associated with patients' mortality status

Variables	OR	p	95% CI (min-max)
APACHE-2	1.073	0.001	1.030–1.118
Mv	0.120	0.046	0.015–0.958
MDR	0.436	0.180	0.129–1.468

OR: Odds ratio; CI: Confidence interval; min: Minimum max: Maximum; APACHE-2: Acute Physiology and Chronic Health Evaluation-2, Mv: Mechanical ventilation; MDR A.b: Multidrug-resistant *A. baumannii*

Table 4. Distribution of *A. baumannii* strains isolated from samples by years

Örnekler	2020 (n=55)	2021 (n=75)	2022 (n=98)	Total	
				n=228	%
ETA and sputum	29	46	60	135	59.2
Blood	18	13	22	53	23.2
Urine	5	9	7	21	9.2
Wound	2	4	6	12	5.3
Catheter tip	1	2	2	5	2.2
Body fluid	0	1	1	2	0.9

ETA: Endotracheal aspirate

were between 94.2% and 96.8% in the carbapenem group (meropenem and imipenem) and between 88.5% and 99.2% in aminoglycosides (amikacin, gentamicin, and tobramycin). Tigecycline resistance rates, on the other hand, decreased in the past 3 years and averaged 54.6%. Colistin resistance was found to be 8.1% on average (Table 5). While the rates of multidrug resistance (MDR) detected in at least three different antibiotic groups against *A. baumannii* were 92.5% in the whole population, it was found to be significantly higher in the mortality group (96.4% vs. 89%, p=0.034).

DISCUSSION

Mortality rates due to *A. baumannii* infections may vary according to countries, regions, and various units of hospitals. In studies conducted with patients in the ICU from Turkey, mortality rates were reported between 64.8% and 82.1%.[8–10] In our study, 28-day mortality was 48.2%, and 90-day mortality was 75%, consistent with the literature.

Age has been reported to be a risk factor for mortality in ICU patients isolated from *A. baumannii*. Park et al.[11] said that the mean age of patients with *A. baumannii* infection who developed mortality was 62 years. However, the age difference between patients who survived was not significant. A study from Turkey reported that the mean age of patients who developed mortality in the ICU was 75.8±21 years, and 75% of the patients were over 75 years old.[8] In our study, the median age was 67.5 in both patients who survived and died, and there was no significant difference between the groups. Tokur et al.[12] reported that 56.4% of the patients with hospital-related *A. baumannii* detected in the ICU were men, and mortality developed in 48% of the men. In another study, it was stated that mortality was significantly higher in the male gender.[13] In our study, 60.1% of the entire population and 61.8% of the mortality group were male. However, no significant difference was found between the groups regarding gender.

Table 5. Antibiotic resistance of *A. baumannii* strains isolated according to the samples (%)

	2020 (n=55)	2021 (n=75)	2022 (n=98)	Total (n=228)
Amikacin	85.5	92	87.6	88.5
Gentamicin	85.5	94.7	93.9	92.1
Tobramycin	100	100	98.6	99.2
İmipenem	93.5	100	96.7	96.8
Meropenem	90.9	95.9	94.9	94.2
TMP-SMX	72.2	76	91.8	81.9
Ciprofloxacin	96.3	100	100	99.1
PIP-TAZO	100	96	97.8	97.6
Ceftazidime	100	97.2	96.6	97.3
Tigecycline	74.1	58.8	44.3	54.6
Colistin	7.7	10.4	8.4	8.1

TMP-SMX: Trimethoprim-sulfamethoxazole; PIP-TAZO: Piperacillin-tazobactam

Chronic respiratory diseases, heart failure, and diabetes mellitus have been reported to be risk factors for mortality in *A. baumannii* bacteremia.[13] However, studies also report that comorbid diseases such as heart failure, diabetes mellitus, cerebrovascular diseases, chronic obstructive pulmonary disease, and chronic kidney failure do not affect mortality.[9,12,14] In our study, none of the comorbid disorders were significantly higher in the mortality group. Sengul et al.[9] reported that the development of acute renal failure significantly affected mortality in patients with *A. baumannii* pneumonia. In our study, 61.1% of the population developed acute renal failure, and RRT was applied. However, there was no significant difference between the groups regarding RTT requirements.

The APACHE-2 score is an important parameter that can predict the prognosis in patients followed in the ICU. It has been

reported that the APACHE-2 score is significantly higher in patients who died from *A. baumannii* bacteremia patients followed in the ICU.[5,8,9] Another study stated that an APACHE-2 score of >16 could predict mortality.[14] Our study's median APACHE-2 score was 25 (11–54) in patients who died, while 21 (6–38) in patients who survived. Consistent with the literature, mortality was significantly higher in those who developed.

A. baumannii bacteremia causes prolonged hospital ICU stays, increasing intensive care bed occupancy rates and severe health expenditures. A study from Turkey stated that the average length of stay in ICU patients with *A. baumannii* bacteremia who developed mortality was 10 days longer.[14] In our study, the median length of stay in the ICU was 16 (3–44) days in the mortality group and 34 (3–103) days in the surviving group. In contrast, the duration of stay in the ICU was found to be significantly higher in the surviving group. Following the literature, we can say that bed occupancy rates and health expenditures increase in patients who do not develop mortality early, leading to prolonged hospital stays in the ICU.

Invasive procedures such as Mv administration, arterial and central venous catheter applications, nasogastric tube, and urinary catheter have been reported to be risk factors for Acinetobacter spp. bacteremia in patients followed up in the ICU.[15,16] Similarly, intubation and mechanical ventilation in ICU patients with *A. baumannii* bacteremia were reported to be risk factors for mortality.[17] In our study, Mv application was also found to be an independent risk factor for mortality (p=0.046, OR=0.120). However, arterial and central catheterization, surgical operation, and the need for blood transfusion were not effective on mortality. Considering the need for percutaneous tracheostomy, it was found that a significantly higher tracheostomy rate was opened in the surviving group (38.1% vs. 11.8%, p<0.001). The loss of patients with poor clinical conditions before tracheostomy can be performed is essential in the emergence of this situation. However, early tracheostomy may benefit patients for whom intubation is inevitable, and extubation is not expected quickly.

Acinetobacter spp. can cause various infections by affecting different organs and systems. Studies from Turkey reported that it was isolated from respiratory tract samples (tracheal aspirate and sputum) at a rate of 65–72.7% and from blood cultures at a rate of 3.6–21%.[5,8,18] In our study, it was most commonly isolated from respiratory tract samples (59.2%) and blood cultures (23.2%).

Carbapenems are among the most critical broad-spectrum antibiotics used to treat *A. baumannii* infections. In the studies reported from Turkey in the past 10 years, it has been reported that resistance to carbapenems develops between 90 and 100%.[18–20] In our study, imipenem resistance was an average of 96.8%, and meropenem resistance was 94.2%. The widespread use of carbapenems in various infections in our ICU may cause very high resistance rates. Due to the high resistance rates in carbapenems in *A. baumannii* bacteremia in ICUs, combined treatment with aminoglycosides is often preferred to increase the success of treatment and prevent the development of antibiotic resistance.[18] In studies reported in recent years, amikacin resistance was between 66% and 89%, while gentamicin resistance was reported between 88% and 95.8%.[10,18] In our study, resistance rates increased in the past 3 years. Mean resistance to amikacin, gentamicin, and tobramycin was found at high rates of 88.5%, 92.1%, and 99.2%, respectively. Resistance rates may increase due to the more widespread use of aminoglycosides in our ICU over the years.

Fluoroquinolones are another group of antibiotics used in the treatment and have increased resistance rates. In studies from Turkey, resistance rates in ciprofloxacin were reported to be 96.1–98.8%, second only to carbapenems.[10,18] In our study, it exceeded carbapenems by 99.1%. Tigecycline is another antibiotic frequently used in Acinetobacter spp. infections. Sahin et al.[10] reported tigecycline resistance as 49.3% in their studies. In our study, however, tigecycline resistance tended to decrease in the past 3 years, and the average was 54.6%. The widespread use of ciprofloxacin in our ICU is influential in determining the high rates of resistance, and less preference for tigecycline may cause a decrease in resistance rates.

MDR *A. baumannii* is defined as resistance to at least three different classes of antibiotics: carbapenems, antipseudomonal penicillins, cephalosporins, aminoglycosides, and quinolones.[21] The relationship between drug resistance and mortality in *A. baumannii* infections is controversial. Sengul et al.[9] reported that they found 70% MDR *A. baumannii* and 30% extreme drug-resistant (XDR, defined as resistant to all antibiotics except colistin and tigecycline) *A. baumannii* in tracheal aspirate cultures of patients with pneumonia. However, no relationship was found between pneumonia due to MDR and XDR *A. baumannii* and mortality. Duran et al.[18] reported MDR *A. baumannii* over 90% of their studies. In our research, while MDR *A. baumannii* was observed in over 90% following the literature, no independent risk factor for mortality was found.

The widespread occurrence of MDR and XDR *A. baumannii* strains leads to the general use of colistin despite its nephrotoxic effect. Although studies report that colistin resistance was not detected in studies from Turkey, there are also studies reporting 9% resistance.[22–24] In our study, colistin resis-

tance was the highest at 10.4% in 2021, while it was detected at an average rate of 8.1%. Using colistin due to the high patient circulation in our ICU and the detection of MDR *A. baumannii*, over 90% lead to increased resistance rates.

Study Limitations

The study's limitations are its single-center, retrospective design, and relatively small sample size. The EUCAST stated that the liquid microdilution method is the only test that gives accurate results in the determination of colistin susceptibility. It has been reported that automated systems such as VITEK-2 can be trusted with the results of colistin resistance. However, it cannot be trusted for sensitive ones.[25] Although some patients used the liquid microdilution method in our study, the results of colistin sensitivity found using VITEK-2 may be misleading.

CONCLUSION

High APACHE-2 scores and Mv were independent risk factors for mortality in patients with *A. baumannii* infection in the ICU. Avoid mechanical ventilation as much as possible and keep early tracheostomy in mind in patients for whom intubation is inevitable and will take a long time. It is crucial to avoid this microorganism's infections, which have high multidrug resistance and mortality rates. Compliance with infection control measures, prevention of healthcare-associated infections and cross-contamination, determination of antibiotic resistance profiles, and application of appropriate treatment guidelines will prevent the development and spread of resistance.

Disclosures

Ethics Committee Approval: The study was approved by the Kanuni Sultan Süleyman Training and Research Hospital Clinical Research Ethics Committee (No: 230, Date: 30/11/2022).

Informed Consent: Written informed consent was obtained from all patients.

Peer-review: Externally peer reviewed.

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