



Antibiotic resistance profile of *Acinetobacter baumannii* isolates identified from blood cultures

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Abstract

Background: *Acinetobacter baumannii* (*A. baumannii*) has emerged as the predominant etiological agent responsible for bloodstream infections among hospitalized patients. The objective of this study was to evaluate antibiotic resistance in *A. baumannii* isolates identified from blood cultures.

Methods: A retrospective cohort evaluation was conducted on 117 *A. baumannii* isolates obtained from blood cultures collected between 2018 and 2019 at the Microbiology Laboratory of Tokat Gaziosmanpaşa University Hospital (Türkiye). The blood culture samples were incubated using the BACT-ALERT 3D system (bioMérieux, Durham, NC, USA). Microorganism identification and antibiotic susceptibility testing were performed using the VITEK 2 (bioMérieux, France) automated system.

Results: Of the 117 samples, 59.8% were obtained from males and 40.2% from females. A total of 90.6% of blood culture samples were collected from the intensive care unit, and 88.9% of isolates were identified as multidrug-resistant (MDR). The highest resistance was observed against meropenem (99.1%), while the lowest resistance was noted for colistin (17.1%) and tigecycline (27.3%). Resistance to amikacin was 74.4%, while resistance levels to gentamicin, tobramycin, cefoxitin, and cefotaxime were within the range of 80–90%. Resistance to imipenem, amoxicillin/clavulanic acid, ampicillin/sulbactam, ceftazidime, cefepime, ciprofloxacin, levofloxacin, meropenem, and ertapenem exceeded 90%.

Conclusion: The increasing number of MDR *A. baumannii* isolates poses a significant threat to all hospitalized patients. However, colistin and tigecycline remain preferable options for the treatment of MDR *A. baumannii* infections. Considering the increasing prevalence of MDR *A. baumannii* isolates, periodic analysis of epidemiological data in healthcare centers is important for managing resistance to colistin and tigecycline.

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Introduction

Acinetobacter baumannii (*A. baumannii*) has shown an increasing ability to enhance survival, evade the immune system, and exhibit other virulence characteristics through various determinants such as capsules, outer membrane proteins, biofilms, siderophores, and more (1,2). *Acinetobacter* spp. are primarily responsible for healthcare-associated infections, including central line-associated bloodstream infections, ventilator-associated pneumonia, and surgical wound infections. Once established, *Acinetobacter* spp. can persist in healthcare settings and are challenging to eliminate. The most notable rise in cases during the first two years of the COVID-19 pandemic involved carbapenem-resistant *Acinetobacter* spp. infections, particularly in countries with a relatively high percentage of carbapenem-resistant cases before the pandemic. According to the European Centre for Disease Prevention and Control and the World Health Organization, the percentages of carbapenem-resistant *Acinetobacter* spp. varied significantly across the region, ranging from below 1% in three (7%) of 45 countries reporting data on this microorganism to 50% or more in 25 (56%) countries in 2021 (3).

A. baumannii has emerged as the predominant etiological agent responsible for bloodstream infections among hospitalized patients. Blood culture, as one of the critical samples analyzed by the clinical microbiology laboratory, serves as the primary and highly sensitive method for diagnosing bloodstream infections. Furthermore, the results of blood cultures play a crucial role in determining the appropriate antimicrobial treatments for patients (4,5).

The clinical properties of bloodstream infections caused by *A. baumannii* can range from transient and benign bacteremia to severe manifestations, such as fulminant disease and septic shock, with an associated mortality rate of up to 46%. Compared to community-acquired cases, hospital-acquired *A. baumannii* infections exhibit a distinct clinical syndrome characterized by intense and severe infection (6).

Due to limited treatment options, patients often receive inadequate care, resulting in significant consequences for their health. The objective of this study is to assess the resistance of *A. baumannii* isolates obtained from blood cultures to antibiotics.

Methods

In this retrospective cohort study, the positive blood culture samples from the records of the Microbiology Laboratory at Tokat Gaziosmanpaşa University

Research and Application Hospital were evaluated. A total of 117 samples with *A. baumannii*-positive blood cultures were identified, excluding repeated samples from the same patient. Blood culture samples were examined in each set of blood culture bottles received at the laboratory using the BacT-Alert 3D system (bioMérieux, Durham, NC, USA). All blood culture bottles were incubated for a duration of five days using the designated system equipment. Blood culture bottles displaying positive growth signals were subjected to Gram staining and inoculated onto blood agar (HiMedia, Türkiye) and eosin methylene blue agar (HiMedia, Türkiye). Microorganism identification and antibiotic susceptibility testing were performed using the VITEK 2 (bioMérieux, France) automated system. The antimicrobial susceptibility tests were interpreted according to the criteria of the European Committee on Antimicrobial Susceptibility Testing (EUCAST) (7).

This study was approved by the Scientific and Ethical Committee of the Tokat Gaziosmanpaşa University Clinical Research Ethics Committee (Ethical Number: 21-KAEK-245). The data were statistically analyzed using SPSS Statistical Program Version 21.0 (SPSS Inc., Chicago, Illinois, USA). Mean and standard deviation were used to describe quantitative variables with a normal distribution, while mean and range were used to characterize non-normally distributed data. Qualitative characteristics were described using numbers and percentages.

Results

A total of 117 samples were analyzed, of which 59.8% were from male patients and 40.2% from female patients. The average age of the patients was 67.31 ± 15.11 years, with 65.8% being 65 years old or older. The majority of *A. baumannii*-positive blood culture samples (90.6%) were obtained from patients admitted to the intensive care unit. The distribution of the isolates across different clinics is presented in Figure 1.

A significant proportion of the *A. baumannii* isolates (88.9%) were identified as multidrug-resistant (MDR). The majority of MDR *A. baumannii* isolates (89.4%) were obtained from patient samples taken from intensive care units. The highest resistance was observed to meropenem (99.1%), while the lowest resistance was seen with colistin (17.1%) and tigecycline (27.3%). Resistance to amikacin was 74.4%, whereas resistance levels for gentamicin, tobramycin, cefoxitin, and cefotaxime ranged between 80–90%. Resistance rates for imipenem, amoxicillin/clavulanic acid, ampicillin/sulbactam, ceftazidime,

cefepime, ciprofloxacin, levofloxacin, meropenem, and ertapenem exceeded 90%. The antibiotic resistance pattern among *A. baumannii* isolates from blood cultures is shown in Table 1.

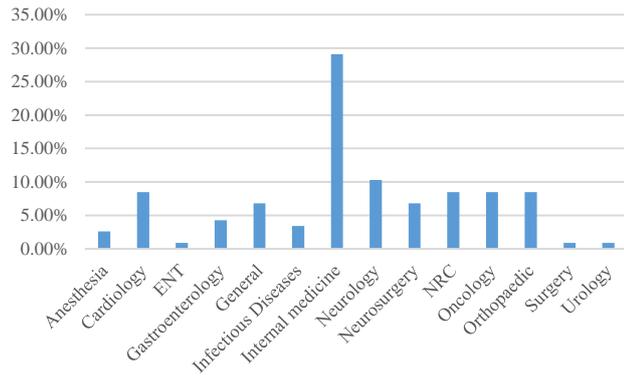


Figure 1. Clinical distribution of *A. baumannii* isolates identified from blood culture samples

Table 1. Antibiotic resistance pattern among *A. baumannii* isolated from blood samples

Antibiotics	Resistant n (Percentage)
Amoxicillin/Clavulanic acid	106 (90.6%)
Ampicillin/Sulbactam	106 (90.6%)
Cefoxitin	97 (82.9%)
Cefotaxime	95 (81.2%)
Ceftazidime	111 (94.9%)
Cefepime	107 (91.5%)
Gentamicin	102 (87.2%)
Amikacin	87 (74.4%)
Tobramycin	96 (82.1%)
Ciprofloxacin	112 (95.7%)
Levofloxacin	111 (94.9%)
Imipenem	93 (79.5%)
Meropenem	116 (99.1%)
Ertapenem	107 (91.5%)
Tigecycline	32 (27.3%)
Colistin	20 (17.1%)

Discussion

Positive blood cultures in a patient with systemic indications of infection identify bloodstream infection, which may be secondary to a documented source or primary, meaning without a recognized cause (8). Bloodstream infections are most commonly caused by Gram-negative bacteria, with *A. baumannii* being one of the most frequent causative agents. In 2023, antibiotic resistance was highlighted in an international prospective observational cohort study (EUROBACT-2) evaluating bloodstream infections in patients hospitalized in intensive care units. *A. baumannii* was found to be responsible for 20.3% of Gram-negative bloodstream infections, with 84.6% of these isolates being carbapenem-resistant. In addition, 50.3% of the isolates were identified as difficult-to-treat resistant, and 2.3% as pan-drug-resistant (9). In Croatia, the prevalence of MDR *A. baumannii* strains isolated from bloodstream infections was reported to be 60.2% (10). During the COVID-19 pandemic, *A. baumannii* was the most frequently isolated bacterium from blood cultures (34%) and showed the highest level of multidrug resistance (100%) among all Gram-negative bacteria (11). In the present study, the prevalence of MDR isolates was found to be 88.9%, a rate comparable to those reported in previous studies. These findings highlight a high prevalence of MDR *A. baumannii* strains not only in the study area but also globally, emphasizing the importance of identifying the most effective antibiotics for determining appropriate treatment strategies.

Carbapenem-resistant *A. baumannii* was identified as one of the highest priorities for antibiotic development and research in 2018. Due to its association with a broad spectrum of concurrent resistance to other antibiotic classes, carbapenem resistance has been selected as a marker (12). A significant increase in imipenem resistance among *A. baumannii* infections was observed from 2011 to 2016, ranging from 73.9% to 77.8%. This resistance rate had dramatically risen compared to the 23.8% reported from 2005 to 2010 in both OECD (Organization for Economic Co-operation and Development) and non-OECD countries (13). Unfortunately, during the 2017-2022 period analyzed, the number of multi-resistant strains of *A. baumannii* continued to increase, with resistance ranging from 28% to 79% for imipenem and 25% to 76% for meropenem (14). Bagherian et al. reported 90.2% resistance to meropenem and 75% to imipenem (15). Similarly, in the present research, resistance rates of 79.5% to imipenem and 99.1% to meropenem were detected, which are consistent with recent findings.

Al-Tamimi et al. reported resistance rates of *A. baumannii* strains to aminoglycosides as 37.2% for tobramycin, 37.1% for amikacin, and 62.6% for gentamicin (16). Jalali et al. reported resistance rates of *A. baumannii* strains as 85% for tobramycin, 85% for amikacin, and 54% for gentamicin (17). In the present study, resistance to these three antibiotics was observed similarly, with the highest resistance noted for gentamicin (87.2%). Resistance to gentamicin, in particular, has increased significantly in *A. baumannii* isolates (14).

In Bratislava, resistance rates of 90% for ceftazidime, 85% for cefepime, 90% for cefotaxime, and 100% for cefuroxime among *A. baumannii* strains have been reported (17). In Jordan, resistance rates of 99.5% for cefoxitin, 77.9% for ceftazidime, and 81.9% for cefepime were observed (16). In the current study, resistance rates of 82.9% for cefoxitin, 94.9% for ceftazidime, and 91.5% for cefepime were noted. High resistance rates were observed for cephalosporins in *A. baumannii* isolates.

Fluoroquinolones have shown effective activity against *A. baumannii* isolates over the past four decades. However, resistance to these drugs has rapidly emerged (18). Recent studies conducted in various countries report high rates of resistance to quinolones among *A. baumannii* isolates (15,17). In the present study, a remarkably high level of resistance to fluoroquinolones was observed, with ciprofloxacin (95.7%) and levofloxacin (94.9%) showing the highest resistance rates after imipenem.

The resistance of *A. baumannii* isolates to tigecycline has been reported as 7.2% in a study conducted in Jordan (16). Similarly, a study involving hospitalized patients in Brazil reported a resistance rate of 7.1% for *A. baumannii* isolates (19). Tewari et al. documented a resistance rate of 20% to tigecycline (20), while Tafreshi et al. indicated a resistance rate of 33.3% to tigecycline in 84 MDR *A. baumannii* isolates (21). In the present study, the resistance rate to tigecycline was determined to be 27.3%. Despite regional variations in resistance rates, tigecycline remains one of the most effective antibiotics against *A. baumannii* isolates. Consequently, tigecycline may be considered an alternative treatment option for MDR *A. baumannii* infections.

Escalating MDR isolates have necessitated the use of colistin, which serves as the last-line treatment option for these isolates (22). Farajnia et al. reported that 41.73% of isolates were MDR, with colistin susceptibility at 76% (23). Resistance to colistin has been reported as lower in other studies (4.2% and 10.6%), and it is noteworthy that resistance varies regionally (24,25). In the present investigation, the prevalence of colistin resistance was reported to be 17.1%. Given that the level of resistance observed in the present study was not significantly high, colistin remains a viable treatment option for patients infected with MDR *A. baumannii* isolates.

Since 2016, EUCAST has recommended broth microdilution (BMD) for determining the minimum inhibitory concentration of colistin (26). However, reference BMD, which requires freshly prepared or frozen antibiotic solutions, is not performed in all clinical laboratories due to laboratory circumstances. Unfortunately, in this study, sensitivity to colistin was determined by the VITEK 2 (bioMérieux, France) automated system and could not be confirmed by BMD. This is a limitation of the study.

Conclusion

Bloodstream infections are a major cause of mortality and morbidity in hospitalized patients worldwide. Increasing rates of antibiotic resistance complicate the treatment of these infections. The growing number of MDR *A. baumannii* isolates poses a significant threat to hospitalized patients. However, colistin and tigecycline are still considered preferable treatment options for MDR *A. baumannii* infections. Given the rising number of MDR *A. baumannii* isolates, periodic analysis of epidemiological data in healthcare centers is crucial to controlling resistance to tigecycline and colistin.

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Ethical statement

This study was approved by the Scientific and Ethical Committee of the Tokat Gaziosmanpaşa University Clinical Research Ethics Committee (21-KAEK-245).

Conflicts of interest

The authors have stated that they have no potential conflicts of interest regarding the research, authorship, and/or publication of this article.

Author contributions

ZFH, USŞC: Research concept and design; USŞC: Collection and/or assembly of data; ZFH, USŞC: Data analysis and interpretation; ZFH, USŞC: Writing the article; USŞC: Critical revision of the article. All authors read and approved the final version of the article.

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