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# Alterations in the Antimicrobial Resistance Profile of *Acinetobacter baumannii* Strains Isolated from Intensive Care Unit Patients: Five-Year Follow-up in Cappadocia

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**Abstract**

**Background**: This study aims to determine alterations in the antibiotic resistance status of *Acinetobacter baumannii* strains isolated from lower respiratory tract samples of patients in intensive care units over the years. **Methods**: In this comprehensive study, *A. baumannii* strains isolated from aspirate and sputum samples of patients hospitalized in intensive care units of a second-stage state hospital between January 2018 and December 2022 were meticulously and retrospectively investigated and analyzed for antimicrobial resistance. **Results**: The rate of aspirate and sputum samples in the study was 18.1% (754/4151); The positivity rate of cultures was 51.7% (390/754); The rate of those associated with *A. baumannii* was found to be 65.6% (256/390).. 90.2% of the isolates were isolated from the general intensive care unit (231/256). The rates of *A. baumannii* isolated from aspirate and sputum samples were 67.4% (213/316) and 58.1% (43/74), respectively. The carbapenem resistance rate in *A. baumannii* isolates grown in aspirate samples was 96.5%, fluoroquinolone resistance was 91.7%; The carbapenem resistance rate in sputum samples was 96.1% and fluoroquinolone resistance was 90.9%. The most effective antibiotics against *A. baumannii* strains isolated from both aspirate and sputum samples were colistin 100% (n=256), TMP/SXT 55.8% (143/256), tigecycline 50.3% (129/256), respectively. **Conclusion**: Our study reveals a concerning trend-a high frequency of multidrug-resistant *A. baumannii* isolates are being identified in the Central Anatolia region of our country. This high prevalence, which is a cause for immediate concern, underscores the urgent and immediate need for robust infection control measures to curb the spread of *A. baumannii* in hospitals.

**Key word:** *Acinetobacter baumannii*, carbapenem resistance, intensive care unit, lower respiratory tract.

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## Introduction

Infections caused by multidrug-resistant organisms are increasingly common in hospitals, particularly in intensive care units (ICUs). These units are critical for providing life support to severely ill or unconscious patients, but they also present a heightened risk for infection due to compromised immune responses, weakened host defenses, and the use of invasive devices such as mechanical ventilators (1).

Although the morbidity and mortality rates associated with such infections have decreased due to the widespread use of antibiotics, the increasing use of antibiotics has exerted selective pressure, leading to the emergence and spread of drug-resistant pathogens (1,2).

*Acinetobacter* species are non-fermentative, Gram-negative coccobacilli belonging to the *Moraxellaceae* family. They are oxidase-negative and catalase-positive bacteria (3). Among these, *Acinetobacter baumannii* is the most virulent and is an opportunistic pathogen responsible for severe nosocomial infections, especially in individuals with underlying health conditions. *A. baumannii* has developed significant resistance to antimicrobials due to various mechanisms such as quorum sensing, biofilm formation, beta-lactamase enzymes, and efflux pumps. In recent years, it has also become resistant to carbapenems, a class of antibiotics known as the "last resort" for treating infections in ICUs (4).

Carbapenems, once the cornerstone of critical infection treatment, now face widespread resistance. The rise of carbapenem-resistant non-fermenting Gram-negative bacilli (NFGNB) in ICUs presents a serious and immediate threat in hospital settings (5,6). Among these, carbapenem-resistant *Acinetobacter baumannii* (CRAB) has emerged as one of the leading causes of healthcare-associated infections, particularly in ICUs (7-10). In the World Health Organization's (WHO) 2017 Global Priority List of Antibiotic-Resistant Bacteria, CRAB was classified as one of the pathogens for which new antibiotics are most urgently needed (11). This highlights the critical need for effective infection control strategies.

Managing and treating CRAB infections in ICUs poses a significant global challenge (12). The mechanisms of CRAB colonization, infection, transmission, and drug resistance in these settings require systematic investigation (10,12).

This study was conducted to assess the changes in antibiotic resistance patterns of *A. baumannii* strains isolated from lower respiratory tract samples of ICU patients over time and to provide guidance for treatment.

## Methods

### Study Setting

The study was conducted at Nevşehir State Hospital, located in the Central Anatolia region of Turkey. This is a state hospital with secondary and tertiary intensive care units (ICUs) that provide healthcare services to both rural and urban patients.

### Study Design

This retrospective study examined data from patients treated in the ICUs of Nevşehir State Hospital between January 2018 and December 2022. Samples evaluated included endotracheal aspirates, bronchoalveolar lavage fluids, nasotracheal aspirates, and sputum from patients over 18 years old who were treated in the ICUs. Only cultures showing *Acinetobacter baumannii* growth that were not deemed contaminants and had accompanying antibiograms were included for analysis.

### Exclusion Criteria

Patients whose demographic data were incomplete were excluded from the study. Likewise, cases of recurrent bacterial growth in the same patient after the first detection were not considered, nor were cultures with polymicrobial growth.

### Data Analysis

Descriptive statistics were expressed as percentages. Bacterial isolates were identified using conventional methods and the automated Vitek2 system (bioMérieux, France). Antimicrobial susceptibility testing was performed following European Committee on Antimicrobial Susceptibility Testing (EUCAST) guidelines, using the Kirby–Bauer disk diffusion method, gradient strip test, and broth microdilution techniques. Results were interpreted according to EUCAST criteria. The Centers for Disease Control and Prevention (CDC) list of common commensal microorganisms was used to distinguish pathogens from contaminants.

### Antibiotic Sensitivity Testing

In this study, bacterial susceptibility was tested against broad-spectrum cephalosporins (ceftazidime, cefepime), beta-lactamase inhibitor combinations (piperacillin/tazobactam), aminoglycosides (gentamicin, amikacin), carbapenems (imipenem, meropenem), folate pathway inhibitors (trimethoprim-sulfamethoxazole), fluoroquinolones (ciprofloxacin, levofloxacin), as well as tigecycline and colistin. Categorical variables were presented as numbers and percentages.

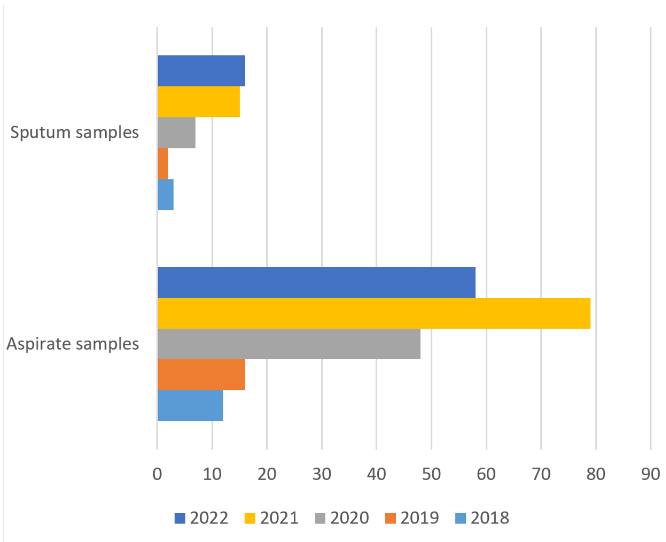
### Ethical Approval

Ethical approval for the study was obtained from the Nevşehir Hacı Bektaş Veli University Non-Invasive Clinical Research Ethics Committee (Decision No: 2023/12, Date: 19.04.2023).

## Results

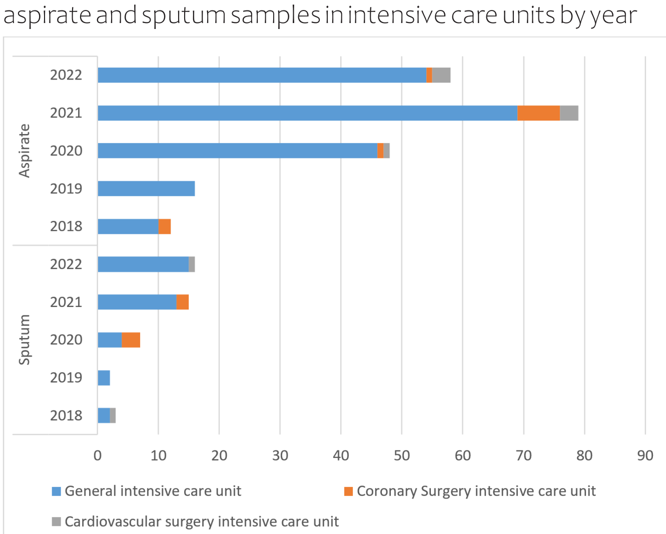
Between January 2018 and December 2022, 4151 samples were studied, of which 18.1% (754/4151) were aspirate and sputum samples. The positivity rate of the cultures was 51.7% (390/754), and the rate of those related to *A. baumannii* was 65.6% (256/390). The average age of the patients is 71.02, and 90.02% (231/256) are male. The proportion of aspirate and sputum samples containing *A. baumannii* was determined as 67.4% (213/316) and 58.1% (43/74), respectively. The year in which *A. baumannii* was detected at the highest rate in both sample groups was 2022 (Figure 1).

**Figure 1**. Distribution of aspirate and sputum samples containing *A. baumannii* by years



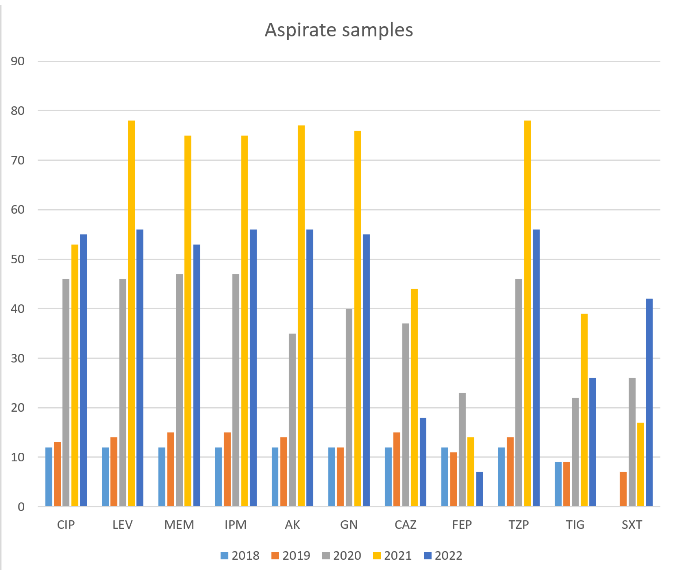

When the distribution of the strains according to the intensive care units (ICU) where they were isolated was examined, it was determined that 90.2% of the isolates were isolated from the general ICU (231/256) (Figure 2).

**Figure 2**. Distribution of *A. baumannii* strains isolated from aspirate and sputum samples in intensive care units by year



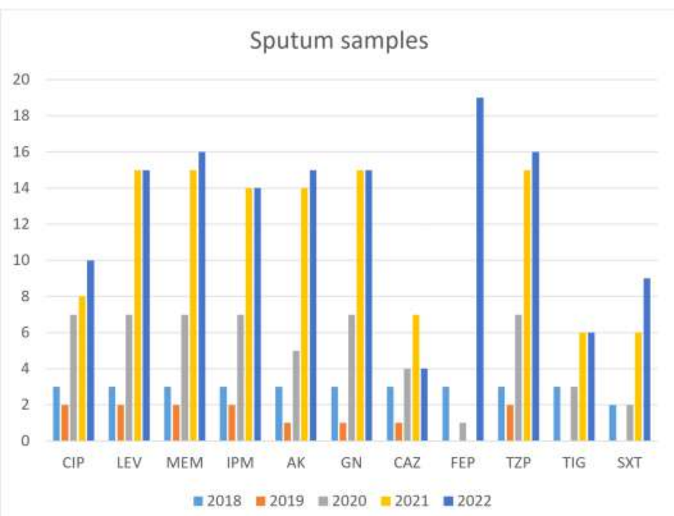
aspirate samples was 96.5%, fluoroquinolone resistance was 91.7%; The carbapenem resistance rate in sputum samples was 96.1% and fluoroquinolone resistance was 90.9%. Similarly, piperacillin/tazobactam also showed a high resistance rate (97.8%). While Tigecycline and Ceftazidime resistance decreased over the years in both samples, all strains were sensitive to colistin. The most effective antibiotics against *A. baumannii* strains isolated from both aspirate and sputum samples were colistin (100%, n=256), Trimethoprim/sulfamethoxazole (TMP/SXT) (55.8%, n=143/256), tigecycline (50.3%, respectively). n=129/256) (Figure 3,4).

**Figure 3**. Resistance of *A. baumannii* strains isolated from aspirate samples to antimicrobials




CIP: Ciprofloxacin, LEV: Levofloxacin, MEM: Meropenem, IPM: Imipenem, AK: Amikacin, GN: Gentamicin, CAZ: Ceftazidime, FEP: Cefepime, TZP: Piperacillin/tazobactam, TIG: Tigecycline, SXT: Trimethoprim/ sulfamethoxazole

**Figure 4**. Resistance of A. baumannii strains isolated from sputum samples to antimicrobials




CIP: Ciprofloxacin, LEV: Levofloxacin, MEM: Meropenem, IPM: Imipenem, AK: Amikacin, GN: Gentamicin, CAZ: Ceftazidime, FEP: Cefepime, TZP: Piperacillin/tazobactam, TIG: Tigecycline, SXT: Trimethoprim/ sulfamethoxazole

When resistance patterns were evaluated by years, fluoroquinolone resistance was observed most in all samples in 2018 and decreased in 2021. Carbapenem resistance is at rates between 93.7% and 100% in all years and in all samples (Figure 3,4).

## Discussion

The emergence of *A. baumannii* strains resistant to most available antimicrobial agents has led to high rates of morbidity and mortality in intensive care unit (ICU) patients (14,15). This study examined *A. baumannii* growth in aspirate and sputum samples from patients hospitalized between January 2018 and December 2022. According to our findings, *A. baumannii* was present in 65.6% (256/390) of aspirate and sputum samples. Similarly, a recent study by Hafız et al. detected *A. baumannii* in 63% of respiratory tract infections, with 262 isolates identified from respiratory samples out of 414 total isolates (16).

According to the latest World Health Organization (WHO) report, clinical laboratories in Turkey recorded an increase in *Acinetobacter* spp. isolates from 2,463 in 2016 to 3,170 in 2020. The report also noted a higher percentage of isolates in men and those aged 65 and over in 2020 (17).

In our study, the highest proportion of isolates was from 2022, with 90.2% (231/256) of patients being men, and the average age of male patients was 69.07 years. These findings suggest an increase in patients towards the end of the pandemic. The region where the study was conducted is a sparsely populated area in Central Anatolia, and the curfews imposed during the pandemic likely reduced the number of samples during times when patients avoided seeking healthcare unless necessary. However, the prevalent misuse of antibiotics during the pandemic may have contributed to the increased antibiotic pressure on patients and the rise in multidrug-resistant *A. baumannii* strains in the post-pandemic period.

*A. baumannii* can survive for prolonged periods in hospital environments (18). Its ability to adhere to plastic surfaces allows it to colonize medical devices such as endotracheal tubes and venous catheters, thus increasing its persistence and transmission among hospitalized patients (19,20). The bacterium has been shown to form biofilms on various materials, including healthcare equipment, porcelain, stainless steel, endotracheal tubes, polycarbonate, and polypropylene plastics (21). This characteristic significantly contributes to the occurrence of medical device-related infections (21,22). In line with these data, we found *A. baumannii* in 67.4% (213/316) of aspirate samples and 58.1% (43/74) of sputum samples from hospitalized patients in our study (Figure 1). *A. baumannii* is an opportunistic pathogen that causes severe nosocomial infections (23).

The global estimated incidence of these bacterial infections is approximately one million cases per year, with high mortality rates, particularly among critically ill patients (24). The clinical significance of *A. baumannii* has risen due to its ability to develop resistance to antibiotics. Indeed, multidrug-resistant, extensively drug-resistant, and panresistant *A. baumannii* isolates have been reported worldwide (25,26).

Over the last 10 years, Turkish healthcare institutions have consistently tested *A. baumannii* against 15 antibiotics: amikacin, gentamicin, imipenem, meropenem, cefoperazone-sulbactam, ceftazidime, cefepime, ampicillin/sulbactam, piperacillin, piperacillin/tazobactam, ciprofloxacin, levofloxacin, trimethoprim-sulfamethoxazole, colistin, and tigecycline. These antibiotics have been tested with considerable frequency, showing that while resistance rates for some antibiotics have remained constant, resistance to others has increased (27). Currently, 45% of *A. baumannii* isolates are classified as multidrug-resistant, with the highest rates observed in America, Asia, and Europe (up to 70%) (28,29). In our study, all isolates were resistant to three or more antimicrobial classes, including almost all carbapenems and fluoroquinolones (Figures 3 and 4).

The Central Asia and Eastern Europe Antimicrobial Resistance Surveillance (CAESAR) 2017 report, which included data from 67 laboratories in Turkey, indicated that 93% of *A. baumannii* isolates were resistant to carbapenems (30). Carbapenem resistance in *A. baumannii* is associated with prolonged hospital stays, increased mortality, and a higher financial burden due to the difficulty in treating these infections (31). Therefore, carbapenem-resistant *A. baumannii* (CRAB) strains must be closely monitored to prevent the spread of epidemic clones in hospitals.

According to WHO's 2020-2022 antimicrobial resistance surveillance report for Europe, *Acinetobacter* spp. carbapenem resistance rates were 91.6% in 2016, 91.5% in 2017, 92.2% in 2018, 90.4% in 2019, and 93.1% in 2020. Fluoroquinolone resistance rates were 92.1% in 2016, 92.6% in 2017, 94.4% in 2018, 90.7% in 2019, and 93.6% in 2020 (29). In our study, carbapenem resistance rates in *A. baumannii* were 96.5% in aspirate samples and 96.1% in sputum samples, while fluoroquinolone resistance rates were 91.7% and 90.9%, respectively. These findings are consistent with the 92% quinolone resistance reported in the CAESAR 2017 report (30).

*A. baumannii* is classified among the most problematic nosocomial ESKAPE pathogens (*Enterococcus faecium, Staphylococcus aureus, Klebsiella pneumoniae, Acinetobacter baumannii, Pseudomonas aeruginosa, and Enterobacter* spp.) and is considered a high priority by WHO (32). In our study, the resistance rate to piperacillin/tazobactam was 97.8%, aligning with findings from Uğur and Genç, who reported over 94% resistance in *A. baumannii* isolates over a three-year period (33).

Aminoglycosides, such as amikacin and gentamicin, are essential drugs for treating *Acinetobacter* infections, but resistance to these antibiotics has also increased (34). Resistance to aminoglycosides primarily arises from ribosomal mutations in 16S rRNA and enzymatic mechanisms (35).

Colistin is considered one of the last-resort treatments for *A. baumannii* infections. However, colistin resistance is associated with increased patient mortality (36,37). Studies show that colistin resistance is higher in Southeast Asia and the Eastern Mediterranean, with an overall prevalence of 11.2% (Germany 0.2%, England 2.3%, India 8.2%, China 11.8%, Lebanon 17.5%) (38). In our study, all strains were susceptible to colistin (Figures 3 and 4). Several studies in Turkey have similarly reported no colistin resistance, or have identified colistin as the most effective antibiotic (33,39). Nevertheless, colistin resistance in *A. baumannii* is diverse and involves mechanisms such as horizontal gene transfer, necessitating a re-evaluation of treatment strategies, including alternatives to conventional antibiotics (40).

Tigecycline, a third-generation tetracycline derivative, can bypass various antibiotic resistance mechanisms, making it a promising drug for *A. baumannii* infections (41). A recent prevalence study showed tigecycline resistance rates of less than 5.5% in Korea, India, and China (42). In our study, tigecycline resistance was 54.2% in aspirate samples and 44.02% in sputum samples. A recent study in Turkey reported tigecycline resistance at 51.6% in *A. baumannii* isolates (43).

This study has some limitations due to its retrospective design. We were unable to evaluate the correlation between risk factors, timing, type, and duration of empirical antimicrobial treatment with resistance and clinical outcomes. For the same reason, we could not confirm the exact resistance mechanisms of *A. baumannii.*

## Conclusions

The results of our study show that multidrug-resistant *A. baumannii* isolates are isolated frequently in the Central Anatolia region of Turkey. These results suggest that surveillance should be further strengthened to identify potential reservoirs of microorganisms, hospital infection control procedures should be updated, and an effective antibiotic stewardship program should be implemented.

## Author contribution statement

**Nazife Akman**: Conceptualization, Investigation, Methodology, Data curation, Writing original draft preparation. **Pelin Özmen**: Supervision, Conceptualization, Data curation, Writing reviewing and editing, Validation. **Mustafa Türk**: Methodoloy, Data curation, Software, Investigation

## Ethics statement

The authors declare that the present study was conducted under the strictest ethical conditions. The research was aproved by Nevşehir Hacı Bektaş Veli University Non-invasive Clinical Research Publication Ethics Committee (Decision number: 2023/12, Date: 19.04.2023).

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None.

## Conflict of interest

The authors declare no conflicts of interest.

## Availability of data

The datasets generated and /or analyzed during current study available from the corresponding author on reasonable request.

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