

Orjinal Araştırma Makalesi/ OriginalPaper

# Antimicrobial Resistance Rates of *Acinetobacter spp*. Isolated from Adult Patients in a State Hospital Between 2017-2021

# 2017-2021 Yılları Arasında Bir Devlet Hastanesinde Erişkin Hastalardan İzole Edilen *Acinetobacter spp*. Antimikrobiyal Direnç Oranları

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#### ÖZET

**Amaç:** *Acinetobacter* türleri, birçok antibiyotiğe karşı son yıllarda saptanan yüksek direnç oranları ile ciddi tedavi sorunları yaratmaktadır. Bu çalışmada, hastanemize başvuran hastalardan izole edilen *Acinetobacter* türlerinin, çeşitli antimikrobiyal ilaçlara karşı direnç profillerinin incelenmesi amaçlanmıştır.

**Materyal ve Metot**: Bandırma Devlet Hastanesi'nde 2017-2021 yıllarında çeşitli klinik örneklerden izole edilen 533 *A. baumannii* suşunun antibiyotiklere direnci retrospektif olarak incelendi. Bakteri identifikasyonu ve antibiyotik duyarlılık testi BD Phoenix (Becton Dickinson, ABD) otomatize sistemi ile yapıldı.

**Bulgular:** Acinetobacter suşlarının çoğu solunum salgılarından (%32.5) ve idrardan (%24.4) izole edilmiştir. Türlerin %63.8'i Acinetobacter baumannii, %34.9'u Acinetobacter baumannii kompleks, %1.1'i diğer Acinetobacter spp., %0.2'si Acinetobacter lwoffii' dir. Antibiyotiklere direnç oranları şu şekilde bulundu: siprofloksasin %91.1, meropenem %91.3, imipenem %89.2, gentamisin %82.5, trimetoprim-sülfametaksasol %78.6, amikasin %66.3 (2020'de enyüksek), ertapenem %100, ampisilin %100, kolistin %4.7 ve levofloksasin %87.1. Serviste ve yoğun bakımda yatan hastalardan alınan örnekler siprofloksasin, levofloksasin, meropenem, imipenem, trimetoprim/sülfametoksazol, gentamisin ve amikasin'e karşı daha dirençli bulundu (p<0,001).

**Sonuç:** *A. baumannii* enfeksiyonlarının başta karbapenem grubu olmak üzere birçok antibiyotiğe direnci yüksek bulunmuş olup tüm hastaların duyarlılık profiline gore tedavi yöntemi belirlenmeli ve yeni tedavi seçenekleri geliştirilmelidir.

Anahtar Kelimeler: Acinetobacter, A.baumanii, Nozokomiyal enfeksiyon.

#### ABSTRACT

**Objective:** Acinetobacter species, high resistance rates detected in recent years against many antibiotics create serious treatment problems. In this study, it was aimed to examine the resistance profiles of *Acinetobacter* species isolated from patients admitted to our hospital against various antimicrobial drugs.

**Material and Method:** Antibiotic resistance of *Acinetobacter* strains isolated from 533 clinical samples collected between 2017-2021 years in Bandırma State Hospital Clinical Microbiology Laboratory were evaluated retrospectively. The identification of isolates and antibiotic susceptibility tests were performed by BD Phoenix (Becton Dickinson, USA) automated system. The vaccinated group and the unvaccinated group were compared in terms of disease severity and outcome.

**Results:** Most of *Acinetobacter* strains were isolated from respiratory secretions (32.5%) and from urine (24.4%). Of species, 63.8% were *Acinetobacter baumannii*, 34.9% *Acinetobacter baumannii* complex, 1.1% other *Acinetobacter sp.*, 0.2% *Acinetobacter lwoffii*. Resistance rates to antibiotics were found as following: ciprofloxacin 91.1%, meropenem 91.3%, imipenem 89.2%, gentamicin 82.5%, trimethoprim-sulfamethaxasol 78.6%, amikacin 66.3% (highest in 2020), ampicillin 100%, ertapenem 100%, colistin 4.7% and levofloxacin 87.1%. The samples collected from patients hospitalized in service and ICU were found more resistant against ciprofloxacin, levofloxacin, meropenem, imipenem, trimethoprim/sulfamethoxazole, gentamicin and amikacin (P<0.0001).

**Conclusion:** *A. baumanii* infections have been observed to have high resistance to numerous antibiotics, particularly the carbapenem group while the treatment method has to be determined in line with the susceptibility profile of all patients and new treatment options have to be developed.

Keywords: Acinetobacter, Acinetobacter baumanii, Nosocomial infection.

Acinetobacter spp. are resistant to numerous antibiotics including carbapenems which render same difficult to treat by virtue of existant antibiotics. Ratiw of

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# INTRODUCTION

carbapenem-resistant *Acinetobacter* strains was below 1% in three countries out of 45 (7%) and 50% or more in 25 countries, especially in Southern and Eastern Europe (56%) according to the World Health Organization's report for 2021 (World Health Organization Regional Office for Europe, 2022).

Increase in number of resistant patients in last two years is directly associated with changes in the provision of healthcare services based on the pandemic conditions. Much as inpatient care institutions apply Prevention and Control rules carefully and seriously, this is not enough for Acinetobacter spp. Resistance (Monnet et al., 2020). Carbapenem-resistant Acinetobacter spp. infections restrict options of treatment there by causing high mortality. Carbapenem-resistant Acinetobacter lead to an estimated 8,500 infections and 700 deaths in hospitalized patients in the U.S.A. in line with the report prepared by CDC in 2017. The CDC applies the goals provided in the US National Action Plan on Antibiotic-Resistant Bacteria published in 2015 and 2020 as regards antimicrobial resistance and it is observed that the budget cost allocated for these said targets has reached significant numbers in 2021 (CDC, 2020). Studies on Acinetobacter resistance have generally been performed in tertiary hospitals until present. On the other hand, there are also very scarce studies on Acinetobacter resistance status in secondary care hospitals of a relatively small settlement place.

The objective of this study is to make research on the antimicrobial resistance of *Acinetobacter* strains isolated between the years of 2017 and 2021 as infectious agents in our hospital.

## MATERIAL and METHOD

This retrospective study included the data of microbiological samples analyzed for *Acinetobacter* strains in the Clinical Microbiology Laboratory of Bandirma State Hospital in Turkiye. All culture samples were isolated from the wounds, blood, tracheal aspirate, abscess, vagina, cerebrospinal fluid (CSF), sputum, and urine samples of 533 patients who were received polyclinic services as outpatients or hospitalized in services or admitted to ICU's between 2017 and 2021. The study protocol was approved by Health Sciences Non-interventional Research Ethical Committee of Bandirma Onyedi Eylul University in Turkiye (Date: 28th Jan 2021, Issue: 2020-50).

Among the clinical samples, the urine samples were inoculated on 5% sheep blood agar and eosin-methylene blue (EMB) agar media while other clinical specimens were inoculated on 5% sheep blood agar, EMB agar and chocolate agar plates. All samples were incubated at 37°C for 24 hours. The growths formed as a result of incubation were evaluated and the culture samples deemed appropriate to be included in the antibiogram were included in the study for bacterial identification.

Blood samples were inoculated in blood culture bottles (Render C/Horacio Lengo N 18, Malaga, Spain) and incubated in an automated system (RENDER BC128, Automated Blood Culture Systems, Jinan, Shandong, China). The samples that gave a reproduction signal within five days were pre-identified by gram staining. Then, the samples were cultivated on 5% sheep blood, chocolate agar and EMB agar and incubated at 35.5-37°C for 18-24 hours.

Identification at the species level for *Acinetobacter* isolate growth observed in the samples of 533 patients were evaluated at the end of 24 hours of incubation period by conventional methods (gram staining, oxidase test, fermentation characteristics) and the resistance rates against antibiotics was determined by using Phoenix 100 (Becton Dickinson, Sparks, Md, BD) automated system. Colistin susceptibility has been analyzed by virtue of Phoenix 100 (Becton Dickinson, Sparks, Md, BD) automated system. Drug sensitivity levels were provided through the automated device subsequent to 24 hours. The results were evaluated in line with the recommendations of the "European Committee on Antimicrobial Susceptibility Testing (EUCAST)".

## Statistical analysis

NCSS (Number Cruncher Statistical System) 2007 (Kaysville, Utah, USA) program was used for the statistical analysis. The study data were evaluated with descriptive statistical methods (Mean, Standard Deviation, Median, Frequency, Ratio, Minimum, Maximum), and the Pearson Chi-Square test was used to compare the qualitative data. The significance was determined at p<0.05 level.

| Type of culture                      | Service (n=138) |       | Polyclinic (n=51) |       | Intensive Care Unit (n=344) |       | Total (n=533) |       |         |
|--------------------------------------|-----------------|-------|-------------------|-------|-----------------------------|-------|---------------|-------|---------|
|                                      | Ν               | %     | Ν                 | %     | Ν                           | %     | Ν             | %     | P value |
| Sputum Culture                       | 29              | 21.0% | 5                 | 9.8%  | 64                          | 18.6% | 87            | 16.3% | 0.207   |
| Urine Culture                        | 33              | 24.0% | 38                | 74.5% | 67                          | 19.5% | 130           | 24.4% | <0.001  |
| Blood Culture                        | 7               | 5.0%  | 0                 | 0.0%  | 45                          | 13.0% | 48            | 9.0%  | 0.001   |
| Catheter Tip Culture                 | 0               | 0.0%  | 0                 | 0.0%  | 1                           | 0.3%  | 1             | 0.2%  | 0.759   |
| <b>Respiratory Secretion Culture</b> | 13              | 9.4%  | 0                 | 0.0%  | 154                         | 44.8% | 173           | 32.5% | <0.001  |
| Wound Culture                        | 56              | 40.6% | 8                 | 15.7% | 13                          | 3.86% | 94            | 17.6% | <0.001  |

Table 1. The distribution of types of culture for Acinetobacter strains according to the medical departments.

#### RESULTS

#### The types of culture for Acinetobacter strains

The mean age of 533 patients whose culture samples were evaluated for the *Acinetobacter* strain was 69.49  $\pm$  16.38 years. 205 of the patients were female (38.5%) while 328 were male patients (61.5%). The mean age of males was 67.63, while the mean age of females was 72.47. Of 533 patients, 138 (25.8%) were patients hospitalized in service, 51 (9.5%) were outpatients treated in the polyclinics and 344 (64.5%) were patients admitted to ICU (Table 1).

The distribution of 533 *Acinetobacter* strains according to the culture samples isolated from patients showed that 32.5% was the respiratory secretion culture, 24.4% was the urine culture, 17.6% wound culture, 16.3% sputum culture, 9% blood culture and 0.2% catheter tip culture (Table 1). Comparison of the distribution of types of culture for *Acinetobacter* strains according to the medical departments showed that

the respiratory secretion and blood cultures were obtained at a higher rate from the patients in ICU compared to other departments (P<0.001 and P=0.001, respectively), while the wound culture was obtained at a higher rate from the patients hospitalized in the services (P<0.001) and the urine culture was obtained at a higher rate from outpatients in polyclinic (P<0.001).

## The growth rates of Acinetobacter species

The growth rate of 533 *A. baumannii* in all culture samples was higher than the other *Acinetobacter spp.* which was 64.5% in the samples collected from the service patients, 56.9% in the samples collected from outpatients and 66.3% in the samples collected from ICU patients (P<0.001 for all). The second most common *Acinetobacter spp.* was A. *baumannii complex* which was 34.3%, 41.2% and 33.7% in the samples collected from service, polyclinic and ICU patients, respectively. Other *Acinetobacter spp.* including *A. lwoffii* rarely growth in all cultures (Table 2).

Table 2. Comparison of the growth rates of *Acinetobacter* species according to the units.

| Acinetobacter Bau- |         |      | Acinetobacter Bau | Acinetobacter |         | Other Acinetobacter |         | Р   |        |
|--------------------|---------|------|-------------------|---------------|---------|---------------------|---------|-----|--------|
| Unit               | mannii  |      | plex              | plex          |         |                     | Spp.    |     | value  |
|                    | N/Total | %    | N/Total           | %             | N/Total | %                   | N/Total | %   | _      |
| Intensive care     | 228/344 | 66.3 | 110/344           | 32.0          | 0/344   | 0.0                 | 6/344   | 1.7 | <0.001 |
| unit               |         |      |                   |               |         |                     |         |     | <0.001 |
| Polyclinic         | 29/51   | 56.9 | 21/51             | 41.2          | 1/51    | 2.0                 | 0/51    | 0.0 | <0.001 |
| Service            | 89/138  | 64.5 | 49/138            | 35.5          | 0/138   | 0.0                 | 0/138   | 0.0 | <0.001 |

Chi-squared Test for Independence

*The distribution of Acinetobacter growth rates according to the departments* 

The distribution of *Acinetobacter* growth rates according to the departments from where the patients were transferred to the units demonstrated that ICU (99.0%), isolated ICU (14.6%), palliative service

(47.1%), urology outpatient clinic (54.9%), chest diseases service (16.7%), internal medicine service (7.2%), 6.5% orthopedics service, 5.8% neurology service, 3.6% general surgery service, and lower rates in other services and outpatient clinics (Table 3).

**Table 3.** The distribution of *Acinetobacter* growth rates according to the departments from where the patients were transferred to the units.

|                        | Unit         |      |               |       |              |                 |  |  |
|------------------------|--------------|------|---------------|-------|--------------|-----------------|--|--|
| Department             | Service (n=1 | 38)  | Polyclinic (n | ı=51) | Intensive Ca | re Unit (n=344) |  |  |
|                        | N/Total      | %    | N/Total       | %     | N/Total      | %               |  |  |
| Intensive care unit    | 0            | 0.0  | 0             | 0.0   | 340/344      | 99.0            |  |  |
| Cardiovascular surgery | 0            | 0.0  | 0             | 0.0   | 4/344        | 1.0             |  |  |
| Palliative care        | 65/138       | 47.1 | 0             | 0.0   | 0            | 0.0             |  |  |
| Chest diseases         | 23/138       | 16.7 | 5/51          | 9.8   | 0            | 0.0             |  |  |
| Internal medicine      | 10/138       | 7.2  | 3/51          | 5.9   | 0            | 0.0             |  |  |
| Urology                | 10/138       | 7.2  | 28/51         | 54.9  | 0            | 0.0             |  |  |
| Orthopedics            | 9/138        | 6.5  | 5/51          | 9.8   | 0            | 0.0             |  |  |
| Neurology              | 8/138        | 5.8  | 0             | 0.0   | 0            | 0.0             |  |  |
| General surgery        | 5/138        | 3.6  | 3/51          | 5.9   | 0            | 0.0             |  |  |
| Infectious diseases    | 4/138        | 2.9  | 1/51          | 2.0   | 0            | 0.0             |  |  |
| Cardiology             | 3/138        | 2.2  | 0             | 0.0   | 0            | 0.0             |  |  |
| Neurosurgery           | 1/138        | 0.7  | 0             | 0.0   | 0            | 0.0             |  |  |
| Home health services   | 0            | 0.0  | 4/51          | 7.8   | 0            | 0.0             |  |  |
| Gynecology             | 0            | 0.0  | 2/51          | 3,9   | 0            | 0.0             |  |  |

*The resistance levels of Acinetobacter strains compared by antibiotic type and by years* 

Overall antibiotic resistance rates of total 533 *Acinetobacter* strains isolated from culture samples were as ciprofloxacin 91.1%, meropenem 91.3%, imipenem 89.2%, gentamicin 82.5%, trimethoprim-sulfamethoxazole 78.6%, amikacin 66.3%, ampiicillin 100%, ertapenem 100%, colistin 4.7% and levofloxacin 87.1%. A comparison of the antibiotic resistance rates by years showed that 100% resistance was detected for all years for ampicillin and ertapenem. (Table 4). The resistance rates decreased during the first three years for ciprofloxacin, meropenem, imipenem, and trimethoprim-sulfamethoxazole while an increase

was observed for each antibiotic in 2020. Colistin susceptibility has been analyzed by virtue of Phoenix 100 (Becton Dickinson, Sparks, Md, BD) automated system. The resistance rates against gentamicin and colistin was observed to increase over the years although the significance was only found in colistin (P<0.001). Colistin resistance was examined in a very few numbers of patients in the last two years, and a resistance was detected in all patients. The amikacin resistance rate was found at a lower rate in 2018 compared to 2017, while an increase has been detected in the last two years (P<0.001). The resistance against levofloxacin was only investigated for the last two years and a high rate of resistance was found (83.9% and 90.2%) without any significant difference between two years. (Table 4).

Table 4. Comparison of the resistance levels of Acinetobacter strains by antibiotic type and by years.

| Antibiotic    | Year    |       |         |       |         |       |         |       |        |
|---------------|---------|-------|---------|-------|---------|-------|---------|-------|--------|
|               | 2017    |       | 2018    |       | 2019    |       | 2020    |       | -      |
|               | N/Total | %     | N/Total | %     | N/Total | %     | N/Total | %     |        |
| Ciprofloxacin | 129/139 | 92.8  | 139/155 | 89.7  | 155/177 | 87.6  | 74/80   | 92.5  | 0.394  |
| Meropenem     | 123/138 | 89.1  | 139/155 | 89.7  | 150/179 | 83.8  | 74/82   | 90.2  | 0.278  |
| Imipenem      | 128/137 | 93.5  | 138/154 | 89.6  | 150/179 | 83.8  | 74/82   | 90.2  | 0.052  |
| Gentamicin    | 110/138 | 79.7  | 120/154 | 77.9  | 149/179 | 83.2  | 75/82   | 91.5  | 0.059  |
| TMP/SXT       | 106/135 | 78.5  | 120/154 | 77.9  | 130/175 | 74.3  | 68/81   | 84.0  | 0.381  |
| Amikacin      | 88/120  | 73.3  | 56/153  | 36.6  | 118/179 | 65.9  | 73/82   | 89.0  | <0.001 |
| Ampicillin    | 184/184 | 100.0 | 142/142 | 100.0 | 150/150 | 100.0 | 66/66   | 100.0 | -      |
| Ertapenem     | 179/179 | 100.0 | 141/141 | 100.0 | 150/150 | 100.0 | 66/66   | 100.0 | -      |
| Colistin      | 1/124   | 0.8   | 5/60    | 8.3   | 5/5     | 100.0 | 1/1     | 100.0 | <0.001 |
| Levofloxacin  | 0       | 0.0   | 0       | 0.0   | 115/137 | 83.9  | 74/82   | 90.2  | 0.189  |

TMP/SXT: Trimethoprim/Sulfamethoxazole

Chi-squared Test for Independence

## *The antibiotic resistance rates of Acinetobacter strains compared by the presence of comorbidities*

The antibiotic resistance rates of *Acinetobacter* strains were compared by the presence of comorbidities including diabetes mellitus, hypertension, heart diseases such as congestive heart failure, renal diseases such as chronic renal failure, chronic obstructive pulmonary disease, Alzheimer, epilepsy, cerebral palsy, Parkinson disease. The resistance rates against gentamicin, colistin, levofloxacin were lower in patients having at least one comorbidity than those without any comorbidity (Table 5). The resistance rates against meropenem, imipenem, ciprofloxacin, trimethoprim-sulfamethoxazole and amikacin were higher in patients with comorbid disease, but no statistically significant difference was found. A 100% resistance rate was found in all patients for ertapenem and ampicillin independent of the presence of comorbidities (Table 5).

| Name of Antibiotic |         |       |         |       |         |
|--------------------|---------|-------|---------|-------|---------|
|                    | Yes     |       | No      |       |         |
|                    | N/Total | %     | Ν       | %     | P value |
| Meropenem          | 228/252 | 90.5  | 223/258 | 86.4  | 0.197   |
| Imipenem           | 225/250 | 90.0  | 224/258 | 86.8  | 0.327   |
| Ciprofloxacin      | 211/227 | 93.0  | 247/280 | 88.2  | 0.100   |
| Ertapenem          | 207/207 | 100.0 | 211/211 | 100.0 | -       |
| Gentamicin         | 205/253 | 81.0  | 212/256 | 82.8  | 0.683   |
| Ampicillin         | 195/195 | 100.0 | 231/231 | 100.0 | -       |
| TMP/SXT            | 187/233 | 80.3  | 203/269 | 75.5  | 0.238   |
| Amikacin           | 156/246 | 63.4  | 161/263 | 61.2  | 0.674   |
| Levofloxacin       | 75/90   | 83.3  | 114/129 | 88.4  | 0.385   |
| Colistin           | 4/83    | 4.8   | 8/76    | 10.5  | 0.289   |

Chi-squared Test

TMP/SXT: Trimethoprim/Sulfamethoxazole

# *The resistance rates of Acinetobacter strains compared by the clinical units and by antibiotic type*

Comparison of the resistance rates in the patients treated in different units by antibiotic type showed that the resistance rate against ampicillin and ertapenem was 100% in all clinical units (Table 6). The resistance rates of all antibiotic types except colistin was found to be highest in ICU patients compared to other clinical units. The highest resistance rate against colistin was found among the service patient, however, the difference was not statistically significant (P=0.344). Significant lower rates of resistances against ciprofloxacin, levofloxacin, meropenem, imipenem, trimethoprim/sulfamethoxazole, gentamicin and amikacin were found among outpatient in polyclinics compared to the service and ICU patients (P<0.001).

| Table 6. Comparison of the resistance rates in the patients treated in different units by ant | ibiotic type. |
|---|---------------|
|---|---------------|

| Name of Antibiotic | Unit            |       |                   |       |                             |       |         |  |  |  |
|--------------------|-----------------|-------|-------------------|-------|-----------------------------|-------|---------|--|--|--|
|                    | Service (n=138) |       | Polyclinic (n=51) |       | Intensive Care Unit (n=344) |       |         |  |  |  |
|                    | N/Total         | %     | N/Total           | %     | N/Total                     | %     | P value |  |  |  |
| Ampicillin         | 184/184         | 100.0 | 46/46             | 100.0 | 196/196                     | 100.0 | -       |  |  |  |
| Ertapenem          | 179/179         | 100.0 | 46/46             | 100.0 | 193/193                     | 100.0 | -       |  |  |  |
| Ciprofloxacin      | 199/216         | 92.1  | 21/46             | 45.7  | 238/245                     | 97.1  | <0.001  |  |  |  |
| Levofloxacin       | 85/94           | 90.4  | 3/18              | 16.7  | 101/107                     | 94.4  | <0.001  |  |  |  |
| Meropenem          | 195/216         | 90.3  | 18/48             | 37.5  | 238/246                     | 96.7  | <0.001  |  |  |  |
| Imipenem           | 194/215         | 90.2  | 18/48             | 37.5  | 237/245                     | 96.7  | <0.001  |  |  |  |
| TMP/SXT            | 171/212         | 80.7  | 15/48             | 31.3  | 204/242                     | 84.3  | <0.001  |  |  |  |
| Gentamicin         | 167/217         | 77.0  | 27/48             | 56.3  | 223/244                     | 91.4  | <0.001  |  |  |  |
| Amikacin           | 120/216         | 55.6  | 14/48             | 29.2  | 183/245                     | 74.7  | <0.001  |  |  |  |
| Colistin           | 7/54            | 13.0  | 1/15              | 6.7   | 4/90                        | 4.4   | 0.171   |  |  |  |

Chi-squared Test for Independence. TMP/SXT: Trimethoprim/Sulfamethoxazole

# DISCUSSION

Increased resistance rates against the antibiotics used in the treatment of A. baumanii infections result in an important health problem all over the world as well as in our country. The antibiotics that should be used against the multi-drug resistant Acinetobacter infections are limited. Antibiotics containing sulbactam alone are not recommended due to the rapidly developing resistance against these infections (Tatman et al., 2004; Jellison et al., 2001). Polymyxin class antibiotics, tigecycline and combined antibiotics are the options in the treatment of multi-drug resistant Acinetobacter infections. Although polymixin antibiotics have been preferred more recently, they cause concerns due to their side effects that create higher toxicity profiles. Therefore, a number of clinicians prefer a treatment based on other agents including sulbactam and tigecycline against the carbapenem-resistant Acinetobacter isolates (Peleg et al., 2008; Fishbain et al., 2010).

A retrospective study found that the combined therapies designed with more than one antibiotic type in the treatment of A. baumannii infections with multidrug resistance yielded more successful results and decreased mortality rates (Batirel et al., 2014). A. baumannii appeared in the first line of the list of "resistant bacteria requiring new antibiotic discovery" published by the World Health Organization (WHO) in 2018 due to the increasing resistance rates of the bacteria (World Health Organization, 2018). These MDR Acinetobacter spp. have increasingly become a serious concern in terms of both nosocomial and community-acquired infections (Peleg et al., 2008). Many studies conducted in different countries have confirmed the increased rates of MDR A.baumannii isolates and revealed that the biofilm production capacity has been rapidly increasing in these isolates (Eze et al., 2018).

Yolbaş et al. investigated the resistance rates against various antibiotics against *A. baumannii* strains of 270 patients by using an automated system (BD Phoenix) and classical methods. In the study, the rate resistance for imipenem was reported as 87%, amikacin 76%, ampicillin/sulbactam 94%, colistin 6%,

cefepime 95%, ceftazidime 95%, ciprofloxacin 93%, aztreonam 96%, meropenem 87%, piperacillin/tazobactam 92%, tetracycline 84%, trimethoprim/sulfamethoxazole 82% (Yolbaş et al., 2013). In our study, over all colistin resistance was found to be lower than this study, as 4.7% which was significantly increasing over years. While the ampicillin resistance rate was 94% for this study, it was found to be 100% in our study. The rates for other antibiotics found in our study were comparable with the literature.

Kurtoğlu et al. examined the antibiotic susceptibilities of the A. baumannii strain in samples of 322 patients by using Phoenix 100 automated identification system and disk diffusion method. In their study, the susceptibilities against tigecycline and cefoperazonesulbactam were determined by the disk diffusion method and other antibiotic susceptibilities were determined by an automated system. Most of the strains (65%) were isolated from the samples collected from the ICU patients and the sputum sample (42% of the strains). The antibiotic resistance rates against A. baumanni strains were as follows: resistance to colistinas 5%, tigecyclineas 16%, cefoperazone-sulbactamas 28%, amikacin as 52%, trimethoprim-sulfamethoxazole as 67%, carbapenems and tetracycline as 70-72%, and other antibiotics between 82-94% (Kurtoğlu et al., 2011). Inconsistent with these findings, the colistin resistance rate measured in our study was found as 4.7% which was highest in patients hospitalized in services. The rate of resistance to the carbapenem group drugs was found to be much higher in our study, particularly among patients admitted to ICU (96.7%) and the rate for ertapenem was found to be 100% independent of the clinical unit. The resistance rates of other antibiotics were also found higher than this study probably due to the high number of hospitalized patients with severe infection selected for the study.

Cesur et al. also used the conventional methods and Phoenix (Becton Dickinson, USA) automated system to conduct the antimicrobial susceptibility tests for 136 *A. baumannii* strains obtained from the clinical samples (Cesur et al., 2017). 109 strains (80.1%) were isolated from the samples of ICU patients and 98 (72%) from the respiratory tract samples. In our study, we isolated 344 (64.5%) *A. baumannii* strains from the samples of ICU patients and most of the culture type was respiratory secretion culture from these samples (44.8%). Cesur et al. determined the antibiotic resistance rates as 5.9% for colistin, 39.7% for amikacin, 73.5% for trimethoprim/sulfamethoxazole, 81.6% for gentamicin, 82.4% for meropenem, 83.1% for imipenem and ciprofloxacin, 83.8% for ceftazidime, and 85.3% for cefepime, piperacillin and piperacillin/tazobactam (Cesur et al., 2017). Again, the colistin resistance was found to be lower in our study. Relatively higher rates of resistance other antibiotics were detected in our study.

Kalem et al. analyzed a total of 275 A. baumannii strains isolated from 136 bronchial aspiration fluid, 41 sputum, 37 blood, 32 urine and 29 wound samples retrospectively by using Vitek 2 Compact (BioMérieux, France) automated system in 2017. All isolates were found to be susceptible to the colistin. The resistance rates were found as follows: 38.9% for amikacin, 64.0% for gentamicin,88.4% for ampicillin/sulbactam,89.5% for imipenem and meropenem, 90.5% for ceftazidime, 93.1% for cefepime, 94.2% for levofloxacin, 94.5% for ciprofloxacin and piperacillin-tazobactam (Kalem et al., 2017). While there was no resistance to colistin in their study, the colistin resistance was observed at a rate of 4.7% in our study. The resistance rates to the other antibiotics were comparable with our findings.

In another study conducted in Northeast Ethiopia, the samples of 238 patients were evaluated by using Vitek automated system. In the study *A. baumannii* isolates showed an antibiotic resistance against the meropenem and ciprofloxacin in a ratio of 33.3% and 44.5%, respectively, and 100% resistance to the ampicillin and piperacine (Motbainor et al., 2020). In our study, the resistance rate for meropenem was 91.3% and those for ciprofloxacin was 91.1% which were higher than the rates of the above-mentioned study. Antibiotic resistance is an emerging problem, associated with excess morbidity and mortality; it has been suggested that this condition might be more prevalent among subjects with comorbid conditions. In a study by Laudisio et al., the presence of antibiotic resistance was found to be independently associated with higher Charlson score which was used to quantify the burden of comorbidity (Laudisio et al., 2016). In our study, the resistance rates against meropenem, imipenem, ciprofloxacin, trimethoprim/sulfamethoxazole and amikacin were relatively higher among the patients with comorbidities. Therefore, these findings are limited to suggest the effect of comorbidities on the antibiotic resistances against *Acinetobacter* strains.

As a result, our study found the resistance rate to colistin lower than those to other antibiotics although the total number of strains which were isolated from outpatients and resistance to levofloxacin and colistin was under 30. Yet, this finding suggested that the colistin could be used as the first option in treatment of Acinetobacter spp. infections. 100% resistance rates were determined against the ampicillin suggesting that these antibiotic may not be used in Acinetobacter treatment. Since the rates of resistance to carbapenem group antibiotics are very high in service and intensive care patients, it is thought that these antibiotics may not be suitable for treatment. In outpatient treated in polyclinics, in addition to colistin, the ciprofloxacin, levofloxacin, meropenem, imipenem, trimethoprim/sulfamethoxazole, gentamicin and amikacin may be accepted as an option in treatment due to the significant decreases in the resistance rates compared to the rates of hospitalized patients in services.

# CONCLUSION

*A. baumannii* infections are difficult to treat and treatment options are restricted based on their increasing resistance to many antibiotics, especially carbapenems. Increasing carbapenem resistance causes a great risk of prolonged hospitalization and increase in mortality. Treatment method should be decided in line with the antibiotic susceptibility profile of all patients and new treatment options have to be developed based on the increasing resistance of *A. baumannii* infections to numerous antibiotics. It is assumed that retrospective and regular examination of this bacterial species, which is a nosocomial factor, will provide major benefits to clinicians in empirical treatment because antibiotic resistance will change according to countries and regions. All microbiologic and molecular studies are significant in order to reach the most appropriate treatment option for nosocomial infectious agents based on increasing resistance to many antibiotics, particularly carbapenems.

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### **Competing Interests**

The authors have no relevant financial or non-financial interests to disclose.

## **Author Contributions**

The author contributed to the study conception and design. The data collection and analysis were performed by DKT. The first draft of the manuscript was written by DKT and DKT commented on previous versions of the manuscript. HD read and approved the final manuscript.

#### Data Availability

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

## **Ethics approval**

This retrospective study involving the data of human participants was in accordance with the ethical standards of the institutional and national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. Approval was granted by Non-Interventional Research Ethics Committee of Bandirma Onyedi Eylül University Health Sciences (Project no: 2020-50, Date: 28th Jan 2021).

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