Journal of Experimental and Clinical Medicine
https://dergipark.org.tr/omujecm

Research Article

J Exp Clin Med
2024; 41(1): 172-176
doi: 10.52142/omujecm.41.1.29

The investigation of beta lactamase in carbapenem-resistant acinetobacter baumannii isolates

Demet GÜR VURAL*, Zeliha SEYFİ, Yeliz TANRIVERDİ ÇAYCI, Kemal BİLGİN, Asuman BİRİNCİ
Department of Medical Microbiology, Faculty of Medicine, Ondokuz Mayıs University, Samsun, Türkiye

Received: 29.02.2024 • **Accepted/Published Online:** 14.03.2024 • **Final Version:** 29.03.2024

Abstract

Acinetobacter baumannii is an opportunistic pathogen that causes nosocomial infections and exhibits multiple antimicrobial resistance. Carbapenems are preferred in the treatment. In recent years, increasing resistance to carbapenems has been reported all over the world. The aim of the study is to investigate the presence of carbapenemases in carbapenem-resistant *A. baumannii* strains by molecular methods.A total of 77 carbapenem-resistant *A. baumannii* isolates, obtained from blood samples collected from catheter hubs of patients hospitalized in the intensive care unit at Ondokuz Mayıs University Faculty of Medicine between from January 2021 and September 2022, were examined. Bacterial identification used traditional methods alongside VITEK® MS (bioMérieux, France). Antibiotic resistance profiles were determined following EUCAST standards using the Vitek2 Compact automated system. Additionally, multiplex polymerase chain reaction (PCR) was utilized to investigate the presence of blaOXA 23-like, blaOXA 24-like, blaOXA 51-like, and blaOXA 58-like oxacillinase genes, as well as blaNDM, blaVIM, and blaIMP metallo-beta-lactamase genes. While all 77 *A. baumannii* isolates were resistant to meropenem, 75 isolates were also resistant to imipenem. In addition, all of the isolates were found to be resistant to ceftazidime, levofloxacin, and ciprofloxacin. Sensitivity to amikacin, gentamicin, and trimethoprim-sulfomethoxazole was 29.8%, 6.4%, and 6.4%, respectively. The blaOXA 51-like gene was found in all *A. baumannii* strains. The blaOXA 23-like gene was detected in 74 (96%) of the strains, and the blaOXA 24-like gene was detected in 16 (20.7%) strains. blaOXA 58-like, blaNDM, blaVIM, and blaIMP genes were not detected positively in any of the isolates. Oxacillinase-type enzymes, notably blaOXA 51-like, blaOXA 23-like, and blaOXA 24-like genes, primarily contribute to carbapenem resistance in *A. baumannii* isolates. The blaOXA 58-like gene and metallo-betalactamase metallo-beta-lactamase resistance genes were not found in the strains. These obtained data revealed reveals the necessity of molecular methods in defining the epidemiological relationship of isolates.

Keywords: acınetobacter baumanni, carbapenem resistant, beta lactamases

1. Introduction

Acinetobacter baumannii is a non-motile, oxidase-negative, nonfermentative gram-negative bacillus (1). *Acinetobacter* species are often isolated from nature, but A. *baumannii* is found in hospital settings, especially in intensive care units (2). *A. baumannii* is responsible for 2-10% of gram-negative bacteria that cause nosocomial infections. For healthy individuals, its virulence is low, and it is difficult to infect. However, it is frequently seen as an infectious agent in individuals whose immune systems are suppressed (3,4). For many reasons, *A. baumannii* is more common in intensive care units. These include its amazing ability to stay alive for a long time on dry, inanimate surfaces, its ability to colonize both patients and healthcare workers, its tendency to stick to the surfaces of medical instruments, and the use of broad-spectrum antibiotics in treatment plans (5).

It has the potential to cause challenging-to-treat infections, including skin and soft tissue infections, urinary tract infections, and meningitis. However, infections like ventilator-associated pneumonia and bacteremia are associated with notably high mortality rates (2). Specifically, mortality rates of 25–34% have been reported in cases of nosocomial *A. baumannii*-related bacteremia, while ventilator-associated pneumonia is linked to even higher mortality rates ranging from 40% to 80% (5).

A. baumannii is one of the six multi-drug-resistant (MDR) microorganisms classified by the Infectious Diseases Society of America (6). While carbapenems are one of the preferred treatments for multidrug-resistant *A. baumannii* infections, the incidence of carbapenem resistance has increased rapidly in recent years (7). According to the European antimicrobial resistance surveillance data, *A. baumannii* carbapenem resistance was reported at 93.3% in 2021 in our country. The World Health Organization prioritized carbapenem-resistant *A. baumannii* for antibiotic research and development in 2018 (8).

The main mechanism of resistance to carbapenems in *A. baumannii* strains is beta-lactamase production. However, various resistance mechanisms, such as modification of penicillin-binding proteins (PBP) and porin exchange, may also be responsible for resistance[7]. The most important carbapenem resistance mechanisms are carbapenemases with serine oxacillinases (OXA types) and metallo beta-lactamases (MBL). These are made by beta-lactamases. Although MBLs identified in *A. baumannii* strains are less common than OXA-type carbapenemases, they have a stronger hydrolyzing effect on carbapenems (9). OXA-51 has been identified in almost all

*Correspondence: demet.gur@yandex.com

A. baumannii strains and has been suggested to be specific to *A. baumannii*. However, it is not found in other *Acinetobacter* species (7,10). OXA23, OXA-24, and OXA-58 are the most commonly acquired oxacilinases among isolates worldwide (11). MBLs are class B beta-lactamases and have the capacity to hydrolyze all beta-lactams, including carbapenems, except aztreonam (9). Although carbapenem-resistant strains are seen worldwide, MBL-producing *A. baumannii* strains have been found to spread only in certain geographical regions. Therefore, the detection of these enzymes is of great importance in the control of *A. baumannii* nosocomial infections (12). The aim of this study is to investigate the presence of class D oxacillinases (blaOXA 23-like, blaOXA 24-like, blaOXA 51-like, and blaOXA 58-like) and metallo-betalactamases (blaNDM, blaVIM, and blaIMP) in carbapenem-resistant *A. baumannii* strains by polymerase chain reaction (PCR).

2. Materials and Methods

2.1. Identification of Isolates and Antibiotic Susceptibility Testing

Seventy strains of *A. baumannii* were studied. They were taken from catheter hub blood samples sent from patients in the intensive care unit to the Medical Microbiology Laboratory of Ondokuz Mayıs University Faculty of Medicine from January 2021 to September 2022. In the process of isolate selection, considerations were given to microbial growths manifesting the same types of microorganisms and the same antibiogram profiles. This evaluation encompassed cultures sent in a minimum of two sets, obtained from both catheter hubs and peripheral veins. Conventional methods (gram stain, oxidase test, motility) and VITEK® MS (bioMérieux, France) were used for species identification of bacteria. The Vitek2 Compact (bioMérieux, France) automated system was used to determine the antibiotic resistance profile. The isolates, whose carbapenem resistance was determined in the automated system, were checked by the gradient strip test (Liofilchem®, Italy) method. Susceptibility test results were evaluated and recorded according to the standards of the European Committee on Antimicrobial Susceptibility Testing (EUCAST, 2023) (13). A single isolate from each patient was included in the study. The first identified isolate in patients with recurrent growth was included in the study.

2.2. Molecular Methods

After identification and determination of carbapenem resistance, DNA extraction was performed by the boiling method (14). Afterwards, the presence of carbapenemase genes in *A. baumannii* strains was investigated by the multiplex PCR method using appropriate primers (Table 1) in an automatic thermal cycler (Eppendorf, Hamburg, Germany). Electrophoresis of the amplification products was carried out on a 1.5% agarose gel at 120 volts for 60 minutes and then stained in ethidium bromide for 20 minutes. It was imaged using the Gel Doc XR (Bio-Rad, USA) instrument and Quantity One (Bio-Rad, USA) software. The primers used were determined after the literature review (10, 15, 16). The PCR of class D oxacillinase resistance genes was performed under the following conditions: Heat denaturation at 94°C for 5 min, 30 cycles of 25 s at 94°C, 40 s at 52°C, 50 s at 72°C, and a final extension step at 72°C for 6 min. The PCR of metallo-betalactamase resistance genes was performed under the following conditions: Heat denaturation at 95°C for 5 min, 35 cycles of 45 s at 95°C, 45 s at 60°C, 1 min at 72°C, and a final extension step at 72°C for 8 min (10, 17).

Table 1. Primer sequences used in multiplex PCR

Target Gene	Primer Direction	Primers Sequence (5'-3')	Amplicon Size (bp)
*bla*OXA 23-like	Forward Reverse	5-GATCGGATTGGAGAACCAGA-3 5-ATTTCTGACCGCATTTCCAT-3	501
*bla*OXA 24-like	Forward Reverse	5-GGTTAGTTGGCCCCCTTAAA-3 5-AGTTGAGCGAAAAGGGGATT-3	246
*bla*OXA 51-like	Forward Reverse	5-TAATGCTTTGATCGGCCTTG-3 5-TGGATTGCACTTCATCTTGG-3	353
*bla*OXA 58-like	Forward Reverse	5-AAGTATTGGGGCTTGTGCTG-3 5-CCCCTCTGCGCTCTACATAC-3	599
*bla*NDM	Forward Reverse	5-GCAGCTTGTCGGCCATGCGGGC-3 5-GGTCGCGAAGCTGAGCACCGCAT-3	782
*bla*VIM	Forward Reverse	5-GTTTGGTCGCATATCGCAAC-3 5-AATGCGCAGCACCAGGATAG-3	389
*bla*IMP	Forward Reverse	5-GGAATAGAGTGGCTTAATTCTC-3 5-CCAAACCACTACGTTATCT-3	188

3. Results

77 carbapenems-resistant *A. baumannii* strains were isolated from catheter blood cultures of patients hospitalized in the intensive care unit. While all isolates were resistant to meropenem, 75 (97.4%) isolates were determined to be resistant to imipenem. In addition, all of the isolates were found to be resistant to ceftazidime, levofloxacin, and ciprofloxacin. A sensitivity of 29.8% to amikacin, 6.4% to gentamicin, and 6.4% to trimethoprim-sulfomethoxazole was found.

After multiplex PCR, the naturally occurring blaOXA 51-like gene in *A. baumannii* was found in all *A. baumannii* strains. The blaOXA 23-like gene was detected in 74 (96%) and the blaOXA 24-like gene was detected in 16 (20.7%) of the strains. The blaOXA 23-like gene was detected in 74 (96%) of the strains, and the blaOXA 24-like gene was detected in 16 (20.7%) strains. blaOXA 58-like, blaNDM, blaVIM, and

blaIMP genes were not positive in any of the isolates. The image of the strains with the blaOXA 23-like, blaOXA 24-like, and blaOXA 51-like genes is presented in Fig. 1. While the blaOXA 51-like gene alone was positive in one strain (1.2%), in 14 (18%) strains, the blaOXA 23-like, blaOXA 24-like, and blaOXA 51-like genes were found to be positive together.

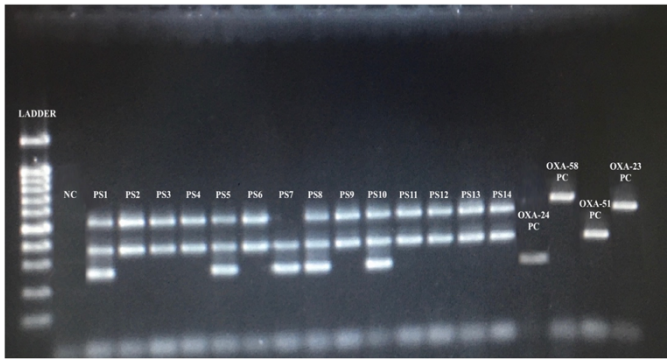

Fig. 1. Electrophoresis image of blaOXA 23-like, blaOXA 24-like and blaOXA 51-like genes. Ladder: 100 bp DNA Ladder Plus; NC: Negative Control; PC: Positive Control; PS1-14: Positive Strains (OXA-23, OXA-24, OXA-51)

4. Discussion

Currently, most *A. baumannii* strains are resistant to aminopenicillins, ureidopenicillins, cephalosporins, aminoglycosides, and quinolones. Recently, emerging multidrug resistance has often led to the use of carbapenems in treatment. However, nowadays, high amounts of carbapenem resistance are seen in *A. baumannii* strains, and it is reported from all over the world. Some strains are resistant to all conventional antimicrobials (7).

In many studies conducted in our country, it is noteworthy that carbapenem resistance has increased over the years. While Gözütok et al. found 91% resistance to carbapenems in their study in 2013, Keskin et al. found resistance to imipenem and meropenem at a rate of 91.5% and 92%, respectively, in 2014 (9,18). In their study, Tümtürk et al. found carbapenem resistance, which was 90.7% in 2014 and increased to 95.9% in 2017. Akyıldız et al. found imipenem and meropenem resistance in *A. baumannii* strains to be 93.2% and 91%, respectively, in 2023 (19,20). In our study, while all strains were resistant to meropenem, 75 (97.4%) strains were determined to be resistant to imipenem.

Resistance to beta-lactam antibiotics is most common in *A. baumannii* strains due to the presence of beta-lactamase. The most important beta-lactamases are carbapenemases, which include metallobeta-lactamases (Ambler class B: IMP, VIM, SIM, and NDM) and serine oxacilinases (Ambler class D: OXA types). Although OXA-type carbapenemases identified in *A. baumannii* strains are more common than MBLs, their hydrolyzing effects on carbapenems are weaker[20].

Although almost all strains of *A. baumannii* have the blaOXA 51-like gene, it has been shown that OXA-51 alone has weak carbapenemase activity but has high-level carbapenem resistance in its overproduction and in combination with other OXA enzymes (21).

Acquired class D oxacillinase was first detected in a strain isolated at Edinburgh University in 1985 and was named OXA-23. The second group is oxacillinases; it includes OXA-24, OXA-25, OXA-26, and OXA-40. Most of the enzymes in this group appear to be variants of each other. The third group is OXA-58, which was detected in France, and it has been reported that it is expressed in *A.baumannii*, reduces the sensitivity to carbapenems, and causes high carbapenem resistance in its overexpression (7).

In the multicenter study of Telli et al. conducted in our country, the blaOXA 23-like gene was found positive in 18 (42%), and the blaOXA 58-like gene was found positive in 5 (12%) of 42 carbapenem-resistant *Acinetobacter* strains isolated from various clinical specimens between 2007 and 2010. The blaOXA 24-like gene was not found in the strains. The naturally occurring blaOXA 51-like gene was found in all *A. baumannii* strains. At the same time, the presence of the blaVIM, blaNDM, and blaIMP genes was investigated, and no positive results were found for the metallo-betalactamase genes (22).

In another multicenter study conducted by Çiftci et al., the blaOXA 51-like gene was found to be positive in all 602 carbapenem-resistant *A. baumannii* strains isolated from various sample species between 2008 and 2011, but the blaOXA 24-like gene was not demonstrated in any strain. The positivity rates for the blaOXA 23-like and blaOXA 58-like genes were found to be 74.4% and 17.3%, respectively (23).

In a 2014 study by Keyik et al., all 105 *A. baumannii* strains resistant to carbapenems isolated from various clinical samples contained the blaOXA 51-like gene. The blaOXA 58-like gene was detected in 56 (53.3%) of the strains, and the blaOXA 23-like gene was detected in 49 (46.7%) strains. blaOXA 24-like gene positivity was not detected in the strains (21).

In a study conducted by Demirci et al. between 2016 and 2018, blaOXA 51-like gene positivity was detected in all 20 *A. baumannii* strains, while blaOXA 23-like was detected in 12 (60%) strains, blaOXA 58-like was detected in 8 (40%) strains, and blaOXA 24-like gene was detected in 1 (5%) strain (24). In a similar study conducted by Vural et al. in our hospital in 2011 with 100 carbapenem-resistant *A. baumannii* strains isolated from various clinical samples, the blaOXA 51-like gene was found positive in all of them, while the blaOXA 23-like gene was found positive in 93 (93%). The blaOXA 24-like and blaOXA 58-like gene regions were not detected in the strains (25). Gözalan et al. investigated blaVIM, blaNDM, and blaIMP genes with the multiplex PCR method in their study with 112 carbapenem-resistant *A. baumannii* strains isolated from blood samples of patients followed up in intensive care units and could not detect positive results of metallo-betalactamase genes (26).

In our study, as in similar studies, the blaOXA 51-like gene specific to *A. baumannii* was found to be positive in all strains, while the positivity rates of the blaOXA 23-like and blaOXA 24-like gene regions were found to be 96% and 20.7%, respectively. blaOXA 58-like, blaVIM, blaNDM, and blaIMP gene regions were not detected in strains. The positivity rates for blaOXA 23-like, blaOXA 24-like, and blaOXA 58-like gene regions varied for each center. Çiftci et al. suggested in their study that blaOXA 58-like gene positivity decreased over the years, while blaOXA 23-like gene positivity increased over the years (23). When we look at the studies conducted in our country, blaOXA 58-like gene positivity is seen at varying rates, but blaOXA 58-like gene positivity was not found in our study. This situation supports the views of Çiftci et al. (23).

In addition, while varying rates of positivity were found in previous studies for the blaOXA 23-like gene region, a high positivity rate of 96% was found in our study. While the blaOXA 24-like gene region was detected at a rate of 5% in the study of Demirci et al., it was not detected in other studies (24). In our study, however, the blaOXA 24-like gene was positive at a rate of 20.7%. For this reason, the possibility that blaOXA 24-like gene positivity may increase over the years has drawn our attention.

It turns out that 94% of the 101 carbapenem-resistant *A. baumannii* bacteria tested by Ning et al. in 2017 were positive for blaOXA 23-like. This is in line with studies done outside of our country on OXA-type carbapenemase genes (27). In Thailand in 2021, Santajit et al. did a study with 172 carbapenem-resistant *A. baumannii.* They found that the blaOXA 51-like gene positivity rate was 100% (172) and the blaOXA 23-like gene positivity rate was 93.60% (161). The blaOXA 24-like gene could not be detected (28).

Again in 2018-2019, in a study conducted with 317 carbapenem-resistant *A. baumannii* strains from different clinical specimens, the presence of the blaOXA 51-like gene was found in all of the strains, and the presence of the blaOXA 23-like gene was found in 94% (n = 298). The blaOXA 58-like gene regions were not detected in the strains (29). In a study conducted by Palavecino et al. between 2019 and 2022, the presence of the blaOXA 23-like gene was found in 63 (67%) of the 94 carbapenem-resistant *A. baumannii* strains, and the presence of the blaOXA 24-like gene was detected in 14 (14.9%) of them. blaOXA 58-like gene positivity was not detected (30).

77 carbapenem resistant *A. baumannii* strains were included in our study. This relatively small number of strains was a limitation for our study. In addition, the fact that we did not have the opportunity to study clonal relationships was a limitation of our research.

In conclusion, our study shows that blaOXA 23-like and blaOXA 51-like genes tend to be found together more often in OXA-type carbapenemases. In our study, the second most common gene accompanying this co-occurrence is blaOXA 24-like. The information gathered is significant because it shows where the OXA-type carbapenemases found in isolates are found and what their epidemiological status is.

Conflict of interest

The authors declared no conflict of interest.

Funding

No funding was used for the study.

Acknowledgments

It was presented as an oral poster presentation at the 40th International Turkish Microbiology Congress (November 16-20, 2022, Antalya,Türkiye.

Authors' contributions

Concept: D.G.V., Design: D.G.V.,Y.T.Ç., Data Collection or Processing: Z.S.Ş, K.B., A.B., Analysis or Interpretation: Y.T.Ç., A.B., Literature Search: Y.T.Ç., K.B., A.B., Writing: D.G.V.

Ethical Statement

The study was approved by Ondokuz Mayıs University Clinical Research Ethics Committee, the study started. The ethics committee decision date is 08/03/2023 and the number of ethical committee decisions is 2023/75.

References

1. Bilgehan H. Klinik Mikrobiyolojik Tanı: Fakülteler Kitabevi Barış Yayınları; 2004.

2. Antunes LC, Visca P, Towner KJ. Acinetobacter baumannii: evolution of a global pathogen. Pathogens and disease. 2014;71(3):292-301.

3. Joly-Guillou M-L. Clinical impact and pathogenicity of Acinetobacter. Clinical microbiology and infection. 2005;11(11):868-73.

4. Şahin AR, Doğruer D, Nazik S, Aktemur A, Öksüz H, Murat A, et al. Hastane kökenli patojenlerde artan antimikrobiyal direnç sorunu: Acinetobacter baumannii. Online Türk Sağlık Bilimleri Dergisi. 2019;4(2):156-69.

5. Savcı Ü, Özveren G, Yenişehirli G, Bulut Y, Özdaş S. Klinik örneklerden izole edilen Acinetobacter baumannii suşlarının in-vitro duyarlılık durumları. Turkish Journal of Clinics and Laboratory. 2015;6(1):24-9.

6. Talbot GH, Bradley J, Edwards Jr JE, Gilbert D, Scheld M, Bartlett JG. Bad bugs need drugs: an update on the development pipeline from the Antimicrobial Availability Task Force of the Infectious Diseases Society of America. Clinical infectious diseases. 2006;42(5):657-68.

7. Çiftci İH, Aşık G. Acinetobacter Baumannii'nin Antibiyotik Direnç Mekanizmalari. Ankem Derg. 2011;25(3):196-207.

8. Temel A, Eraç B. Küresel bir tehdit: Acinetobacter baumannii enfeksiyonları, antimikrobiyal dirençte güncel durum ve alternatif tedavi yaklaşımları. Turkish Bulletin of Hygiene & Experimental Biology/Türk Hijyen ve Deneysel Biyoloji. 2020;77(3).

9. Keskin H, Tekeli A, Dolapçı İ, Öcal D. Klinik örneklerden izole edilen Acinetobacter baumannii suşlarında beta-laktamaz kaynaklı direncin moleküler karakterizasyonu. Mikrobiyol Bul. 2014;48(3):365-76.

10. Woodford N, Ellington MJ, Coelho JM, Turton JF, Ward ME, Brown S, et al. Multiplex PCR for genes encoding prevalent OXA carbapenemases in Acinetobacter spp. International journal of antimicrobial agents. 2006;27(4):351-3.

11. Mertins S, Higgins PG, Thunissen C, Magein H, Gilleman Q, Mertens P, et al. Development of an immunochromatographic lateral flow assay to rapidly detect OXA-23-, OXA-40-, OXA-58- and NDM-mediated carbapenem resistance determinants in Acinetobacter baumannii. Journal of Medical Microbiology. 2023;72(4):001681.

12. Ikonomidis A, Ntokou E, Maniatis AN, Tsakris A, Pournaras S. Hidden VIM-1 metallo-β-lactamase phenotypes among Acinetobacter baumannii clinical isolates. Journal of clinical microbiology. 2008;46(1):346-9.

13. European Committee on Antimicrobial Susceptibility Testing. Breakpoint tables for interpretation of MICs and zone diameters. Version 13.0, 2023.

14. Tshabalala R, Kabelinde A, Tchatchouang C-DK, Ateba CN, Manganyi MC. Effect of Clove (Syzygium aromaticum) spice as microbial inhibitor of resistant bacteria and Organoleptic Quality of meat. Saudi Journal of Biological Sciences. 2021;28(7):3855-63.

15. Doyle D, Peirano G, Lascols C, Lloyd T, Church DL, Pitout JD. Laboratory detection of Enterobacteriaceae that produce carbapenemases. Journal of clinical microbiology. 2012;50(12):3877-80.

16. Ellington MJ, Kistler J, Livermore DM, Woodford N. Multiplex PCR for rapid detection of genes encoding acquired metallo-β-lactamases. Journal of antimicrobial chemotherapy. 2007;59(2):321-2.

17. Tanrıverdi Çaycı Y HÜK, Karacan Temür G, Güney DB, Ertokatlı M, Birinci A. Escherichia coli izolatlarında O25b-ST131 klonu sıklığı ile karbapenem ve fosfomisin direnç genlerinin varlığının araştırılması: Escherichia coli O25b-ST131 izolatlarında Türkiye'den ilk fosA3 tespiti. Mikrobiyol Bul 2023;57(3):454-462.

18. Gözütok F, Sarigüzel FM, Çelik İ, Berk E, Aydin B, Güzel D. hastane infeksiyonu etkeni acinetobacter baumannii suşlarinin antimikrobiyal direnç oranlarinin araştirilmasi. aNKEM dERG. 2013;27(1):7-12.

19. Tümtürk A, Tekçe AYT, Şanal L. Nozokomiyal infeksiyon etkeni Gram negatif bakterilerde karbapenem direnç oranları: Üçüncü basamak bir hastaneden retrospektif bir çalışma. Ortadoğu Tıp Dergisi. 2019;11(4):422-6.

20. Akyildiz E, Saral A, Tuba K, Beriş FŞ, Düzgün AÖ. Trabzon Fatih Devlet Hastanesinden İzole Edilen Klinik Acinetobacter baumannii ve Pseudomonas aeruginosa Suşlarında Antibiyotik Direnç Genlerinin Araştırılması. Gümüşhane Üniversitesi Sağlık Bilimleri Dergisi. 2023;12(2):450-5.

21. Keyik S, Arslan U, Türk Dağı H, Seyhan T, Fındık D. Karbapenemlere dirençli Acinetobacter baumannii suşlarında OXA tipi beta-laktamazların araştırılması ve PFGE ile genotiplendirilmesi. Mikrobiyol Bul. 2014;48(4):556-65.

22. Telli M, Eyigör M, Korkmazgil B, Aydın N, Atalay MA. Acinetobacter spp. klinik izolatlarında karbapenem direncinin moleküler epidemiyolojisi. 2017.

23. Çiftci İH, Aşık G, Karakeçe E, Öksüz L, Yağcı S, Sesli Çetin E, et al. Acinetobacter baumannii izolatlarında blaOXA genlerinin dağılımı: Çok merkezli bir çalışma. 2013.

24. Demirci M, Yiğin A, Demir C. Karbapeneme dirençli Acinetobacter baumannii suşlarında OXA tipi karbapenemaz genlerinin dağılımının gerçek zamanlı polimeraz zincir reaksiyonu yöntemiyle incelenmesi. Klimik Dergisi. 2019;32(2):123-6.

25. Gür Vural D, Durupınar B. Karbapenem Dirençli Acinetobacter baumannii Klinik İzolatlarında Sınıf D Beta Laktamaz Varlığının Araştırılması. Türk Mikrobiyol Cem Derg 46(4):181-187, 2016

26. Gözalan A, Ünaldı Ö, Kırca F, Çöplü N, Müderris T, Açıkgöz Z, et al. Yoğun bakım ünitelerinde kan dolaşımı enfeksiyonu etkeni karbapenem dirençli Acinetobacter baumannii izolatlarının moleküler yöntemlerle karakterizasyonu. Turk Hijiyen Ve Deneysel Biyoloji Dergisi Turkish Bulletin Of Hygiene And Experimental Biology. 2020;77(1).

27. Ning N-z, Liu X, Bao C-m, Chen S-m, Cui E-b, Huang J, et al. Molecular epidemiology of bla OXA-23-producing carbapenem-resistant Acinetobacter baumannii in a single institution over a 65-month period in north China. BMC infectious diseases. 2017;17(1):1-8.

28. Santajit S, Bhoopong P, Kong-Ngoen T, Tunyong W, Horpet D, Paehoh-Ele W, et al. Phenotypic and Genotypic Investigation of Carbapenem-Resistant Acinetobacter baumannii in Maharaj Nakhon Si Thammarat Hospital, Thailand. Antibiotics. 2023;12(3):580.

29. Sharma S, Banerjee T, Yadav G, Kumar A. Susceptibility profile of blaOXA-23 and metallo-β-lactamases co-harbouring isolates of carbapenem resistant Acinetobacter baumannii (CRAB) against standard drugs and combinations. Frontiers in Cellular and Infection Microbiology. 2023;12:1068840.

30. Palavecino E, Greene SR, Kilic A. Characterisation of carbapenemase genes and antibiotic resistance in carbapenem-resistant Acinetobacter baumannii between 2019 and 2022. Infectious Diseases. 2022;54(12):951-3.