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# Determination of PER-1 and OXA-10-like Extended-Spectrum Beta-Lactamases Frequency in Ceftazidime-Resistant *Pseudomonas aeruginosa* Strains Isolated in Kastamonu Training and Research Hospital, Turkey

## Kastamonu Eğitim ve Araştırma Hastanesinden İzole Edilen Seftazidime Dirençli *Pseudomonas aeruginosa* Suşlarında PER-1 ve OXA-10 Benzeri Genişlemiş Spektrumlu Beta-Laktamaz Sıklığının Belirlenmesi

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### ABSTRACT

***Introduction:*** *Detecting Pseudomonas aeruginosa strains producing extended-spectrum beta-lactamase (ESBL) in the hospital setting and taking necessary precautions against them is important for infection control and public health. This study aimed to investigate PER-1 and OXA-10-like ESBLs production frequency in ceftazidime-resistant P. aeruginosa obtained from Kastamonu Training and Research Hospital.*

***Materials and Methods:*** *Forty-two ceftazidime-resistant P. aeruginosa strains from different patients between April 2018 and March 2020 were included in the study. Identification of the strains and antibiotic susceptibility tests were studied according to the European Committee on Antimicrobial Susceptibility Testing (EUCAST) criteria by VITEK 2 Compact automated system (BioMerieux, France). ESBL production of the strains was studied by combined disk test, phenotypically. The presence of PER-1 and OXA-10-like genes was investigated by polymerase chain reaction (PCR). Confirmation of the PCR product was done using DNA sequencing on an ABI PRISM 3130XL Genetic Analyzer (Applied Biosystems, Foster City, CA, USA).*

***Results:*** *The resistance rates of the strains were: 19%, 81%, 88%, 88%, 91%, 95%, and 95% for amikacin, gentamicin, meropenem, cefepime, imipenem, piperacillin-tazobactam, and ciprofloxacin, respectively. Twenty-seven (64%) strains had the ESBL phenotype. Only one strain had PER-1 gene. OXA-10-like gene was not found in any strains. PER-1 sequence was identical and corresponded to the published sequences for PER-1 gene in GenBank at the National Center for Biotechnology Information.*

***Conclusion:*** *These results showed that PER-1 and OXA-10-like genes were not common among ceftazidime-resistant P. aeruginosa strains obtained from our hospital. ESBL production can be determined phenotypically in ceftazidime-resistant P. aeruginosa strains. However, confirming the results with molecular tests is significant for epidemiological studies.*

***Key Words:*** *Ceftazidime; OXA-10-like; PER-1; PCR; Pseudomonas aeruginosa*

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## ÖZ

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***Giriş:*** *Bir hastanede genişlemiş spektrumlu beta-laktamaz (GSBL) üreten Pseudomonas aeruginosa suşlarının tespit edilmesi ve onlara karşı gerekli önlemlerin alınması infeksiyon kontrolü ve halk sağlığı açısından önem arz etmektedir. Bu çalışmada Kastamonu Eğitim ve Araştırma Hastanesinden elde edilen seftazidime dirençli P. aeruginosa suşlarında PER-1 ve OXA-10 benzeri GSBL üretim sıklığının belirlenmesi amaçlanmıştır.*

***Materyal ve Metod:*** *Çalışmaya Nisan 2018-Mart 2020 tarihleri arasında farklı hastalardan izole edilen 42 seftazidime dirençli P. aeruginosa suşu dahil edilmiştir. Suşların tanımlanması ve antibiyotik duyarlılık testleri VITEK 2 Kompakt otomatize sistem (BioMerieux, Fransa) kullanılarak Avrupa Antimikrobiyal Duyarlılık Testi (EUCAST) kriterleriyle çalışılmış ve değerlendirilmiştir. Suşların GSBL üretimi fenotipik olarak kombine disk testiyle belirlenmiştir. PER-1 ve OXA-10 benzeri genlerin varlığı ise polimeraz zincir reaksiyonu (PZR) ile araştırılmıştır. PZR ürününün doğrulanması "ABI PRISM 3130XL Genetic Analyzer" (Applied Biosystems, Foster City, CA, ABD) cihazında DNA dizileme yöntemi ile yapılmıştır.*

***Bulgular:*** *Suşların amikasin, gentamisin, meropenem, sefepim, imipenem, piperasilin-tazobaktam ve siprofloksasin antibiyotiklerine direnç oranları sırasıyla %19, %81, %88, %88, %91, %95 ve %95 olarak tespit edilmiştir. Yirmi yedi suşun (%64) GSBL fenotipine sahip olduğu bulunmuştur. Sadece bir suşta PER-1 geni tespit edilmiştir. OXA-10 benzeri gen hiçbir suşta saptanmamıştır. Elde edilen PER-1 dizisinin Ulusal Biyoteknoloji Bilgi Merkezi GenBank veri tabanındaki PER-1 geni için yayınlanan dizilerle özdeş olduğu belirlenmiştir.*

***Sonuç:*** *Bu sonuçlar, hastanemizden izole edilen seftazidime dirençli P. aeruginosa suşlarında PER-1 ve OXA-10 benzeri genlerin yaygın olarak bulunmadığını göstermiştir. Seftazidime dirençli P. aeruginosa suşlarında GSBL üretimi fenotipik olarak tespit edilebilir. Ancak sonuçların moleküler testlerle doğrulanması özellikle epidemiyolojik çalışmalar açısından önem taşımaktadır.*

***Anahtar Kelimeler:*** *Seftazidim; OXA-10-benzeri; PER-1; Pseudomonas aeruginosa; PZR*

## INTRODUCTION

Beta-lactam group antibiotics are commonly used antibiotics to combat infectious diseases. However, their misuse and overuse have increased the spread of resistance in bacteria[1]. Extended-spectrum beta-lactamases (ESBLs) are enzymes that hydrolyze beta-lactam group antibiotics other than cephamycins (cefoxitin, cefotetan, cefmetazol, etc.) and carbapenems (meropenem, imipenem, etc.). ESBLs can be inactivated by beta-lactamase inhibitors such as clavulanic acid, sulbactam, and tazobactam[2]. Although these enzymes have been reported especially in *Enterobacterales* members, they have also been reported in *Pseudomonas aeruginosa* strains in recent years[3,4].

PER-1 (Pseudomonas extended resistances) and OXA-10-like (oxacillinases) type ESBLs, which are found in Ambler class A and class D, respectively, have been reported to be commonly found in *P. aeruginosa* strains in Turkey[5]. The genes encoding ESBLs can be transferred onto other bacteria, as they are carried on transferable genetic elements. This can accelerate the spread of resistance among bacteria and lead to threats to public health[6]. Also, it is known that morbidity and mortality are increased in ESBL-producing *P. aeruginosa* infections[7]. As a result, it is significant for public health to detect ESBL-producing strains in the hospital, monitor their spreading, and take necessary precautions.

PER-1 and OXA-10-like type ESBL production in clinical *P. aeruginosa* strains may vary based on geographic distribution and even hospitals in Turkey. This study was aimed to investigate ESBL production phenotypically and the presence of PER-1 and OXA-10-like genes in ceftazidime-resistant *P. aeruginosa* strains isolated from inpatients and outpatients at Kastamonu Training and Research Hospital (TRH).

## MATERIALS and METHODS

### Bacterial Strains

In this study, 42 ceftazidime-resistant *P. aeruginosa* strains isolated from clinical samples of the patients from Kastamonu TRH between April 2018 and March 2020 were included. Of the strains, 32 were obtained from intensive care units, seven from inpatient services, and three from outpatients. The clinical samples from which the strains were isolated were as follows: respiratory secretions (n= 29/42), urine (n= 6/42), wound (n= 4/42), and blood cultures (n=3/42). The strains were identified using conventional methods and VITEK 2 Compact automated system (BioMérieux, France). The strains were named with KPA (K: Kastamonu P: *Pseudomonas* A: *aeruginosa*) code and isolate number. The strains were stored at -80°C in nutrient broth (Merck, Darmstadt, Germany) containing 20% glycerol until studied.

### Antibiotic Susceptibility Profile

Antibiotic susceptibility to piperacillin-tazobactam (TZP), ceftazidime (CAZ), cefepime (FEP), gentamicin (CN), amikacin (AK), and ciprofloxacin (CIP) as antipseudomonal antibiotics were studied and evaluated by using the EUCAST standards[8] by VITEK 2 Compact automated system.

### Phenotypic Detection of ESBL Production

ESBL production of the strains was studied by the combined disc test (CDT) phenotypically. Briefly, fresh cultures of the strains grown on nutrient agar (Merck) were adjusted to 0.5 McFarland turbidity and inoculated on Mueller Hinton Agar (MHA) (Merck). Cefotaxime (CTX) and ceftazidime (CAZ) disks (30 µg) with and without clavulanic acid (10 µg) were put on the MHA plate at a distance of 30 mm (center to center) from each other. After incubation at 37°C for 18 ± 2 hours, if the zone diameter of the discs containing clavulanic acid was ≥5 mm than those without, the ESBL was considered positive. Cefepime (FEP) discs (30 µg) with or without clavulanic acid (10 µg) were also used in this study to avoid false-negative results for ESBL as a result of overexpression of AmpC type beta-lactamase (Ambler class C). *Klebsiella pneumoniae* ATCC 700603 and *Escherichia coli* ATCC 25922 were used as positive and negative control, respectively[9].

### Searching for PER-1 and OXA-10-like Genes

The detection of PER-1 and OXA-10-like genes was investigated by polymerase chain reaction (PCR) using the specific primers listed in Table 1. Total DNA was extracted from the strains using the standard boiling method[10]. PCR amplification was performed in Techne TC-512 thermal cycler (Techne, Staffordshire, UK) as follows: 94°C for 5 min for initial denaturation; 35 cycles of 40 s at 94°C, 1 min at 55°C, and 50 s at 72°C; and a final extension of 5 min at 72°C[11]. PCR reactions were prepared to contain the following ingredients; 2 µL DNA template, 0.4 µL 10 pmol/µL of each primer (sense and antisense), 4 µL 5x FIREPol® Master Mix (SolisBioDyne, Tartu, Estonia), and ultra-pure water up to 20 µL. A *P. aeruginosa* strain known to be positive for PER-1 and OXA-10-like genes was used as a positive control, and *P. aeruginosa* ATCC 27853 strain was used as a negative control. The PCR products were electrophoresed on a 1.2% agarose gel

**Table 1. Primers used for detecting PER-1 and OXA-10-like genes**

| Gene | Primer | Sequence (5′ → 3′) | Product Size (bp) | Reference |
|---|---|---|---|---|
| PER-1 | PERA | ATGAATGTCATTATAAAAGC | 926 bp | [11] |
| | PERD | AATTTGGGCTTAGGGCAGAA | | |
| OXA-10-like | OPR1 | GTCTTTCGAGTACGGCATTA | 720 bp | |
| | OPR2 | ATTTTCTTAGCGGCAACTTAC | | |

stained with RedSafe™ Nucleic Acid Staining Solution (iNtRON Biotechnology Inc.) in 1x Tris-acetate-EDTA buffer. The results were evaluated in the presence of a DNA size marker (GeneRuler 1 kb, Thermo Scientific, CA, ABD), visualized under a UV transilluminator. Purified PCR product was sequenced using an ABI PRISM 3130XL Genetic Analyzer (Applied Biosystems, Foster City, CA, USA) by the REFGEN Biyoteknoloji (Ankara, Turkey). The obtained sequences were compared to sequences deposited in GenBank at the National Center for Biotechnology Information.

### Statistical Analysis

Statistical analysis was done by Chi-square test using the SPSS version 23 for Windows, and $p< 0.05$ was considered as statistically significant.

## RESULTS

All strains were resistant to ceftazidime. The resistance rates of the strains to other antipseudomonal antibiotics are presented in Table 2. Resistance rates of the isolates to piperacillin/tazobactam (TZP), cefepime (FEP), imipenem (IPM), meropenem (MEM), gentamicin (CN), amikacin (AK), and ciprofloxacin (CIP) were 95% (n= 40/42), 88% (n= 37/42), 91% (n= 38/42), 88% (n= 37/42), 81% (n= 34/42), 19% (n= 8/42), and 95% (n= 40/42), respectively. The ESBL phenotype was present in 27 (64%) strains (Figure 1). There was no significant difference ($p> 0.05$) in resistance rates to antipseudomonal antibiotics between ESBL positive and negative strains (Table 2).

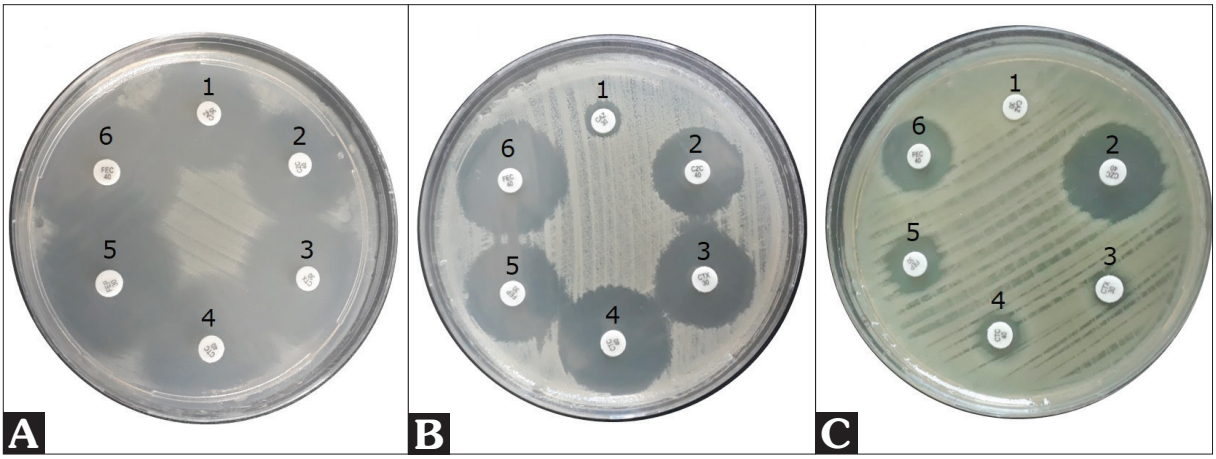


**Figure 1.** Combined disk test using cephalosporins with and without clavulanic acid. **(A)**: *E. coli* ATCC 25922 (negative control), **(B)**: *K. pneumoniae* ATCC 700603 (positive control), **(C)**: KPA-10 [1: Ceftazidime (CAZ), 2: Ceftazidime + clavulanic acid (CZC), 3: Cefotaxime (CTX), 4: Cefotaxime + clavulanic acid (CTC), 5: Cefepime (FEP), 6: Cefepime + clavulanic acid (FEC)].

**Table 2. The resistance rates of ESBL positive and negative strains to antipseudomonal antibiotics**

| | Number of resistant strains (%) | | |
|---|---|---|---|
| **Antibiotic** | **ESBL Positive (n= 27)** | **ESBL Negative (n= 15)** | **Total (n= 42)** |
| TZP | 26 (96%) | 14 (93%) | 40 (95%) |
| FEP | 24 (89%) | 13 (87%) | 37 (88%) |
| IPM | 24 (89%) | 14 (93%) | 38 (91%) |
| MEM | 23 (85%) | 14 (93%) | 37 (88%) |
| CN | 22 (82%) | 12 (80%) | 34 (81%) |
| AK | 4 (15%) | 4 (27%) | 8 (19%) |
| CIP | 27 (100%) | 13 (87%) | 40 (95%) |

ESBL: Extended-spectrumbeta-lactamase, TZP: Piperacillin-tazobactam, FEP: Cefepime, IPM: Imipenem, MEM: Meropenem, CN: Gentamicin, AK: Amikacin, CIP: Ciprofloxacine. There was no significant difference ($p> 0.05$) in resistance rates to antipseudomonal antibiotics between ESBL positive and negative strains.

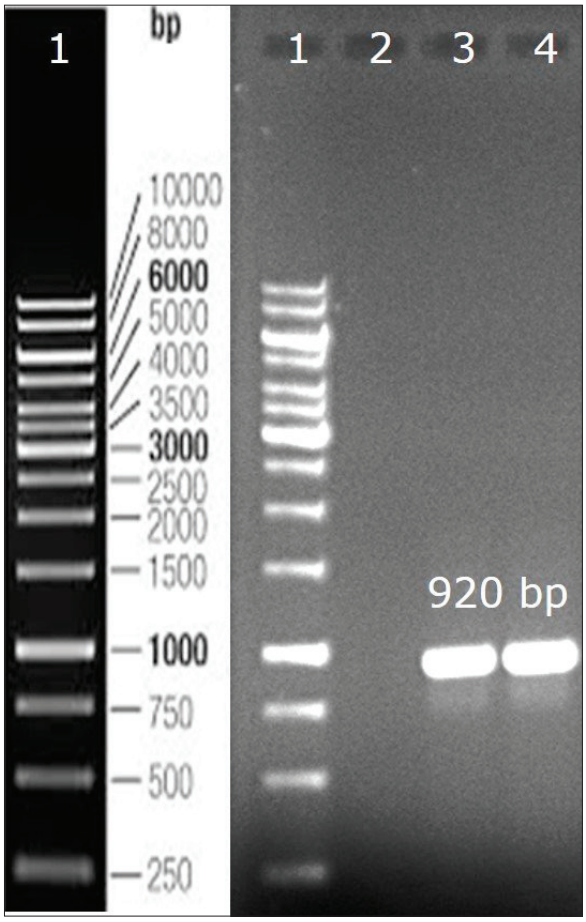


**Figure 2.** PCR products on agarose gel electrophoresis for PER-1 gene. Lane 1: DNA size marker (GeneRuler 1 kb, ThermoScientific, CA, USA); lane 2: Negative control; lane 3: Positive control; lane 4: KPA-10.

Based on the PCR results, PER-1 gene positivity was detected in a strain (2%) designed as KPA-10 (Figure 2). OXA-10-like gene was not found in any of the isolates. When the PER-1 gene was sequenced, the PER-1 sequence was identical and corresponded to the published sequences for the PER-1 gene. GenBank accession number taken for PER-1 sequence is MZ203413.

## DISCUSSION

*P. aeruginosa* is an opportunistic pathogen that can cause bloodstream infections, pneumonia, urinary tract, and wound infections in humans. In particular, patients with respirators and catheters, as well as patients with wounds from post-operative or burns, are at risk for *P. aeruginosa* infections[12]. Ceftazidime is frequently preferred in the treatment of infections caused by *P. aeruginosa* strains. However, ceftazidime resistance in *P. aeruginosa* strains is mainly occurred due to the overexpression of AmpC type beta-lactamase or by ESBL enzymes[13]. In the current study, it was found that ceftazidime-resistant *P. aeruginosa* strains were often resistant to beta-lactam group antibiotics as well as other antibiotics such as gentamicin and ciprofloxacin. This could be due to plasmids carrying ESBL genes might also contain genes encoding resistance to other antibiotics. On the other hand, the lower rate of resistance to amikacin compared to other antibiotics might be due to the less frequent use of amikacin in Kastamonu TRH. These results suggest that the options available except amikacin for the treatment of ceftazidime-resistant *P. aeruginosa* infections are currently limited in Kastamonu TRH.

The ESBL production in ceftazidime-resistant *P. aeruginosa* strains isolated from Turkey has been reported to be between 30.7% and 64%[14,15], and this frequency was found to be 64% in our hospital. These results showed that ESBL production in ceftazidime-resistant *P. aeruginosa* strains could be a potential threat to Kastamonu TRH.

PER-1 and OXA type enzymes are detected in high prevalence in ESBL producing *P. aeruginosa* strains isolated from Turkey[5]. PER-1 was first reported in a *P. aeruginosa* strain isolated from a Turkish patient in France in 1991[16], and its frequency has increased in Turkey[17,18] and Middle Eastern countries after this date[19,20]. However, it is remarkable that PER-1 frequency in ceftazidime-resistant *P. aeruginosa* strains has decreased in Turkey in recent years. For example, PER-1 gene was not detected in any of 195 ceftazidime-resistant *P. aeruginosa* strains in a study conducted in Turkey[14]. Similarly, the frequency of PER-1 positivity by PCR was found to be 2% in 42 ceftazidime-resistant *P. aeruginosa* strains (as 4% in 27 ESBL producing strains) in this study. OXA-10-like gene was not found in any strains in the current study. These results showed that PER-1 and OXA-10-like genes were not commonly found in Kastamonu TRH. Our findings suggest that ESBL positive strains in this

study might have other ESBL genes rather than PER-1 and OXA-10-like.

## CONCLUSION

As a result, the presence of ESBL-producing *P. aeruginosa* strains in our hospital may become a serious problem as they may exhibit a broad range of resistance to other antibiotic classes. Ceftazidime-resistant *P. aeruginosa* strains isolated in our hospital should be routinely examined in terms of ESBL production. Besides, the confirmation of the results with molecular tests is important for epidemiological studies. It is suggested to investigate the presence of other ESBL genes in these strains in further studies.

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## ETHICS COMMITTEE APPROVAL

This study was approves by Karabük University Non-invasive Clinical Research Ethics Committee (Date: 02.05.2018, Decision no: 5/4).

## CONFLICT of INTEREST

The authors declare that they have no conflict of interest.

## AUTHORSHIP CONTRIBUTIONS

Concept and Design: EFT, MCB, NÇ

Data Collection or Processing: SA, ÇK, YÇA

Analysis/Interpretation: EFT, SA, ÇK

Literature Search: NÇ, MCB, YÇA

Writing: EFT, SA, YÇA

Final Approval: NÇ, MCB, ÇK

## REFERENCES

1. *Pandey N, Cascella M. Beta Lactam Antibiotics. [Updated 2021 Jan 16]. In: StatPearls. Treasure Island (FL): StatPearls Publishing; 2021. Available from: https://www.ncbi.nlm.nih.gov/books/NBK545311/*
2. *Rawat D, Nair D. Extended-spectrum β-lactamases in gram negative bacteria. J Glob Infect Dis 2010;2(3):263-74. https://doi.org/10.4103/0974-777X.68531*
3. *Laudy AE, Róg P, Smolińska Król K, Ćmiel M, Słoczyńska A, Patzer J, et al. Prevalence of ESBL-producing Pseudomonas aeruginosa isolates in Warsaw, Poland, detected by various phenotypic and genotypic methods. PLoS One 2017;12(6):e0180121. https://doi.org/10.1371/journal.pone.0180121*
4. *Qing Y, Cao KY, Fang ZL, Huang YM, Zhang XF, Tian GB, et al. Outbreak of PER-1 and diversity of β-lactamases among ceftazidime-resistant Pseudomonas aeruginosa clinical isolates. J Med Microbiol 2014;63(3):386-92. https://doi.org/10.1099/jmm.0.069427-0*
5. *Aktaş Z, Satana D, Kayacan C, Can B, Gönüllü N, Küçükbasmacı O. Pseudomonas aeruginosa suşlarında antibiyotik duyarlılık oranları ve beta-laktam direnç mekanizmalarının tiplendirilmesi. Mikrobiyol Bul 2012;46(3):386-97.*
6. *Bush K, Jacoby GA. Updated functional classification of beta-lactamases. Antimicrobial Agents Chemotherapy 2010;54(3):969-76. https://doi.org/10.1128/AAC.01009-09*
7. *Hu YJ, Ogyu A, Cowling BJ, Fukuda K, Pang HH. Available evidence of antibiotic resistance from extended-spectrum β-lactamase-producing Enterobacteriaceae in paediatric patients in 20 countries: a systematic review and meta-analysis. Bull World Health Organ 2019;97(7):486-501B. https://doi.org/10.2471/BLT.18.225698*
8. *The European Committee on Antimicrobial Susceptibility Testing. Breakpoint tables for interpretation of MICs and zone diameters, version 11.0, 2021. Available from: http://www.eucast.org/clinical_breakpoints/*
9. *The European Committee on Antimicrobial Susceptibility Testing. EUCAST guidelines for detection of resistance mechanisms and specific resistances of clinical and/or epidemiological importance, version 2.0, 2017. Available from: http://www.eucast.org/resistance_mechanisms/*
10. *Ahmed OB, Asghar AH, Elhassan MM. Comparison of three DNA extraction methods for polymerase chain reaction (PCR) analysis of bacterial genomic DNA. Afr J Microbiol Res 2014;8(6):598-602. https://doi.org/10.5897/AJMR2013.6459*
11. *Aktaş Z, Poirel L, Midilli K, Nordmann P. PER-1-and OXA-10-like β-lactamases in ceftazidime-resistant Pseudomonas aeruginosa isolates from intensive care unit patients in Istanbul, Turkey. Clin Microbiol Infect 2005;11(3):193-8. https://doi.org/10.1111/j.1469-0691.2004.01067.x*
12. *Centers for Disease Control and Prevention (CDC). Antibiotic Resistance Threats in the United States, 2019. Atlanta, GA: U.S. Department of Health and Human Services CDC 2019.*
13. *Picão RC, Poirel L, Gales AC, Nordmann P. Diversity of beta-lactamases produced by ceftazidime-resistant Pseudomonas aeruginosa isolates causing bloodstream infections in Brazil. Antimicrob Agents Chemother 2009;53(9):3908-13. https://doi.org/10.1128/AAC.00453-09*

14. *Er H, Altındiş M, Aşık G, Demir C. Seftazidime dirençli Pseudomonas aeruginosa izolatlarında beta-laktamazların moleküler epidemiyolojisi. Mikrobiyol Bul 2015;49(2):156-65. https://doi.org/10.5578/mb.8901*

15. *Ünlü Söğüt M, Yildirim T, Birinci A, Durupinar B. Determination of PER-1 and OXA-10-like β-lactamases in ceftazidime-resistant Pseudomonas aeruginosa isolates by molecular methods. Turkiye Klinikleri J Med Sci 2011;31(5):1227-35. https://doi.org/10.5336/medsci.2010-22180*

16. *Nordmann P, Ronco E, Naas T, Duport C, Michel-Briand Y, Labia R. Characterization of a novel extended-spectrum beta-lactamase from Pseudomonas aeruginosa. Antimicrob Agents Chemother 1993;37(5):962-9. https://doi.org/10.1128/AAC.37.5.962*

17. *Vahaboglu H, Dodanlı S, Eroğlu C, Oztürk R, Soyletir G, et al. Characterization of multiple-antibiotic-resistant Salmonella Typhimurium strains: molecular epidemiology of PER-1 producing isolates and evidence for nosocomial plasmid exchange by a clone. J Clin Microbiol 1996;34(12):2942-6. https://doi.org/10.1128/jcm.34.12.2942-2946.1996*

18. *Atilla A, Eroğlu C, Esen S, Sünbül M, Leblebicioğlu H. Hastane kaynaklı Pseudomonas aeruginosa izolatlarında PER-1 tipi beta-laktamaz sıklığının ve antibiyotiklere direnç oranlarının araştırılması. Mikrobiyol Bul 2012;46(1):1-8.*

19. *Amirkamali S, Naserpour-Farivar T, Azarhoosh K, Peymani A. Distribution of the blaOXA, blaVEB-1, and blaGES-1 genes and resistance patterns of ESBL-producing Pseudomonas aeruginosa isolated from hospitals in Tehran and Qazvin, Iran. Rev Soc Bras Med Trop 2017;50(3):315-20. https://doi.org/10.1590/0037-8682-0478-2016*

20. *Elhariri M, Hamza D, Elhelw R, Dorgham SM. Extended-spectrum beta-lactamase-producing Pseudomonas aeruginosa in camel in Egypt: potential human hazard. Ann Clin Microbiol Antimicrob 2017;16(1):21. https://doi.org/10.1186/s12941-017-0197-x*

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