JIDC | THE JOURNAL OF INFECTION IN DEVELOPING COUNTRIES

Original Article

Ceftolozane-tazobactam and ceftazidime-avibactam efficacy against *K. pneumoniae*: first *NDM-5* and *OXA-232* report from Türkiye

Belgin Altun[1], Gülşen Hazırolan[2], Deniz Gür[2]

[1] *Vocational School of Health Services, Hacettepe University, Ankara, Turkey*
[2] *Department of Medical Microbiology, Faculty of Medicine, Hacettepe University, Ankara, Turkey*

Abstract

Introduction: Ceftolozane-tazobactam (CLZ-TAZ) and ceftazidime-avibactam (CAZ-AVB) are recently developed β-lactam/β-lactamase inhibitor combinations active against resistant Gram-negative bacteria. This study compared the in vitro activities of ceftazidime, meropenem, piperacillin-tazobactam (PIP-TAZ), CLZ-TAZ, and CAZ-AVB in *Klebsiella pneumoniae* isolates from Hacettepe University hospitals and investigated the carbapenemase types detected over the past five years.

Methodology: A total of 550 *K. pneumoniae* isolates were collected consecutively from invasive clinical samples between 2015 and 2022 according to the SENTRY protocol. Identification was performed using matrix-assisted laser desorption ionization–time of flight mass spectrometry (MALDI-TOF MS). Susceptibility testing for ceftazidime, meropenem, PIP-TAZ, CLZ-TAZ, and CAZ-AVB was carried out by broth microdilution and interpreted according to EUCAST standards. Carbapenemase genes were determined by whole-genome sequencing.

Results: Isolates were obtained from blood (n = 191), skin/soft tissue (n = 130), urine (n = 102), respiratory (n = 86), and intra-abdominal (n = 41) samples. Resistance rates were 62.3% for ceftazidime, 29.7% for meropenem, 60.4% for PIP-TAZ, 43.1% for CLZ-TAZ, and 8.7% for CAZ-AVB. The predominant carbapenemases were OXA-48, OXA-232, NDM-1, OXA-181, and KPC-2. Multiple carbapenemases coexisted in 10% of carbapenem-resistant isolates.

Conclusions: CAZ-AVB demonstrated superior activity compared to CLZ-TAZ in this high-resistance setting, While OXA-48 and NDM-1 remain the most frequent carbapenemases, emerging enzymes including OXA-181, OXA-232, KPC-3, and NDM-5 were also detected. The coexistence of multiple enzymes in single isolates highlights a growing therapeutic challenge, emphasizing the need for continued surveillance and effective antimicrobial stewardship.

Key words: *K. pneumoniae*, carbapenem-resistance, ceftolozan-tazobactam, ceftazidime-avibactam, OXA-232, NDM-5.

J Infect Dev Ctries 2026; 20(1):98-103. doi:10.3855/jidc.21385

(Received 26 January 2025 – Accepted 15 May 2025)

Introduction

Klebsiella pneumoniae is one of the primary microorganisms that pose significant challenges in the treatment of hospital-acquired infections because of its resistance to multiple antibiotics. Antimicrobial resistant *K. pneumoniae* isolates are prevalent in Turkey and treatment options for infections caused by these isolates, especially those resistant to carbapenems, are limited [1–4].

Resistance to carbapenems is mostly due to carbapenemases [5,6]. These beta-lactamases hydrolize carbapenems, as well as extended-spectrum beta-lactams, cephalosporins, and cephamycins. These enzymes are categorized in Class A, B, and D based on Ambler's classification. Class A carbapenemases (e.g. *Klebsiella pneumoniae* carbapenemase (KPC) enzyme) and Class D enzymes (oxacillinase, OXA-type)) are serine enzymes; while Class B enzymes (such as verona integron-encoded metallo-β-lactamase (VIM), imipenemase metallo-β-lactamase (IMP), and New Delhi metallo-β-lactamase (NDM beta-lactamase)) are metalloenzymes which need zinc ions for their activity [5,6].

Carbapenemase production and antibiotic resistance in *K. pneumoniae* isolates have become an increasing public health concern in Turkey. Several carbapenemases have been reported in *K. pneumoniae* from Turkey including OXA-48, NDM, VIM, and IMP [2,3,7–10].

New beta-lactam/beta-lactamase inhibitor combinations have been developed which can be active against carbapenemase producing isolates [11]. CAZ-AVB is particularly effective against Class A and Class D enzyme producing *K. pneumoniae* strains and is considered an important option for treating such resistant infections. However, its efficacy against metallo-beta-lactamase (MBL)-producing strains is limited. CLZ-TAZ, on the other hand, has low activity against carbapenemases [11]. Surveillance studies which provide local data on the distribution of the carbapanemeases are essential for guiding the empirical therapy of infections caused by these isolates.

The Hacettepe University Hospitals have participated in the SENTRY Antimicrobial Surveillance Program (JMI Laboratories, North Liberty, IA, USA) since 1997. SENTRY is a global surveillance study of antimicrobial resistance with participation from many centers across Latin America, North America, Europe, and Asia-Western Pacific countries. In this study, the in vitro activity of ceftazidime, meropenem, piperacillin-tazobactam (PIP-TAZ), ceftolozane-tazobactam (CLZ-TAZ), and ceftazidime-avibactam (CAZ-AVB) against 550 *K. pneumoniae* isolates obtained at Hacettepe University Hospitals and sent to SENTRY between 2015 and 2022 were determined, with a focus on the types of carbapenemase enzymes identified in resistant isolates in the last 5 years.

Methodology

Isolates

K. pneumoniae isolates were obtained between 2015 and 2022 from blood, respiratory tract, skin and soft tissue, urine, and intra-abdominal samples from several different wards, mostly from the intensive care unit (ICU), oncology, and internal medicine. The isolates were consecutive in accordance with the SENTRY protocol and only one sample per patient was included. Only the first isolate was included in the case of more than one isolation from the same patient. A total of 20–100 isolates are collected according to the SENTRY protocol, including all types of microorganisms, depending on the type of infection. A total of 550 *K. pneumoniae* isolates were included in the study between 2015–2022.

Species identification was performed on the day of isolation by matrix-assisted laser desorption ionization–time of flight mass spectrometry (MALDI-TOF MS) using a Bruker Daltonics MALDI Biotyper apparatus (Billerica, MA, USA) according to the manufacturer's instructions The isolates were kept at – 80 °C until the day of the study. The isolates were first thawed at room temperature, then vortexed and subcultured on 5% sheep blood agar / eosin methelene blue agar. The isolates were subcultured twice before susceptibility testing.

Antibiotic susceptibility testing

Antibiotic susceptibilities for ceftazidime, meropenem, PIP-TAZ, CLZ-TAZ, and CAZ-AVB were determined by the microdilution method. Validated MIC panels for testing antibiotic susceptibilities were manufactured at JMI Laboratories (North Liberty, IA, USA). The testing medium was cation-adjusted Mueller-Hinton broth [12]. Quality control (QC) was performed using *E. coli* ATCC 25922 and ATCC 35218; and *K. pneumoniae* ATCC 700603, BAA-1705, and BAA-2814.

Molecular testing

Isolates with MIC values for meropenem of ≥ 4 mg/L were selected for further analysis. The types of carbapenemases were investigated in isolates collected in 2018–2022 with the whole genome sequencing method as described in the SENTRY protocol [13]. Total genomic DNA was extracted using the Nextera XT library construction protocol and index kit (Illumina, San Diego, CA) according to the manufacturer's instructions, and sequencing was performed on a MiSeq system (Illumina, San Diego, CA) with a target coverage of 30X. The resulting FASTQ files for each sample were independently assembled de novo using SPAdes version 3.9.0 with K-values of 21, 33, 55, 77, and 99; with the "careful" mode enabled to reduce mismatches, producing FASTA format files with the best N50 values. The assembled sequences were then analyzed using an in-house–designed software tool, which aligned the target sequences against resistance determinants in the NCBI Bacterial Antimicrobial Resistance Reference Gene Database [14], to identify β-lactamase and other resistance genes based on the criteria of > 94% identity and ≥ 40% minimum coverage length.

Table 1. In vitro resistance of *Klebsiella pneumoniae* isolates to antibiotics (2015–2022).

Years (number of isolates)	Ceftazidime %		Meropenem %		PIP-TAZ*, %	CLZ-TAZ *, %	CAZ-AVB *, %
	I	R	I	R	R	R	R
2015 (n = 61)	1.6	59.0	1.6	21.3	54.1	36.1	13.1
2016 (n = 69)	1.4	58.0	0.0	15.9	59.4	30.4	4.3
2017 (n = 61)	3.3	44.3	0.0	18.0	45.9	18.0	8.2
2018 (n = 92)	1.1	64.1	2.2	28.3	57.6	50.0	4.4
2019 (n = 95)	2.1	68.4	3.2	27.4	75.8	58.9	9.5
2020 (n = 62)	1.6	54.8	0.0	30.6	58.1	37.1	1.6
2021 (n = 53)	7.5	56.6	1.9	52.8	66.0	54.7	15.1
2022 (n = 57)	3.5	66.7	0.0	38.6	59.6	50.9	17.5
TOTAL (n = 550)	2.5	59.8	1.3	28.4	60.4	43.1	8.7

*: There is no category I according to EUCAST criteria. PIP-TAZ: piperacillin-tazobactam; CLZ-TAZ: ceftolozane-tazobactam; CAZ-AVB: ceftazidime-avibactam.

Results

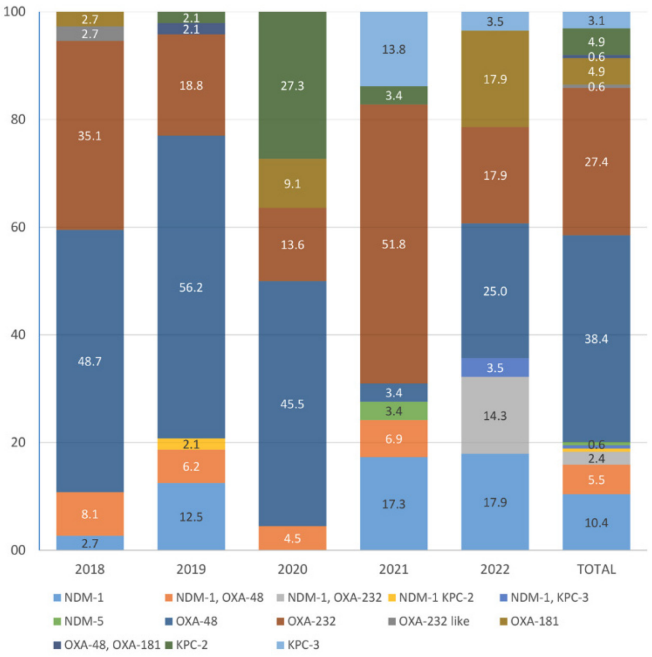
A total of 550 *K. pneumoniae* isolates were obtained from blood (n = 191), skin and soft tissue (n = 130), urine (n = 102), respiratory tract (n = 86), and intra-abdominal (n = 41) samples. Antibiotic susceptibilities of the isolates, and MIC_{50}, MIC_{90} of the antibiotics are presented in Tables 1 and 2 respectively.

Overall resistance to ceftazidime among hospital isolates of *K. pneumoniae* had been over 40% since 2015. Resistance to meropenem fluctuated until 2021 with a sharp peak of 52.8% in 2021. CLZ-TAZ resistance was the lowest in 2017 (18.0%), but remained higher than 30% during the study period with an increase above 50% in the last two years. CAZ-AVB was the most effective antibiotic in vitro against these isolates.

The percentages of carbapenemase types identified in *K. pneumoniae* isolates by year are presented in Figure 1. The most frequent enzymes were OXA-48 (n = 63 alone; n = 10 in combination), followed by OXA-232 (n = 45 alone; n = 4 in combination), and NDM-1 (n = 17 alone; n = 15 in combination).

No information was available regarding the travel history of patients identified with OXA-232. A limitation of the study was that OXA-232 source verification could not be performed.

Figure 1. Percentages of carbapenemase enzymes detected in Klebsiella pneumoniae isolates.



KPC: Klebsiella pneumoniae carbapenemase; NDM: New Delhi metallo-beta-lactamase; OXA: oxacillinase.

Discussion

In this study, more than half of the *K. pneumoniae* isolates were resistant to ceftazidime and PIP-TAZ. Meropenem is the drug of choice in *K. pneumoniae* resistant to cephalosporins [15]. However, the overall resistance to meropenem in the isolates had reached 28.4%, with the highest level of resistance of 52.8% in 2021.

CLZ-TAZ and CAZ-AVB are two recent alternative antibiotics for multi drug resistant (MDR) Gram-negative bacteria. CLZ-TAZ is more effective against Class A penicillinases, but it has no activity against carbapenemase enzymes [11,16]. Resistance rates to CLZ-TAZ range between 10–20% in the Americas and Europe [13,17–19]. In this study, the overall resistance to CLZ-TAZ was 43.1%. This high rate can be explained by the presence of carbapenemase enzymes [3,20]. Therefore, it is not an appropriate choice of antibiotic in the initial empirical treatment of critically ill patients infected with or suspected of systemic infection by *K. pneumoniae* at our center and others with considerable carbapenem resistance. New guidelines for carbapenem resistant isolates recommend meropenem-vaborbactam or CAZ-AVB, if active in vitro. The aztreonam and CAZ-AVB combination is recommended for patients with severe infections caused by metalloenzyme- producing and/or resistant isolates to new antibiotic therapies [4]. There is no evidence to recommend for or against the use of imipenem-relebactam and fosfomycin monotherapy for carbapenem resistant isolates [4].

In the ceftazidime/avibactam combination, cefazidime provides antibacterial activity by inhibiting bacterial cell wall synthesis, while avibactam causes inhibition against β-lactamases. CAZ-AVB is a beta-lactamase inhibitor combination effective against Class A and C beta-lactamases, but has variable activity against Class D beta-lactamases and is inactive against

Table 2. MIC_{50}, MIC_{90}, and MIC ranges in *K. pneumoniae* isolates (n = 550).

Antibiotics	MIC_{50} (µg/mL)	MIC_{90} (µg/mL)	Range (µg/mL)
Ceftazidime	16	> 32	0.06 to >32
Meropenem	0.06	> 32	≤ 0.015 to > 32
Piperacillin-tazobactam	64	> 64	0.5 to 64
Ceftolozane-tazobactam	1	> 16	≤ 0.12 to > 16
Ceftazidime-avibactam	0.25	2	≤ 0.015 to > 32

MIC: minimum inhibitory concentration.

metallo-beta-lactamases [16,21,22]. According to the SENTRY Antimicrobial Surveillance Program results from 2016 to 2019, resistance to CAZ-AVB was reported as 0% in the United States and 0.8% in Western Europe [13]. Similarly, another surveillance study conducted between 2016 and 2020 identified resistance rates of 11.8% in Asia, 6.2% in China, and 6.0% in Latin America [23]. Resistance to CAZ-AVB was 8.7% among the isolates with an increasing trend since 2021.

Class D carbapenemases (OXA-48 and OXA-232) were the most frequently identified resistance mechanisms to carbapenems, followed by Class A and Class B carbapenemases. These enzymes have been reported in many Gram-negative bacteria in Turkey [2,8,24–26]. The OXA-48 enzyme is globally recognized as a prevalent carbapenemase. Variants such as OXA-232 and OXA-181 are also frequently reported. Studies indicate that the OXA-48 enzyme is most commonly identified in Europe and Africa-Central Asia, while OXA-232 and OXA-181 rank as the second most frequently reported variants in these regions. OXA-232 was predominantly reported in the Asia-Pacific regions between 2016 and 2020, and OXA-181 was most commonly identified in Africa and Central Asia [27].

In Turkey, the OXA-48 enzyme has significantly increased in prevalence since its first identification in 2001 and has now become endemic [2,10,16]. National studies report that OXA-48 accounts for 80–90% of carbapenemase enzymes detected in clinical isolates [2,3].

Until recent years, KPC was not observed in Enterobacterales [17,20]; but KPC enzymes have been reported in more recent studies [3,9,10]. In this study KPC-2 and KPC-3 were detected alone and in combination with NDM-1. NDM type carbapenemases are metallo enzymes, and CAZ-AVB is not active against isolates harboring this enzyme. Although NDM type enzymes have been reported in several studies, the NDM-5 enzyme is reported for the first time in Turkish isolates. This is very concerning since CAZ-AVB cannot be used in therapy against *K. pneumoniae* which produce this enzyme. Overall, 33 isolates (20.1%) were NDM producers in this study. It is an interesting finding that NDM-5 has not been found since 2021 in our isolates and not reported in any other part of Turkey up till now. This may be due to the fact that carbapenemase typing is not performed in routine laboratories or that NDM-5 is not very common in Turkey. One limitation of this study is that genotyping was only performed on isolates after 2018.

In a global study, OXA-181 and OXA-232 enzymes were detected at rates of 2% and 6.3% respectively in Europe, and 6.1% and 38.8% in Latin America [27]. OXA-181 albeit rarely, has been reported in Turkish isolates; but OXA-232 was identified for the first time in this study. It is interesting that this enzyme was found in 15 of 29 (51.7%) carbapenem resistant isolates in 2021, and this could be due to an outbreak or cluster in the hospital.

Conclusions

Antibiotic resistance in *K. pneumoniae* isolates obtained from the hospital was high. CAZ-AVB appeared to be more effective than CLZ-TAZ due to the carbapenemases. Although less common than OXA-48, OXA-181, OXA-232, KPC-3, and NDM-5 may also be responsible for carbapenem resistance, and multiple enzymes may coexist in a single isolate. This finding suggests that the mechanisms of carbapenem resistance should be monitored and the type of carbapenemase identified when posssible.

Acknowledgements

We would like to thank Prof. Dr. Ömrüm Uzun for her valuable contribution to this manuscript in terms of revision.

Corresponding author

Belgin Altun, PhD.
Hacettepe University Vocational School of Health Services, Adnan Saygun Street,
D-Blocks 3rd Floor, 06230-Samanpazarı, Ankara, Turkey.
Tel: + 90 0312 305 14 33
Fax: + 90 0312 310 27 30
Email: altunb@hacettepe.edu.tr

Conflict of interest

No conflict of interest is declared.

References

1. Rice LB (2010) Progress and challenges in implementing the research on ESKAPE pathogens. Infect Control Hosp Epidemiol Suppl 1: 7–10. doi: 10.1086/655995.
2. Çakar A, Akyön Y, Gür D, Karatuna O, Öğünç D, Özhak Baysan B, Çöplü N, Çağatay M, Kılıç A, Baysallar M, Bakıcı Z, Çelik C, Gülay Z, Aydemir Ş, Tünger A, Kılıç H, Erçal BD, Aşçı Toraman Z, Zer Y, Büyüktaş A, Ay S, Aktaş Z, Kayacan Ç, Bayramoğlu G, Aydın F, Dündar D, Hasdemir U, Ayaş R, Yanık K, Günaydın M, Güdücüoğlu H, Parlak M (2016) Investigation of carbapenemases in carbapenem-resistant *Escherichia coli* and *Klebsiella pneumoniae* strains isolated in 2014 in Turkey Mikrobiyol Bul 50: 21–33. doi: 10.5578/mb.10695.
3. Süzük Yildiz S, Şimşek H, Bakkaloğlu Z, Numnoğlu Çevik Y, Hekimoğlu CH, Kılıç S, Alp Meşe E, Ulusal Karbapenemaz Sürveyans Çalışma Grubu (2021) The epidemiology of

carbapenemases in *Escherichia coli* and *Klebsiella pneumoniae* isolated in 2019 in Turkey. Mikrobiyol Bul 55: 1–16. doi: 10.5578/mb.20124.
4. Paul M, Carrara E, Retamar P, Tänβgdén T, Bitterman R, Bonomo RA, de Waele J, Daikos GL, Akova M, Harbarth S, Pulcini C, Garnacho-Montero J, Seme K, Tumbarello M, Lindemann PC, Gandra S, Yu Y, Bassetti M, Mouton JW, Tacconelli E, Rodríguez-Baño J (2022) European Society of Clinical Microbiology and Infectious Diseases (ESCMID) guidelines for the treatment of infections caused by multidrug-resistant Gram-negative bacilli (endorsed by European Society of Intensive Care Medicine). Clin Microbiol Infect 28: 521–547. doi: 10.1016/j.cmi.2021.11.025.
5. Boyd SE, Livermore DM, Hooper DC, Hope WW (2020) Metallo-β-lactamases: structure, function, epidemiology, treatment options, and the development pipeline. Antimicrob Agents Chemother 64: e00397-20. doi: 10.1128/AAC.00397-20.
6. Bradford PA, Castanheira M (2023) Mechanisms of resistance to antibacterial agents. In Pfaller MA, Carroll CK editors. Manual of Clinical Microbiology 13th edition, Washington DC: ASM Press. 1375–1410.
7. Candevir Ulu A, Güven Gökmen T, Kibar F, Kurtaran B, Önlen C, Kuşçu F, İnal AS, Kömür S, Yaman A, Aksu HSZ, Taşova Y (2017) Molecular epidemiology of carbapenem-resistant *Klebsiella pneumoniae* at a Turkish centre: is the increase of resistance a threat for Europe? J Glob Antimicrob Resist 11: 10–16. doi: 10.1016/j.jgar.2017.06.012.
8. Grundmann H, Glasner C, Albiger B, Aanensen DM, Tomlinson CT, Andrasević AT, Cantón R, Carmeli Y, Friedrich AW, Giske CG, Glupczynski Y, Gniadkowski M, Livermore DM, Nordmann P, Poirel L, Rossolini GM, Seifert H, Vatopoulos A, Walsh T, Woodford N, Monnet DL, European Survey of Carbapenemase-Producing Enterobacteriaceae (EuSCAPE) Working Group (2017) Occurrence of carbapenemase-producing *Klebsiella pneumoniae* and *Escherichia coli* in the European survey of carbapenemase-producing Enterobacteriaceae (EuSCAPE): a prospective, .multinational study, Lancet Infec Dis 17: 153–163. doi: 10.1016/S1473-3099(16)30257-2.
9. Özad Düzgün A (2021) From Turkey: first Report of KPC-3- and CTX-M-27-producing multidrug-resistant *Klebsiella pneumoniae* ST147 clone carrying *OmpK36* and *Ompk37* porin mutations. Microb Drug Resist 27: 1265–1270. doi: 10.1089/mdr.2020.0274.
10. Tanrıverdi Caycı Y, Bıyık I, Korkmaz F, Birinci A (2021) Investigation of *NDM*, *VIM*, *KPC*, and *OXA-48* genes, blue-carba and CIM in carbapenem resistant Enterobacterales isolates. J Infect Dev Ctries 15: 696–703. doi: 10.3855/jidc.13345.
11. van Duin D, Bonomo RA (2016) Ceftazidime/avibactam and ceftolozane/tazobactam: second-generation β-lactam/β-lactamase inhibitor combinations. Clin Infect Dis 63: 234–241. doi: 10.1093/cid/ciw243.
12. EUCAST (2024) Breakpoint tables for interpretation of MIC's and zone diameters, Version 14.0, European Committee on Antimicrobial Susceptibility Testing. Available: https://www.eucast.org/clinical_breakpoints/. Accessed: 9 September 2025.
13. Castanheira M, Kimbrough JH, DeVries S, Mendes RE, Sader HS (2023) Trends of β-lactamase occurrence among *Escherichia coli* and *Klebsiella pneumonia* in United States hospitals during a 5-year period and activity of antimicrobial agents against isolates stratified by β-lactamase type. Open Forum Infect Dis 10: ofad038. doi: 10.1093/ofid/ofad038.
14. NCBI (2016) Bacterial antimicrobial resistance reference gene database. Available: https://www.ncbi.nlm.nih.gov/bioproject/PRJNA313047. Accessed: 9 September 2025.
15. Lynch JP 3rd, Clark NM, Zhanel GG (2021) Escalating antimicrobial resistance among Enterobacteriaceae: focus on carbapenemases. Expert Opin Pharmacother 22: 1455–1473. doi: 10.1080/14656566.2021.1904891.
16. Lee YL, Chen Hii IM, Hsueh PR (2022) Carbapenemase-producing Enterobacterales infections: recent advances in diagnosis and treatment. Int J Antimicrob Agents 59: 106528. doi: 10.1016/j.ijantimicag.2022.106528.
17. Pfaller M, Bassetti M, Duncan LR, Castanheira M (2017) Ceftolozane/tazobactam activity against drug-resistant Enterobacteriaceae and *Pseudomonas aeruginosa* causing urinary tract and intraabdominal infections in Europe: report from an antimicrobial surveillance programme (2012–15). J Antimicrob Chemother 72: 1386–1395. doi: 10.1093/jac/dkx009.
18. Castanheira M, Duncan L, Mendes RE, Sader HS, Shortridge D (2018) Activity of ceftolozane-tazobactam against *Pseudomonas aeruginosa* and Enterobacteriaceae isolates collected from respiratory tract specimens of hospitalized patients in the United States during 2013 to 2015. Antimicrob Agents Chemother 62: e02125–17. doi: 10.1128/AAC.02125-17.
19. Wang Y, Wang J, Wang R, Cai Y (2020) Resistance to ceftazidime-avibactam and underlying mechanisms. J Glob Antimicrob Resist 22: 18–27. doi: 10.1016/j.jgar.2019.12.009.
20. Gur D, Hasdemir U, Cakar A, Plazomicin Study Group (2020) Comparative in vitro activity of plazomicin and older aminoglyosides against Enterobacterales isolates; prevalence of aminoglycoside modifying enzymes and 16S rRNA methyltransferases. Diagn Microbiol Infect Dis 97: 115092. doi: 10.1016/j.diagmicrobio.2020.115092.
21. Zhang H, Xu YC, Jia PY, Zhu Y, Zhang G, Zhang JJ, Duan SM, Kang W, Wang T, Jing R, Cheng JW, Liu YL, Yang QW (2020) Global trends of antimicrobial susceptibility to ceftaroline and ceftazidime-avibactam: a surveillance study from the ATLAS program (2012–2016). Antimicrob Resist Infect Control 9: 166. doi: 10.1186/s13756-020-00829-z.
22. Mojica MF, De La Cadena E, García-Betancur JC, Porras J, Novoa-Caicedo I, Páez-Zamora L, Pallares C, Appel TM, Radice MA, Castañeda-Méndez P, Gales AC, Munita JM, Villegas MV (2023) Molecular mechanisms of resistance to ceftazidime/avibactam in clinical isolates of Enterobacterales and *Pseudomonas aeruginosa* in Latin American hospitals. mSphere 8: e00651–22. doi: 10.1128/msphere.00651-22.
23. Yin D, Wu S, Yang Y, Shi Q, Dong D, Zhu D, Hu F, China Antimicrobial Surveillance Network (CHINET) Study Group (2019) Results from the China Antimicrobial Surveillance Network (CHINET) in 2017 of the in vitro activities of ceftazidime-avibactam and ceftolozane-tazobactam against clinical isolates of Enterobacteriaceae and *Pseudomonas aeruginosa*. Antimicrob Agents Chemother 6: e02431–18. doi: 10.1128/AAC.02431-18.
24. Poirel L, Héritier C, Tolün V, Nordmann P (2004) Emergence of oxacillinase-mediated resistance to imipenem in *Klebsiella pneumoniae*. Antimicrob Agents Chemother 48: 15–22. doi: 10.1128/AAC.48.1.15-22.2004.

25. Gur D, Korten V, Unal S, Desphande LM, Castanheira M (2008) Increasing carbapenem resistance due to the clonal dissemination of oxacillinase (OXA-23 and OXA-58)-producing *Acinetobacter baumannii*: report from the Turkish SENTRY Program sites. J Med Microbiol 57: 1529–1532. doi: 10.1099/jmm.0.2008/002469-0.
26. Roca I, Mosqueda N, Altun B, Espinal P, Akova M, Vila J (2014) Molecular characterization of NDM-1 producing *Acinetobacter pittii* isolated from Turkey in 2006, J Antimicrob Chemother 69: 3437–3438. doi: 10.1093/jac/dku306.
27. Stone G, Wise M, Utt E (2024) In vitro activity of ceftazidime-avibactam and comparators against OXA-48-like Enterobacterales collected between 2016 and 2020. Microbiol Spectr 12: e0147323. doi: 10.1128/spectrum.01473-23.