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LETTER TO THE EDITOR / EDİTÖRE MEKTUP

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Ceftazidime-Avibactam Susceptibility Patterns of Carbapenem-Resistant *Klebsiella pneumoniae* and *Pseudomonas aeruginosa* Clinical Strains in a Tertiary-Care Educational Hospital in Türkiye

Türkiye'deki Üçüncü Basamak Eğitim Hastanesinde Karbapenem Dirençli *Klebsiella pneumoniae* ve *Pseudomonas aeruginosa* Klinik Suşlarının Seftazidim-Avibaktam Duyarlılık Paternleri

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Dear Editor,

Healthcare-associated infections caused by carbapenem-resistant gram-negative bacilli (CRGNB) are becoming increasingly significant. A substantial part of CRGNB are resistant to multiple drugs and are increasingly resistant to most available antibiotics[1]. The increasing prevalence of CRGNB also constitutes a serious threat to global public health due to the limited treatment options available and the historically slow pace of development in the new gram-negative bacteria-oriented antimicrobial agents[2].

Ceftazidime-avibactam (CAZ-AVI) is the first-line treatment in carbapenem-resistant *Klebsiella pneumoniae* and the second-line treatment after ceftolozane/tazobactam which is not available in Türkiye for *Pseudomonas aeruginosa* in IDSA guidelines[3]. Herein, we aimed to investigate the in vitro efficacy of CAZ-AVI, against clinical strains of carbapenem-resistant *K. pneumoniae* and *P. aeruginosa*.

A total of 170 strains isolated from different clinical specimens in the bacteriology laboratory between February 1 and August 31, 2021, were evaluated. In the case of duplicate isolates, the first strain isolated from each patient was included in the study. Species-level identification of bacteria was performed by MALDI-TOF MS (bioMérieux, France). The susceptibility testing of the strains was performed using the Kirby-Bauer disk diffusion method and VITEK 2 (bioMérieux, France), an automated microdilution method in accordance with EUCAST recommendations[4]. CAZ-AVI susceptibility was determined by the disc diffusion method[5]. *Enterobacterales* isolates (susceptible, ≥13 mm; resistant, <13 mm) and *P. aeruginosa* isolates (susceptible, ≥17 mm; resistant, <17 mm) were interpreted with EUCAST breakpoints[4]. In addition to CAZ-AVI, resistance rates of amikacin, gentamicin, imipenem, ertapenem, meropenem, and ciprofloxacin were also analyzed.

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Of the 170 strains examined, 140 (82.3%) were identified as *K. pneumoniae* and 30 (17.6%) as *P. aeruginosa*. Approximately 33.8% were isolated from respiratory samples, 30.3% from urinary samples, 15.6% from the blood culture, and 19% from soft tissue infections. While 52.8% of the examined isolates were isolated from inpatients, 27% were isolated from emergency room patients. Additionally, 24.4% of inpatients were in the intensive care units. In *K. pneumoniae* strains, resistance to imipenem, meropenem, ertapenem, ciprofloxacin, amikacin, gentamicin, and CAZ-AVI were 94.3%, 95%, 100%, 98.6%, 39.28%, 47.14%, and 26.42%, respectively. Imipenem, meropenem, ciprofloxacin, amikacin, and CAZ-AVI resistance rates in *P. aeruginosa* strains were 93.3%, 80%, 90%, 60%, and 60%, respectively.

CAZ-AVI was the most effective antibiotic against *K. pneumoniae*. CAZ-AVI and amikacin were the most effective antibiotics in *P. aeruginosa*. We also analyzed the sensitivity to CAZ-AVI in strains resistant to gentamicin and amikacin, as well as in strains sensitive to gentamicin and amikacin. We found sensitivities of 60.5% (46/76) and 78.4% (40/51), respectively.

In two studies from Sakarya, CAZ-AVİ resistance was reported to be 21.8% in carbapenem-resistant *P. aeruginosa* and 27% in carbapenem-resistant *K. pneumoniae*[6,7]. In another study from Ankara and Adana with 102 meropenem-resistant *P. aeruginosa* strains, the CAZ-AVİ resistance rate was determined as 17%[8]. While our CAZ-AVİ resistance rate in *K. pneumoniae* (26.42%) was consistent with the findings of Terzi et al., the CAZ-AVİ resistance rate in *P. aeruginosa* (60%) was higher than that reported by Aydemir et al. and Mirza et al[6-8]. We may speculate that this discrepancy may be due to the possible molecular epidemiology difference in our setting. However, we could not perform molecular analysis.

As a limitation of our study, we did not analyze the molecular epidemiology and clinical outcomes of the patients. However, our data suggest that, while not applicable to all strains, approximately 40% of *P. aeruginosa* strains and 75% of the *K. pneumoniae* strains indicate a potential for patients to be treated with CAZ-AVİ, as recommended by the IDSA guidelines[3].

In conclusion, CAZ-AVİ continues to exhibit a high susceptibility rate, and accurate susceptibility testing is crucial for optimal patient management. Furthermore, we recommend heightened efforts in implementing effective infection control measures against CRGNB.

CONFLICT of INTEREST

The authors have no conflicts of interest to declare that are relevant to the content of this article.

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