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Activity of Aztreonam-avibactam and other β-lactamase inhibitor combinations against Gram-negative bacteria isolated from patients hospitalized with pneumonia in United States medical centers (2020–2022)

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Abstract

Background Initial antimicrobial therapy for pneumonia is frequently empirical and resistance to antimicrobial agents represents a great challenge to the treatment of patients hospitalized with pneumonia. We evaluated the frequency and antimicrobial susceptibility of Gram-negative bacteria causing pneumonia in US hospitals.

Methods Bacterial isolates were consecutively collected (1/patient) from patients hospitalized with pneumonia and the susceptibility of Gram-negative bacilli (3,911 Enterobacterales and 2,753 non-fermenters) was evaluated by broth microdilution in a monitoring laboratory. Isolates were collected in 69 medical centers in 2020–2022. Aztreonam-avibactam was tested with avibactam at fixed 4 mg/L and a pharmacokinetic/pharmacodynamic susceptible (S) breakpoint of ≤ 8 mg/L was applied for comparison. Carbapenem-resistant Enterobacterales (CRE; isolates with MIC values of > 2 mg/L for imipenem and/or meropenem) isolates were screened for carbapenemases by whole genome sequencing.

Results Gram-negative bacilli represented 71.1% of organisms. The most common Gram-negative species were *Pseudomonas aeruginosa* (22.4% of organisms), *Klebsiella pneumoniae* (8.8%), *Escherichia coli* (6.6%), *Serratia marcescens* (6.2%), *Stenotrophomonas maltophilia* (4.9%), and *Enterobacter cloacae* complex (4.8%). Aztreonam-avibactam inhibited 100.0% of Enterobacterales at ≤ 8 mg/L and 99.9% at ≤ 4 mg/L and showed potent activity against CRE ($MIC_{50/90}$, 0.25/1 mg/L). Ceftazidime-avibactam and meropenem-vaborbactam were active against 89.4% and 88.5% of CREs, respectively. Aztreonam-avibactam retained activity against Enterobacterales non-susceptible to ceftazidime-avibactam and/or meropenem-vaborbactam ($n = 19$; $MIC_{50/90}$, 0.25/4 mg/L). The most common carbapenemases were KPC (69.2% of CREs), NDM (9.6%), and SME (4.8%). A carbapenemase gene was not identified in 16.3% of CREs. Ceftazidime-avibactam and meropenem-vaborbactam were highly active against KPC and SME producers but showed limited activity against MBL producers. The most active comparators against CRE were tigecycline (95.2%S),

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amikacin (73.1%S), and gentamicin (60.6%S). Among *Pseudomonas aeruginosa*, 79.1% were inhibited at ≤ 8 mg/L of aztreonam-avibactam, 77.2% were meropenem susceptible, and 77.2% were piperacillin-tazobactam susceptible. Aztreonam-avibactam was highly active against *S. maltophilia*, inhibiting 99.5% of isolates at ≤ 8 mg/L.

Conclusions Aztreonam-avibactam displayed potent in vitro activity against a large collection of contemporary Gram-negative organisms isolated from patients hospitalized with pneumonia, including CRE isolates resistant to ceftazidime-avibactam and/or meropenem-vaborbactam. Results of surveillance programs are valuable for planning empiric antimicrobial therapy guidelines and infection control measures.

Keywords Nosocomial pneumonia, Enterobacterales, CRE, *Pseudomonas aeruginosa*, *Stenotrophomonas maltophilia*, Metallo-beta-lactamase, KPC

Introduction

Bacterial pneumonia represents one of the most frequent healthcare-associated infections and it is generally related to prolonged hospitalization and increased morbidity and mortality [1]. Moreover, resistance to antimicrobial agents represents a great challenge to the treatment of patients hospitalized with pneumonia. Antimicrobial therapy is frequently empirical, and the most effective regimen is determined mainly by recognizing the most common causative pathogens and their antimicrobial susceptibility. The application of timely and effective antimicrobial therapy is crucial to reduce complications and mortality [2].

A few antimicrobial agents with potent activity against Gram-negative organisms were licensed in the last few years, including ceftazidime-avibactam, meropenem-vaborbactam, imipenem-relebactam, and cefiderocol [3]. The approval of these antimicrobials represented a significant improvement in the treatment of infections caused by multidrug-resistant Gram-negatives, including carbapenem-resistant Enterobacterales (CRE); however, with the exception of cefiderocol, these agents are not active against metallo-β-lactamase (MBL)-producing strains [4]. Furthermore, resistance to recently approved β-lactamase inhibitor combinations (BLICs), such as ceftazidime-avibactam and meropenem-vaborbactam, appears to be increasing among CRE in some US hospitals [5].

Aztreonam-avibactam is under clinical development to treat patients with Gram-negative infections, including those caused by MBL-producing CRE [6]. Aztreonam is not hydrolysed by MBLs, but it can be inactivated by serine β-lactamases, such as extended-spectrum β-lactamases, chromosomal derepressed AmpC, and *Klebsiella pneumoniae* carbapenemases (KPC). Since MBL-producing Enterobacterales isolates usually coproduce a serine β-lactamase, aztreonam was combined with avibactam. In the present study, we evaluated the frequency and antimicrobial susceptibility of Gram-negative bacteria causing pneumonia in United States (US) hospitals.

Materials and methods

Organism collection

Bacterial isolates were provided by clinical microbiology laboratories as part of the International Network for Optimal Resistance Monitoring (INFORM) Program. Each participating center was requested to provide 120 consecutive collected bacterial isolates each year from lower respiratory tract specimens. Only isolates determined to be significant by local criteria as the reported probable cause of pneumonia was included in the investigation. Medical records were not available to the participant laboratories to make clinical inferences about the infection (e.g., community-acquired or hospital-acquired); thus, this category includes patients hospitalized for any reason who were diagnosed with pneumonia while in the hospital. Isolates from invasive sampling (transtracheal aspiration, bronchoalveolar lavage, protected brush samples, etc.) or qualified sputum samples were accepted. The participating laboratory identified bacterial isolates to the species level and then the monitoring laboratory (Element Iowa City [JMI Laboratories]; North Liberty, Iowa, USA) confirmed bacterial identifications by standard algorithms and/or by matrix-assisted laser desorption ionization-time of flight mass spectrometry.

A total of 10,258 bacterial isolates were collected (1/patient) in 2020–2022 from 69 US medical centers. Among those, 3,911 Enterobacterales, 2,130 *Pseudomonas aeruginosa*, and 200 *Stenotrophomonas maltophilia* were evaluated in the present study. CRE was defined as any isolate displaying MIC values of > 2 mg/L for imipenem and/or meropenem. Imipenem was not applied for *Proteus mirabilis* or indole-positive Proteeae due to their intrinsically elevated MIC values.

Susceptibility methods

All isolates were susceptibility tested at JMI Laboratories by the broth microdilution method specified by Clinical and Laboratory Standard Institute (CLSI) standards [7]. Validated MIC panels (frozen-form) were manufactured at Element Iowa City (JMI Laboratories).

Aztreonam-avibactam was tested with avibactam at a fixed concentration of 4 mg/L.

A tentative aztreonam-avibactam pharmacokinetic/pharmacodynamic (PK/PD) susceptible breakpoint of ≤8 mg/L was applied for comparison [6]. Aztreonam-avibactam breakpoints recently (April 2024) published by the European Committee on Antimicrobial Susceptibility Testing (EUCAST; ≤4 mg/L for susceptible and >4 mg/L for resistant) were also applied. CLSI breakpoints were generally applied to the comparators, whereas US Food and Drug Administration (FDA) and/or EUCAST breakpoints were applied where CLSI breakpoints were not available [8–10].

Screening for β-lactamases

CRE isolates were tested for β-lactamase–encoding genes using Next-Generation Sequencing (NGS). Total genomic DNA was extracted using the fully automated Thermo Scientific™ KingFisher™ Flex Magnetic Particle Processor (Cleveland, Ohio, USA). DNA extracts were quantified using the Qubit™ High Sensitivity DS-DNA assay (Invitrogen, ThermoFisher Inc.) and normalized to 0.2 ng/μL. A total of 1 ng high-quality genomic DNA was used as input material for library construction using the Nextera XT™ DNA library preparation kit (Illumina, San Diego, California, USA). Libraries were normalized using the bead-based normalization procedure (Illumina) and sequenced on MiSeq. The generated FASTQ files were assembled using SPAdes Assembler and subjected to proprietary software (Element Iowa City [JMI Laboratories]) for screening of β-lactamase genes [11].

Results

The most common organisms isolated from patients hospitalized with pneumonia are shown in Fig. 1 and include *Staphylococcus aureus* (26.7%), *P. aeruginosa* (22.4%), *K. pneumoniae* (8.8%), *E. coli* (6.6%), *S. marcescens* (6.2%), *S. maltophilia* (4.9%), and *E. cloacae* species complex (4.8%). Gram-negative bacilli represented 71.1% and Enterobacterales 38.1% of bacteria isolated from patients with pneumonia. Notably, *S. maltophilia* ranked sixth and represented almost 5.0% of organisms (Fig. 1).

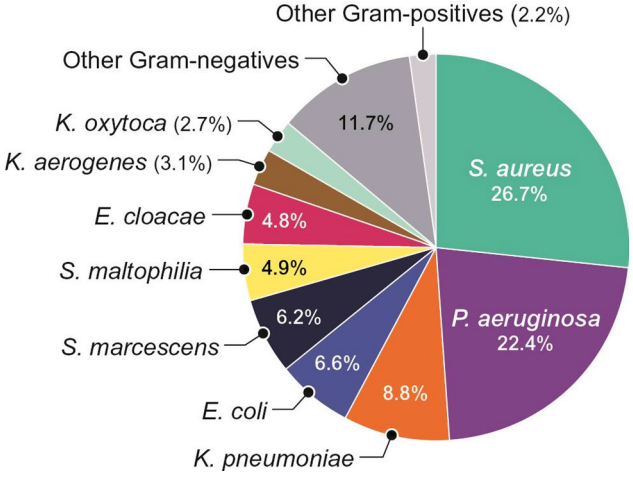

Fig. 1 Frequency of organisms isolated from patients with pneumonia in US medical centers (2020–2022)

Aztreonam-avibactam inhibited 100.0% of Enterobacterales at ≤8 mg/L and 99.9% at ≤4 mg/L ($MIC_{50/90}$, 0.06/0.25 mg/L) and showed potent activity against CRE ($MIC_{50/90}$, 0.25/1 mg/L; Table 1; Fig. 2). Ceftazidime-avibactam ($MIC_{50/90}$, 0.12/0.5 mg/L; 99.6% susceptible) and meropenem-vaborbactam ($MIC_{50/90}$, 0.03/0.06 mg/L; 99.7% susceptible) were also highly active against Enterobacterales, but these compounds showed somewhat limited activity against CRE with susceptibility rates of 89.4% for ceftazidime-avibactam ($MIC_{50/90}$, 1/>32 mg/L) and 88.5% for meropenem-vaborbactam ($MIC_{50/90}$, 0.06/8 mg/L). Imipenem-relebactam was slightly less active than ceftazidime-avibactam or meropenem-vaborbactam against Enterobacterales overall ($MIC_{50/90}$, 0.12/0.5 mg/L; 95.2% susceptible) and CRE ($MIC_{50/90}$, 0.12/8 mg/L; 79.8% susceptible) (Table 1; Fig. 2). Notably, aztreonam-avibactam retained activity against Enterobacterales non-susceptible to ceftazidime-avibactam and/or meropenem-vaborbactam ($n=19$; $MIC_{50/90}$, 0.25/4 mg/L [data not shown]). Cefiderocol was only tested against CRE isolates and inhibited 95.2% of isolates at the CLSI and US FDA susceptible breakpoint of ≤4 mg/L (Table 1).

Meropenem was the most active carbapenem against Enterobacterales with 97.3% susceptibility. The aminoglycosides gentamicin and amikacin were also very active against Enterobacterales with susceptibility rates of 91.0% and 95.1%, respectively; however, these compounds showed limited activity against CRE, with susceptibility rates of 60.6% for gentamicin and 73.1% for amikacin (Table 1).

The most active compounds against *P. aeruginosa* were imipenem-relebactam ($MIC_{50/90}$, 0.25/1 mg/L; 97.1% susceptible), ceftolozane-tazobactam ($MIC_{50/90}$, 0.5/2 mg/L; 96.9% susceptible), ceftazidime-avibactam ($MIC_{50/90}$, 2/8 mg/L; 96.1% susceptible), and tobramycin ($MIC_{50/90}$, 0.5/2 mg/L; 89.4% susceptible; Table 1; Fig. 2). Aztreonam-avibactam ($MIC_{50/90}$, 0.25/1 mg/L) inhibited 79.1% of isolates at the PK/PD breakpoint of ≤8 mg/L, which is comparable to the susceptibility rates for piperacillin-tazobactam (77.2%), meropenem (77.2%), and ceftazidime (81.2%; Table 1; Fig. 2).

Very few compounds exhibited adequate in vitro activity against *S. maltophilia*. Aztreonam-avibactam ($MIC_{50/90}$, 2/4 mg/L) inhibited 99.5% of isolates at ≤8 mg/L, trimethoprim-sulfamethoxazole ($MIC_{50/90}$, ≤0.12/0.5 mg/L) inhibited 97.5% of isolates at the CLSI susceptible breakpoint of ≤2 mg/L and minocycline

Table 1 Antimicrobial susceptibility of organisms from patients hospitalized with pneumonia in US medical centers (2020–2022)

Antimicrobial agent	% Susceptible per CLSI and/or FDA criteria (no. of isolates)				
	Enterobacterales (3,911)	**CRE (104)**	***K. pneumoniae* (961)**	***P. aeruginosa* (2,130)**	***S. maltophilia* (200)**
Aztreonam-avibactam	100.0 [a]	100.0 [a]	100.0 [a]	79.1 [a]	99.5 [a]
Aztreonam	78.7	5.8	78.7	68.8	
Ceftazidime-avibactam	99.6	89.4	99.6	96.1	
Meropenem-vaborbactam	99.7	88.5	99.5	[c]	
Imipenem-relebactam	95.2 [b]	79.8 [b]	98.7	97.1	
Ceftolozane-tazobactam	88.6	11.5	91.6	96.9	
Piperacillin-tazobactam	79.4	6.7	78.4	77.2	
Cefiderocol [d]		95.2			
Ceftriaxone	74.8	5.8	77.9		
Ceftazidime	79.5	11.5	78.1	81.2	22.0
Cefepime	85.5	14.4	78.9	83.3	
Ertapenem	95.2	2.7	95.3		
Imipenem	92.0 [b]	1.9 [b]	95.6	76.5 [b]	
Meropenem	97.3	6.7	95.2	77.2	
Ciprofloxacin	81.7	30.5	77.4	79.3	
Levofloxacin	84.3	35.6	81.6	70.6	83.5
Gentamicin	91.0	60.6	88.6		
Amikacin	95.1	73.1	96.1		
Tobramycin				89.4	
Tigecycline	96.2	95.2	97.0	--	91.5 [e]
TMP-SMX					97.5
Minocycline					93.5

[a] % inhibited at ≤ 8 mg/L

[b] All Enterobacterales species were included in the analysis, but CLSI excludes *Morganella*, *Proteus*, and *Providencia* species

[c] Meropenem-vaborbactam is not approved to treat *P. aeruginosa* infections in the US

[d] Cefiderocol was only tested against CRE isolates

[e] At ≤ 2 mg/L

Abbreviations CLSI, Clinical and Laboratory Standards Institute; FDA, Food and Drug Administration; CRE, carbapenem-resistant Enterobacterales; TMP-SMX, trimethoprim-sulfamethoxazole

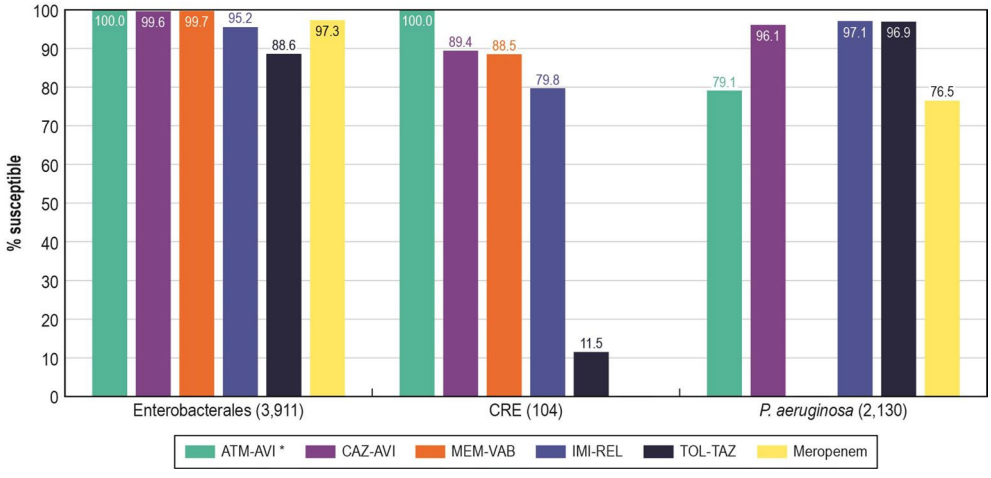

Fig. 2 Antimicrobial activity of β-lactamase inhibitor combinations and meropenem against Enterobacterales, CRE, and *P. aeruginosa* isolated from patients hospitalized with pneumonia in US medical centers (2020–2022). *Abbreviations* CRE, carbapenem-resistant Enterobacterales; ATM-AVI, aztreonam-avibactam; CAZ-AVI, ceftazidime-avibactam; MEM-VAB, meropenem-vaborbactam; IMI-REL, imipenem-relebactam; TOL-TAZ, ceftolozane-tazobactam. * Inhibited at ≤ 8 mg/L

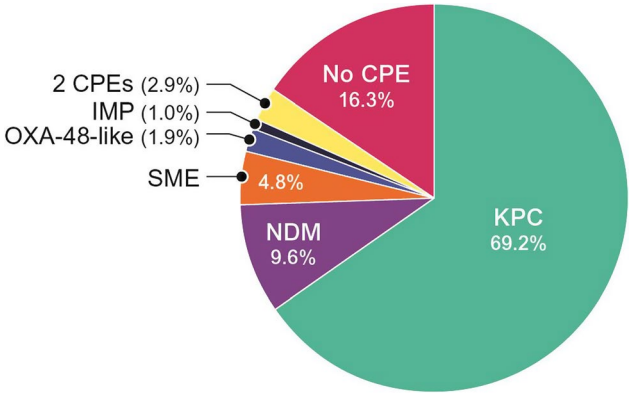

Fig. 3 Frequency of carbapenemases (CPE) among carbapenem-resistant Enterobacterales isolates from patients hospitalized with pneumonia in US medical centers. The "2 CPEs" group include 3 isolates, 1 isolate with an IMP-4 and a KPC-3, 1 isolate with a KPC-3 and an NDM-1, and 1 isolates with an NDM-5 and an OXA-181

($MIC_{50/90}$, 0.5/1 mg/L) inhibited 93.5% of isolates at the 2024 CLSI susceptible breakpoint of ≤ 1 mg/L (Table 1). It is important to note that CLSI is currently revising *S. maltophilia* breakpoints and these susceptibility rates may change. Moreover, tigecycline ($MIC_{50/90}$, 1/2 mg/L) inhibited 91.5% of isolates at ≤ 2 mg/L (CLSI breakpoint for Enterobacterales) but only 49.5% at ≤ 0.5 mg/L (EUCAST breakpoint for *E. coli*; data not shown) and levofloxacin was active against 83.5% of isolates per current CLSI criteria.

A carbapenemase gene was identified in 83.7% (87/104) of CRE isolates. The most common carbapenemase genes identified among CRE isolates were bla_{KPC} (69.2% of CRE isolates), bla_{NDM} (9.6%), and bla_{SME} (4.8%; Fig. 3). Overall, 10.6% of CREs produced an MBL and were resistant to ceftazidime-avibactam, meropenem-vaborbactam, and imipenem-relebactam (Fig. 3). Aztreonam-avibactam retained potent activity against carbapenemase-producing CRE independent of carbapenemase type ($MIC_{50/90}$, 0.25/0.5 mg/L; highest MIC, 2 mg/L). Ceftazidime-avibactam and meropenem-vaborbactam were highly active against KPC and SME producers but showed limited activity against MBL producers. Cefiderocol was active against 72.7% of MBL producers and 96.6% of carbapenemase producers overall (Fig. 4).

Discussion

Antimicrobial treatment of patients hospitalized with pneumonia continues to represent a major challenge for clinicians. Timely introduction of effective antimicrobial therapy is probably the most critical factor that drives the outcome [12]. However, the constant change in the epidemiology of antimicrobial resistance complicates the selection of appropriate empiric therapy. It has been well demonstrated that introduction of inappropriate antimicrobial treatment for healthcare associated pneumonia leads to increased hospital post-infection onset length of stay, cost, morbidity, and risk of mortality [13, 14]. Thus, it is vital for clinicians to have access to contemporary epidemiology of organisms causing pneumonia in the hospital setting.

We evaluated microbiology data from more than 10,000 patients hospitalized with pneumonia in 69 US medical centers. One of the strengths of surveillance program evaluated in this investigation is the fact that the organisms are consecutively collected (1/patient), which allows

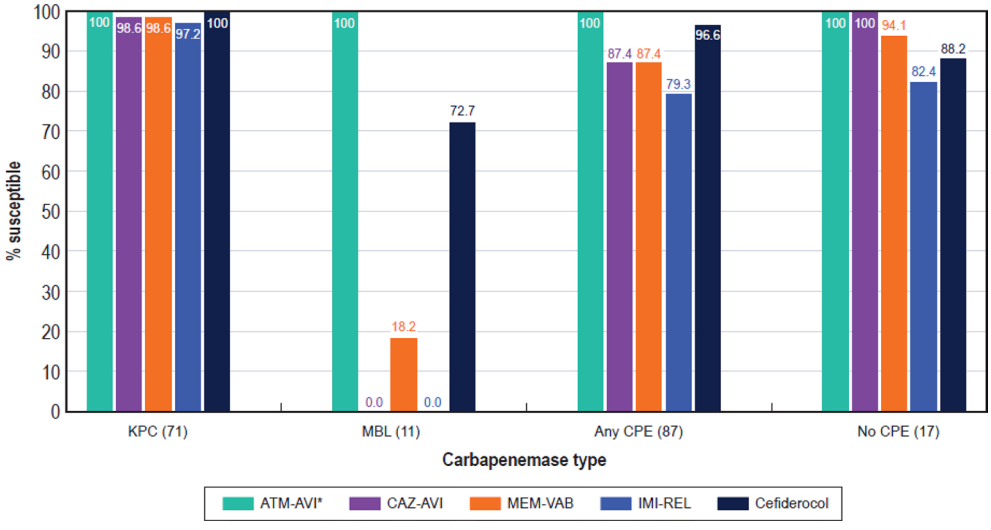

Fig. 4 Antimicrobial activity of β-lactamase inhibitor combinations and cefiderocol against carbapenemase-producing CRE stratified by main carbapenemase types. *Abbreviations* CRE, carbapenem-resistant Enterobacterales; ATM-AVI, aztreonam-avibactam; CAZ-AVI, ceftazidime-avibactam; MEM-VAB, meropenem-vaborbactam; IMI-REL, imipenem-relebactam; MBL, metallo-β-lactamase; Any CPE: Include isolates with KPC, NDM, SME, OXA-48-like, and/or IMP; No CPE, a carbapenemase gene was not identified. * Inhibited at ≤ 8 mg/L

the evaluation of the occurrence of organisms causing pneumonia in hospitalized patients [5]. The most common bacterial organisms were *S. aureus*, *P. aeruginosa*, and Enterobacterales species such as *K. pneumoniae*, *E. coli*, *S. marcescens*, and *E. cloacae*. Enterobacterales plus *S. maltophilia*, which were very susceptible to aztreonam-avibactam, represented 43% of organisms isolated from patients hospitalized with pneumonia.

The results on the organism occurrence corroborate other recent investigations. Zilberberg et al. [14] evaluated data from 17,819 patients from approximately 200 US hospitals in 2012–2019 and found that the most common organisms were *S. aureus*, *P. aeruginosa*, *K. pneumoniae*, and *E. coli*. Moreover, the most recent data published by the CDC National Healthcare Safety Network showed *S. aureus*, *P. aeruginosa*, *K. pneumoniae*, *E. cloacae*, and *E. coli* as the 5 most common organisms isolated from patients with ventilator-associated pneumonia (VAP) [15]. The most interesting finding on the organism frequency was the higher prevalence of *S. maltophilia* (4.9%) when compared to other studies [14, 15]. The frequency of *S. maltophilia* among organisms isolated from patients hospitalized with pneumonia has been consistently elevated (around 3 to 5%) in the SENTRY Program for many years and appears to be increasing recently [16, 17]. Growing rates of *S. maltophilia* infections have been reported by other investigators and appear to be related to advances in immunocompromised patient care and increasing use of invasive devices and broad-spectrum antimicrobial agents [18].

Although other investigators have evaluated antimicrobial susceptibility data from organisms recovered from patients with pneumonia, those evaluations usually rely on susceptibility results provided by the participant institutions and may have some limitations. Participant centers apply distinct susceptibility testing methods and/or breakpoint interpretative criteria, may test different agents within a drug class, or may perform selected testing (cascade testing). All these factors can introduce bias. Moreover, data on the activity of recently approved antimicrobial agents, such as meropenem-vaborbactam and imipenem-relebactam, are scarce [15, 19].

Our results on the antimicrobial susceptibility of Enterobacterales indicates that the prevalence of CRE appears to be stable in the last few years at around 1.0%, but the epidemiology of carbapenemases among CRE has been changing, mainly due to the decrease of KPC and increase of MBLs, which can hydrolyze newer β-lactamase inhibitor combination, such as ceftazidime-avibactam, meropenem-vaborbactam, and imipenem-relebactam [5]. Estabrook et al. [20] evaluated 5,728 Enterobacterales collected in 2018 and 2019 from North American hospitals and found that 1.9% of isolates were meropenem nonsusceptible, and 15.5% of those were MBL producers.

The results of this investigation on the antimicrobial susceptibility of *P. aeruginosa* are also comparable to data recently published by other investigators. Karlowski et al. [21] evaluated 2,361 *P. aeruginosa* collected in 2018–2020 from 24 US medical centers through the SMART Surveillance Program and found susceptibility rates of 96.4% for ceftolozane-tazobactam, 91.5% for imipenem-relebactam, 94.4% for ceftazidime-avibactam, and 77.0% for piperacillin-tazobactam, which are similar to those reported here (Table 1). *P. aeruginosa* susceptibility rates remained stable in the last few years. Results from the first 20 years of the SENTRY Program (1997–2016) showed susceptibility rates of 77.4% for piperacillin-tazobactam, 77.3% for meropenem, and 82.2% for ceftazidime [16]. More recent data on *P. aeruginosa* from patients hospitalized with pneumonia also showed susceptibility rates similar to those reported here. A total of 2,215 isolates collected in 2017–2018 from 70 US medical centers were evaluated and susceptibility rates were 75.0% for piperacillin-tazobactam, 72.6% for meropenem, and 79.8% for ceftazidime [22]. Susceptibility rates reported for ceftazidime-avibactam (96.0%) and ceftolozane-tazobactam (95.9%) were also similar to this investigation (96.1% and 96.9%, respectively; Table 1) [22]. Notably, the percentage of *P. aeruginosa* inhibited at aztreonam-avibactam PK/PD breakpoint of ≤8 mg/L (79.1%) was comparable to the susceptibility rates for commonly used anti-Pseudomonal drugs such as piperacillin-tazobactam (77.2%) and meropenem (77.2%). It is also important to note that susceptibility rates are usually lower among isolates from patients with pneumonia compared to other infection types [23].

Although *S. maltophilia* exhibited high susceptibility rates for some antimicrobial agents based on current CLSI criteria [8], such as trimethoprim-sulfamethoxazole and minocycline, these results should be interpreted with caution since those breakpoints were established in the 1980s, i.e., before the knowledge of pharmacokinetic/pharmacodynamic parameters that are currently used to establish breakpoints. CLSI is currently revising these breakpoints and these susceptibility rates may change markedly.

Our study has several strengths and some limitations. The absence of a definition for "clinically relevant organism" in the study protocol is a limitation of the study since these criteria may vary among participating medical centers. The lack of differentiation between community-acquired pneumonia that needs hospitalization and healthcare-associated pneumonia and between VAP and non-VAP is certainly another limitation. Although they should be considered when interpreting the results and

conclusions, it is unlikely that these limitations have introduced important bias to the study.

In summary, aztreonam-avibactam displayed potent in vitro activity against a large collection of contemporary Gram-negative organisms isolated from patients hospitalized with pneumonia in US hospitals, including CRE isolates resistant to ceftazidime-avibactam, meropenem-vaborbactam, and/or imipenem-relebactam. Aztreonam-avibactam was active against 100.0% of Enterobacterales, showed anti-Pseudomonal activity similar to piperacillin-tazobactam and meropenem, and exhibited potent in vitro activity against *S. maltophilia.* The results of this investigation emphasize the importance of continued monitoring of resistance phenotypes and resistance mechanisms via large, well-designed surveillance programs. Due to the clinical importance of these rapid fluctuations in the epidemiology of β-lactam resistance mechanisms, the results of surveillance programs are valuable to plan empiric antimicrobial therapy guidelines and infection control measures.

Abbreviations

CLSI	Clinical and Laboratory Standards Institute
CRE	Carbapenem-resistant Enterobacterales
EUCAST	European Committee on Antimicrobial Susceptibility Testing
FDA	Food and Drug Administration
KPC	Klebsiella pneumoniae carbapenemase
MBL	Metallo-β-lactamase
NGS	Next-Generation Sequencing
US	United States

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12890-025-03500-8.

Supplementary Material 1

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Author contributions
HSS: Conceptualization, Formal Analysis, Data Curation, Writing– Original Draft, Visualization, Funding Acquisition. REM: Conceptualization, Validation, Resources, Writing– Review & Edit, Supervision, Funding Acquisition. SJR: Methodology, Formal Analysis, Investigation, Data Curation, Software, Validation, Supervision. TBD: Methodology, Formal Analysis, Investigation, Data Curation, Review & Edit, Software, Validation, Supervision. MC: Conceptualization, Validation, Resources, Writing– Review & Edit, Supervision, Funding Acquisition. All authors reviewed and approved the manuscript.

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Data availability
The datasets generated and/or analysed during the current study are available in the Sequence Read Archive (SRA) repository [https://www.ncbi.nlm.nih.gov/] under BioProject ID PRJNA1201045. Also, DNA sequencing results are provided in supplemental material.

Declarations

Ethics approval and consent to participate
This study does not include factors necessitating patient consent. The study used bacterial isolates stored by clinical laboratories and the participant laboratories did not provide patient identification.

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

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