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Antimicrobial Activity of Aztreonam-Avibactam against Enterobacterales Isolated from Patients with Ventilator-Associated Pneumonia (VAP)

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CONCLUSIONS

ATM-AVI exhibited potent activity against Enterobacterales isolated from patients with VAP, non-VAP, and BSI, and retained potent activity against CRE, MDR, and XDR isolates.

The activities of CAZ-AVI, MEM-VAB, and IMI-REL against CRE and XDR isolates were compromised by the increased frequency of MBL producers.

Resistance to ceftolozane-tazobactam and old β-lactam agents, such as ceftazidime and piperacillin-tazobactam, was higher among isolates from VAP compared to non-VAP and BSI.

INTRODUCTION

- Aztreonam-avibactam (ATM-AVI) was recently approved for clinical use by the United States (US) Food and Drug Administration (FDA) and has demonstrated potent activity against carbapenem-resistant Enterobacterales (CRE), including MBL producers.
- We evaluated the activities of ATM-AVI and other β-lactamase inhibitor combinations against Enterobacterales causing ventilator-associated pneumonia (VAP) in US medical centers.

METHODS

- Enterobacterales isolates were consecutively collected from 92 US medical centers in 2018–2025.
- The organism collection included 2,106 isolates from VAP, 3,204 isolates from patients with non-ventilator-associated pneumonia (non-VAP), and 16,404 isolates from bloodstream infection (BSI).
- Isolates were susceptibility tested by Clinical and Laboratory Standards Institute (CLSI) M07 broth microdilution methods at a monitoring laboratory.
- Cefiderocol was tested in iron-depleted media against CRE only.
- Susceptibility results from VAP isolates were compared to isolates from non-VAP and BSI.
- CRE was defined as resistant to meropenem and/or imipenem, multidrug-resistant (MDR) as nonsusceptible to ≥1 agent in ≥3 antimicrobial classes, and extensively drug-resistant (XDR) as susceptible to ≤2 classes.
- CRE isolates from VAP (*n*=43) were screened for carbapenemases (CBases) by whole genome sequencing.

Table 1. Antimicrobial susceptibility of Enterobacterales

Antimicrobial agent	% Susceptible (no. of isolates tested)[a]		
	VAP (2,106)	Non-VAP [b] (3,204)	BSI (16,404)
Aztreonam-avibactam	>99.9	99.9	99.9
Ceftazidime-avibactam	99.4	99.6	99.6
Meropenem-vaborbactam	99.5	99.7	99.6
Imipenem-relebactam	95.4	95.2	94.9
Ceftolozane-tazobactam	89.4	91.8	95.4
Piperacillin-tazobactam	79.7	83.0	89.5
Ceftazidime	80.7	82.6	84.1
Cefepime	85.8	87.0	86.0
Meropenem	98.1	98.2	99.0
Imipenem	93.2	92.8	93.4
Levofloxacin	86.6	84.0	78.8
Amikacin	96.2	95.6	94.8
Gentamicin	92.1	91.7	89.9

Abbreviations: VAP, ventilator-associated pneumonia; BSI, bloodstream infections.
[a] Susceptibility per CLSI and/or US FDA criteria.
[b] Pneumonia excluding VAP.

Table 2. Antimicrobial susceptibility of isolates from VAP

Antimicrobial agent	% Susceptible (no. of isolates tested)[a]		
	CRE (43)	MDR (539)	XDR (14)
Aztreonam-avibactam	100.0	100.0	100.0
Ceftazidime-avibactam	74.4	97.6	50.0
Meropenem-vaborbactam	76.7	98.0	38.3
Imipenem-relebactam	76.7	95.4	33.3
Cefiderocol	97.7	NT[b]	90.0
Levofloxacin	51.2	60.5	14.3
Amikacin	65.1	90.4	21.4
Gentamicin	60.5	73.5	14.3

Abbreviations: VAP, ventilator-associated pneumonia; CRE, carbapenem-resistant Enterobacterales; MDR, multidrug-resistant; XDR, extensively drug-resistant.
[a] Susceptibility per CLSI and/or US FDA criteria.
[b] NT, not tested.

RESULTS

- The most common Enterobacterales species from VAP were *K. pneumoniae* (23.0%), *S. marcescens* (17.0%), *E. coli* (16.4%), and *E. cloacae* (14.2%; Figure 1).
- ATM-AVI was highly active against VAP isolates ($MIC_{50/90}$, 0.06/0.25 mg/L; >99.9% susceptible [S]) and retained activity against 100.0% of CRE, MDR, and XDR isolates from VAP (Tables 1 and 2).
- Ceftazidime-avibactam (CAZ-AVI) and meropenem-vaborbactam (MEM-VAB) were very active against Enterobacterales (99.4–99.5% S) and MDR isolates (97.6–98.0% S) from VAP but exhibited limited activity against CRE (74.4–76.7% S) and XDR isolates (38.3–50.0%; Table 2).
- Susceptibility to ceftolozane-tazobactam, piperacillin-tazobactam, and ceftazidime was lower among isolates from VAP compared to non-VAP and BSI (Table 1).
- CRE rates were higher among isolates from VAP (2.0%) compared to non-VAP (1.7%) and BSI (0.9%; Figure 2).
- MDR rates were higher among isolates from VAP (25.6%) compared to non-VAP (22.9%) and BSI (22.6%; Figure 2).
- A CBase was identified in 69.8% of CREs from VAP and the most common CBases were KPC (48.8% of CREs), NDM (14.0%), and VIM (7.0%).

Figure 1. Frequency of Enterobacterales species isolated from patients with VAP

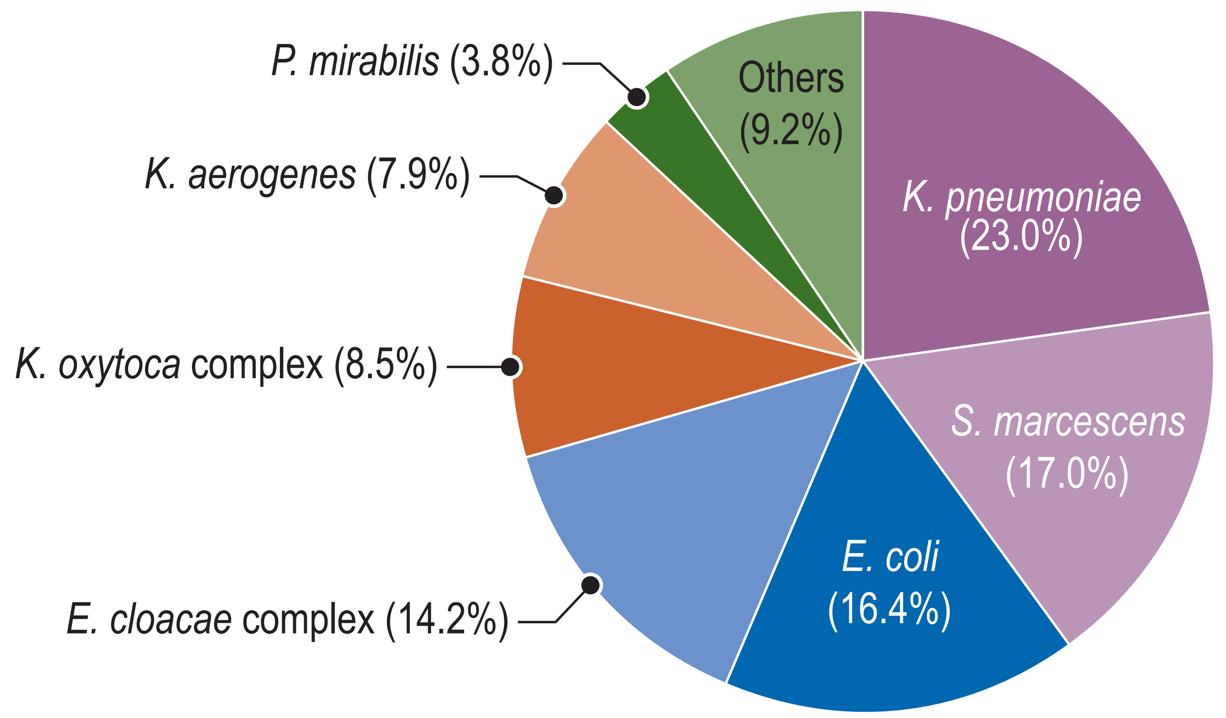
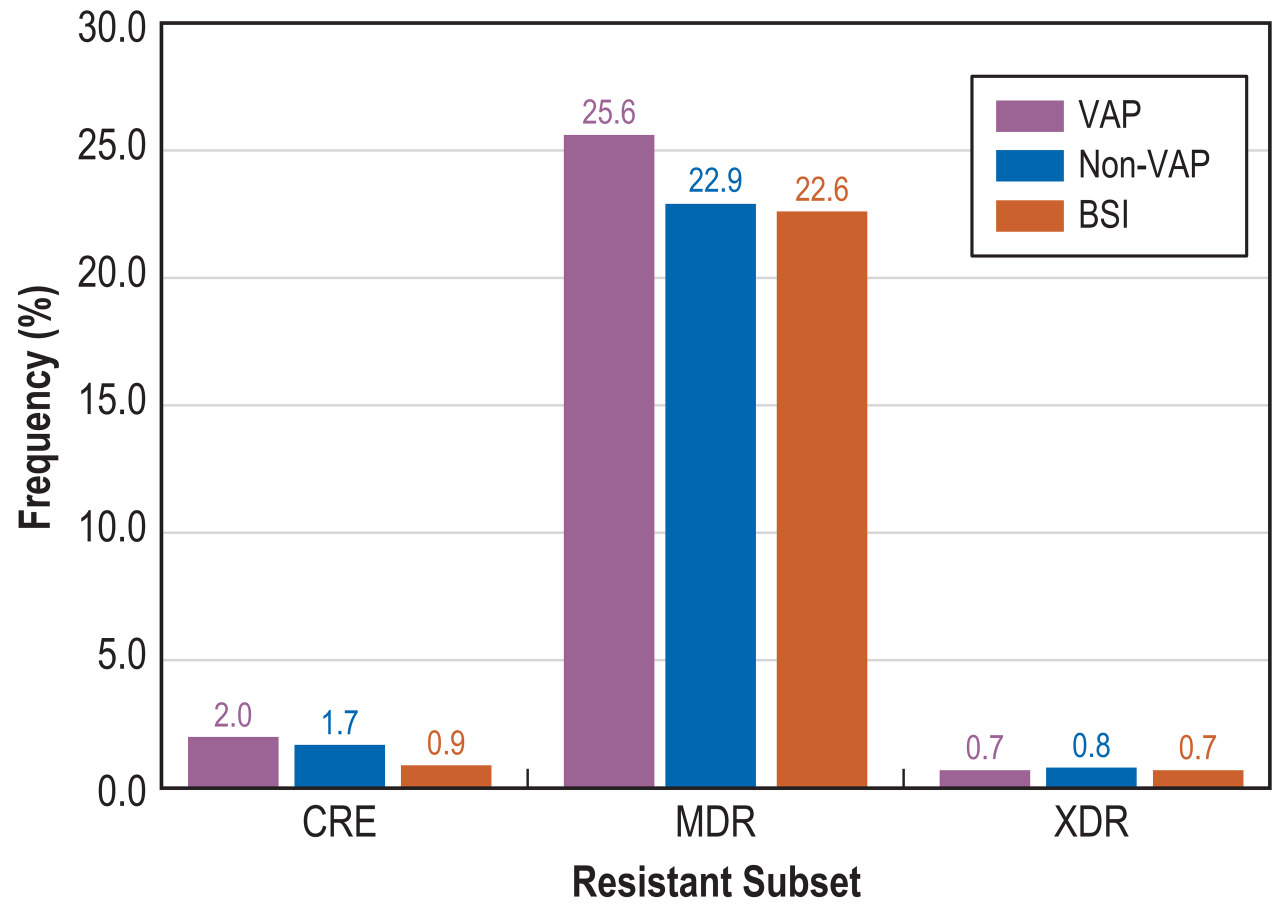

P. mirabilis (3.8%)
Others (9.2%)
K. aerogenes (7.9%)
K. pneumoniae (23.0%)
K. oxytoca complex (8.5%)
S. marcescens (17.0%)
E. coli (16.4%)
E. cloacae complex (14.2%)

Figure 2. Frequency of resistant subsets


30.0
25.0
20.0
15.0
10.0
5.0
0.0
Frequency (%)
VAP
Non-VAP
BSI
2.0
1.7
0.9
25.6
22.9
22.6
0.7
0.8
0.7
CRE
MDR
XDR
Resistant Subset

Abbreviations: VAP, ventilator-associated pneumonia; BSI, bloodstream infection; CRE, carbapenem-resistant Enterobacterales; MDR, multidrug-resistant; XDR, extensively drug-resistant.

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