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Antimicrobial Susceptibility and Molecular Characterization of Carbapenem-Resistant *Klebsiella pneumoniae* from United States Medical Centers (2020–2025)

Helio S. Sader[1], Mariana Castanheira[1], Todd Riccobene[2], John H. Kimbrough[1], Krisztina M. Papp-Wallace[1]

[1] *Element Iowa City (JMI Laboratories), North Liberty, Iowa, USA;* [2] *AbbVie Inc., Chicago, Illinois, USA*

CONCLUSIONS

- ATM-AVI demonstrated potent and consistent activity against CR-KPN over time.
- The proportion of CR-KPN isolates that produce MBL increased drastically during the study period.
- The activities of CAZ-AVI, MEM-VAB, and IMI-REL decreased markedly during the study period due to the increasing frequency of MBL producers.
- These results emphasize the importance of comprehensive surveillance programs to monitor the epidemiology of resistance mechanisms to antimicrobial agents.

INTRODUCTION

- The frequency of metallo-β-lactamase (MBL)-producing Enterobacterales has been increasing in the United States (US) and effective antibiotics to treat infections caused by these organisms are limited.
- Aztreonam-avibactam (ATM-AVI) was recently (February 2025) approved by the US Food and Drug Administration (FDA) and has shown potent activity against MBL-producing Enterobacterales.
- We evaluated the antimicrobial susceptibility and carbapenemase (CBase) production of carbapenem-resistant *K. pneumoniae* (CR-KPN) isolates from US hospitals.

METHODS

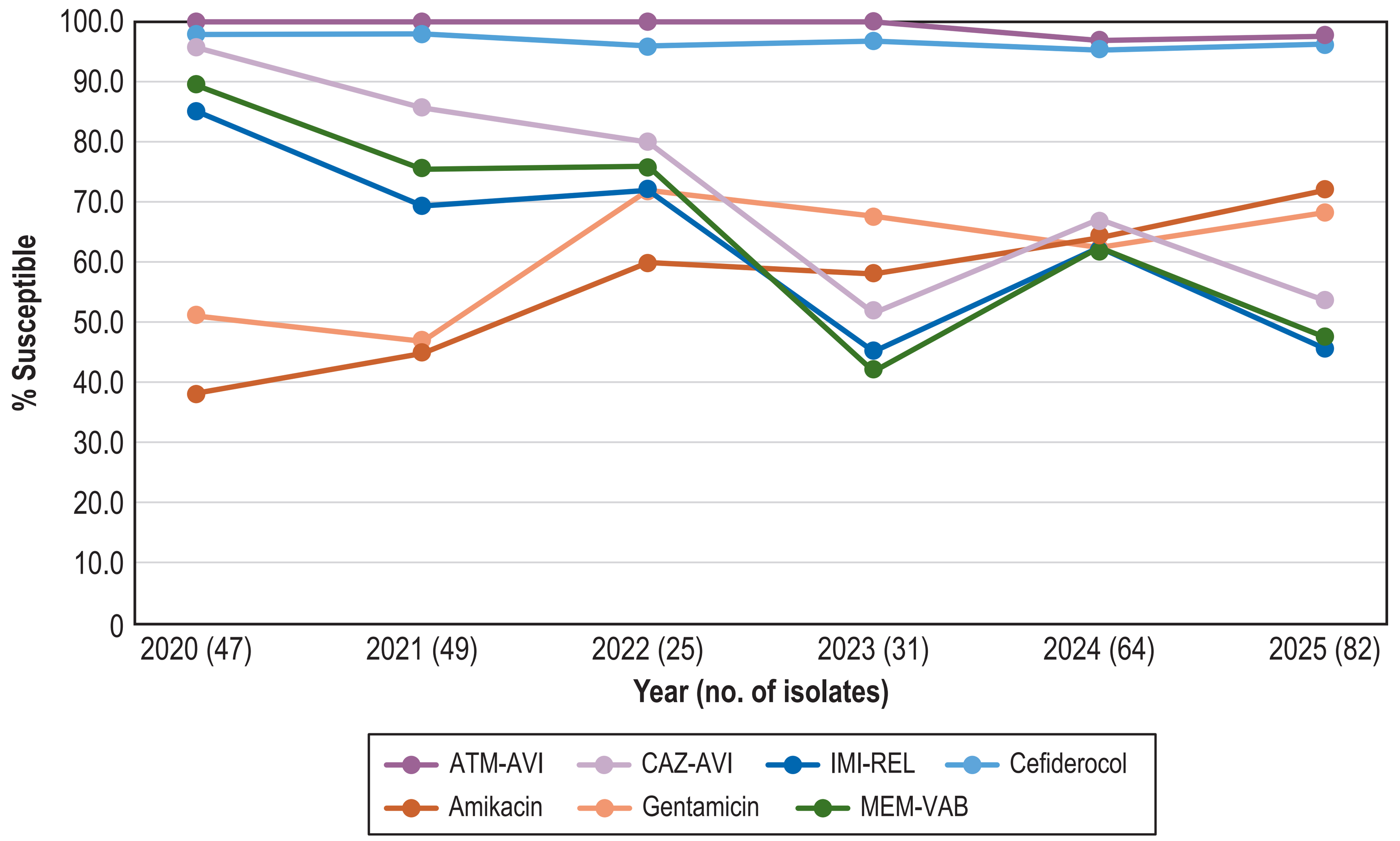
- A total of 10,254 *K. pneumoniae* isolates were consecutively collected from 86 US medical centers in 2020–2025.
- Among those, 298 (2.9%) were CR-KPN, defined as resistant (MIC ≥4 mg/L) to meropenem and/or imipenem.
- Only bacterial isolates determined to be significant by local criteria as the reported probable cause of infection were included in the study.
- Isolates were susceptibility tested by Clinical and Laboratory Standards Institute (CLSI) M07 broth microdilution methods at a monitoring laboratory.
- β-lactamase screening and characterization of resistance mechanisms were performed on all CR-KPN isolates by whole genome sequencing.
- Susceptibility results were stratified by year and CBase type.

Table 1. Antimicrobial susceptibility of CR-KPN from US hospitals (2020–2025)

Antimicrobial agent	mg/L		Susceptibility[a]		
	MIC_{50}	MIC_{90}	%S	%I	%R
Aztreonam-avibactam	0.12	0.5	98.7	0.7	0.7
Ceftazidime-avibactam	1	>32	70.5		29.5
Meropenem-vaborbactam	0.5	>32	63.8	3.7	32.6
Imipenem-relebactam	0.25	>8	61.6 [b]	3.0	35.4
Cefiderocol	1	4	96.6	1.0	2.3
Aztreonam	>16	>16	7.4	1.7	90.9
Ciprofloxacin	>4	>4	17.1	3.7	79.1
Levofloxacin	16	>32	16.8	11.1	72.1
Gentamicin	1	>16	61.1	4.4	34.6
Amikacin	4	>32	58.1	9.1	32.9
Tigecycline	0.5	2	96.3	3.7	0.0
Colistin	0.25	1		92.2	7.8

[a] Based on breakpoint criteria as published by CLSI and/or US FDA
[b] All Enterobacterales species were included in the analysis, but CLSI and EUCAST exclude organisms from the family Morganellaceae.
Abbreviations: CR-KPN, carbapenem-resistant *K. pneumoniae*; S, susceptible; I, intermediate; R, resistant.

Figure 1. Antimicrobial susceptibility of CR-KPN from US hospitals stratified by year

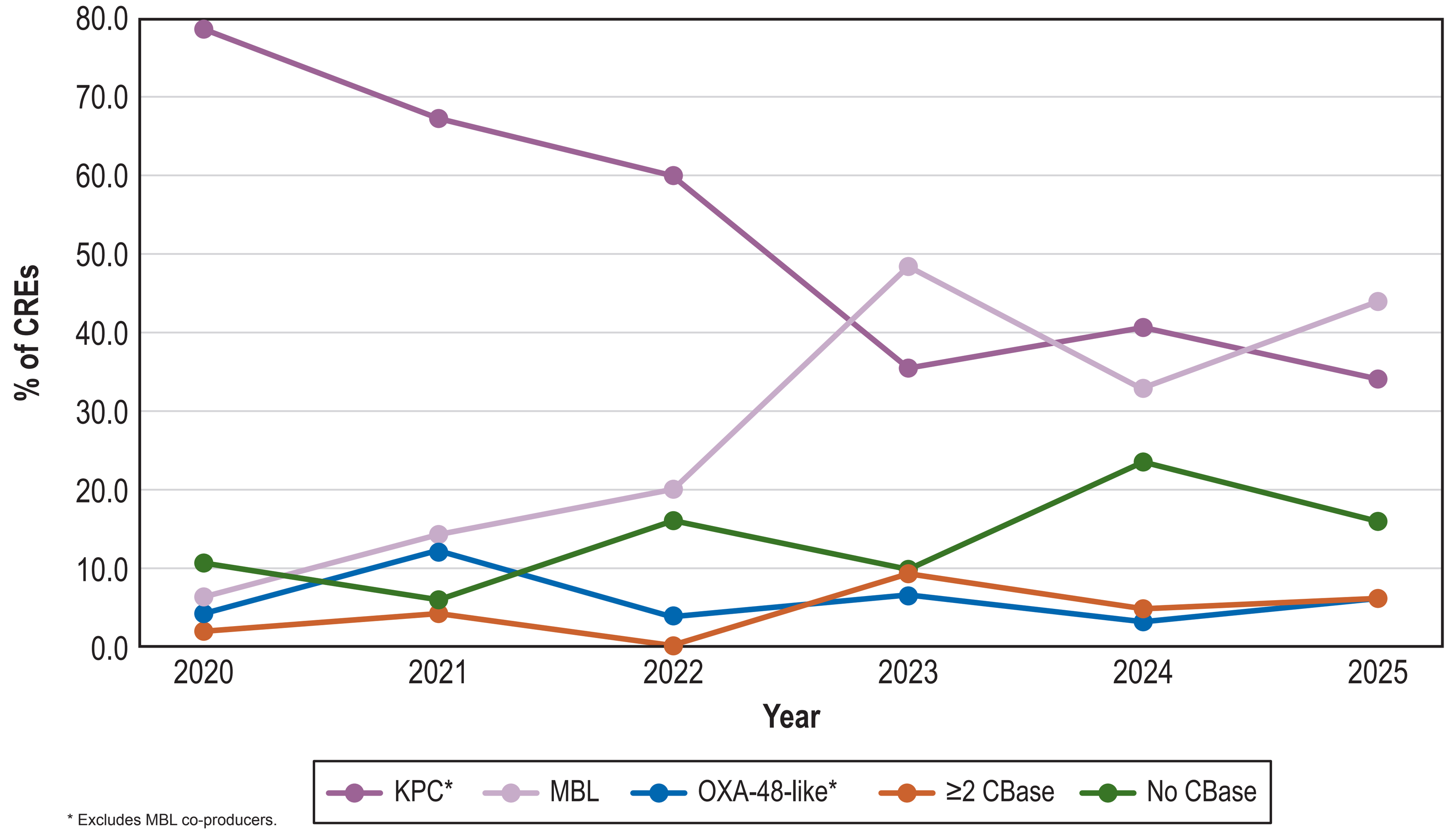


% Susceptible
Year (no. of isolates)
2020 (47)
2021 (49)
2022 (25)
2023 (31)
2024 (64)
2025 (82)
ATM-AVI
CAZ-AVI
IMI-REL
Cefiderocol
Amikacin
Gentamicin
MEM-VAB

RESULTS

- The most active agents against CR-KPN were ATM-AVI ($MIC_{50/90}$, 0.12/0.25; 98.7% susceptible [S]), cefiderocol ($MIC_{50/90}$,1/4 mg/L; 96.6%S), and ceftazidime-avibactam (CAZ-AVI; $MIC_{50/90}$, 1/>32 mg/L; 70.5%S; Table 1).
- ATM-AVI and cefiderocol displayed consistent activity over the years, whereas the activities of CAZ-AVI, meropenem-vaborbactam (MEM-VAB), and imipenem-relebactam (IMI-REL) decreased markedly during the investigation (Figure 1).
- Notably, the activities of amikacin (Figure 1) and gentamicin improved substantially during the same period.
- The proportion of KPC producers among CR-KPN decreased from 78.7% in 2020 to 34.1% in 2025, while the proportion of MBL producers increased from 6.4% to 43.9% in the same period (Figure 2).
- All β-lactamase inhibitor combinations (BLICs) and cefiderocol exhibited potent activity against KPC producers, but only ATM-AVI (100.0%S) and cefiderocol (93.1%S) retained good activity against MBL producers (Figure 3).
- The most common sequence types among CR-KPN were 258 (14.7%), 147 (13.1%), and 45 (7.2%).

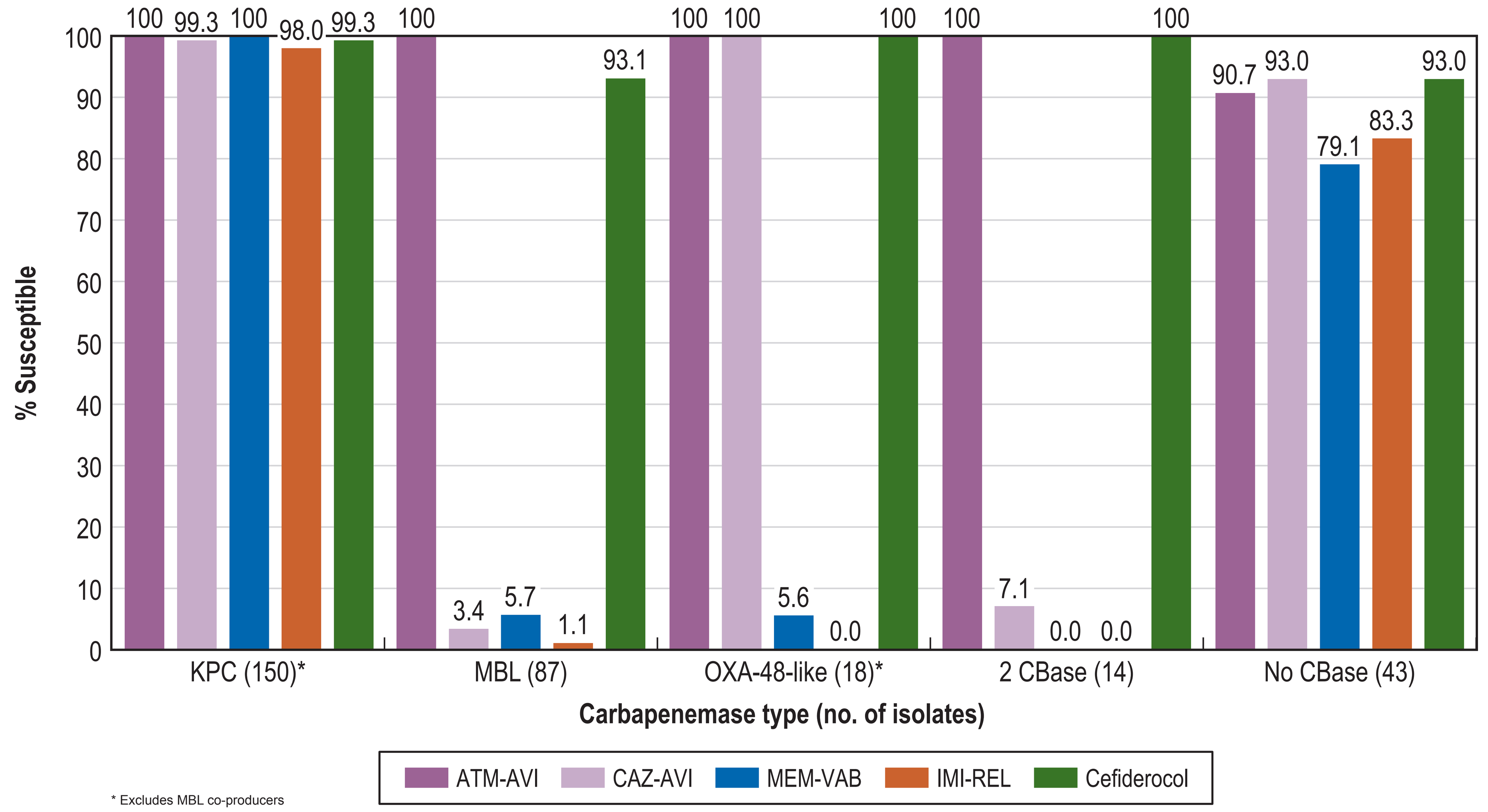
Figure 2. Annual frequency of carbapenemase (CBase) types among CR-KPN isolates



% of CREs
Year
KPC*
MBL
OXA-48-like*
≥2 CBase
No CBase

* Excludes MBL co-producers.

Figure 3. Activity of ATM-AVI and comparators against CR-KPN isolates stratified by carbapenemase type



% Susceptible
100 99.3 100 98.0 99.3
100 3.4 5.7 1.1 93.1
100 100 5.6 0.0 100
100 7.1 0.0 0.0 100
90.7 93.0 79.1 83.3 93.0
KPC (150)*
MBL (87)
OXA-48-like (18)*
2 CBase (14)
No CBase (43)
Carbapenemase type (no. of isolates)
ATM-AVI
CAZ-AVI
MEM-VAB
IMI-REL
Cefiderocol

* Excludes MBL co-producers

Contact Information

Helio S. Sader, MD, PhD, FIDSA
Element Iowa City (JMI Laboratories)
345 Beaver Kreek Centre, Suite A
North Liberty, IA 52317
Phone: (319) 665-3370
Email: helio.sader@element.com

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