Frequency and Antimicrobial Susceptibility of Gram-negative Bacteria Isolated from Patients with Bloodstream Infections in United States (US) Medical Centers (2020–2021)

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CONCLUSIONS



CAZ-AVI and MEM-VAB were the most active agents against



C-T, IMI-REL, and tobramycin were the most active agents against P. aeruginosa.



The newer β-lactamase inhibitor combinations represent valuable treatment options for infections caused by MDR Enterobacterales and P. aeruginosa.



CAZ-AVI exhibited a more balanced spectrum against Enterobacterales and P. aeruginosa when compared to other β-lactamase inhibitor combinations.





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This study was supported by AbbVie. HS Sader, RE Mendes, CG Carvalhaes, MD Huband, D Shortridge, and M Castanheira are employees of JMI Laboratories, which was paid consultant to AbbVie in connection with the development of this

Acknowledgments The authors thank all the participant centers for their work in providing isolates.

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INTRODUCTION

- Antimicrobial resistance among Gram-negative bacteria (GNB) is a major problem in US hospitals.
- The development of various β-lactamase inhibitor combinations markedly increased the armamentarium to treat infections caused by GNB in recent years.
- · We evaluated the frequency and antimicrobial susceptibility of GNB causing bloodstream infection (BSI) in US medical centers.

METHODS

- A total of 5,796 isolates were consecutively collected from patients with BSI in 31 US medical centers.
- Among those isolates, 2,893 (49.9%) were GNB and selected for evaluation, including 2,434 Enterobacterales and 296 Pseudomonas aeruginosa isolates.
- Only isolates determined to be significant by local criteria as the reported probable cause of infection were included in the program.
- Carbapenem-resistant Enterobacterales (CRE) isolates were defined as displaying imipenem and/or meropenem MIC ≥4 mg/L; imipenem was not applied to *Proteus mirabilis* and indole-positive Proteeae due to their intrinsically elevated MIC values.
- Multidrug resistance (MDR) was defined as nonsusceptible (CLSI breakpoints) to at least 3 antimicrobial classes (Magiorakos et al., 2012).
- Isolates were susceptibility tested by the CLSI broth microdilution test method.

Figure 1. Frequency of Gram-negative bacteria

isolated from patients with bloodstream infections in

US medical centers (2020–2021)

K. oxytoca (3.5%)

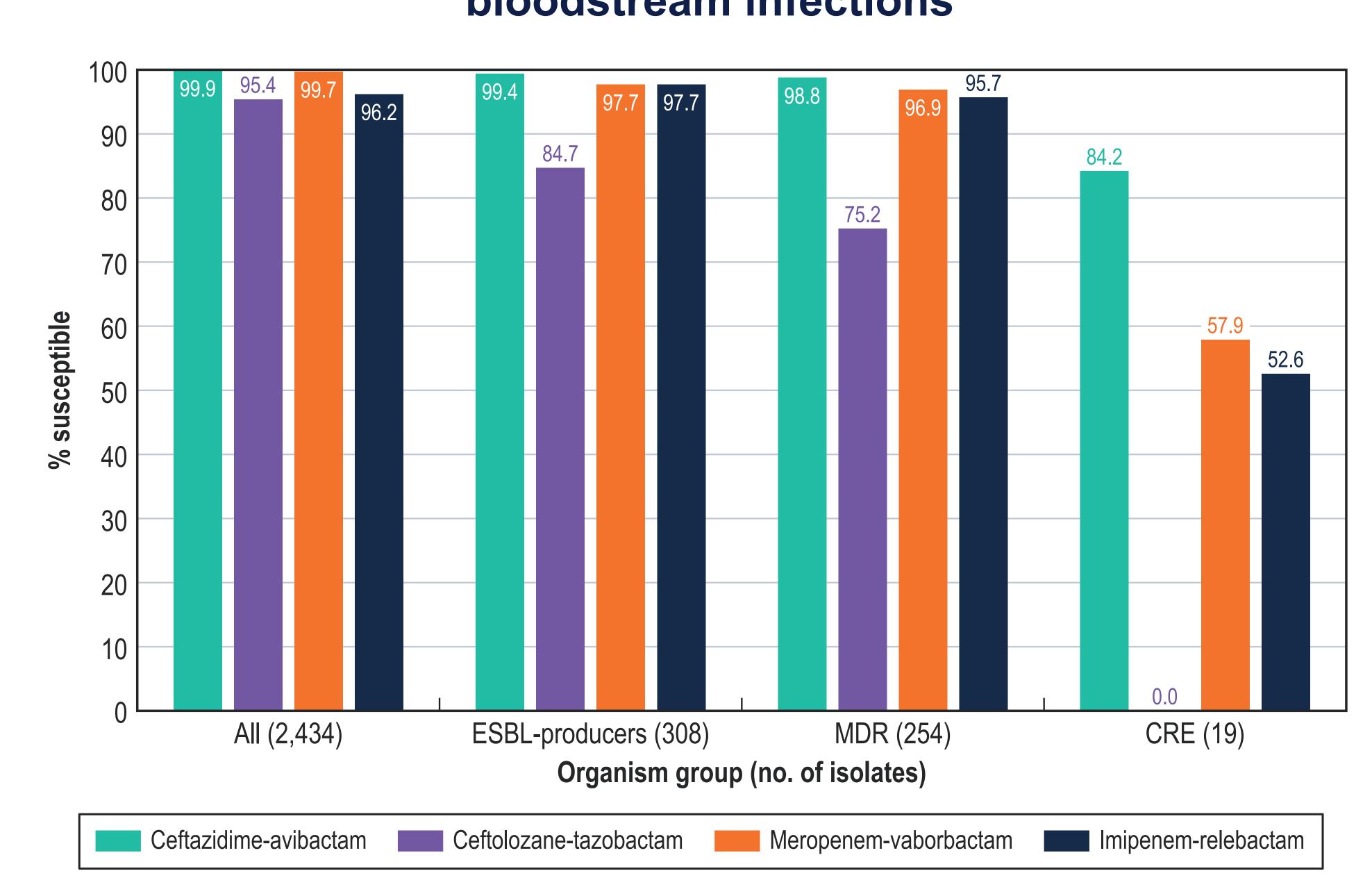
P. aeruginosa -

P. mirabilis (4.0%) —

E. cloacae complex -

• Enterobacterales with elevated MIC values for selected β-lactams (ceftazidime, ceftriaxone, aztreonam, and/or cefepime) were screened for β-lactamase genes by whole genome sequencing.

Figure 2. Ceftazidime-avibactam, ceftolozane-tazobactam, meropenem-vaborbactam, and imipenem-relebactam activities against Enterobacterales from patients with bloodstream infections



viations: ESBL, extended-spectrum β-lactamase; MDR, multidrug-resistant; CRE, carbapenem-resistant Enterobacterales.

Figure 3. Ceftazidime-avibactam, ceftolozane-tazobactam, meropenem-vaborbactam, and imipenem-relebactam activities against P. aeruginosa isolates from patients with bloodstream

• The most common GNBs isolated from BSI were E. coli (41.9%), K. pneumoniae (16.1%), P. aeruginosa (10.2%), and Enterobacter

- Imipenem-relebactam (IMI-REL; 96.2% S) exhibited potent activity against Enterobacterales, except *P. mirabilis* and indole-positive

- Ceftolozane-tazobactam (C-T; 95.4% S) showed limited activity against *E. cloacae* complex, ESBL-phenotype (84.7% S), and MDR

• Ceftriaxone susceptibility rates were 80.1%, 82.9%, and 74.0% for *E. coli*, *K. pneumoniae*, and *E. cloacae* complex, respectively (data

• CAZ-AVI (97.6% S), C-T (97.6% S), IMI-REL (99.0% S), and tobramycin (98.3% S) were the most active agents against P. aeruginosa

• Ceftazidime-avibactam (CAZ-AVI; 99.9% susceptible [S]) and meropenem-vaborbactam (MEM-VAB; 99.7% S) showed almost

• CAZ-AVI, MEM-VAB, and IMI-REL were active against 84.2%, 57.9%, and 52.6% of CRE isolates, respectively (Figure 2).

and retained good activity against isolates nonsusceptible to piperacillin-tazobactam or meropenem and against MDR isolates

• P. aeruginosa susceptibility to piperacillin-tazobactam, meropenem, and ceftazidime were 86.1%, 88.5%, and 88.5%, respectively

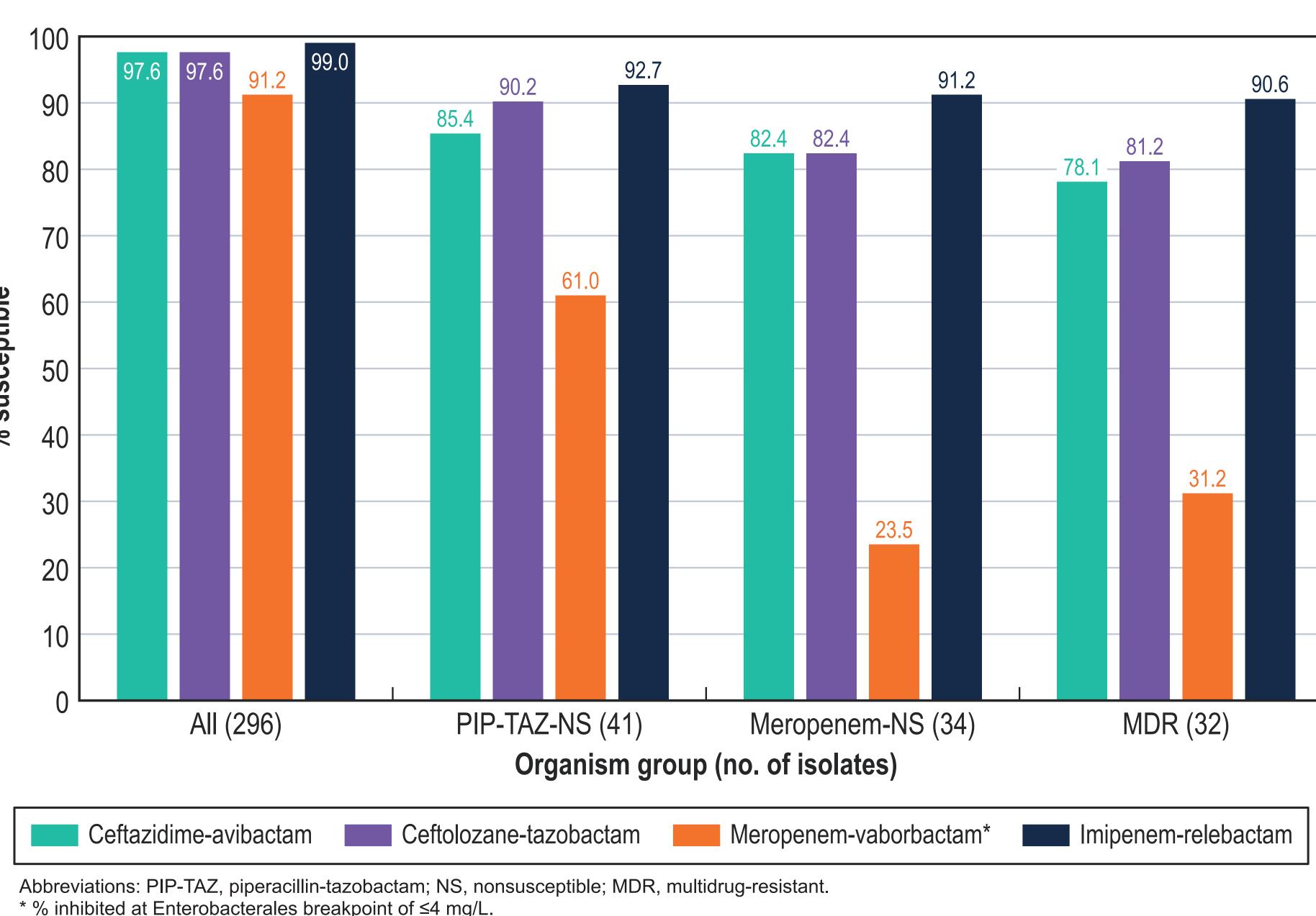


Table 1. Antimicrobial susceptibility of Enterobacterales (*n*=2,434) isolated from patients with BSI in US medical centers (2020–2021)

K. pneumoniae

ntimicrobial agent	MIC in mg/L		CLSIa			
	MIC ₅₀	MIC ₉₀	%S	%I	%R	
eftazidime-avibactam	0.12	0.25	99.9		0.1	
eftolozane-tazobactam	0.25	1	95.4	1.2	3.4	
eropenem-vaborbactam	0.03	0.06	99.7	0.0	0.3	
nipenem-relebactam	0.12	0.5	96.2 ^b	3.0	0.8	
iperacillin-tazobactam	2	16	88.0	4.3	7.7	
mpicillin-sulbactam	16	64	49.4	15.2	35.4	
efuroxime	4	>64	69.9 ^c	4.1	26.0	
eftriaxone	≤0.06	>8	80.7	0.7	18.5	
eftazidime	0.25	32	84.1	2.1	13.8	
efepime	0.06	32	86.0	2.0	12.0	
rtapenem	0.015	0.06	97.7	0.7	1.6	
nipenem	≤0.12	1	95.1	3.4	1.4	
eropenem	0.03	0.06	99.1	0.2	0.7	
iprofloxacin	0.03	>4	74.9	3.1	22.0	
evofloxacin	0.06	16	77.1	3.2	19.7	
entamicin	0.5	8	89.4	0.7	9.9	
mikacin	2	4	99.5	0.4	0.1	

b Not approved to treat P. aeruginosa infections in the United States; Enterobacterales breakpoints of ≤4/8/≥16 mg/L (S/I/R) were applied for comparison.

Table 2. Antimicrobial susceptibility of 296 P. aeruginosa isolated from natients with BSI in US medical centers (2020–2021)

RESULTS

not shown).

(Table 2 and Figure 3).

(Table 2 and Figure 3).

cloacae complex (6.8%; Figure 1).

Proteeae isolates (Table 1 and Figure 2).

isolates (75.2%; Table 1 and Figure 2).

complete activity against Enterobacterales (Table 1 and Figure 2).

• Frequency of β-lactamases found in Enterobacterales is shown in Table 3.

Antimicrobial agent	MIC in mg/L		CLSIa		
	MIC ₅₀	MIC ₉₀	%S	%I	%R
Ceftazidime-avibactam	2	4	97.6		2.4
Ceftolozane-tazobactam	0.5	2	97.6	1.4	1.0
Meropenem-vaborbactam	0.25	4	[91.2] ^b	[4.4] ^b	[4.4] ^b
Imipenem-relebactam	0.25	1	99.0	0.3	0.7
Piperacillin-tazobactam	4	32	86.1	7.5	6.4
Ceftazidime	2	16	88.5	1.7	9.8
Cefepime	2	16	89.5	5.4	5.1
Imipenem	1	8	87.5	2.4	10.2
Meropenem	0.5	4	88.5	2.7	8.8
Ciprofloxacin	0.12	2	84.4	4.7	10.8
Levofloxacin	0.5	8	79.7	5.8	14.6
Tobramycin	0.5	1	98.3	0.0	1.7

CTX-M-27 CTX-M-55 CTX-M-14 Other CTX-M enzymes

CTX-M type

2 carbapenemases

2 CTX-M enzymes OXA type CTX-M + OXA-1/30 SHV type 45.1% Carbapenemase KPC type 58.8% OXA-48 type 35.3% NDM type 11.8%

Table 3. Frequency of extended-spectrum

β-lactamases (ESBLs) and carbapenemases

produced by Enterobacterales from BSI

93.8%

12.0%

5.9%

^bAll Enterobacterales species were included in the analysis, but CLSI excludes *Morganella*, *Proteus*, and *Providencia* species. ^c Using parenteral breakpoints.