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Antimicrobial Activity of Ceftazidime-Avibactam and Other New β-Lactamase Inhibitor Combinations Tested against Bacterial Isolates from Pediatric Patients from US Medical Centers (2020–2021)

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CONCLUSIONS

- Ceftazidime-avibactam and meropenem-vaborbactam were the most active agents against Enterobacterales.
- Ceftazidime-avibactam and ceftolozane-tazobactam were the most active agents against *P. aeruginosa*.
- Susceptibility rates to comparator agents varied among age groups and infection types.

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References

1. CLSI. 2018. M07Ed11. Methods for dilution antimicrobial susceptibility tests for bacteria that grow aerobically; approved standard: 11th edition. Clinical and Laboratory Standards Institute. Wayne, PA.
2. CLSI. 2021. M100Ed31. Performance standards for antimicrobial susceptibility testing: 32nd informational supplement. Clinical and Laboratory Standards Institute, Wayne, PA.
3. Lake JG, Weiner LM, Milstone AM, et al. 2018. Pathogen distribution and antimicrobial resistance among pediatric healthcare-associated infections reported to the National Healthcare Safety Network, 2011-2014. Infect Control Hosp Epidemiol 39:1-11.
4. Sader HS, Castanheira M, Streit JM, Carvalhaes CG, Mendes RE. 2020. Frequency and antimicrobial susceptibility of bacteria causing bloodstream infections in pediatric patients from United States (US) medical centers (2014-2018): therapeutic options for multidrug-resistant bacteria. Diagn Microbiol Infect Dis 98:115108.

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INTRODUCTION

- The US FDA expanded the approval of ceftazidime-avibactam to include pediatric patients aged ≥3 months in 2019.
- We evaluated the *in vitro* activities of ceftazidime-avibactam, ceftolozane-tazobactam, meropenem-vaborbactam, imipenem-relebactam, and comparators against Enterobacterales and *P. aeruginosa* isolates causing infection in pediatric patients in US medical centers.

METHODS

- Among the 21,332 organisms (1/patient) collected in 2020–2021 from the INFORM Surveillance Program, 2,805 (13.1%) were from pediatric patients (≤17 years old [yo]).
- The collection included 2,391 Enterobacterales and 414 *P. aeruginosa*.
- These isolates were consecutively collected from 69 US medical centers and susceptibility tested by CLSI broth microdilution method.
- Susceptibility results were stratified by infection type and patient age: ≤1 yo (1,040 isolates), 2 to 5 yo (580), 6 to 12 yo (651), and 13 to 17 yo (534; Figure 1).
- Enterobacterales with elevated MIC values for selected β-lactams were screened for β-lactamase genes by whole genome sequencing.

RESULTS

- Isolates were mainly from urinary tract (47.2%), pneumonia (26.0%), and bloodstream infection (BSI; 14.4%; Figure 1).
- Ceftazidime-avibactam and meropenem-vaborbactam showed complete activity (100.0% susceptible [S]) against Enterobacterales, whereas ceftolozane-tazobactam and imipenem-relebactam showed limited activity against some organisms (Table 1 and Figure 2).
- Meropenem, ceftriaxone, and gentamicin were active against 99.8%, 87.5%, and 93.0% of Enterobacterales, respectively (Table 1).
- The susceptibility of Enterobacterales to ceftriaxone varied from 84.7% (6-12 yo) to 89.8% (13-17 yo; Table 1) and was 87.9% and 86.9% among isolates from pneumonia and BSI, respectively (data not shown).
- The frequency of the multidrug-resistant (MDR) phenotype varied from 3.7% (≤1 yo) to 4.8% (13-17 yo; Figure 3).
- The frequency of ESBL-producing Enterobacterales was 5.3% among patients ≤1 yo and ranged from 6.3% to 6.6% among the other age groups (Figure 3).
- Among ESBL producers, 97.2% (140/144) produced a CTX-M, the most common being CTX-M-15 (*n*=97; 67.4% of ESBL-producers) and CTX-M-27 (*n*=21; 14.6%); 34.0% (49/140) of CTX-M producers also had an OXA-1/30 (Table 2).
- Carbapenemase genes were not detected among isolates submitted to WGS (ESBL phenotype).
- Ceftazidime-avibactam (99.5%S), ceftolozane-tazobactam (99.8%S), and imipenem-relebactam (98.4%S) were the most active agents against the *P. aeruginosa* collection, but ceftazidime-avibactam and ceftolozane-tazobactam showed greater activity than imipenem-relebactam against *P. aeruginosa*-resistant subsets (Figure 4).
- Meropenem-vaborbactam and meropenem exhibited similar activity against *P. aeruginosa* (91.3% inhibited at ≤2 mg/L for both agents; data not shown).
- *P. aeruginosa* susceptibility to piperacillin-tazobactam (87.4%S) varied from 85.1% (6 to 12 yo) to 90.1% (13 to 17 yo; Table 1).
- *P. aeruginosa* susceptibility to meropenem (87.3%S) varied from 87.3% (13 to 17 yo) to 93.2% (2 to 5 yo; Table 1).

Table 1. Antimicrobial activity of ceftazidime-avibactam and comparator agents tested against Enterobacterales and *P. aeruginosa* isolates stratified by patient age group

Organism/antimicrobial agent	% Susceptible by age group[a]				
	≤1 yo	2–5 yo	6–12 yo	13–17 yo	All
Enterobacterales (no. of isolates)	(919)	(492)	(517)	(463)	(2,391)
Ceftazidime-avibactam	100.0	100.0	100.0	100.0	100.0
Ceftolozane-tazobactam	95.9	98.6	96.1	98.3	96.9
Meropenem-vaborbactam	100.0	100.0	100.0	100.0	100.0
Imipenem-relebactam	98.3	95.1	97.3	95.3	96.9
Piperacillin-tazobactam	91.2	94.9	90.7	93.7	92.3
Ceftriaxone	86.8	89.6	84.7	89.8	87.5
Meropenem	99.7	99.8	100.0	100.0	99.8
Levofloxacin	94.1	88.6	90.5	87.4	90.9
Gentamicin	94.0	92.7	91.9	92.6	93.0
Amikacin	99.5	100.0	100.0	99.8	99.7
P. aeruginosa (no. of isolates)	(121)	(88)	(134)	(71)	(414)
Ceftazidime-avibactam	100.0	100.0	99.3	98.6	99.5
Ceftolozane-tazobactam	100.0	100.0	99.3	100.0	99.8
Meropenem-vaborbactam	[93.4][b]	[96.6][b]	[94.8][b]	[97.2][b]	[95.2][b]
Imipenem-relebactam	98.9	100.0	96.9	97.8	98.4
Piperacillin-tazobactam	87.6	88.6	85.1	90.1	87.4
Ceftazidime	92.6	93.2	86.6	91.5	90.6
Meropenem	90.9	93.2	92.5	87.3	91.3
Levofloxacin	90.0	81.8	76.9	76.1	81.6
Tobramycin	99.2	95.5	95.5	90.1	95.7

[a] Criteria as published by CLSI.
[b] Percentage inhibited at the Enterobacterales breakpoint of ≤4 mg/L.
Abbreviations: yo, year(s) old

Table 2. Frequency of extended-spectrum β-lactamases (ESBLs) produced by sequenced Enterobacterales isolates (*n*=144) from pediatric patients

β-Lactamase	No. of isolates	% of ESBL producers
CTX-M type	140	97.2%
CTX-M-15	97	67.4%
CTX-M-27	21	14.6%
CTX-M-55	12	8.3%
CTX-M-14	7	4.9%
CTX-M-3	2	1.4%
CTX-M-173	2	1.4%
CTX-M + OXA-1/30	49	34.0%
SHV type	6	4.2%
≥2 ESBLs	51	35.4%

Figure 1. Distributions of patients by age group (1A) and infection type (1B)

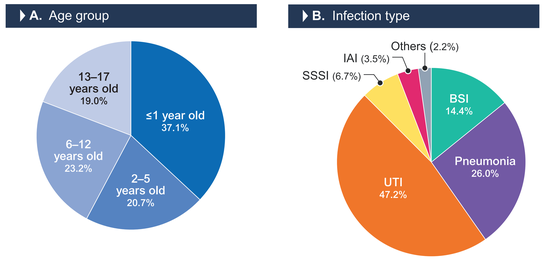
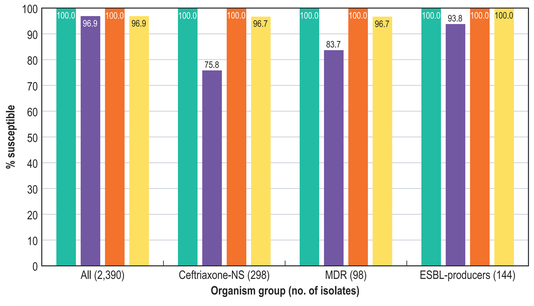


Figure 2. Ceftazidime-avibactam, ceftolozane-tazobactam, meropenem-vaborbactam, and imipenem-relebactam activities against Enterobacterales from pediatric patients



Abbreviations: NS, nonsusceptible; MDR, multidrug-resistant; ESBL, extended-spectrum β-lactamase.

Figure 3. Frequency of ESBL producers among Enterobacterales and isolates with a multidrug-resistant (MDR) phenotype stratified by age group

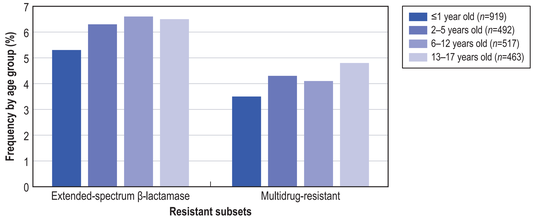
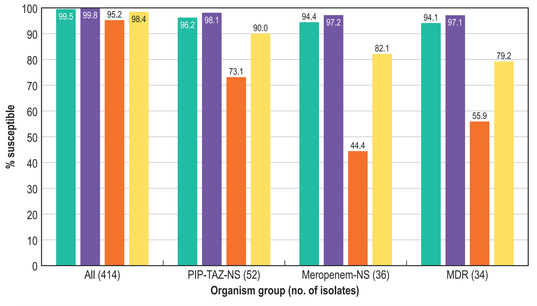


Figure 4. Ceftazidime-avibactam, ceftolozane-tazobactam, meropenem-vaborbactam, and imipenem-relebactam activities against *P. aeruginosa* isolates from pediatric patients



Abbreviations: PIP-TAZ, piperacillin-tazobactam; NS, nonsusceptible; MDR, multidrug-resistant.
* % inhibited at Enterobacterales breakpoint of ≤4 mg/L.