ORIGINAL ARTICLE

In vitro activity of ceftazidime-avibactam against clinical isolates of Enterobacterales and *Pseudomonas aeruginosa* collected in Malaysia: Results from the ATLAS Programme, 2013 to 2019

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ABSTRACT

Introduction: There has been a steady rise in antimicrobial resistance among common pathogens in Malaysia. This study aims to determine the *in vitro* antimicrobial activities of ceftazidime-avibactam and its comparators against clinical isolates of Enterobacterales and *Pseudomonas aeruginosa* collected in Malaysia from 2013 to 2019, and to determine the rates of resistance among these isolates.

Materials and Methods: In this retrospective study, four participating study centres located in East (N = 1) and West (N = 3) Malaysia contributed to the collection of clinical isolates of Enterobacterales and *P. aeruginosa* from 2013 to 2019. Antimicrobial minimum inhibitory concentrations (MICs) and percentage susceptibilities were interpreted according to Clinical Laboratory Standards Institute (CLSI) breakpoints, except for tigecycline and colistin, which utilised the United States Food and Drug Administration (US FDA) and European Committee on Antimicrobial Susceptibility Testing (EUCAST) breakpoints, respectively.

Results: A total of 1,073 isolates of Enterobacterales and 332 isolates of *P. aeruginosa* were collected in Malaysia from the four centres. Among Enterobacterales isolates, the highest percentages of susceptibility were seen with ceftazidime-avibactam (99.2%), meropenem (98.9%), and tigecycline (96.9%). Whereas *P. aeruginosa* isolates demonstrated the highest susceptibilities to colistin (95.6%), followed by ceftazidime-avibactam (93.1%) and cefepime (87.1%). All metallo-β-lactamase (MBL)-negative isolates of Enterobacterales, including ceftazidime-nonsusceptible, meropenem-nonsusceptible, and colistin-resistant phenotypes, were susceptible to ceftazidime-avibactam. Furthermore, ceftazidime-avibactam demonstrated the highest percentage of susceptibility (97.1%) against multidrug-resistant (MDR) isolates of Enterobacterales.

Conclusion: Ceftazidime-avibactam exhibited potent *in vitro* activity against clinical isolates of Enterobacterales and *P. aeruginosa* collected in Malaysia from 2013 to 2019. The results of this study show that ceftazidime-avibactam should be considered in the treatment of indicated infections caused by susceptible strains of aerobic Gram-negative pathogens and is a valuable alternative to carbapenems.

KEYWORDS:
ATLAS, carbapenem-resistant, ceftazidime-avibactam, colistin-resistant, Enterobacterales, Gram-negative, Malaysia, Pseudomonas aeruginosa, surveillance

INTRODUCTION

Rising antimicrobial resistance has led to increased morbidity and mortality rates associated with infectious diseases and is now an alarming global issue. The rising resistance rates, including the emergence of multidrug-resistant (MDR) organisms, can be attributed to the excessive and suboptimal use of antibiotics in clinical practice.[1,2] Similarly in Malaysia, a steady rise in antimicrobial resistance among common pathogens has been observed.[2] Of note, the World Health Organisation (WHO) has classified both carbapenem-resistant Enterobacterales (CRE) and carbapenem-resistant *Pseudomonas aeruginosa* as critical priority pathogens for research and development, whereas the Centers for Disease Control and Prevention (CDC) has classified CRE as an urgent threat that requires aggressive action.[3,4] CREs produce carbapenemases, enzymes that hydrolyse the β-lactam antibiotics (e.g. carbapenems, cephalosporins, penicillins, and aztreonam) and are resistant against most β-lactamase inhibitors.[5] Common carbapenemases include class A *Klebsiella pneumoniae* carbapenemases (KPCs), class B metallo-β-lactamases (MBLs) including imipenemase (IMP), New Delhi MBL (NDM), and Verona Integron-encoded MBL (VIM) types, and class D Oxacillinase (OXA) β-lactamases.[1]

Ceftazidime-avibactam is a combination of the third-generation cephalosporin, ceftazidime, and the novel, non-β-lactam β-lactamase inhibitor, avibactam. Avibactam has potent *in vitro* activity against a broad range of β-lactamases, including Ambler class A (extended-spectrum β-lactamases, KPCs), class C (AmpC), and some class D (OXA-48) enzymes. Therefore, combination with avibactam extends ceftazidime's spectrum of activity to cover MDR

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Enterobacterales and *P. aeruginosa* strains; however, an important limitation of the combination is its inability to inhibit MBL-producing isolates (i.e. NDM, VIM, IMP).[6,7]

Ceftazidime-avibactam is approved for the treatment of adults with complicated intra-abdominal infections (in combination with metronidazole), complicated urinary tract infections (including pyelonephritis), and hospital-acquired pneumonia (including ventilator-associated pneumonia). In Europe, ceftazidime-avibactam is also approved for the treatment of adult patients with other infections caused by aerobic Gram-negative organisms with limited treatment options.[7,8] Currently, there is a lack of studies that specifically describe the *in vitro* activity of ceftazidime-avibactam against clinical isolates of Enterobacterales and *P. aeruginosa* in Malaysia. This study aims to determine the *in vitro* antimicrobial activities of ceftazidime-avibactam and its comparators against clinical isolates of Enterobacterales and *P. aeruginosa* collected in Malaysia from 2013 to 2019, and to determine the rates of resistance among these isolates, using the data from the Antimicrobial Testing Leadership and Surveillance (ATLAS) programme.

MATERIALS AND METHODS

In this retrospective study, four participating study centres located in East (N = 1) and West (N = 3) Malaysia contributed to the collection of clinical isolates of Enterobacterales (i.e., *Citrobacter* spp., *Enterobacter* spp., *Escherichia* spp., *Serratia* spp., *Klebsiella* spp., and *Proteus* spp.) and *P. aeruginosa* from 2013 to 2019. Relevant clinical isolates were obtained from hospitalised patients with complicated intra-abdominal infections, complicated urinary tract infections, complicated skin and skin structure infections, lower respiratory tract infections, and bloodstream infections.[9] The isolates were then identified by each participating study centre and stored in tryptic soy broth (supplied by the International Health Management Associates [IHMA]) with glycerol at –70°C, and shipped to a central laboratory (IHMA Inc., Schaumburg, IL, USA) for susceptibility testing.[9] Only isolates identified as a potential causative agent of a patient's infection were included in these studies.[9] Isolate identification was confirmed by IHMA using matrix-assisted laser desorption ionisation–time of flight mass spectrometry (MALDI Biotyper; Bruker Daltonics, Billerica, MA, USA).

Antimicrobial susceptibility testing was performed following the Clinical and Laboratory Standards Institute (CLSI) standard method and the European Committee on Antimicrobial Susceptibility Testing (EUCAST) guidelines of the European Society of Clinical Microbiology and Infectious Diseases, using custom 96-well broth microdilution panels prepared in-house at IHMA or by Trek (Thermo Fisher Scientific, Oakwood Village, OH, USA).[10] The minimum inhibitory concentrations (MICs) were interpreted using current CLSI breakpoints[11] with the following exceptions: Tigecycline and colistin MICs were interpreted using the United States Food and Drug Administration (US FDA)[12] and EUCAST[13] breakpoints, respectively. Polymerase chain reaction and Sanger sequencing or whole-genome sequencing were used to screen isolates of Enterobacterales and *P. aeruginosa* for the presence of known resistant mechanisms, such as the presence or alteration in genes encoding β-lactamases and penicillin-binding proteins.

Data considered evaluable by IHMA were collated by a data management team and incorporated by Micron Research (Micron, Ely, UK) into the ATLAS database, an interactive platform available at www.atlas-surveillance.com.[14] In this study, the data were analysed for ceftazidime-avibactam, and the following comparator agents: imipenem, meropenem, cefepime, ceftazidime, tigecycline, colistin, and piperacillin-tazobactam. The data for this study were extracted in June 2021; however, the ATLAS database is continuously updated, with new resources being added regularly (i.e. every 6–8 months).[14] Ethical clearance was obtained from the National Medical Research and Ethics Committee (MREC), Ministry of Health Malaysia. This study was registered under the National Medical Research Registry (NMRR-18-1271-39749).

RESULTS

Over the 7-year period, 1,405 isolates (1,073 isolates of Enterobacterales; 332 isolates of *P. aeruginosa*) were collected from participating hospitals, including Hospital Kuala Lumpur, Hospital Sultanah Aminah, Hospital Sungai Buloh, and Sarawak General Hospital. Of the 1,073 isolates of Enterobacterales tested, 99.2% were susceptible to ceftazidime-avibactam (MIC_{90}, 0.25 mg/L), with lower percentages of susceptibility observed with meropenem (98.9%), tigecycline (96.9%), imipenem (91.1%), piperacillin-tazobactam (89.5%), colistin (85.9%), ceftazidime alone (75.9%), and cefepime (75.3%). Ceftazidime-avibactam MIC_{90} values for each species or species group within the Enterobacterales order ranged from 0.06 mg/L (*Proteus* spp.) to 0.5 mg/L (*Enterobacter* spp., *K. pneumoniae* and *Serratia* spp.), whereas percentages of susceptibility to ceftazidime-avibactam were 98.1%, 98.4%, and 100% among *Enterobacter* spp., *K. pneumoniae*, and among other species or species groups of Enterobacterales isolates (*E. coli, K. aerogenes, K. oxytoca, K. variicola, Citrobacter* spp., *Proteus* spp., and *Serratia* spp.), respectively. Isolates of *Proteus* and *Serratia* demonstrate nonsusceptibility to colistin as they are naturally resistant to polymyxins.[15] Among isolates of Enterobacterales, only eight MBL-positive isolates were found within groups of *K. pneumoniae* (6/400 isolates,1.5%) and *Enterobacter* spp. (2/122 isolates,1.6%). Hence, percentages of susceptibility to ceftazidime-avibactam were 1.6% and 1.9% higher for MBL-negative isolates of *K. pneumoniae* and *Enterobacter* spp., respectively, compared with data sets that included all isolates. All Enterobacterales isolates that were MBL-negative exhibited 100% susceptibility to ceftazidime-avibactam. The susceptibility of Enterobacterales isolates to imipenem (91.1%) was lower compared with meropenem (98.9%) owing to the presence of 73 isolates of *Proteus* spp. (6.8% of all Enterobacterales isolates); the genus *Proteus* has innately higher imipenem MICs compared with meropenem.[11] Among the 332 isolates of *P. aeruginosa*, 95.6% (MIC_{90}, 2 mg/L), 93.1% (MIC_{90}, 8 mg/L), 87.1%, 83.4%, 83.4%, 81.6%, and 78.6% were susceptible to colistin, ceftazidime-avibactam, cefepime, ceftazidime alone, meropenem, piperacillin-tazobactam, and imipenem, respectively. When only MBL-negative isolates of *P. aeruginosa* were considered, the percentage of susceptibility to ceftazidime-avibactam was the highest (97.9%) compared with the other agents (Table I).

Table I: *In vitro* activities of ceftazidime-avibactam and comparator antimicrobial agents tested against isolates of Enterobacterales and *Pseudomonas aeruginosa*[a]

Organism	Antimicrobial agent	MIC (mg/L)				
		N	50%	90%	Range	% susceptible[b]
Enterobacterales	Ceftazidime-avibactam	956	0.12	0.25	≥0.015 to ≤256	99.2
	Ceftazidime	1,073	0.25	64	≥0.03 to ≤256	75.9
	Cefepime	1,073	0.12	32	≥0.12 to ≤64	75.3
	Piperacillin-tazobactam	1,073	2	32	≥0.12 to ≤256	89.5
	Imipenem	956	0.25	1	≥0.06 to ≤16	91.1
	Meropenem	1,073	0.06	0.12	≥0.015 to ≤32	98.9
	Colistin	703	0.5	8	≥0.12 to ≤16	85.9
	Tigecycline	1,073	0.5	2	≥0.06 to ≤16	96.9
Enterobacterales, MBL-negative	Ceftazidime-avibactam	948	0.12	0.25	≥0.015 to ≤4	100
	Ceftazidime	1,065	0.25	32	≥0.03 to ≤256	76.4
	Cefepime	1,065	0.12	32	≥0.12 to ≤64	75.9
	Piperacillin-tazobactam	1,065	2	16	≥0.12 to ≤256	90.1
	Imipenem	948	0.25	1	≥0.06 to ≤8	91.9
	Meropenem	1,065	0.06	0.06	≥0.015 to ≤4	99.6
	Colistin	695	0.5	8	≥0.12 to ≤16	85.8
	Tigecycline	1,065	0.5	2	≥0.06 to ≤16	96.9
Klebsiella pneumoniae	Ceftazidime-avibactam	365	0.12	0.5	≥0.015 to ≤256	98.4
	Ceftazidime	400	0.5	128	≥0.03 to ≤256	63.0
	Cefepime	400	0.12	32	≥0.12 to ≤64	62.8
	Piperacillin-tazobactam	400	4	128	≥0.5 to ≤256	81.0
	Imipenem	365	0.25	0.5	≥0.06 to ≤16	97.3
	Meropenem	400	0.06	0.12	≥0.015 to ≤32	97.8
	Colistin	275	0.5	1	≥0.12 to ≤16	98.9
	Tigecycline	400	0.5	2	≥0.25 to ≤16	97.8
Klebsiella pneumoniae, MBL-negative	Ceftazidime-avibactam	359	0.12	0.5	≥0.015 to ≤4	100
	Ceftazidime	394	0.25	64	≥0.03 to ≤256	64.0
	Cefepime	394	0.12	32	≥0.12 to ≤64	63.7
	Piperacillin-tazobactam	394	4	128	≥0.5 to ≤256	82.2
	Imipenem	359	0.25	0.5	≥0.06 to ≤4	98.9
	Meropenem	394	0.12	0.12	≥0.015 to ≤4	99.2
	Colistin	269	0.5	1	≥0.12 to ≤16	98.9
	Tigecycline	394	0.5	2	≥0.25 to ≤16	97.7
Klebsiella spp. (other than *Klebsiella pneumoniae*)[c]	Ceftazidime-avibactam	20	0.12	0.25	≥0.06 to ≤0.25	100
	Ceftazidime	26	0.25	2	≥0.06 to ≤32	92.3
	Cefepime	26	0.12	0.5	≥0.12 to ≤0.5	100
	Piperacillin-tazobactam	26	4	4	≥0.5 to ≤32	92.3
	Imipenem	20	0.5	2	≥0.12 to ≤2	90.0
	Meropenem	26	0.06	0.12	≥0.03 to ≤0.12	100
	Colistin	18	0.25	0.5	≥0.12 to ≤2	100
	Tigecycline	26	0.5	0.5	≥0.06 to ≤1	100
Enterobacter spp.[d]	Ceftazidime-avibactam	105	0.25	0.5	≥0.03 to ≤256	98.1
	Ceftazidime	122	0.5	64	≥0.06 to ≤256	80.3
	Cefepime	122	0.12	8	≥0.12 to ≤64	83.6
	Piperacillin-tazobactam	122	2	16	≥0.5 to ≤256	91.8
	Imipenem	105	0.5	2	≥0.06 to ≤16	87.6
	Meropenem	122	0.06	0.12	≥0.015 to ≤32	98.4
	Colistin	76	0.5	16	≥0.12 to ≤16	85.5
	Tigecycline	122	0.5	1	≥0.12 to ≤2	100
Enterobacter spp., MBL-negative	Ceftazidime-avibactam	103	0.25	0.5	≥0.03 to ≤2	100
	Ceftazidime	120	0.5	32	≥0.06 to ≤256	81.7
	Cefepime	120	0.12	8	≥0.12 to ≤64	85.0
	Piperacillin-tazobactam	120	2	16	≥0.5 to ≤256	93.3
	Imipenem	103	0.5	2	≥0.06 to ≤4	89.3
	Meropenem	120	0.12	0.12	≥0.015 to ≤0.5	100
	Colistin	74	0.5	16	≥0.12 to ≤16	85.1
	Tigecycline	120	0.5	1	≥0.12 to ≤2	100

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Table I: *In vitro* activities of ceftazidime-avibactam and comparator antimicrobial agents tested against isolates of Enterobacterales and *Pseudomonas aeruginosa*[a]

Organism	Antimicrobial agent	MIC (mg/L)				
		N	50%	90%	Range	% susceptible[b]
Escherichia coli	Ceftazidime-avibactam	321	0.06	0.25	≥0.015 to ≤4	100
	Ceftazidime	359	0.25	32	≥0.03 to ≤256	80.2
	Cefepime	359	0.12	32	≥0.12 to ≤64	77.7
	Piperacillin-tazobactam	359	2	8	≥0.12 to ≤256	95.5
	Imipenem	321	0.25	0.25	≥0.06 to ≤2	99.7
	Meropenem	359	0.03	0.06	≥0.015 to ≤1	100
	Colistin	229	0.5	1	≥0.12 to ≤4	96.5
	Tigecycline	359	0.25	0.5	≥0.06 to ≤8	99.2
Citrobacter spp.[e]	Ceftazidime-avibactam	40	0.12	0.25	≥0.03 to ≤2	100
	Ceftazidime	41	0.25	64	≥0.12 to ≤256	78.1
	Cefepime	41	0.12	32	≥0.12 to ≤64	82.9
	Piperacillin-tazobactam	41	4	128	≥1 to ≤256	85.4
	Imipenem	40	0.25	0.5	≥0.12 to ≤2	95.0
	Meropenem	41	0.06	0.06	≥0.015 to ≤2	97.6
	Colistin	28	0.25	1	≥0.12 to ≤1	100
	Tigecycline	41	0.25	0.5	≥0.12 to ≤1	100
Proteus spp.[f]	Ceftazidime-avibactam	73	0.06	0.06	≥0.03 to ≤0.12	100
	Ceftazidime	73	0.06	0.25	≥0.03 to ≤8	98.6
	Cefepime	73	0.12	2	≥0.12 to ≤32	91.8
	Piperacillin-tazobactam	73	0.25	1	≥0.25 to ≤128	98.6
	Imipenem	73	2	4	≥0.25 to ≤8	23.3
	Meropenem	73	0.06	0.12	≥0.06 to ≤1	100
	Colistin	51	16	16	≥8 to ≤16	0
	Tigecycline	73	2	4	≥0.25 to ≤8	75.3
Serratia spp.[g]	Ceftazidime-avibactam	32	0.25	0.5	≥0.06 to ≤0.5	100
	Ceftazidime	52	0.5	1	≥0.06 to ≤256	92.3
	Cefepime	52	0.12	0.5	≥0.12 to ≤64	94.2
	Piperacillin-tazobactam	52	2	8	≥0.25 to ≤128	96.2
	Imipenem	32	1	1	≥0.25 to ≤2	96.9
	Meropenem	52	0.06	0.12	≥0.03 to ≤0.25	100
	Colistin	26	16	16	≥4 to ≤16	0
	Tigecycline	52	1	2	≥0.25 to ≤4	94.2
Pseudomonas aeruginosa	Ceftazidime-avibactam	303	2	8	≥0.5 to ≤256	93.1
	Ceftazidime	332	2	32	≥0.5 to ≤256	83.4
	Cefepime	332	2	16	≥0.5 to ≤64	87.1
	Piperacillin-tazobactam	332	8	128	≥0.25 to ≤256	81.6
	Imipenem	303	2	16	≥0.25 to ≤16	78.6
	Meropenem	332	0.5	8	≥0.06 to ≤32	83.4
	Colistin	274	1	2	≥0.25 to ≤8	95.6
Pseudomonas aeruginosa, MBL-negative	Ceftazidime-avibactam	288	2	4	≥0.5 to ≤256	97.9
	Ceftazidime	317	2	16	≥0.5 to ≤256	79.8
	Cefepime	317	2	8	≥0.5 to ≤64	55.8
	Piperacillin-tazobactam	317	8	32	≥0.25 to ≤256	85.5
	Imipenem	288	2	16	≥0.25 to ≤16	25.0
	Meropenem	317	0.5	4	≥0.06 to ≤32	82.3
	Colistin	260	1	2	≥0.25 to ≤8	95.4

[a]Isolates of Enterobacterales (N = 1,073) and *Pseudomonas aeruginosa* (N = 332) were collected in Malaysia as part of the ATLAS program from 2013 to 2019.
[b]Percentage susceptibilities were interpreted according to CLSI breakpoints, except for tigecycline and colistin, which utilised US FDA and EUCAST breakpoints, respectively.
[c]*Klebsiella* spp. (other than *Klebsiella pneumoniae*) included *Klebsiella aerogenes* (N = 14), *Klebsiella oxytoca* (N = 6) and *Klebsiella variicola* (N = 6).
[d]The *Enterobacter* spp. included *Enterobacter aerogenes* (N = 20), *Enterobacter asburiae* (N = 8), *Enterobacter cloacae* (N = 84), *Enterobacter kobei* (N = 3), *Enterobacter xiangfangensis* (N = 5), and *Enterobacter*, non-speciated (N = 2).
[e]The *Citrobacter* spp. included *Citrobacter amalonaticus* (N = 1), *Citrobacter freundii* (N = 5), and *Citrobacter koseri* (N = 35).
[f]*Proteus* spp. included *Proteus hauseri* (N = 1), *Proteus mirabilis* (N = 57), and *Proteus vulgaris* (N = 15).
[g]*Serratia* spp. included *Serratia marcescens* (N = 51) and *Serratia rubidaea* (N = 1).

Table II: *In vitro* activities of ceftazidime-avibactam and comparator antimicrobial agents tested against ceftazidime-nonsusceptible isolates of Enterobacterales and *Pseudomonas aeruginosa*[a]

Organism	Antimicrobial agent	N	MIC (mg/L)			% susceptible[b]
			50%	90%	Range	
Enterobacterales	Ceftazidime-avibactam	228	0.25	1	≥0.015 to ≤256	96.5
	Ceftazidime	259	32	256	≥8 to ≤256	0
	Cefepime	259	32	64	≥0.12 to ≤64	12.7
	Piperacillin-tazobactam	259	16	256	≥0.5 to ≤256	63.3
	Imipenem	228	0.25	1	≥0.12 to ≤16	92.5
	Meropenem	259	0.06	0.25	≥0.015 to ≤32	95.4
	Colistin	172	0.5	1	≥0.12 to ≤16	93.0
	Tigecycline	259	0.5	2	≥0.06 to ≤8	97.3
Enterobacterales, MBL-negative	Ceftazidime-avibactam	220	0.25	1	≥0.015 to ≤4	100
	Ceftazidime	251	32	256	≥8 to ≤256	0
	Cefepime	251	32	64	≥0.12 to ≤64	13.2
	Piperacillin-tazobactam	251	8	256	≥0.5 to ≤256	65.3
	Imipenem	220	0.25	1	≥0.12 to ≤4	95.9
	Meropenem	251	0.12	0.12	≥0.015 to ≤4	98.4
	Colistin	164	0.5	1	≥0.12 to ≤16	92.7
	Tigecycline	251	0.5	2	≥0.06 to ≤8	97.2
Klebsiella spp.	Ceftazidime-avibactam	138	0.25	1	≥0.03 to ≤256	95.7
	Ceftazidime	150	32	256	≥8 to ≤256	0
	Cefepime	150	32	64	≥0.12 to ≤64	4.7
	Piperacillin-tazobactam	150	16	256	≥0.5 to ≤256	52.7
	Imipenem	138	0.25	1	≥0.12 to ≤16	92.8
	Meropenem	150	0.06	0.25	≥0.015 to ≤32	94.0
	Colistin	96	0.5	1	≥0.12 to ≤4	97.9
	Tigecycline	150	1	2	≥0.25 to ≤8	96.7
Klebsiella spp., MBL-negative	Ceftazidime-avibactam	132	0.25	1	≥0.03 to ≤4	100
	Ceftazidime	144	32	256	≥8 to ≤256	0
	Cefepime	144	32	64	≥0.12 to ≤64	4.9
	Piperacillin-tazobactam	144	16	256	≥0.5 to ≤256	54.9
	Imipenem	132	0.25	1	≥0.12 to ≤4	97.0
	Meropenem	144	0.12	0.25	≥0.015 to ≤4	97.9
	Colistin	90	0.5	1	≥0.12 to ≤4	97.8
	Tigecycline	144	1	2	≥0.25 to ≤8	96.5
Enterobacter spp.	Ceftazidime-avibactam	18	0.5	256	≥0.12 to ≤256	88.9
	Ceftazidime	24	64	256	≥8 to ≤256	0
	Cefepime	24	8	64	≥0.25 to ≤64	41.7
	Piperacillin-tazobactam	24	16	128	≥1 to ≤256	58.3
	Imipenem	18	1	8	≥0.25 to ≤16	83.3
	Meropenem	24	0.12	0.5	≥0.03 to ≤32	91.7
	Colistin	17	0.5	8	≥0.25 to ≤16	82.4
	Tigecycline	24	0.5	2	≥0.25 to ≤2	100
Enterobacter spp., MBL-negative	Ceftazidime-avibactam	16	0.5	1	≥0.12 to ≤2	100
	Ceftazidime	22	64	128	≥8 to ≤256	0
	Cefepime	22	8	64	≥0.25 to ≤64	45.5
	Piperacillin-tazobactam	22	16	64	≥1 to ≤256	63.6
	Imipenem	16	0.5	1	≥0.25 to ≤2	93.8
	Meropenem	22	0.12	0.5	≥0.03 to ≤0.5	100
	Colistin	15	0.5	8	≥0.25 to ≤16	80.0
	Tigecycline	22	0.5	2	≥0.25 to ≤2	100
Escherichia coli	Ceftazidime-avibactam	61	0.12	0.25	≥0.015 to ≤4	100
	Ceftazidime	71	32	64	≥8 to ≤256	0
	Cefepime	71	32	64	≥0.12 to ≤64	18.3
	Piperacillin-tazobactam	71	4	32	≥0.5 to ≤256	88.7
	Imipenem	61	0.25	0.5	≥0.12 to ≤2	98.4
	Meropenem	71	0.12	0.12	≥0.015 to ≤1	100
	Colistin	50	0.5	4	≥0.12 to ≤4	90.0
	Tigecycline	71	0.25	0.5	≥0.06 to ≤2	100

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Table II: *In vitro* activities of ceftazidime-avibactam and comparator antimicrobial agents tested against ceftazidime-nonsusceptible isolates of Enterobacterales and *Pseudomonas aeruginosa*[a]

Organism	Antimicrobial agent	N	MIC (mg/L)			% susceptible[b]
			50%	90%	Range	
Citrobacter spp.	Ceftazidime-avibactam	9	0.25	2	≥0.12 to ≤2	100
	Ceftazidime	9	64	256	≥32 to ≤256	0
	Cefepime	9	32	64	≥0.25 to ≤64	22.2
	Piperacillin-tazobactam	9	128	256	≥4 to ≤256	44.4
	Imipenem	9	0.25	2	≥0.12 to ≤2	77.8
	Meropenem	9	0.12	2	≥0.03 to ≤2	88.9
	Colistin	7	0.5	1	≥0.25 to ≤1	100
	Tigecycline	9	0.5	0.5	≥0.12 to ≤0.5	100
Other Enterobacterales[c]	Ceftazidime-avibactam	2	0.5	0.5	≥0.06 to ≤0.5	100
	Ceftazidime	5	16	256	≥8 to ≤256	0
	Cefepime	5	4	64	≥0.5 to ≤64	20.0
	Piperacillin-tazobactam	5	4	128	≥1 to ≤128	80.0
	Imipenem	2	4	4	≥0.5 to ≤4	50.0
	Meropenem	5	0.12	0.25	≥0.06 to ≤0.25	100
	Colistin	2	16	16	≥8 to ≤16	0
	Tigecycline	5	2	4	≥1 to ≤4	60.0
Pseudomonas aeruginosa	Ceftazidime-avibactam	50	8	256	≥2 to ≤256	58.0
	Ceftazidime	55	64	256	≥16 to ≤256	0
	Cefepime	55	32	64	≥2 to ≤64	1.8
	Piperacillin-tazobactam	55	128	256	≥4 to ≤256	10.9
	Imipenem	50	16	16	≥0.5 to ≤16	10.0
	Meropenem	55	4	32	≥0.06 to ≤32	43.6
	Colistin	46	1	2	≥0.5 to ≤4	93.5
Pseudomonas aeruginosa, MBL-negative	Ceftazidime-avibactam	35	4	32	≥2 to ≤256	82.9
	Ceftazidime	40	32	256	≥16 to ≤256	0
	Cefepime	40	16	64	≥2 to ≤64	2.5
	Piperacillin-tazobactam	40	128	256	≥4 to ≤256	15.0
	Imipenem	35	2	16	≥0.5 to ≤16	14.3
	Meropenem	40	1	16	≥0.06 to ≤32	60.0
	Colistin	32	1	2	≥0.5 to ≤4	90.6

[a]Isolates of ceftazidime-nonsusceptible Enterobacterales (N = 259) and *Pseudomonas aeruginosa* (N = 55) were collected in Malaysia as part of the ATLAS program from 2013 to 2019.
[b]Percentage susceptibilities were interpreted according to CLSI breakpoints, except for tigecycline and colistin, which utilised US FDA and EUCAST breakpoints, respectively.
[c]Other Enterobacterales included *Serratia marcescens* (N = 4) and *Proteus mirabilis* (N = 1).

Table II shows the *in vitro* activity of ceftazidime-avibactam and comparator agents against ceftazidime-nonsusceptible isolates of Enterobacterales and *P. aeruginosa*. Among the 259 isolates of Enterobacterales that were ceftazidime-nonsusceptible (24.1% of all Enterobacterales isolates), 96.5% were susceptible to ceftazidime-avibactam (MIC_{90}, 1 mg/L), with MIC_{90} values against individual species or species groups of Enterobacterales ranging from 0.25 mg/L (*E. coli*) to 256 mg/L (*Enterobacter* spp.) and percentages of susceptibility to ceftazidime-avibactam ranged from 88.9% (*Enterobacter* spp.) to 100% susceptible (*E. coli*, *Citrobacter* spp., *S. Marcescens*, and *P. mirabilis*). Compared with ceftazidime-avibactam, the pooled collection of ceftazidime-nonsusceptible Enterobacterales exhibited lower susceptibility rates to the other antimicrobial agents, except for tigecycline (97.3% susceptible; MIC_{90}, 2 mg/L). However, among MBL-negative isolates of ceftazidime-nonsusceptible Enterobacterales, ceftazidime-avibactam exhibited the highest percentage of susceptibility (100%; MIC_{90}, 1 mg/L). Of the 55 isolates of *P. aeruginosa* that were ceftazidime-nonsusceptible (16.6% of all *P. aeruginosa* isolates), 58% were susceptible to ceftazidime-avibactam (MIC_{90}, 256 mg/L). Lower susceptibility rates (from 1.8% [cefepime] to 43.6% [meropenem]) were seen among the other agents included in this study apart from colistin (93.5%; MIC_{90}, 2 mg/L). The percentage of susceptibility to ceftazidime-avibactam was higher among MBL-negative isolates of *P. aeruginosa* (82.9% susceptible; MIC_{90}, 32 mg/L) compared with the pooled isolates of ceftazidime-nonsusceptible *P. aeruginosa*.

Table III depicts the *in vitro* activity of ceftazidime-avibactam and comparator agents against isolates of Enterobacterales and *P. aeruginosa* with a meropenem-nonsusceptible phenotype. Among the 12 isolates of Enterobacterales that were meropenem-nonsusceptible (1.1% of all Enterobacterales isolates), 33.3% were susceptible to ceftazidime-avibactam (MIC_{90}, 256 mg/L). The highest susceptibility was seen with tigecycline (100% susceptible; MIC_{90}, 1 mg/L), followed by colistin (91.7% susceptible; MIC_{90}, 2 mg/L); only 8.3% (MIC_{90}, 16 mg/L) of the

Table III: *In vitro* activities of ceftazidime-avibactam and comparator antimicrobial agents tested against meropenem-nonsusceptible isolates of Enterobacterales and *Pseudomonas aeruginosa*[a]

Organism	Antimicrobial agent	N	MIC (mg/L)			% susceptible[b]
			50%	90%	Range	
Enterobacterales[c]	Ceftazidime-avibactam	12	256	256	≥1 to ≤256	33.3
	Ceftazidime	12	256	256	≥128 to ≤256	0
	Cefepime	12	64	64	≥32 to ≤64	0
	Piperacillin-tazobactam	12	128	256	≥128 to ≤256	0
	Imipenem	12	8	16	≥0.25 to ≤16	8.3
	Meropenem	12	16	32	≥2 to ≤32	0
	Colistin	12	0.25	2	≥0.25 to ≤4	91.7
	Tigecycline	12	0.5	1	≥0.12 to ≤1	100
Enterobacterales, MBL-negative	Ceftazidime-avibactam	4	2	4	≥1 to ≤4	100
	Ceftazidime	4	256	256	256	0
	Cefepime	4	64	64	≥32 to ≤64	0
	Piperacillin-tazobactam	4	128	256	≥128 to ≤256	0
	Imipenem	4	2	4	≥0.25 to ≤4	25.0
	Meropenem	4	2	4	≥2 to ≤4	0
	Colistin	4	0.25	4	≥0.25 to ≤4	75.0
	Tigecycline	4	1	1	≥0.12 to ≤1	100
Pseudomonas aeruginosa	Ceftazidime-avibactam	51	8	256	≥1 to ≤256	60.8
	Ceftazidime	55	16	256	≥1 to ≤256	34.6
	Cefepime	55	16	64	≥1 to ≤64	9.1
	Piperacillin-tazobactam	55	32	256	≥2 to ≤256	38.2
	Imipenem	51	16	16	≥2 to ≤16	0
	Meropenem	55	16	32	≥4 to ≤32	0
	Colistin	46	1	2	≥0.25 to ≤4	97.8
Pseudomonas aeruginosa, MBL-negative	Ceftazidime-avibactam	36	4	32	≥1 to ≤256	86.1
	Ceftazidime	40	8	256	≥1 to ≤256	47.5
	Cefepime	40	8	32	≥1 to ≤64	12.5
	Piperacillin-tazobactam	40	16	256	≥2 to ≤256	52.5
	Imipenem	36	16	16	≥2 to ≤16	0
	Meropenem	40	8	16	≥4 to ≤32	0
	Colistin	32	1	2	≥0.25 to ≤4	96.9

[a]Isolates of meropenem-nonsusceptible Enterobacterales (N = 12) and *Pseudomonas aeruginosa* (N = 55) were collected in Malaysia as part of the ATLAS program from 2013 to 2019.
[b]Percentage susceptibilities were interpreted according to CLSI breakpoints, except for tigecycline and colistin, which utilised US FDA and EUCAST breakpoints, respectively.
[c]Enterobacterales included *Klebsiella pneumoniae* (N = 9), *Enterobacter cloacae* (N = 2), and *Citrobacter koseri* (N = 1).

meropenem-nonsusceptible isolates of Enterobacterales were susceptible to imipenem and none were susceptible to ceftazidime, cefepime, or piperacillin-tazobactam. When only MBL-negative isolates were considered, all isolates were susceptible to ceftazidime-avibactam (100% susceptible; MIC_{90}, 4 mg/L). Among 55 isolates of *P. aeruginosa* that were meropenem-nonsusceptible (16.6% of all *P. aeruginosa* isolates), 60.8% were susceptible to ceftazidime-avibactam (MIC_{90}, 256 mg/L). Apart from colistin (97.8% susceptible; MIC_{90}, 2 mg/L), lower susceptibility rates (from 0% [imipenem] to 38.2% [piperacillin-tazobactam]) were observed with all the other agents included in this study. The percentage of susceptibility to ceftazidime-avibactam was higher among MBL-negative isolates of *P. aeruginosa* (86.1% susceptible; MIC_{90}, 32 mg/L) compared with the pooled isolates of meropenem-nonsusceptible *P. aeruginosa*.

Table IV describes the *in vitro* activity of ceftazidime-avibactam and comparator agents against colistin-resistant isolates of Enterobacterales and *P. aeruginosa*. Among the 22 colistin-resistant isolates of Enterobacterales (2.1% of all Enterobacterales isolates), 100% (MIC_{90}, 1 mg/L) were susceptible to ceftazidime-avibactam, imipenem, and tigecycline. Susceptibility to other agents ranged from 54.5% (ceftazidime) to 95.5% (meropenem). Among 12 colistin-resistant isolates of *P. aeruginosa* (3.6% of all *P. aeruginosa* isolates), 100% (MIC_{90}, 4 mg/L) were susceptible to ceftazidime-avibactam and cefepime. Other agents demonstrated susceptibilities ranging from 75% (ceftazidime and piperacillin-tazobactam) to 91.7% (meropenem). No MBL-positive isolates were detected among colistin-resistant isolates of Enterobacterales and *P. aeruginosa*.

Table V shows the *in vitro* activity of ceftazidime-avibactam and comparator agents against MDR isolates of Enterobacterales and *P. aeruginosa*. MDR is defined in the ATLAS database as resistance to any three of the following groups of antimicrobial agents: cephalosporins, carbapenems, quinolones, aminoglycosides, polymyxins, monobactams, and penicillin combination.[14] The MDR

Table IV: *In vitro* activities of ceftazidime-avibactam and comparator antimicrobial agents tested against colistin-resistant isolates of Enterobacterales and *Pseudomonas aeruginosa*[a]

Organism	Antimicrobial agent	N	MIC (mg/L)			% susceptible[b]
			50%	90%	Range	
Enterobacterales[c]	Ceftazidime-avibactam	22	0.12	1	≥0.03 to ≤2	100
	Ceftazidime	22	4	128	≥0.12 to ≤256	54.5
	Cefepime	22	0.25	32	≥0.12 to ≤64	68.2
	Piperacillin-tazobactam	22	4	64	≥1 to ≤256	81.8
	Imipenem	22	1	1	≥0.12 to ≤1	100
	Meropenem	22	0.06	0.25	≥0.03 to ≤2	95.5
	Colistin	22	4	16	≥4 to ≤16	0
	Tigecycline	22	0.5	1	≥0.12 to ≤2	100
Pseudomonas aeruginosa	Ceftazidime-avibactam	12	2	4	≥1 to ≤8	100
	Ceftazidime	12	2	16	≥1 to ≤16	75.0
	Cefepime	12	2	4	≥2 to ≤8	100
	Piperacillin-tazobactam	12	8	32	≥4 to ≤64	75.0
	Imipenem	12	2	4	≥0.5 to ≤8	83.3
	Meropenem	12	0.5	2	≥0.25 to ≤4	91.7
	Colistin	12	4	8	≥4 to ≤8	0

[a]Isolates of colistin-resistant Enterobacterales (N = 22) and *Pseudomonas aeruginosa* (N = 12) were collected in Malaysia as part of the ATLAS program from 2013 to 2019. None of the colistin-resistant isolates were MBL-positive.
[b]Percentage susceptibilities were interpreted according to CLSI breakpoints, except for tigecycline and colistin, which utilised US FDA and EUCAST breakpoints, respectively.
[c]Enterobacterales included *Enterobacter* spp. (N = 11), *Escherichia coli* (N = 8), and *Klebsiella pneumoniae* (N = 3). *Proteus* spp. and *Serratia* spp. were excluded as they are intrinsically resistant to colistin.

Table V: *In vitro* activities of ceftazidime-avibactam and comparator antimicrobial agents tested against MDR isolates of Enterobacterales and *Pseudomonas aeruginosa*[a]

Organism	Antimicrobial agent	N	MIC (mg/L)			% susceptible[b]
			50%	90%	Range	
Enterobacterales[c]	Ceftazidime-avibactam	279	0.25	1	≥0.015 to ≤256	97.1
	Ceftazidime	286	32	256	≥0.06 to ≤256	21.0
	Cefepime	286	32	64	≥0.12 to ≤64	22.4
	Piperacillin-tazobactam	286	8	256	≥0.25 to ≤256	65.7
	Imipenem	279	0.25	2	≥0.06 to ≤16	90.0
	Meropenem	286	0.06	0.25	≥0.015 to ≤32	95.8
	Colistin	221	0.5	4	≥0.12 to ≤16	89.1
	Tigecycline	286	0.5	2	≥0.06 to ≤8	96.2
Pseudomonas aeruginosa	Ceftazidime-avibactam	38	32	256	≥2 to ≤256	44.7
	Ceftazidime	39	256	256	≥4 to ≤256	10.3
	Cefepime	39	32	64	≥4 to ≤64	10.3
	Piperacillin-tazobactam	39	128	256	≥16 to ≤256	7.7
	Imipenem	38	16	16	≥1 to ≤16	21.1
	Meropenem	39	16	32	≥0.5 to ≤32	18.0
	Colistin	36	1	2	≥0.5 to ≤2	100

[a]MDR isolates of Enterobacterales (N = 286) and *Pseudomonas aeruginosa* (N = 39) were collected in Malaysia as part of the ATLAS program from 2013 to 2019. According to the ATLAS database, MDR is defined as resistance to any three of the following groups: cephalosporins, carbapenems, quinolones, aminoglycosides, polymyxins, monobactams, and penicillin combination (i.e., piperacillin-tazobactam).
[b]Percentage susceptibilities were interpreted according to CLSI breakpoints, except for tigecycline and colistin, which utilised US FDA and EUCAST breakpoints, respectively.
[c]Enterobacterales included *Klebsiella pneumoniae* (N = 143), *Escherichia coli* (N = 98), *Enterobacter* spp. (N = 24), *Proteus* spp. (N = 11), *Citrobacter* spp. (N = 9), and *Serratia marcescens* (N = 1).

phenotype was present in 286 (26.7%) of all Enterobacterales isolates. Among these, 97.1% were susceptible to ceftazidime-avibactam (MIC_{90}, 1 mg/L). Lower susceptibility rates were observed with all other antibacterials included in this study—from 21% (ceftazidime) to 96.2% (tigecycline). Separately, the MDR phenotype was present in 39 (11.7%) *P. aeruginosa* isolates. Ceftazidime-avibactam demonstrated a percentage of susceptibility of 44.7% (MIC_{90}, 256 mg/L), which was higher than that observed for all other agents except colistin (100% susceptible; MIC_{90}, 2 mg/L).

DISCUSSION

This study reports the *in vitro* antimicrobial susceptibility and the prevalence of resistant phenotypes among clinical isolates of Enterobacterales and *P. aeruginosa* collected in Malaysia from 2013 to 2019. Among Enterobacterales isolates, the highest percentages of susceptibility were seen with ceftazidime-avibactam (99.2%), meropenem (98.9%), and tigecycline (96.9%). The reduced percentage of susceptibility of colistin in the pooled Enterobacterales group is attributed to the presence of 73 isolates of *Proteus* spp. and 52 isolates of *Serratia* spp., which are intrinsically resistant to colistin (Table I).[15] When these bacterial species were excluded from the pooled Enterobacterales group, colistin demonstrated a percentage of susceptibility of 96.5%. Separately, *P. aeruginosa* isolates demonstrated the highest susceptibilities to colistin (95.6%), followed by ceftazidime-avibactam (93.1%) and cefepime (87.1%) (Table I).

In Malaysia, there are limited data on the *in vitro* activity of ceftazidime-avibactam against clinical isolates of Enterobacterales and *P. aeruginosa*. However, the recent 2015–2017 INFORM study (which included Asia-Pacific countries such as Australia, Japan, South Korea, Malaysia, Philippines, Taiwan, and Thailand) found that Enterobacterales and *P. aeruginosa* also displayed the highest susceptibility rates to ceftazidime-avibactam, colistin, and meropenem. In the INFORM study, 98.1% and 97.7% of Enterobacterales isolates were susceptible to ceftazidime-avibactam and meropenem, respectively. Among isolates of *P. aeruginosa*, 99.7% and 92.7% were susceptible to colistin and ceftazidime-avibactam, respectively.[8]

Specific to Malaysia, isolates of Enterobacterales collected from Asia-Pacific countries as part of the 2012–2015 INFORM programme exhibited a percentage of susceptibility of 99.7% to ceftazidime-avibactam; of note, this value is comparable to the rate of susceptibility reported in this study (99.2%). Across the Asia-Pacific countries studied, the percentage of susceptibility of Enterobacterales isolates to ceftazidime-avibactam ranged from 97% (Philippines) to 100% (Hong Kong and Korea). Ceftazidime-avibactam demonstrated a 94.7% susceptibility against isolates of *P. aeruginosa* collected in Malaysia, slightly higher (1.6%) compared with the rate of susceptibility in this study. Percentages of susceptibility ranged from 83.1% (Thailand) to 100% (Hong Kong) across the Asia-Pacific countries.[16]

It is important to consider MBL-producing isolates when evaluating the *in vitro* activity of ceftazidime-avibactam against clinical isolates of Enterobacterales and *P. aeruginosa*. In this study, the resistance of Enterobacterales isolates to ceftazidime-avibactam was only observed in eight isolates (0.8% [8/956] of all ceftazidime-avibactam-tested isolates), all of which were MBL-positive. All MBL-negative isolates of Enterobacterales, including resistant subsets of Enterobacterales isolates (i.e. ceftazidime-nonsusceptible, meropenem-nonsusceptible, and colistin-resistant phenotypes) (Table I-IV), were susceptible to ceftazidime-avibactam. This susceptibility may be attributed to the broad-spectrum coverage of ceftazidime-avibactam, which effectively inhibits Ambler Class A, C, and D.[7] In this study, 21 isolates (6.9% [21/303] of all ceftazidime-avibactam-tested isolates) of *P. aeruginosa* were resistant to ceftazidime-avibactam; 15 of which were MBL-positive. MBL-negative isolates of *P. aeruginosa* exhibited a 4.8% higher susceptibility (97.9%) to ceftazidime-avibactam compared with the pooled collection of *P. aeruginosa*. This result is consistent with that reported in the Asia-Pacific 2012–2015 INFORM study.[16]

Among resistant subsets in this study, tigecycline exhibited high percentages of susceptibility against ceftazidime-nonsusceptible (97.3%), meropenem-nonsusceptible (100%), and colistin-resistant (100%) isolates of Enterobacterales, whereas colistin demonstrated the highest percentages of susceptibility among ceftazidime-nonsusceptible (93.5%), meropenem-nonsusceptible (97.8%), and MDR (100%) isolates of *P. aeruginosa*. These outcomes were expected as tigecycline and colistin are widely recognised as 'last resort antibiotics' and remain highly active against carbapenem-resistant and MDR isolates.[17–19] However, there are growing reports of carbapenem and colistin resistance in Southeast Asia,[1] making ceftazidime-avibactam an important addition to the antimicrobial armamentarium. One study investigating the efficacy of ceftazidime-avibactam versus colistin for CRE infections revealed that ceftazidime-avibactam was associated with a 64% probability of better outcome (95% confidence interval, 57%–71%) compared with colistin.[20]

The increased prevalence of MDR isolates is a growing issue despite continuous efforts to increase awareness of antibiotic resistance.[21] In this study, MDR isolates accounted for 26.7% of all Enterobacterales isolates. Alarmingly, this is much higher than MDR Enterobacterales rates reported in the INFORM study, where only 9.1% of the isolates collected from Malaysia were identified as MDR. Furthermore, the rates of MDR Enterobacterales isolates ranged from 2.7% (Australia) to 19.4% (Thailand) across the Asia-Pacific countries studied.[16]

Among *P. aeruginosa* isolates in this study, 11.7% were MDR. According to the results from the Asia-Pacific 2012–2015 INFORM study, only 7.1% of *P. aeruginosa* isolates collected in Malaysia were MDR, while rates of MDR *P. aeruginosa* in other Asia-Pacific countries varied between 5.7% (Australia) and 24% (Philippines).[16] In this study, ceftazidime-avibactam remained the most active agent (97.1%) against MDR isolates of Enterobacterales and second most active agent (44.74%), after colistin, against MDR isolates of *P. aeruginosa*. It is important to note that the isolates collected from Malaysia in the Asia-Pacific 2012–2015 and 2015–2017 INFORM studies were included in this study as well.

One of the limitations of this study is the low number of isolates collected over the 7-year period, which may be insufficient to establish the prevalence of resistant subsets in Malaysia. Furthermore, antibacterial surveillance data were not collected from Malaysia in the year 2017 and were not available in the ATLAS database. This gap year makes it difficult to establish the prevalence and pattern of antibiotic resistance over time. In addition, the use of ceftazidime-avibactam was not yet approved in Malaysia when the data was collected (2013–2019), and thus the local resistance pattern of ceftazidime-avibactam cannot be determined as there had not been clinical usage in the country. Nevertheless, as there have been limited antimicrobial surveillance studies in Malaysia that reports susceptibility data of antibiotics, the results of this study will serve as a valuable resource to inform healthcare professionals of the local antimicrobial activities of commonly used antibiotics and to guide their optimal use. With its recent entry into the Malaysian healthcare system, more susceptibility data on the use of ceftazidime-avibactam among Enterobacterales and *P. aeruginosa* will be available in the near future.

CONCLUSION

Clinical isolates of Enterobacterales and *P. aeruginosa* collected from hospitals in Malaysia from 2013 to 2019 were highly susceptible to ceftazidime-avibactam. Additionally, ceftazidime-avibactam consistently displayed comparable, and often, higher percentages of susceptibility as compared with meropenem at all outcome measures. This shows that ceftazidime-avibactam is a valuable alternative to carbapenems. Ceftazidime-avibactam exhibited potent *in vitro* activity against MBL-negative isolates of Enterobacterales and *P. aeruginosa*, including isolates with ceftazidime-nonsusceptible, meropenem-nonsusceptible, and colistin-resistant phenotypes, making it a potential alternative to last-resort antimicrobial agents such as colistin and tigecycline. Furthermore, ceftazidime-avibactam demonstrated the highest percentage of susceptibility against MDR isolates of Enterobacterales. Based on the potent *in vitro* activity of ceftazidime-avibactam in Malaysia, and its established clinical efficacy,[22–26] ceftazidime-avibactam should be considered in the treatment of indicated infections caused by susceptible strains of aerobic Gram-negative pathogens.

DECLARATION OF CONFLICT OF INTEREST

Salvinder S, Chen VSY are employees of Pfizer Malaysia Sdn Bhd.

ETHICAL APPROVAL

Individual patient's informed consent was not required as this study was an antimicrobial surveillance programme (NMRR-18-1271-39749). Ethical approval for this study was obtained from MREC, Ministry of Health Malaysia.

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