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FULL PAPER

Extent and Resistance Patterns of Gram-negative Bacteria Isolated From 13 Hospitals in Shaoxing, Zhejiang Province

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SUMMARY

Gram-negative bacteria are increasingly recognized as the sauce of severe infections. In recent years, epidemiological data has indicated that the drug resistance rate of Gram-negative bacteria has significantly increased. We analyzed the epidemiological surveillance data of gram-negative bacteria in Shaoxing City in 2021 by retrospectively collecting drug susceptibility data of *Escherichia coli*, *Klebsiella pneumoniae*, *Proteus mirabilis*, *Enterobacter cloacae*, *Pseudomonas aeruginosa*, *Acinetobacter baumannii*, and *Burkholderia cepacian* from thirteen tertiary hospitals. A total of 24,142 strains were collected from thirteen hospitals. The isolation rates of *E. coli*, *K. pneumoniae*, *P. aeruginosa*, *A. baumannii*, *P. mirabilis*, *E. cloacae,* and *B. cepacian* were 29.25%, 18.83%, 11.03%, 8.43%, 3.80%, 3.12%, and 0.75%, respectively. Among them, 2.86% were carbapenem-resistant *E. coli*, 12.98% were CRKP, 31.27% were CRPA, and 34.77% were CRAB. Carbapenem-resistant *Enterobacterales* were more sensitive to ceftazidime-avibactam and polymyxin. The drug resistance rates of *P. aeruginosa* and *A. baumannii* to polymyxin were 0 and 1.3%, but the resistance rates to ceftazidime-avibactam were 10.5% and 26.0%, respectively. Based on results from epidemiological data, CRKP had a high isolation rate and non-fermenting bacteria had a high resistance rate to ceftazidime-avibactam. All hospitals should strengthen monitoring and enact continuous intervention to reduce the generation and spread of drug-resistant bacteria.

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INTRODUCTION

Gram-negative bacteria such as *Escherichia coli*, *Klebsiella pneumoniae*, *Pseudomonas aeruginosa*, and *Acinetobacter species* are the most common organisms involved in hospital-acquired infections (Agarwal *et al.*, 2018; Brink, 2019; Holmes CL, 2021; Li *et al.*, 2022). In recent years, multidrug-resistant bacteria, especially carbapenem-resistant *Enterobacterales* (CRE), have shown rapid growth, which has created concern regarding clinical anti-infection treatments (Brink, 2019; Doi, 2019). The main drug resistance mechanisms are KPC-2, NDM, and OXA-48-like carbapenemase production (Han *et al.*, 2020). Carbapenem-resistant *Pseudomonas aeruginosa* (CRPA) and *Acinetobacter baumannii* (CRAB) infections remain major causes of high mortality, predominantly in hospital-acquired infections (Brink, 2019). CRPA infection occurs predominantly due to a chromosome mutation leading to a high expression of efflux pumps, while CRAB infection mainly produces metallo-β-lactamase (MBL) and OXA-types (Eichenberger and Thaden, 2019).

Given the clinical importance of gram-negative bacteria and their high drug resistance rate in Zhejiang Province (Hu *et al.*, 2020), a bacterial antibiotic resistance monitoring platform was established in Shaoxing City in 2018. Thus, a better understanding and monitoring of these isolates could help limit the spread of antimicrobial resistance and provide a reference for empirical clinical antibiotic use.

Herein, we investigated the prevalence of gram-negative bacteria from 13 hospitals in Shaoxing, Zhejiang, to understand the in vitro activities of carbapenems, polymyxin, ceftazidime-avibactam, and other antibiotics; we also aimed to provide a reference for controlling the spread of multidrug-resistant bacteria.

Key words:
Gram-negative bacteria, carbapenem-resistant enterobacteriaceae, antibiotic, ceftazidime-avibactam, Polymyxin.

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MATERIALS AND METHODS

Data collection

We analyzed 24,142 consecutive and non-duplicated isolates (the same strain was isolated multiple times from the same patient, and the first isolate was selected) from 13 hospitals in Shaoxing City, Zhejiang province in 2021. All hospitals involved in the study are secondary or tertiary hospitals and are accredited to perform pathogen identification and antimicrobial susceptibility testing. The hospitals are distributed across Shaoxing City, including Shaoxing People's Hospital, Shaoxing Second Hospital, Shaoxing Maternal and Child Health Hospital, Shaoxing Central Hospital, Affiliated Hospital of Shaoxing University, Shaoxing Seventh People's Hospital, Shangyu People's Hospital, Zhuji People's Hospital, Zhuji Second People's Hospital, Shengzhou People's Hospital, The People's Hospital of Xinchang, Shaoxing Hospital of Traditional Chinese Medicine, Shaoxing Keqiao District Hospital of Traditional Chinese Medicine. Isolates were identified by the Vitek 2 Compact system (bioMerieux, France), VITEK-MS automated microbial identification system (bioMerieux, France), or Matrix-assisted laser desorption/ionization time-of-flight mass spectrometry (Bruker Daltonics, Bremen, Germany) as per the manufacturers' instructions.

Antimicrobial susceptibility testing

Antimicrobial susceptibility testing of the isolates for common clinically used antibiotics was performed using the Vitek 2 Compact system (bioMerieux, France), the AST-N 334 model was used for *Enterobacterales*, and AST-N335 was used for non-fermentative bacteria. This analysis was conducted at Shaoxing People's Hospital, Affiliated Hospital of Shaoxing University, Shaox-

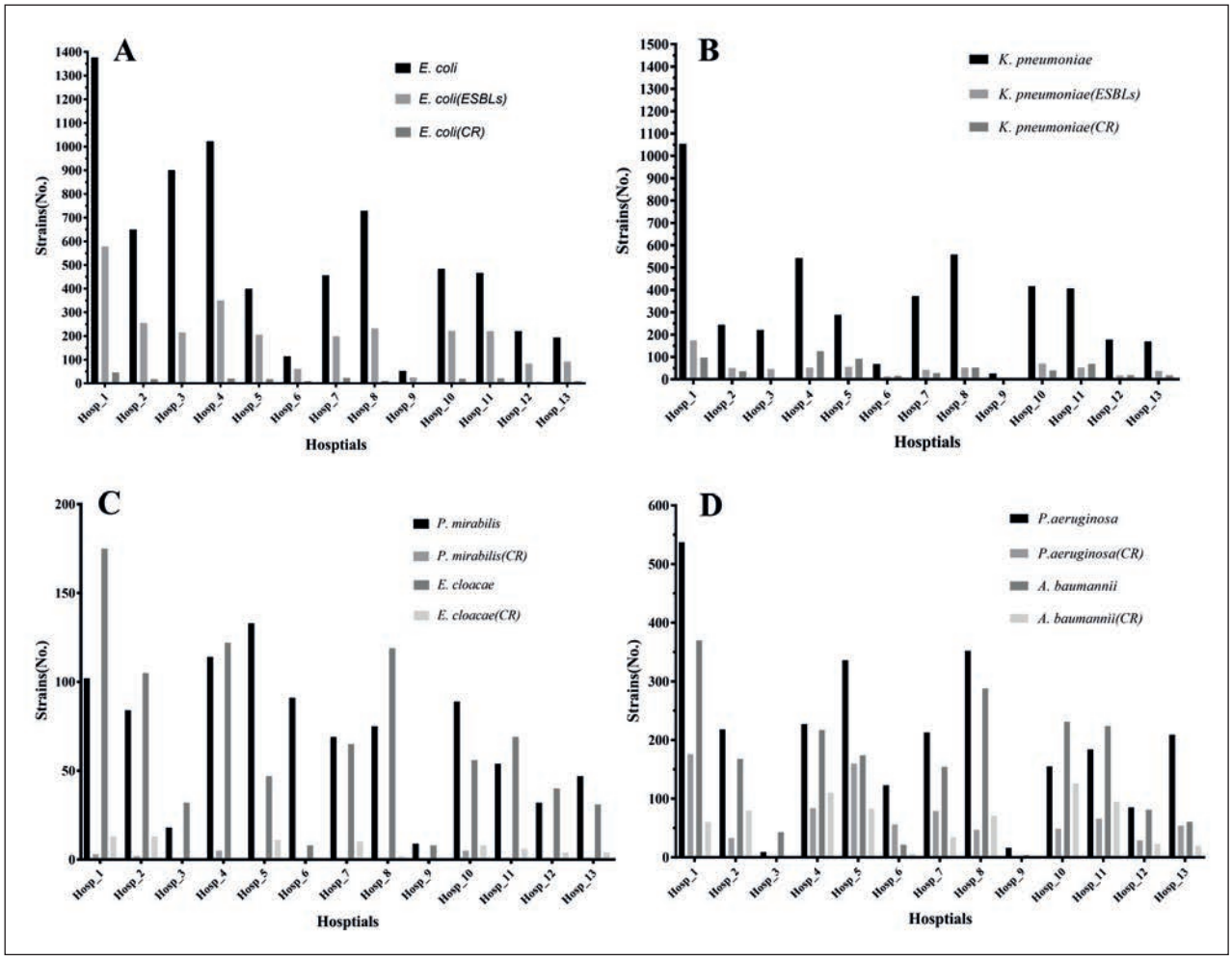

Figure 1 - *Distribution of gram-negative bacteria.*
The detection rate of E. coli (A) and K. pneumoniae (B), and the proportion of production of Extended-Spectrum β-lactamase and carbapenem-resistant strains in 13 hospitals. The detection rate of P. mirabilis (C), E. cloacae (C), P. aeruginosa (D), and A. baumannii (D), and the proportion of carbapenem-resistant strains in 13 hospitals. Diamonds and dashed lines indicate the number of beds in the 13 hospitals; hosp_1 to hosp_13 were 1827, 1040, 600, 1000, 1400, 700, 850, 1500, 285, 1000, 1112, 1000 and 400 beds, respectively.

ing Hospital of Traditional Chinese Medicine, Shengzhou People's Hospital, and The People's Hospital of Xinchang. AST-GN13 and AST-GN16 models of the Vitek compact system (bioMerieux, France) were used by other hospitals for bacterial susceptibility testing. The Kirby-Bauer method was used to detect Fosfomycin trometamol (200 µg; Oxoid Ltd., UK) susceptibility, according to the Clinical and Laboratory Standards Institute (CLSI) protocol. The broth microdilution method was used to detect ceftazidime avibactam (Biokont Ltd., Wenzhou, Zhejiang) susceptibility. To allow comparison of the identification and susceptibility results among hospitals, the same reference strain and standard operating procedures were used for each method, as suggested by the National Health Commission of the People's Republic of China. The susceptibility results were interpreted according to annual CLSI-M100 documents (https://www.clsi.org/). *K. pneumoniae* ATCC 700603, *E. coli* ATCC25922, and *P. aeruginosa* ATCC 27853 were used as quality control strains.

Statistical analysis

Data were collected using WHONET5.6 software (http://www.whonet.org.cn/news/19_509.html). Statistical software (Excel 2016, Microsoft, Redmond, Washington, USA) was used for data analysis after data were exported and verified. Drug susceptibility data were expressed as percentages.

RESULTS

Distribution of gram-negative bacteria

A total of 15,754 *Enterobacterales* strains, including 1,487 (9.44%) CRE, were isolated from 13 hospitals in 2021. The resistance rate of *Enterobacterales* to the compound enzyme inhibitors, amikacin, fosfomycin trometamol, carbapenem, tigecycline, and polymyxin was less than 10%.

The isolation rate of carbapenem-resistant *E. coli* was 7.89% in Hosp_5 and was less than 5% in other hospitals (*Figure 1A*). *E. coli* producing extended-spectrum beta-lactamases (ESBLs) was more than 50% in Hosp_5 and Hosp_6, and less than 50% in other hospitals (*Figure 1A*). The prevalence of *K. pneumoniae*-producing ESBLs (ESBL-KP) was less than 25% in all hospitals (*Figure 1B*). The carbapenem-resistant *K. pneumoniae* (CRKP) isolation rates of Hosp_2, Hosp_3, Hosp_6, Hosp_9, and Hosp_13 were higher

Table 1 - *In vitro activities of antibiotics tested against E. coli, ESBLs-E. coli and CR-E. coli.*

Antibiotics	*MIC Range*	*E. coli*				*ESBLs- E. coli*				*CR- E. coli*			
		R(%)	MIC_{50}	MIC_{90}	*No.*	*R(%)*	MIC_{50}	MIC_{90}	*No.*	*R(%)*	MIC_{50}	MIC_{90}	*No.*
Ampicillin/ sulbactam	1-64	48.4	16	64	1472	65.5	32	64	663	96	32	64	25
Cefuroxime	0.5-128	52.6	64	128	2076	98.8	128	128	807	97.7	128	128	43
Cefazolin	2-.128	40.9	4	64	2464	98.5	64	64	823	95	64	128	20
Ceftriaxone	0.125-128	45.4	1	128	6994	98.3	64	128	2730	72.8	64	128	202
Ceftazidime	0.06-128	18.9	1	32	4569	34.7	8	32	1868	81.8	64	128	77
Cefepime	0.06-128	18.2	1	16	6532	36.7	4	64	2481	78.7	32	64	89
Cefoxitin	2-128	8.6	4	16	5056	11.5	4	32	2070	36.1	4	128	166
Aztreonam	0.5-128	26.1	1	64	4007	58.0	16	64	1532	42.5	4	64	153
Piperacillin/ tazobactam	2-256	2.3	4	4	7031	2.3	4	8	2726	31.7	4	256	199
Cefoperazone/ sulbactam	4-128	3.7	8	16	3121	6.0	8	32	1208	82	64	128	50
Ceftazidime/ avibactam	–	1.9	–	–	478	0	–	–	192	4.2	–	–	24
Amikacin	1-128	1.0	2	4	6941	1.8	2	4	2732	5.6	2	8	198
Levoflfloxacin	0.06-16	44.8	1	16	7019	66.3	8	16	2719	61.4	8	16	202
Ciproflfloxacin	0.125-8	51.1	1	4	3997	73.3	4	8	1527	64.5	2	4	152
Ertapenem	0.06-16	1.0	0.25	0.5	6962	0.5	0.25	0.5	2728	40.4	0.5	16	193
Imipenem	0.125-32	2.3	0.5	1	7061	2.3	0.5	1	2725	86.5	24	32	200
Meropenem	0.125-1	2.3	0.125	0.25	608	0.5	0.125	0.125	192	53.8	–	–	13
Fosfomycin/ trometamol	–	4.3	–	–	512	7.4	–	–	244	23.1	–	–	13
Tobramycin	0.5-32	8.0	1	8	3997	14.3	1	16	1531	11.9	1	16	151
Sulfamethoxazole/ trimethoprim	1-512	46.1	16	256	6552	58.1	16	256	2482	52.4	16	256	191
Tigecycline	0.25-16	0.1	0.5	0.5	5574	0.1	0.5	0.5	2066	0.6	0.5	0.5	176
Polymyxin	0.25-1	–	–	–	–	–	–	–	–	0	0.5	1	20

'-', not detected.

than 20%, with the highest at 23.08% in Hosp_9 (*Figure 1B*). Although the rate of *Enterobacter cloacae* isolation was low, the carbapenem resistance (CR) rate was high in certain hospitals (23.4% in Hosp_5) (*Figure 1C*).

CRPA and CRAB were not detected in Hosp_3 and Hosp_9. In addition, the detection rate of CRPA was the lowest in Hosp_8, at 13.35%, while in other hospitals it was 30-40% (*Figure 1D*). The lowest detection rate of CRAB was in Hosp_1, at 16.22%, whereas the detection rate in other hospitals had a wide range of 20-55% (*Figure 1D*).

Drug susceptibility of E. coli

E. coli, *E. coli* producing ESBL (ESBL-*E. coli*), and CR-*E. coli* isolation rates were 29.25%, 38.69%, and 2.86%, respectively. ESBLs-*E. coli* demonstrated good sensitivity to cefoxitin, β-lactamase inhibitor complex, amikacin, carbapenems, fosfomycin trometamol, and tigecycline.

Alternatively, CR-*E. coli* showed high sensitivity to amikacin, tigecycline, ceftazidime-avibactam, and polymyxin (*Table 1*).

Drug susceptibility of K. pneumoniae

K. pneumoniae, ESBLs- *K. pneumoniae* (ESBLs-KP) and CRKP isolation rates were 18.83%, 14.74%, and 12.98%, respectively. ESBLs- KP demonstrated high sensitivity to cefoxitin, β-lactam combinations, amikacin, carbapenems, fosfomycin trometamol, and tigecycline, whereas CRKP exhibited high sensitivity only to amikacin, ceftazidime avibactam and polymyxin (*Table 2*).

Resistance of other enterobacteria and non-fermentative bacteria

A total of 917 (3.80%) *P. mirabilis* and 753 (3.12%) *E. cloacae* strains were isolated. No cefoperazone-sulbactam-resistant strains were isolated from *P. mirabilis*, and imipenem and meropenem resistance rates were 6.3% and 3.3%, respectively. *E. cloacae* had the lowest resistance rate to amikacin (1.1%), followed by meropenem (1.2%); the resistance rate to imipenem was 6.0% (*Table 3*).

A total of 2,664 (11.03%) strains of *P. aeruginosa* and 2,036 (8.43%) strains of *A. baumannii* were isolated; the CRPA and CRAB were 25.7% and 27.35%, respec-

Table 2 - *In vitro activities of antibiotics tested against K. pneumoniae, ESBLs-KP and CRKP.*

Antibiotics	*MIC Range*	*KP*				*ESBLs-KP*				*CRKP*			
		R(%)	MIC_{50}	MIC_{90}	*No.*	*R(%)*	MIC_{50}	MIC_{90}	*No.*	*R(%)*	MIC_{50}	MIC_{90}	*No.*
Ampicillin/ sulbactam	1-64	38.8	8	64	891	84.7	32	64	163	96	32	64	177
Cefuroxime	0.5-128	25.8	4	128	1681	92.8	128	128	235	99.4	64	128	161
Cefazolin	2-128	24.5	4	64	1187	95.0	64	64	181	93	64	64	86
Ceftriaxone	0.125-128	23.7	1	64	4507	93.0	64	128	670	85.8	64	128	586
Ceftazidime	0.06-128	18.8	0.5	64	3122	42.8	8	64	477	88	64	128	440
Cefepime	0.06-128	14.6	1	32	4122	40.1	2	64	621	76.6	32	128	508
Cefoxitin	2-128	12.3	4	64	3216	20.3	4	64	508	71.4	64	128	350
Aztreonam	0.5-128	19.3	1	64	2330	66.1	16	64	357	73.4	64	128	334
Piperacillin/ tazobactam	2-256	11.6	4	128	4527	16.5	4	128	666	79.8	128	256	590
Cefoperazone/ sulbactam	4-128	11.0	8	64	2256	21.0	16	128	314	87.8	64	128	262
Ceftazidime/ avibactam	–	4.7	–	–	300	0	–	–	51	4	–	–	50
Amikacin	1-128	5.8	2	2	4475	5.8	2	4	670	43.8	4	128	577
Levoflfloxacin	0.06-16	17.3	0.25	8	4537	44.5	1	16	670	76.3	8	16	590
Ciproflfloxacin	0.125-8	27.9	0.25	4	2320	74.5	1	4	357	73.6	4	8	333
Ertapenem	0.06-16	8.3	0.25	0.5	4426	9.2	0.5	1	654	81.9	8	16	524
Imipenem	0.125-32	10.9	1	8	4545	8.2	0.5	2	657	93.3	16	32	582
Meropenem	0.125-32	8.1	0.125	16	454	3.9	0.25	32	51	79.2	32	32	24
Fosfomycin/ trometamol	–	4.8	–	–	418	11.5	–	–	78	51.7	–	–	29
Tobramycin	0.5-32	8.0	1	8	2317	15.4	2	16	357	43.5	8	32	333
Sulfamethoxazole/ trimethoprim	1-128	20.1	16	128	4119	54.1	16	256	601	50.7	16	256	503
Tigecycline	0.25-16	5.8	1	2	3579	11.4	2	8	490	34.6	2	8	387
Polymyxin	–	–	–	–		–	–	–	–	0	0.5	1	35

'-', not detected.

Table 3 - *In vitro activities of antibiotics tested against Proteus mirabilis and Enterobacter cloacae.*

Antibiotics	*P. mirabilis*					*E. cloacae*				
	MIC Range	*R(%)*	MIC_{50}	MIC_{90}	*No.*	*MIC Range*	*R(%)*	MIC_{50}	MIC_{90}	*No.*
Ampicillin/sulbactam	1-64	41.3	16	64	300	2-32	48.2	16	32	110
Cefuroxime	0.5-128	39.1	2	128	207	0.5-128	35.6	16	128	250
Cefazolin	2-128	51.9	64	128	289	2-128	97.6	64	128	461
Ceftriaxone	0.125-128	38.1	1	128	909	0.125-128	30	1	64	723
Ceftazidime	0.06-128	10.3	0.5	16	633	0.06-128	26.1	1	64	494
Cefepime	0.06-128	9.1	1	8	834	0.06-128	8.8	1	8	683
Cefoxitin	2-128	4.5	4	16	554	2-128	96.6	64	128	438
Aztreonam	0.5-128	9.2	1	2	587	0.5-128	23	1	64	505
Piperacillin/tazobactam	2-256	0.7	4	4	916	2-256	8.7	4	64	750
Ceftazidime/avibactam	–	1.5	–	–	67	–	7.1	–	–	98
Cefoperazone/sulbactam	4-32	0	8	8	340	4-128	8.5	4	32	282
Amikacin	1-128	5.9	2	16	825	1-128	1.1	2	2	752
Levoflfloxacin	0.06-16	44.9	1	16	917	0.06-16	12.1	0.25	4	753
Ciproflfloxacin	0.125-8	56.8	2	8	588	0.125-8	19.0	0.25	4	505
Ertapenem	0.06-16	1.1	0.25	0.5	894	0.06-16	7.7	0.5	0.5	703
Imipenem	0.25-8	6.3	0.5	4	558	0.125-32	6.0	1	2	736
Meropenem	0.125-1	3.3	0.125	1	61	0.125-1	1.2	0.125	0.5	82
Fosfomycin/trometamol	–	22.5	–	–	40	–	4.5	–	–	67
Tobramycin	0.5-32	22.7	2	32	587	0.5-32	4.4	1	8	505
Sulfamethoxazole/ trimethoprim	0.25-512	60.2	16	256	829	0.125-512	16.4	12	24	696
Tigecycline	0.25-16	10.7	4	8	615	0.25-16	3.0	1	2	529

'-', not detected.

tively. The resistance rates of *P. aeruginosa* and *A. baumannii* to polymyxin were 0 and 1.3%, respectively, and the resistance rates to ceftazidime-avibactam were 10.5% and 26.0%, respectively. Furthermore, the tigecycline resistance rate of A. baumannii was 2.1% (*Table 4*).

Drug susceptibility of Burkholderia cepacia

A total of 181 (0.75%) strains of *B. cepacia* strains were isolated, of which no ceftazidime-avibactam-resistant strains were found. The drug resistance rates for sulfamethoxazole and ceftazidime were 8.5% and 12.5%, respectively (*Table 4*).

DISCUSSION

In recent years, carbapenem-resistant gram-negative bacilli, especially carbapenem-resistant *Enterobacterales* (CRE), have become a global problem (Holmes CL, 2021). The bacterial drug resistance rates from 13 hospitals in Shaoxing in 2021 showed that the drug resistance rates of *E. coli* and *K. pneumoniae* to carbapenems were similar to or lower than those of the CHINET monitoring results (Hu *et al.*, 2022). The positive rates of ESBLs detection in *E. coli* and *K. pneumoniae* were lower than those of CHINET (Hu *et al.*, 2022). With regard to the CRE strain, it should be noted that when carbapenemases and other ESBLs are present in the same CRE strain, the traditional automated drug sensitivities using CLSI phenotypic methods to detect ESBLs may produce false negatives (Hu *et al.*, 2016). In this case, using third-generation cephalosporins such as ceftriaxone may be a more accurate measure of the positive rate of ESBLs. Currently, there are certain differences in the recommendations provided by China and other countries in the selection of antibiotic therapy for ESBLs- producing strains; however, carbapenems are still used as the preferred drug for the treatment of severe infection (Tamma *et al.*, 2021). It is worth noting that the isolation rate of CRKP in some hospitals is high; therefore, it is recommended that the hospital infection management department should actively intervene to prevent the emergence of these drug-resistant bacteria. In addition, the amikacin resistance rate of CRKP across 13 hospitals was significantly higher than that found in 6 hospitals in 2019; this difference may be related to the increased use of amikacin as a combined treatment for multidrug-resistant bacteria (Liang *et al.*, 2022).

P. mirabilis is another pathogen with a high detection rate in *Enterobacterales*. It has a high drug resistance rate to imipenem (6.3%), with an intermediary rate of 13.3%, which is higher than the surveillance results in China (Hu *et al.*, 2022). *P. mirabilis* is naturally insensitive to imipenem; this insensitivity may be due to the loss of porins and functional defects of

Table 4 - *In vitro activities of antibiotics tested against Pseudomonas aeruginosa, Acinetobacter baumannii and Burkholderia cepacian.*

Antibiotics	*P. aeruginosa*					*A. baumannii*					*B. cepacian*				
	MIC Range	R(%)	MIC_{50}	MIC_{90}	No.	MIC Range	R(%)	MIC_{50}	MIC_{90}	No.	MIC Range	R(%)	MIC_{50}	MIC_{90}	No.
Ceftazidime	0.06-128	18.8	4	64	2012	0.5-128	37.9	8	64	1387	1-128	12.5	2	32	96
Cefepime	0.06-128	11.6	2	32	2429	0.06-128	33.5	4	64	1861					
Aztreonam	1-64	15.1	4	32	556	16-128	80.4	32	64	270					
Piperacillin/ tazobactam	2-256	15.3	8	128	2575	2-256	38.6	8	128	982					
Ceftazidime/ avibactam	–	10.5	–	–	323	–	26.0	–	–	169	–	0	–	–	165
Cefoperazone/ sulbactam	4-128	16.1	8	64	1096	4-128	20.4	8	64	881	4-128	22.8	16	128	55
Amikacin	1-128	2.4	2	8	2634	1-4	18.2	1	2	247					
Levoflfloxacin	0.06-16	21.0	0.5	8	2664	0.06-16	25.9	0.25	8	2025	0.25-16	46.2	2	16	181
Ciproflfloxacin	0.125-8	19.8	0.25	4	2626	0.125-8	35.9	0.25	4	1811					
Sulfame-thoxazole/ trimethoprim											1-64	8.5	2	16	164
Minocycline											0.5-32	16.7	8	32	47
Tobramycin	0.5-32	5.7	1	1	2550	0.5-32	17.3	1	16	1810					
Imipenem	0.125-32	25.7	2	32	2735	0.125-32	34.4	1	16	2036					
Meropenem	0.125-32	20.8	0.5	16	1329	0.125-32	35.8	0.25	16	872	1-32	76.6	4	32	46
Tigecycline						0.25-16	2.1	0.5	4	1524	0.25-16	52.9	8	16	135
Polymyxin	0.5-2	0	0.5	2	218	0.5-16	1.3	0.5	2	230					

'-', not detected.

penicillin-binding proteins (Girlich *et al*., 2020), or because it produces β-lactamase, *K. pneumoniae* carbapenemase (KPC), and OXA-23(Potron *et al*., 2019; Yang *et al*., 2020; Lombes A, 2022). Currently, most automated drug sensitivity meters may falsely identify resistance when detecting the imipenem sensitivity of *Proteobacteria*. Therefore, it is advisable to use the disk diffusion or broth dilution methods to review imipenem susceptibility results. The drug resistance rates of the two β-lactam-β-lactamase inhibitor combinations, namely cefoperazone-sulbactam and piperacillin-tazobactam, to *P. mirabilis* were lower than those of the other two carbapenems, namely ertapenem and meropenem. This drug resistance was also observed to be lower than the national surveillance results (Hu F.P. *et al*., 2022). Therefore, according to pharmacokinetic/pharmacodynamic modeling, these two β-lactam-β-lactamase inhibitor combinations may be used for the treatment of infections caused by *P. mirabilis*.

The rate of CR of *E. cloacae* in the observed geographical region is high, constituting more than 20% of total *E. cloacae* strains in some hospitals; this high resistance to carbapenem in *E. cloacae* may be attributed to the total number of isolates being small, which may lead to insufficient attention to its resistance. *E. cloacae* also possess multiple drug resistance mechanisms. Polymyxin-resistant strains have also been found in the Zhejiang province, and plasmid-mediated drug resistance is a potential factor leading to horizontal transmission (Liu *et al.*, 2021). Susceptibility to polymyxin was not detected in this study, and the status of drug resistance in this area is not clear at present. Therefore, it is necessary to strengthen monitoring in the future.

Ceftazidime-avibactam is a new β-lactam mixture approved by the United States Food and Drug Administration (FDA) for the treatment of complex intra-abdominal infections, hospital-acquired pneumonia, and ventilator-associated pneumonia caused by CRE (Yahav *et al.*, 2020). The main antibacterial mechanism of avibactam is the inhibition of various types of β-lactamases. These enzymes include class A enzymes (e.g., KPC), class C enzymes, and some class D enzymes (e.g., OXA-48); nonetheless, they have no inhibitory effect on class B metalloenzymes, thereby pro-

tecting the bactericidal effect of ceftazidime (Yahav *et al*., 2020). As a first-line drug for carbapenem-resistant *Enterobacterales*, ceftazidime-avibactam was found to be efficacious against these *Enterobacterales*. Our single-center study found that this was mainly related to the production of NDM, IMP, and other metalloenzymes (data not shown). The combined drug susceptibility test of CRE strains showed that ceftazidime-avibactam had different degrees of synergistic effects with fosfomycin and aztreonam, providing laboratory evidence for clinical anti-infection.

The resistance rate of non-fermentative bacteria to ceftazidime-avibactam was higher than that of *Enterobacterales*; in particular, the resistance rate of *A. baumannii* reached 26%, which is higher than CHINET and SMART results in China (Hsueh *et al*., 2019; Guo *et al*., 2022). The resistance rates of *P. aeruginosa* and *A. baumannii* to polymyxin remained low. Although colistin has nephrotoxic and neurotoxic effects, it is the first-line treatment option for multidrug-resistant bacteria when facing increasingly severe drug resistance (Zhang *et al.*, 2020).

B. cepacia is naturally resistant to many antimicrobial agents, including carbapenems, polymyxin, and aminoglycosides (Sfeir, 2018). *B. cepacia* isolation is increasing, especially in pulmonary diseases such as cystic fibrosis, which is difficult to treat (Lord *et al*., 2020). At present, there is a lack of large-scale epidemiological investigations and randomized control trials on treatments (Lord *et al.*, 2020). An in vitro prospective multicenter study on *B. cepacia* infection in patients with cystic fibrosis in Germany showed that ceftazidime-avibactam had good activity (Schaumburg *et al*., 2022). In our study, *B. cepacia* showed a low resistance rate to ceftazidime-avibactam, ceftazidime, minocycline, and sulfamethoxazole, suggesting these drugs could be used for the treatment of *B. cepacia* infection.

In summary, our research demonstrated that the isolation rates and drug resistance of bacterial strains in different hospitals in the same geographical area are different. While focusing on the continuous growth of multidrug-resistant *Enterobacterales* and maintaining a high drug resistance rate of non-fermenting bacteria, it is necessary to pay attention to the CR of relatively rare bacteria, such as *P. mirabilis*. Hospitals should take targeted measures to prevent the emergence of drug-resistant bacteria according to their unique isolation situation.

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Data Availability

All data analyzed during the study are included in this published article.

Author contributions

All authors contributed to the study's conception and design. Material preparation, data collection, and analysis were performed by MC, XJ, and LL. The first draft of the manuscript was written by YQ. QL commented on previous versions of the manuscript. GF read and approved the final manuscript.

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Ethical Statement

This study is conducted on already available data from the Shaoxing antimicrobial resistance Surveillance platform. Ethical approval was approved by the Ethics Committee of Shaoxing People's Hospital (Number: 110).

Conflict of Interest

No potential conflict of interest was reported by the authors.

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