Risk Factors for Carbapenem-Resistant *Pseudomonas aeruginosa*, Zhejiang Province, China

Yan-Yan Hu, Jun-Min Cao, Qing Yang, Shi Chen, Huo-Yang Lv, Hong-Wei Zhou, Zuowei Wu, Rong Zhang

Carbapenem-resistant *Pseudomonas aeruginosa* (CRPA) is a public health concern worldwide, but comprehensive analysis of risk factors for CRPA remains limited in China. We conducted a retrospective observational study of carbapenem resistance in 71,880 *P. aeruginosa* isolates collected in Zhejiang Province during 2015–2017. We analyzed risk factors for CRPA, including the type of clinical specimen; the year, season, and region in which it was collected; patient information, including age, whether they were an outpatient or inpatient, and whether inpatients were in the intensive care unit or general ward; and the level of hospital submitting isolates. We found CRPA was more prevalent among isolates from patients ≥60 years of age and in inpatients, especially in intensive care units. In addition, specimen types and seasons in which they were collected were associated with higher rates of CRPA. Our findings can help hospitals reduce the spread of *P. aeruginosa* and optimize antimicrobial drug use.

The bacterium *Pseudomonas aeruginosa* is a particularly concerning nosocomial pathogen because of its intrinsic resistance to multiple antimicrobial agents (*1*,*2*). In 2016, surveillance of nosocomial infections in China showed *P. aeruginosa* was the fifth most frequently isolated pathogen, accounting for 8.7% of hospital-acquired infections, and the fourth most common (8.0%) in Zhejiang Province (*3*,*4*). *P. aeruginosa* often causes severe infections and results in high rates of illness and death among infected patients (*1*). A survey in the United States revealed that *P. aeruginosa* was the second-leading cause of nosocomial pneumonia (14%–16%), third main contributor of urinary tract infections (7%–11%), and seventh major cause of bloodstream infections (2%–6%) (*5*,*6*).

Author affiliations: Second Affiliated Hospital of Zhejiang University, School of Medicine, Hangzhou, China (Y.-Y. Hu, H.-W. Zhou, R. Zhang); First Affiliated Hospital of Zhejiang University, School of Medicine, Hangzhou (Q. Yang); Zhejiang Provincial Hospital of Traditional Chinese Medicine, Hangzhou (J.-M. Cao, H.-Y. Lv); Hangzhou Third People's Hospital, Hangzhou (S. Chen); Iowa State University, Ames, Iowa, USA (Z. Wu)

DOI: https://doi.org/10.3201/eid2510.181699

Carbapenems are the most effective antimicrobial agents against severe *P. aeruginosa* nosocomial infections involving bacteria producing cephalosporinase AmpC or extended-spectrum β-lactamases (*7*). However, *P. aeruginosa* has become increasingly resistant to carbapenems. A 2016 World Health Organization survey ranked carbapenem-resistant *P. aeruginosa* (CRPA) as the second most critical-priority bacterium among 20 antimicrobial-resistant bacterial species (*8*).

CHINET surveillance (http://www.chinets.com) revealed that CRPA in Zhejiang Province, China, increased annually from 22% in 2015 to 38.67% in 2017 and that Zhejiang had the highest rates of CRPA of all provinces in China in 2017. In addition, Zhejiang reported the local emergence of carbapenem-resistant *Klebsiella pneumoniae* carbapenemase–producing *P. aeruginosa* in 2015 (*9*). Given the clinical importance of CRPA, we analyzed short-term trends and various risk factors related to the occurrence of carbapenem resistance in *P. aeruginosa* in Zhejiang, as well as co-resistance to other commonly used antimicrobial agents.

Materials and Methods

Bacterial Species and Strain Identification

We obtained data from the Annual Review of Hospital Infection Resistance Survey in Zhejiang Province, collected during 2015–2017 (*4*,*10*,*11*). Each of the ≥78 secondary or tertiary hospitals enrolled in the surveillance each year (Table 1) imported and shared data of routine antimicrobial susceptibility testing using WHONET 5.6 software (http://www.whonet.org). Enrolled hospitals are distributed in 11 cities of Zhejiang Province: Hangzhou, Huzhou, Jiaxing, Shaoxing, Ningbo, Taizhou, Jinhua, Quzhou, Lishui, Wenzhou, and Zhoushan. Each hospital laboratory cultured isolates on blood agar plates and identified antimicrobial-resistant strains by using matrix-assisted laser desorption/ionization time of flight (MALDI-TOF) mass spectrometry, the VITEK 2 Compact system (bioMérieux, https://www.biomerieux.com), or the Phoenix 100 system (Becton Dickinson, https://www.bd.com).

Table 1. *Pseudomonas aeruginosa* isolates obtained from hospitals in Zhejiang Province, China, 2015–2017

Year	No. hospitals*					No. isolates	Isolation rate, %†	Gram-negative isolates, %	Imipenem-resistant isolates, %
	Total	3A	3B	2A	2B				
2015	78	41	23	13	1	22,464	8.1	11.9	35.4
2016	88	44	23	19	2	24,303	8.0	12.0	37.1
2017	84	41	24	18	1	25,113	7.8	12.0	39.1

*Hospital classification is performed by the National Health Commission of China on the basis of the number of beds and comprehensive evaluation scores. Comprehensive evaluation covers the number of departments, staffing levels, management, technical level, work quality, and supporting facilities. Class 3 hospitals have >500 beds, class 2 hospitals have 100–499 beds. Grade levels are given on the basis of scores from a comprehensive evaluation; grade A hospitals received >900 points, grade B hospitals received 750–899 points.
†*P. aeruginosa* was the fourth most commonly isolated pathogen in the region in each of the reported years.

Antimicrobial Susceptibility Testing

We performed antimicrobial susceptibility testing on 71,880 *P. aeruginosa* isolates submitted during 2015–2017. We tested for susceptibility to gentamicin, amikacin, piperacillin/tazobactam, ceftazidime, cefepime, aztreonam, imipenem, meropenem, ciprofloxacin, levofloxacin, colistin, and polymyxin B. We selected these 12 antimicrobial agents because all are used routinely in clinical settings in the province and we could include 1–2 from each antimicrobial category, per guidelines from the Clinical and Laboratory Standards Institute (CLSI; *12*). We imported susceptibility data into WHONET, deleted duplicated strains, used only the first isolate from each patient, and interpreted results according to CLSI guidelines (*12*).

Hospitals prepared isolates for susceptibility testing by using the Kirby-Bauer method and interpreted results manually according to CLSI guidelines (*12*) or by using broth microdilution for analysis by VITEK 2 or Phoenix 100 automated systems. To ensure comparable susceptibility tests between hospitals, each used the same reference strain, *P. aeruginosa* ATCC27853, and standardized procedures, following guidelines from the National Health Commission of China. We considered possible inaccuracies of susceptibility tests for colistin and polymyxin B in automated systems, especially by the Kirby-Bauer method, because of poor and slow diffusion in agar plates (*13*) and applied strict quality control practices by comparing results against our reference strain.

We conducted imipenem susceptibility testing of 71,880 isolates and meropenem susceptibility testing of 26,916 (37.44%). We used imipenem resistance as an indicator of carbapenem resistance and separately analyzed imipenem-resistant (IMP-R) and imipenem-susceptible (IMP-S) *P. aeruginosa* isolates against the other antimicrobial agents.

Classifications

We used year as an independent variant for occurrence analysis of IMP-R *P. aeruginosa.* Then, we calculated other variants by year. For our analysis, we categorized patient age into 6 groups: 0–2, 3–9, 10–19, 20–39, 40–59, and ≥60 years of age. Then we analyzed specific specimen types: blood, sputum, and urine. We analyzed outpatient and inpatient data and divided inpatients into 2 categories: those in intensive care units (ICUs) and those in standard patient wards (non-ICUs). To assess seasonality of CRPA, we analyzed quarters of the year, January–March, April–June, July–September, and October–December.

We grouped hospitals into 4 levels, 3A, 3B, 2A, and 2B, according to classifications designated by the National Health Commission of China, which classifies hospitals on the basis of the number of beds and scores on a comprehensive evaluation. Class 3 hospitals have >500 beds, and class 2 hospitals have 100–499 beds. The National Health Commission grades hospitals using scores from a comprehensive evaluation of the number of departments, staffing levels, management, technical level, work quality, and supporting facilities. Grade A hospitals received >900 points; grade B hospitals received 750–899 points.

We grouped geographic regions by city (Figure 1). Then, we analyzed each variant by year (Appendix Figure 1, http://wwwnc.cdc.gov/EID/article/25/10/18-1699-App1.pdf).

Statistical Analysis

We analyzed antimicrobial resistance patterns of *P. aeruginosa* isolates exported from WHONET. We used unconditional logistic regression models to estimate odds ratios (ORs) and 95% CIs for univariable analysis of risk factors associated with IMP-R *P. aeruginosa*. We used either Pearson χ^2 test or Fisher exact test to compare the frequency distribution of categorical variables. For all models, we considered $p<0.05$ statistically significant and then performed 2-sided probability on those results by using SPSS version 23.0 (IBM, https://www.ibm.com). We classified both intermediate and resistant isolates as IMP-R.

Results

Surveillance Data

Approximately 80 hospitals from 11 administrative districts in Zhejiang Province participated in the annual survey of antimicrobial resistance. *P. aeruginosa* was the fourth most frequently isolated nosocomial pathogen identified, accounting for 8.0% of all bacteria obtained and 12.0%

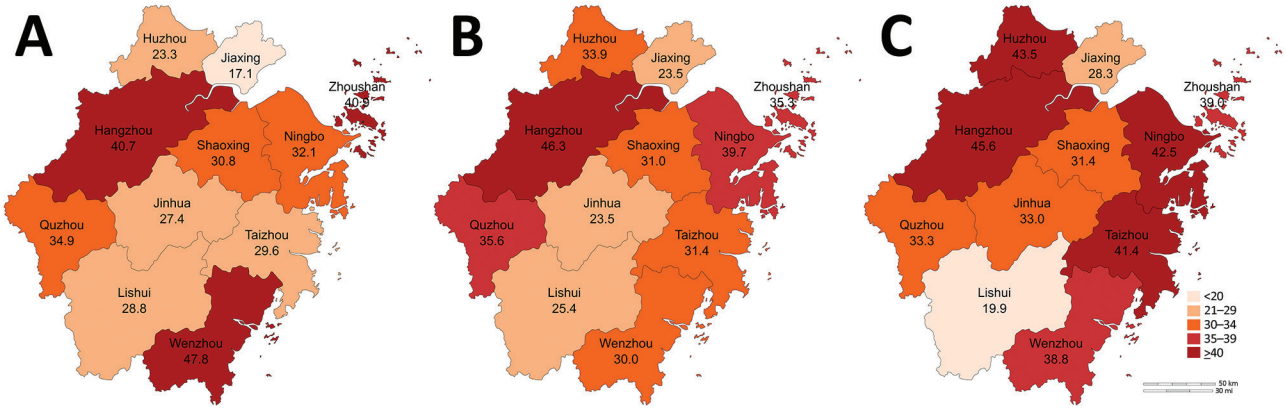

Figure 1. Heatmap of rates of carbapenem-resistant *Pseudomonas aeruginosa* each year in administrative districts in Zhejiang Province, China. A) 2015; B) 2016; C) 2017.

of gram-negative bacteria collected in Zhejiang. During 2015–2017, hospitals submitted 71,880 *P. aeruginosa* isolates, >20,000 each year; this total is much higher than the numbers analyzed in studies from the United States and Europe (*14*,*15*). The large number of isolates provides a strong dataset for our statistical analysis.

We found that 26,789 isolates (37.26%) were resistant to imipenem. The rate of IMP-R *P. aeruginosa* was >35% in each year and increased gradually during the study period. The meropenem resistance rate of ≈29% was slightly lower than that of imipenem resistance in the 3 years analyzed. In addition, we found that 29.54% of isolates were resistant to piperacillin/tazobactam and 25.11% were resistant to cefepime (Table 1; Figure 2; Appendix Table 1).

Correlation of IMP-R *P. aeruginosa* with Risk Factors

We examined the correlation between IMP-R *P. aeruginosa* and risk factors by using OR (Table 2). We investigated quarter of the year, geographic region, patient age, inpatient or outpatient status, and ICU or non-ICU status as risk factors. Our analysis showed that the year isolates were collected had a statistically significant effect on the OR for IMP-R *P. aeruginosa*: OR 1.072 (95% CI 1.032–1.115) in 2016 compared with 2015 and OR 1.167 (95% CI 1.124–1.213) for 2017 compared with 2015. Seasonality was also a factor; *P. aeruginosa* isolates collected during January–March, April–June, and October–December were more likely to be IMP-R than those collected during July–September. We found that the capital of Zhejiang, Hangzhou, as well as Huzhou, Ningbo, Taizhou, Zhoushan, Wenzhou, and Quzhou, had higher IMP-R *P. aeruginosa* rates than other cities.

Isolates from inpatients had higher rates of imipenem resistance than those from outpatients, and isolates from patients in ICUs were more likely to be IMP-R than those from patients in non-ICU wards. When analyzed for patient age, the highest proportion of resistant isolates were collected from patients ≥60 years of age. We found no statistically significant difference in risk for IMP-R among isolates collected from patients 0–2 and 3–9 years of age. However, in other age groups, OR increased with age. In addition, we found that isolates from blood and sputum cultures were more likely to be IMP-R than isolates from urine (Table 2).

Antimicrobial Resistance Patterns of *P. aeruginosa*

Overall, *P. aeruginosa* showed high susceptibility to lipopeptides (99.07% to colistin and 98.5% to polymyxin B) and aminoglycosides (93.06% to amikacin and 85.88% to gentamicin) but high resistance to cephalosporins and fluquinolones (≈20%–30% susceptibility) and aztreonam (35.65% susceptibility) (Table 3). When we classified isolates into IMP-R and IMP-S groups, we

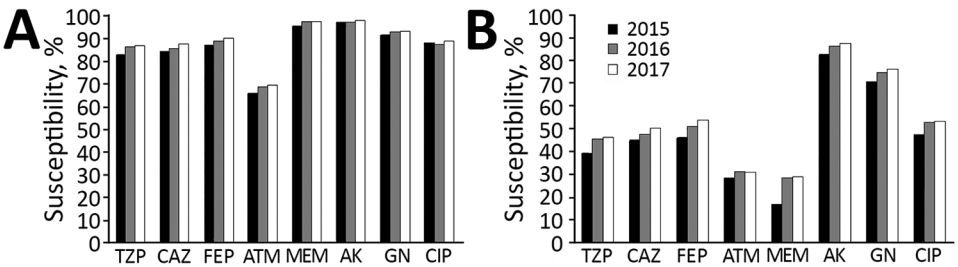

Figure 2. Annual susceptibility rates to antimicrobial agents among imipenem-susceptible (A) and imipenem-resistant (B) *Pseudomonas aeruginosa* isolates Zhejiang Province, China. AK, amikacin; ATM, aztreonam; CAZ, ceftazidime; CIP, ciprofloxacin; FEP, cefepime; GN, gentamicin; MEM, meropenem; TZP, piperacillin/tazobactam.

Table 2. Annual odds ratios for risk factors associated with carbapenem-resistant *Pseudomonas aeruginosa*, Zhejiang Province, China, 2015–2017*

	2015		2016		2017	
Characteristics	OR (95% CI)	p value	OR (95% CI)	p value	OR (95% CI)	p value
District						
Jiaxing	Referent		Referent		Referent	
Hangzhou	3.22 (2.85–3.63)	**<0.001**	2.83 (2.52–3.19)	**<0.001**	2.10 (1.91–2.31)	**<0.001**
Huzhou	1.42 (1.16–1.75)	**0.001**	1.68 (1.41–2.00)	**<0.001**	1.92 (1.55–2.38)	**<0.001**
Ningbo	2.23 (1.94–2.56)	**<0.001**	2.16 (1.89–2.47)	**<0.001**	1.85 (1.64–2.07)	**<0.001**
Taizhou	1.97 (1.65–2.36)	**<0.001**	1.50 (1.29–1.75)	**<0.001**	1.77 (1.51–2.07)	**<0.001**
Zhoushan	3.24 (2.63–4.00)	**<0.001**	1.79 (1.46–2.18)	**<0.001**	1.61 (1.31–1.97)	**<0.001**
Wenzhou	4.30 (3.75–4.94)	**<0.001**	1.40 (1.18–1.65)	**<0.001**	1.59 (1.40–1.80)	**<0.001**
Quzhou	2.99 (2.48–3.61)	**<0.001**	1.81 (1.53–2.14)	**<0.001**	1.25 (1.09–1.45)	**0.002**
Jinhua	1.77 (1.51–2.08)	**<0.001**	0.99 (0.85–1.15)	0.893	1.24 (1.09–1.40)	**0.001**
Shaoxing	2.09 (1.77–2.47)	**<0.001**	1..47 (1.26–1.71)	**<0.001**	1.10 (0.96–1.25)	0.165
Lishui	1.90 (1.59–2.27)	**<0.001**	1.11 (0.89–1.39)	0.345	0.62 (0.49–0.79)	**<0.001**
Specimen type						
Urine	Referent		Referent		Referent	
Blood	1.23 (0.99–1.53)	0.067	1.68 (1.35–2.08)	**<0.001**	1.44 (1.66–1.77)	**0.001**
Sputum	1.87 (1.66–2.96)	**<0.001**	1.97 (1.76–2.22)	**<0.001**	2.13 (1.90–2.39)	**<0.001**
Patient age, y						
0–2	Referent		Referent		Referent	
3–9	0.93 (0.58–1.49)	0.764	0.83 (0.56–1.23)	0.362	1.06 (0.73–1.54)	0.768
10–19	1.66 (0.99–2.48)	0.055	1.23 (0.84–1.80)	0.295	1.57 (1.08–2.29)	**0.018**
20–39	3.51 (2.48–4.97)	**<0.001**	2.28 (1.70–3.06)	**<0.001**	2.62 (1.95–3.55)	**<0.001**
40–59	3.93 (2.82–5.48)	**<0.001**	2.57 (1.95–3.39)	**<0.001**	3.09 (2.33–4.10)	**<0.001**
>60	4.34 (3.13–6.02)	**<0.001**	2.83 (2.15–3.71)	**<0.001**	3.24 (2.45–4.27)	**<0.001**
Quarter						
Jul–Sep	Referent		Referent		Referent	
Jan–Mar	2.11 (1.46–3.03)	**<0.001**	1.30 (1.17–1.44)	**<0.001**	1.90 (1.75–2.07)	**<0.001**
Apr–Jun	NA	NA	1.09 (0.97–1.22)	0.136	1.56 (1.42–1.70)	**<0.001**
Oct–Dec	NA	NA	1.28 (1.15–1.43)	**<0.001**	1.21 (1.11–1.31)	**<0.001**
Hospital level†						
2B	Referent		Referent		Referent	
2A	1.36 (0.71–2.63)	0.355	1.46 (0.96–2.20)	0.073	1.84 (1.11–3.04)	**0.016**
3B	1.13 (0.59–2.18)	0.712	0.95 (0.63–1.44)	0.819	1.35 (0.82–2.25)	0.239
3A	1.93 (1.01–3.71)	**0.044**	1.10 (0.72–1.68)	0.653	1.58 (0.95–2.63)	3.175
Type of patient						
Outpatient	Referent		Referent		Referent	
Inpatient, ward					1.15 (1.01–1.31)	**0.039**
Non-ICU	Referent		Referent		Referent	
ICU	2.60 (2.42–2.79)	**<0.001**	2.66 (2.49–2.85)	**<0.001**	2.57 (2.38–2.78)	**<0.001**

*Isolates from patients with missing values on the variables are not included in the analysis. Bold text indicates statistical significance. NA, not available; OR, odds ratio.

†Hospital classification is performed by the National Health Commission of China on the basis of the number of beds and comprehensive evaluation scores. Comprehensive evaluation covers the number of departments, staffing levels, management, technical level, work quality, and supporting facilities. Class 3 hospitals have >500 beds, class 2 hospitals have 100–499 beds. Grade levels are given on the basis of scores from a comprehensive evaluation; grade A hospitals received >900 points, grade B hospitals received 750–899 points.

found statistically significant differences (p<0.001) in resistance rates between resistant and susceptible isolates for all analyzed antimicrobial drugs except lipopeptides. IMP-R isolates exhibited statistically lower susceptibility than IMP-S isolates to all antimicrobial drugs except the lipopeptides, colistin and polymyxin B. We saw a 2–3-fold difference in MIC_{50} (MIC needed to inhibit 50% of cells) between IMP-S isolates and IMP-R isolates. In contrast, for each antimicrobial drug except lipopeptides, most IMP-R strains belonged to the MIC_{90} group (MIC needed to inhibit 90% of cells), whereas the IMP-S isolates were more prevalent in the MIC_{50} group. Similarly, the IMP-R group was highly resistant (25.36%) to meropenem, but IMP-S group was highly susceptible (96.97%) (Figure 2).

Discussion

Carbapenems are the most effective antimicrobial agents against serious infections caused by multidrug-resistant gram-negative bacilli. However, the resistance rate of *P. aeruginosa* to carbapenems has been consistently high (*3*,*16*–*18*). Clarifying resistance trends of CRPA and related risk factors can guide antimicrobial use and selection of effective treatment plans.

In our study, rates of IMP-R *P. aeruginosa* increased annually and were higher in Zhejiang Province than reported for other provinces in national surveillance through CHINET (*3*,*17*,*18*). For instance, 2017 CHINET surveillance reported national rates of 27.3% for IMP-R *P. aeruginosa* and 25.1% for meropenem-resistant *P. aeruginosa* (*18*), but in Zhejiang Province the rates were 39.3% for

Table 3. Antimicrobial resistance patterns of imipenem-resistant and imipenem-susceptible *Pseudomonas aeruginosa* isolates, Zhejiang Province, China, 2015–2017*

Antimicrobial drugs	No. isolates (susceptibility rate, %)		p value	Total susceptibility rate, %	MIC_{50}, μg/mL		MIC_{90}, μg/mL	
	IMP-S	IMP-R			S	R	S	R
Piperacillin/tazobactam	41,145 (85.70)	23,721 (44.01)	**<0.001**	70.46	8	64	64	128
Ceftazidime	30,326 (86.26)	18,348 (47.93)	**<0.001**	71.81	4	16	32	64
Cefepime	42,492 (89.01)	24,947 (50.83)	**<0.001**	74.89	2	8	16	64
Aztreonam	24,215 (68.07)	13,823 (30.32)	**<0.001**	54.35	8	32	32	64
Amikacin	42,106 (97.38)	24,748 (85.69)	**<0.001**	93.06	2	4	8	64
Gentamicin	41,207 (92.80)	24,618 (74.29)	**<0.001**	85.88	1	2	4	16
Ciprofloxacin	42,442 (88.28)	25,063 (51.64)	**<0.001**	74.67	0.25	1	2	4
Levofloxacin	41,982 (89.06)	24,593 (53.17)	**<0.001**	75.80	0.5	2	4	8
Meropenem	17,166 (96.97)	9,750 (25.36)	**<0.001**	71.03	1	8	1	16
Colistin	1,624 (99.08)	627 (99.04)	NA	99.07	1	1	1	2
Polymyxin B	5,012 (98.60)	3,746 (98.37)	0.452	98.50	1	1	2	2

*MIC_{50} and MIC_{90} were generated from the minimal inhibitory concentrations of antimicrobial drugs. Bold text indicates p values <0.05. IMP-R, imipenem-resistant; IMP-S, imipenem-susceptible; NA, not applicable; R, resistant; S, susceptible.

IMP-R and 28.1% for meropenem-resistant isolates. Both the CHINET surveillance and our data indicated CRPA poses a severe challenge in Zhejiang Province. The slightly lower resistance rate we saw for meropenem could be because we tested fewer isolates for meropenem resistance (n = 26,916) than for imipenem resistance (n = 71,880) or could be the result of other mechanisms, such as mutation or loss of the oprD2 in some isolates (*19*).

When we examined risk factors, we found that patient type and ward were associated with a higher prevalence of IMP-R *P. aeruginosa*. Inpatients and those admitted to an ICU had higher IMP-R rates than outpatients and those in non-ICU wards, in accordance with previous studies (*20*), indicating ICU admission is a risk factor for IMP-R *P. aeruginosa.* Patient age also factors into IMP-R *P. aeruginosa* occurrence in Zhejiang (*21*), which could be a result of the low immune function of patients ≥60 years of age. We saw an increase in the rate of IMP-R with increased patient age but did not see increased rates for patients 0–2, 3–9, or 10–19 years of age. However, the IMP-R rate was >10% in 2015 and increased to 20.9% in 2017 in the 10–19-year age group (data not shown), which could signal a potential increasing trend of IMP-R in subsequent years. Further studies with clinical information and data are needed to investigate this issue.

A previous study in India showed that *P. aeruginosa* isolates from sputum and blood samples from patients in the ICU were more resistant than isolates from urine (*22*). Other studies in China also have observed this discrepancy of *P. aeruginosa* from various specimen types (*16*,*23*). We found this observation was true, not only for isolates from patients in the ICU but for all patient isolates included in our study, indicating IMP-R *P. aeruginosa* might be a less likely agent in urinary tract infection.

Previous studies also stated that the occurrence of *P. aeruginosa* infection was associated with seasons (*24*,*25*) and that the isolation rate usually was higher in summer than in winter. However, we observed a reverse outcome for IMP-R *P. aeruginosa*: a higher prevalence in winter than in summer (data not shown). The seasonal effect on IMP-R *P. aeruginosa* rates is unknown, but our finding could potentially inform clinical recommendations.

By OR analysis, we found that IMP-R *P. aeruginosa* was more prevalent in 7 administrative districts: Hangzhou, Huzhou, and Quzhou in the northwest and Ningbo, Taizhou, Zhoushan, and Wenzhou in the southeast of the province. However, we found no statistical differences in IMP-R related to hospital classification in Zhejiang, which is worth noting because patients in class 2 hospitals usually have mild or moderate illnesses and patients in class 3 hospitals have more severe conditions or are immunocompromised and more susceptible to infection. We weighted class 2 hospitals differently than class 3 hospitals in our statistical analysis to account for the difference in patient types. However, because we saw no statistically significant difference in imipenem resistance rates related to the hospital level, we should put the same weight on both classes of hospitals in future analyses.

Although our study showed *P. aeruginosa* was highly resistant to carbapenems and multiple other drugs, it remains highly susceptible to colistin and has some sensitivity to cephalosporins and fluoroquinolones. IMP-R *P. aeruginosa* is most sensitive to colistin in vitro, and colistin is effective against multidrug-resistant *P. aeruginosa* nosocomial infections (*26*). Despite its strong neurotoxicity and ototoxicity, colistin was reapproved for clinical applications in China in September 2017. However, efficacy of colistin monotherapy has been questioned in clinical trials (*27*), and colistin should be used in combination with other antimicrobial agents in clinical therapy.

Novel antimicrobial agents approved by the US Food and Drug Administration, such as ceftolozane/tazobactam or ceftazidime/avivactam, could be other treatment options. These drug combinations have good efficacy against CRPA isolates (*28*,*29*) but currently are not approved for use in China. Of note, ceftolozane/tazobactam might not be useful against carbapenemase-producing *P. aeruginosa* (*30*), and prerequisite identification of resistance mechanisms would

be needed to develop rational antimicrobial drug regimens. In addition, a novel plasmid-mediated colistin-resistant gene, *mcr*, has emerged in *Enterobacteriaceae* (*31–33*). To reduce the chances of its dissemination to *P. aeruginosa* under antimicrobial drug selection pressure, clinicians should prioritize colistin only for severe cases of *P. aeruginosa* infection in clinical practice. Because of limitations of susceptibility testing methods (*13*), MICs for polymyxins might be less reliable in strains with MICs close to the breakpoint. Therefore, clinicians also should choose polymyxin therapies carefully.

Our study had some limitations. We excluded strains without a corresponding field from the classification analysis, such as patient age, patient type, or isolation time, which might have caused a distortion in the resistance rate. A disproportionate number of class 3 to class 2 hospitals participated in the surveillance, and class 2 hospitals inevitably were biased in the statistical antimicrobial resistance rate because they submit fewer isolates. In addition, we could not include therapeutic regimens, patient outcomes, or the molecular mechanisms of resistance for CRPA strains because they were not available, but these measures could inform clinical decisions and should be included in further surveillance studies.

In summary, we conducted a comprehensive analysis of risk factors associated with CRPA in Zhejiang Province, China. We investigated potential risk factors for IMP-R *P. aeruginosa* because Zhejiang Province has higher rates of carbapenem resistance compared with other provinces (*34*). Our research provides insights into CRPA in China and indicates an imperative for medical institutions in China to strengthen surveillance for this organism.

Acknowledgments

We thank all the members of the Zhejiang Province Surveillance of Antimicrobial Resistance Program for supplying the data.

This work was funded by the National Natural Science Foundation of China (grant nos. 81501805 and 81772250) and Natural Science Foundation of Zhejiang Province (grant no. LQ16H200002).

Contributions: Y.-Y.H. and R.Z. were involved in the conception and design of the study. J.-M.C., S.C., Q.Y., H.Y.-L., and H.-W.Z. collected the data. Y.-Y.H. and R.Z. analyzed and interpreted the data. Y.-Y.H., Z.W., and R.Z. wrote the manuscript. All authors read and approved the final manuscript.

About the Author

Dr. Hu is a clinical laboratory technician at the Second Affiliated Hospital of Zhejiang University, School of Medicine, Zhejiang University, Hangzhou, China. Her primary research interest is antibiotic resistance mechanisms of gram-negative bacteria.

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Address for correspondence: Rong Zhang, Zhejiang University, Second Affiliated Hospital of Zhejiang University, School of Medicine, 88 Jiefang Rd, Hangzhou 310009, China; email: zhang-rong@zju.edu.cn; Zuowei Wu, Iowa State University, Department of Veterinary Microbiology and Preventive Medicine, 1113 Vet Med, 1800 Christensen Dr, Ames, IA 50011-1134, USA; email: wuzw@iastate.edu

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Article DOI: https://doi.org/10.3201/eid2510.181699

Risk Factors for Carbapenem-Resistant *Pseudomonas aeruginosa*, Zhejiang Province, China

Appendix

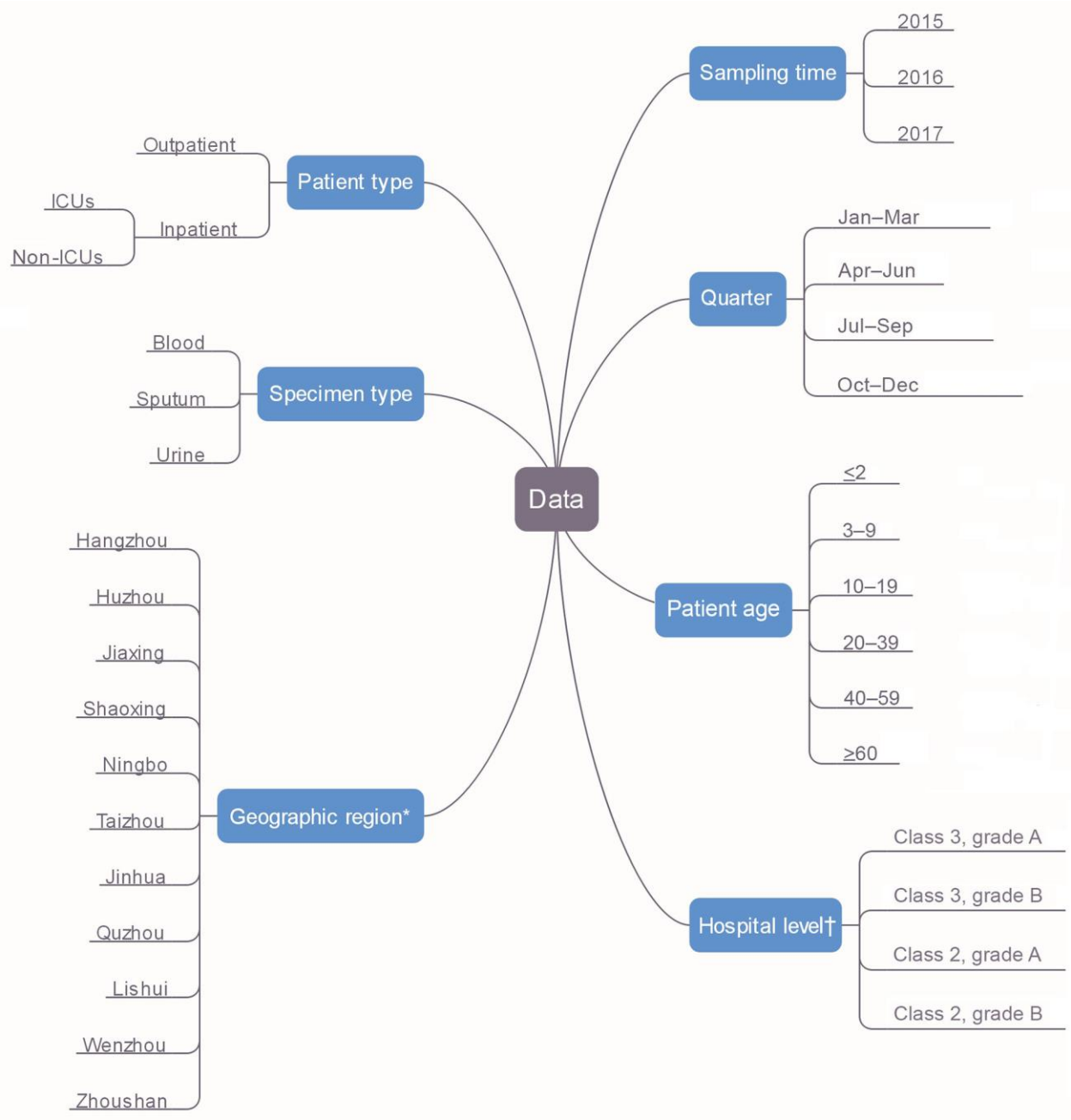
Appendix Table. Surveillance for carbapenem-resistant *Pseudomonas aeruginosa* in hospitals, Zhejiang Province, China, 2015–2017*

Hospitals by city	Level†	Strain identification method‡	Years excluded§
Hangzhou			
First 17 People's Liberation Army Hospital	3A	VITEK 2 Compact	
Hangzhou Red Cross Hospital	3A	VITEK 2 Compact	
Hangzhou First People's Hospital	3A	MALDI-TOF MS	
Hangzhou Children's Hospital	3A	VITEK 2 Compact	
Hangzhou Hospital of Chinese Traditional Hospital	3A	Phoenix 100, VITEK 2 Compact	
Hangzhou Cancer Hospital	3A	VITEK 2 Compact	
Xixi Hospital of Hangzhou	3A	VITEK 2 Compact	
Sir Run Run Shaw Hospital, School of Medicine, Zhejiang University	3A	MALDI-TOF MS	
The Children's Hospital of Zhejiang University School of Medicine	3A	MALDI-TOF MS	
Women's Hospital, School of Medicine, Zhejiang University	3A	VITEK 2 Compact	
The First Affiliated Hospital of Medical School of Zhejiang University	3A	MALDI-TOF MS	
The Second Affiliated Hospital of Zhejiang University School of Medicine	3A	MALDI-TOF MS	
Hangzhou Second People's Hospital	3A	MALDI-TOF MS	
Zhejiang People's Armed Police Corps Hospital, Hangzhou	3A	Phoenix 100	
Xinhua Hospital of Zhejiang Province	3A	VITEK 2 Compact	
Zhejiang Provincial People's Hospital	3A	MALDI-TOF MS	
Zhejiang Provincial Hospital of Traditional Chinese Medicine	3A	MALDI-TOF MS	
Tongde Hospital of Zhejiang Province	3A	VITEK 2 Compact	
Zhejiang Hospital	3A	MALDI-TOF MS	
Zhejiang Cancer Hospital	3A	MALDI-TOF MS	
Hangzhou Third People's Hospital	3B	VITEK 2 Compact	
The First People's Hospital of Jiande	3B	VITEK 2 Compact	2017
First People's Hospital of Yuhang Distrcit, Hangzhou	3B	Phoenix 100	
Linan People's Hospital	2A	VITEK 2 Compact	2017
The First People's Hospital of Chunan	2A	VITEK 2 Compact	2015
Shulan Hospital	3A	Phoenix 100 system	2015, 2017
The First People's Hospital of Tonglu	2A	VITEK 2 Compact	2015
Huzhou			
The First People's Hospital of Huzhou	3B	VITEK 2 Compact	
Huzhou Central Hospital	3A	MALDI-TOF MS	2017
Changxing County People's Hospital	2A	VITEK 2 Compact	2017
Deqing People's hospital	2A	VITEK 2 Compact	2015
Jiaxing			
Jiaxing Maternity and Child Health Care Hospital	3A	Phoenix 100	
The Second Hospital of Jiaxing	3A	MALDI-TOF MS	
The First Hospital of Jiaxing	3A	MALDI-TOF MS	
Chinese medicine hospital of Jiaxing City	3A	VITEK 2 Compact	
The First People's Hospital of Jiashan	3B	VITEK 2 Compact	
The First People's Hospital of Pinghu	2A	VITEK 2 Compact	
The Second People's Hospital of Tongxiang	2A	VITEK 2 Compact	
Zhejiang Haining People's Hospital	3B	MALDI-TOF MS	2016
The First People's Hospital of Tongxiang	3B	VITEK 2 Compact	2016

Hospitals by city	Level†	Strain identification method‡	Years excluded§
Haiyan People's Hospital	2A	VITEK 2 Compact	
Haiyan County Chinese Medicine Hospital	2B	VITEK 2 Compact	2017
The Third Hospital of Jiaxing	2A	VITEK 2 Compact	2015, 2016
Shaoxing			
Shangyu People's Hospital	3B	VITEK 2 Compact	
The Second Hospital of Shaoxing	3B	VITEK 2 Compact	
Zhejiang Shengzhou People's Hospital	3B	VITEK 2 Compact	
Zhuji People's Hospital of Zhejiang Province	3B	VITEK 2 Compact	
Shaoxing Maternity and Child Health Care Hospital	3A	VITEK 2 Compact	
Shaoxing People's Hospital	3A	VITEK 2 Compact	
Xinchang County People's Hospital	3B	VITEK 2 Compact	2016, 2017
Ningbo			
The Affiliated Hospital of School of Medicine of Ningbo University	3A	MALDI-TOF MS	
Ningbo Women and Children's Hospital	3A	VITEK 2 Compact	
Ningbo Medical Central Lihuili Hospital	3A	VITEK 2 Compact	
Ningbo Second Hospital	3A	VITEK 2 Compact	
Ningbo First Hospital	3A	MALDI-TOF MS	
Beilun People's Hospital	3B	VITEK 2 Compact	
Maternal and Child Care Service Centre	3B	Phoenix 100	
People's Hospital of Cixi City	3B	VITEK 2 Compact	
Yinzhou People's Hospital	3B	MALDI-TOF MS	2015
Yuyao People's Hospital of Zhejiang Province	3B	VITEK 2 Compact	2017
Fenghua People's Hospital	2A	VITEK 2 Compact	
Ningbo No.7 Hospital	2A	VITEK 2 Compact	
Ningbo Fourth Hospital	3B	VITEK 2 Compact	2015, 2016
Taizhou			
Taizhou Municipal Hospital of Zhejiang Province	3B	VITEK 2 Compact	
The First People's Hospital of Taizhou	3B	VITEK 2 Compact	2017
Taizhou Hospital of Zhejiang Province	3A	MALDI-TOF MS	2015
Taizhou Central Hospital	3A	MALDI-TOF MS	2017
The First People's Hospital of Wenling	3B	VITEK 2 Compact	
Yuhuan People's Hospital	2A	VITEK 2 Compact	2015
Jinhua			
Dongyang People's Hospital	3B	MALDI-TOF MS	
Jinhua Central Hospital	3B	MALDI-TOF MS	
The First People's Hospital of Yongkang	3B	Phoenix 100	2015
Jinhua Municipal Central Hospital	3A	VITEK 2 Compact	
Lanxi People's Hospital	2A	VITEK 2 Compact	
Panan People's Hospital	2A	VITEK 2 Compact	
Pujiang People's Hospital	2A	VITEK 2 Compact	
Wuyi First People's Hospital	2A	VITEK 2 Compact	2015
Yiwu Central Hospital	3B	Phoenix 100	2015, 2016
Quzhou			
Quzhou People's Hospital	3A	MALDI-TOF MS	
Jiangshan People's Hospital	2A	Phoenix 100	
People's Hospital of Changshan	2A	VITEK 2 Compact	2016, 2017
Longyou County People's Hospital	2A	VITEK 2 Compact	
Zhejiang Quhua Hospital	3B	Phoenix 100	2015
Quzhou Kecheng Hospital	2A	Phoenix 100	2015, 2016
Lishui			
Lishui People's Hospital	3A	MALDI-TOF MS	2017
The Second People's Hospital of Lishui	3A	VITEK 2 Compact	2015
Lishui Central Hospital	3A	VITEK 2 Compact	
Qingtian Country People's Hospital	2A	VITEK 2 Compact	2017
Qingyuan County People's Hospital	2A	VITEK 2 Compact	2017
Jingning County People's Hospital	2B	MALDI-TOF MS	
Jinyun County People's Hospital	2A	VITEK 2 Compact	2015, 2016
Wenzhou			
The Second Affiliated Hospital of Wenzhou Medical College	3A	MALDI-TOF MS	
The First Affiliated Hospital of Wenzhou Medical College	3A	MALDI-TOF MS	
Wenzhou People's Hospital	3A	VITEK 2 Compact	
People's Hospital of Yueqing City	3B	MALDI-TOF MS	
The People's Hospital of Pingyang	3B	Phoenix 100	2015, 2017
The People's Hospital of Cangnan	3B	VITEK 2 Compact	2015, 2016
Hospital of Integrated Traditional Chinese and Western Medicine of Wenzhou	3A	MALDI-TOF MS	2015, 2016
Zhoushan			
Zhoushan Hospital	3A	Phoenix 100	

Hospitals by city	Level†	Strain identification method‡	Years excluded§

*MALDI-TOF MS, matrix assisted laser desorption ionization-time of flight mass spectrometry.
†Hospital classification is performed by the Ministry of Health of China on the basis of the number of beds and comprehensive evaluation scores. Comprehensive evaluation covers the number of departments, staffing levels, management, technical level, work quality, and supporting facilities. Class 3 hospitals have >500 beds, class 2 hospitals have 100–499 beds. Grade levels are given on the basis of scores from a comprehensive evaluation; grade A hospitals received >900 points, grade B hospitals received 750–899 points.
‡ VITEK 2 Compact system (bioMérieux, https://www.biomerieux.com); Phoenix 100 system (Becton Dickinson, https://www.bd.com).
§Hospitals were excluded for years in which they submitted <3 isolates.



Appendix Figure. Diagram of data collected for determining risk factors for carbapenem-resistant *Pseudomonas aeruginosa* in Zhejiang Province, China, 2015–2017. *****Administrative districts are designated by city names from the region. †Hospital classification is performed by the National Health Commission of China on the basis of the number of beds and comprehensive evaluation scores. Comprehensive evaluation covers the number of departments, staffing levels, management, technical level, work quality, and supporting facilities. Class 3 hospitals have >500 beds, class 2 hospitals have 100–499 beds. Grade levels are given on the basis of scores from a comprehensive evaluation; grade A hospitals received >900 points, grade B hospitals received 750–899 points.