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ORIGINAL PAPER

Patterns of Drug-Resistant Bacteria in a General Hospital, China, 2011–2016

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Abstract

Drug-resistant bacteria has been a threat to public life and property. We described the trends and changes in antibiotic resistance of important pathogens in a general hospital in Zhengzhou, China from 2011 to 2016, to control antimicrobial-resistant bacteria in hospital and provide support to clinicians and decision-making departments.

Five dominant bacteria were enrolled based on the data from the general hospital during 6 years. The results of antimicrobial susceptibility testing were interpreted according to Clinical and Laboratory Standards Institute (CLSI). From 2011 to 2016, a total of 19,260 strains of bacteria were isolated, of which *Klebsiella pneumoniae*, *Escherichia coli*, *Staphylococcus aureus*, *Pseudomonas aeruginosa* and *Acinetobacter baumannii* accounted for 51.98%. The resistance rate of *K. pneumoniae* and *E. coli* to carbapenem was less than 15%, but resistance of *K. pneumoniae* to carbapenems increased with time and resistance of *E. coli* to meropenem increased. The rate of extended-spectrum beta-lactamase (ESBL) production among *K. pneumoniae* and *E. coli* was decreasing. For most antibiotics, the resistance rate of ESBL-positive isolates was higher than that of ESBL-negative isolates, excluding carbapenems and cefoxitin. For *S. aureus*, the rate of methicillin-resistant *S. aureus* (MRSA) was stable. Resistance of *S. aureus* to mostly antibiotics decreased with time. Besides polymyxin B, *P. aeruginosa* and *A. baumannii* showed high resistance to other antibiotics. For *A. baumannii*, the resistance rate to mostly antibiotics was increasing. The bacteria showed high levels of resistance and multiple drug resistance. Continuous surveillance and optimizing the use of antibiotics are essential.

Key words: antimicrobial resistance, Gram-negative bacteria, ESBL, MRSA, surveillance

Introduction

The emergence and spread of drug-resistant bacteria have always been a public concern. With the increase of resistance to available antimicrobial agents and the emergence of multi-drug resistant bacteria, antimicrobial resistance has caused serious threats to public health in the world (Livermore 2012; Rossolini et al. 2014; Yang et al. 2017). It can cause damage to human health and, at the same time, it can lead to a situation where there is no cure. The research reported that antimicrobial resistance causes about 700 000 deaths worldwide each year, and if no effective action is taken, it is expected to cause 10 million deaths a year by 2050 (Hoffman et al. 2015).

Simultaneously, antibiotics that become ineffective against bacteria have been reported (Liu et al. 2016). The bacterial resistance crisis has been greatly attributed to the overuse and misuse of these antibiotics (Pathak et al. 2013; Michael et al. 2014; Tang et al. 2018). Monitoring of the epidemiology of resistance provides useful information for prevention and helps clinicians prescribe the effective antibiotic therapy (Ventola 2015), as well as optimize the use of antibiotics, which has become one of the most important parts of drug resistance control (Lafaurie et al. 2012; Wang et al. 2018). In this study, the significant changes and trends in antibiotic resistance of clinically important pathogens isolated from a general hospital in Zhengzhou, Henan Province, China, from 2011 to 2016 were described to provide a more complete picture of bacterial infections and to help clinicians and decision-making departments undertake the proper decisions for patients and antibiotic use.

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Experimental

Materials and Methods

Based on the data from a general hospital in Zhengzhou, Henan province, China from 2011 to 2016, five dominant bacteria (*Klebsiella pneumoniae*, *Escherichia coli*, *Staphylococcus aureus*, *Pseudomonas aeruginosa*, and *Acinetobacter baumannii*) were investigated in this study. The antibiotic susceptibilities of the isolates were determined using the broth dilution method according to Clinical and Laboratory Standards Institute (CLSI 2017). In this study, the intermediate was attributed as the resistant. The differences in proportions were compared using the chi-squared test and the variation tendency was compared using the chi-squared for trend. Two-sided test with $p < 0.05$ were taken as statistically significant, with the use of SAS 9.1.

Results

From 2011 to 2016, a total of 19 260 bacterial isolates were obtained, with five dominant bacteria being *K. pneumoniae* (17.71%), *E. coli* (14.45%), *S. aureus* (7.42%), *P. aeruginosa* (6.64%), and *A. baumannii* (5.75%). Overall, these isolates accounted for 51.98% of all reported isolates. Also, a wavy increase was observed in the detection rates of these isolates (Table I).

During the study period, the detection rate of *K. pneumoniae* isolates was stable, meanwhile, the rate of extended-spectrum beta-lactamase (ESBL)-producing *K. pneumoniae* (ESBL-*K. pneumoniae*) showed a downward trend ($\chi^2 = -4.6619$, $p < 0.0001$). A significant increase of resistance was observed for cefotaxime, meropenem, and imipenem to *K. pneumoniae* and ESBL-*K. pneumoniae*. But a significant decrease of resistance was seen for nitrofurantoin. Beyond that, the resistance rates of ampicillin, levofloxacin, cefepime, and piperacillin-tazobactam against *K. pneumoniae* increased from 97.1% to 100%, from 34.42% to 35.05%, from 23.91% to 34.91%, and from 21.74% to 30.58%, respectively. In addition, the rate of trimethoprim-sulfamethoxazole decreased from 71.38% to 55.07%. These results are shown in Table II and Table S-I. The resistance rates of ESBL-*K. pneumoniae* isolates to cefuroxime, ceftriaxone, ampicillin-sulbactam, trimethoprim-sulfamethoxazole, gentamicin, cefotaxime, cefepime, nitrofurantoin, levofloxacin were higher than the rates displayed by ESBL-negative *K. pneumoniae* isolates ($p < 0.05$) (Table S-II).

During the study period, the detection rates of *E. coli* and ESBL-producing *E. coli* (ESBL-*E. coli*) showed a declining trend ($\chi^2 = -4.7904$, $p < 0.0001$ and $\chi^2 = -2.1785$, $p = 0.0294$, respectively). A significant increase of resistance against *E. coli* and ESBL-*E. coli* was observed for cefotaxime, ceftazidime, and meropenem. But a significant decrease of resistance was seen for trimethoprim-

Table I
Distribution of bacterial isolates in relation to years and type of samples.

Category	No. isolates	*Klebsiella pneumoniae*		*Escherichia coli*		*Staphylococcus aureus*		*Pseudomonas aeruginosa*		*Acinetobacter baumannii*		Total	
		n	%	n	%	n	%	n	%	n	%	n	%
Year													
2011	1429	276	19.31	213	14.91	96	6.72	108	7.56	68	4.76	761	53.25
2012	3350	524	15.64	531	15.85	248	7.40	236	7.04	114	3.40	1653	49.34
2013	3143	486	15.46	493	15.89	219	6.98	168	5.35	114	3.63	1480	47.09
2014	3073	605	19.69	477	15.52	213	6.93	248	8.07	224	7.29	1767	57.50
2015	3750	781	20.83	522	13.92	254	6.77	259	6.91	292	7.89	2108	56.21
2016	4515	739	16.37	548	12.18	400	8.86	259	5.74	296	6.56	2242	49.66
Total	19260	3411	17.71	2784	14.45	1430	7.42	1278	6.64	1108	5.75	10011	51.98
χ^2			1.5767		−4.7904		2.5513		−1.7311		7.8954		1.9893
p			0.1149		< 0.0001		0.0107		0.0834		< 0.0001		0.0467
Samples													
Sputum		2741	80.36	493	17.71	81	5.66	1023	80.05	910	82.13	5248	27.25
Urine		382	11.2	1565	56.21	249	17.41	110	8.61	87	7.85	2393	12.42
Blood		104	3.05	265	9.52	275	19.23	30	2.35	24	2.17	698	3.62
Secretion		92	2.7	217	7.79	620	43.36	65	5.09	41	3.70	1035	5.37
Throat swabs		27	0.79	8	0.29	6	0.42	3	0.23	3	0.27	47	0.24
Others		65	1.91	236	8.48	199	13.92	47	3.68	43	3.88	590	3.06

Table II
The resistance rates of *K. pneumoniae* to 15 antimicrobial agents in the years 2011 to 2016.

Antimicrobial agent	MIC breakpoints	2011	2012	2013	2014	2015	2016	Total	χ^2	*p*
	I (μg/ml)	n = 276	n = 524	n = 486	n = 605	n = 781	n = 739	n = 3411		
Ampicillin	16	97.1	99.05	98.97	99.5	100	100	99.38	5.2285	< 0.0001
Cefotaxime	2	52.17	54.39	45.27	56.86	100	100	73.67	26.9374	< 0.0001
Nitrofurantoin	64	76.81	65.84	49.59	56.36	54.16	58.59	58.49	–4.711	< 0.0001
Trimethoprim--sulfamethoxazole	4/76	71.38	70.61	52.06	35.7	37	55.07	50.78	–9.1411	< 0.0001
Ampicillin-sulbactam	16/8	52.54	49.81	46.09	40.17	47.25	47.9	46.79	–1.1923	0.2332
Cefuroxime	16	50.72	49.81	43.21	42.64	47.76	51.01	47.46	0.51	0.6101
Ceftriaxone	2	48.91	53.24	43.21	37.52	46.09	48.71	46.06	–0.9744	0.3299
Gentamicin	8	44.93	43.7	33.74	31.74	40.46	40.46	38.82	–0.8754	0.3813
Cefoxitin	16	40.58	43.51	34.77	31.9	39.44	39.51	38.17	–0.6514	0.5148
Levofloxacin	4	34.42	33.21	22.02	26.12	37.26	35.05	31.78	2.3291	0.0199
Cefepime	16	23.91	33.59	22.84	26.28	35.47	34.91	30.69	3.7816	0.0002
Piperacillin-tazobactam	32/4–64/4	21.74	24.81	18.93	23.64	32.01	30.58	26.41	4.7683	< 0.0001
Amikacin	32	26.09	26.53	16.05	18.02	28.55	23	23.19	0.376	0.7069
Meropenem	2	0	0	0	0.99	10.12	11.37	4.95	12.3843	< 0.0001
Imipenem	2	0	0	0	1.49	9.22	7.98	4.1	10.4364	< 0.0001

Table III
The resistance rates of *E. coli* to 16 antimicrobial agents in the years 2011 to 2016.

Antimicrobial agent	MIC breakpoints	2011	2012	2013	2014	2015	2016	Total	χ^2	*p*
	I (μg/ml)	n = 213	n = 531	n = 493	n = 477	n = 522	n = 548	n = 2784		
Ampicillin	16	92.49	93.03	90.06	86.37	87.16	88.87	89.4	–3.0413	0.0024
Cefotaxime	2	69.01	72.88	71.4	73.17	100	100	82.79	16.5655	< 0.0001
Trimethoprim--sulfamethoxazole	4/76	93.9	93.03	81.74	77.99	70.69	69.16	79.63	–11.9199	< 0.0001
Ampicillin-sulbactam	16/8	76.06	73.63	80.53	67.92	60.15	62.96	69.43	–6.7117	< 0.0001
Cefuroxime	16	70.42	73.45	71.81	67.51	60.92	62.59	67.42	–4.8433	< 0.0001
Levofloxacin	4	73.71	71.56	67.95	65.62	66.67	61.13	67.1	–4.0714	< 0.0001
Ceftriaxone	2	69.01	72.5	68.97	64.36	60.15	62.23	65.88	–4.3853	< 0.0001
Gentamicin	8	74.18	65.73	60.45	59.75	51.34	52.92	59.2	–6.7725	< 0.0001
Cefepime	16	49.77	54.24	46.25	38.36	30.65	38.32	42.21	–7.1678	< 0.0001
Ceftazidime	8	17.84	1.32	48.48	43.61	34.29	36.31	31.25	9.9654	< 0.0001
Cefoxitin	16	30.52	29.57	29.41	21.17	12.07	10.77	21.19	–10.1704	< 0.0001
Nitrofurantoin	64	28.17	27.31	16.02	14.47	10.73	11.13	16.88	–8.6556	< 0.0001
Piperacillin-tazobactam	32/4–64/4	14.55	18.64	13.18	13.63	6.7	10.77	12.72	–4.6131	< 0.0001
Amikacin	32	18.31	15.25	10.75	8.39	8.24	8.03	10.78	–5.3067	< 0.0001
Imipenem	2	0.94	1.51	2.43	1.26	1.15	1.64	1.54	–0.1060	0.9156
Meropenem	2	0	0.56	0.2	1.05	0.96	2.01	0.9	3.1604	0.0016

sulfamethoxazole, ampicillin-sulbactam, gentamicin, cefepime, cefoxitin, nitrofurantoin, and amikacin. A marked decrease of resistance against *E. coli* was observed for cefuroxime and ceftriaxone, i.e., from 70.42% to 62.59%, and from 69.01% to 62.23%, respectively. However, the resistance rates of these two antimicrobial agents to ESBL-*E. coli* showed an increasing trend (both from 95.6% to 100%). All the ESBL-*E. coli* isolates were resistant to ampicillin. These data are presented in Table III and Table S-III. The resistance

rates of ESBL-*E. coli* isolates to ceftriaxone, cefuroxime, ampicillin-sulbactam, cefepime, ampicillin, cefotaxime, levofloxacin, ceftazidime, gentamicin, and trimethoprim-sulfamethoxazole were higher than the rates of the ESBL-negative *E. coli* isolates ($p < 0.05$) (Table S-IV).

During the study period, the detection rate of *S. aureus* showed an upward trend ($\chi^2 = 2.5513$, $p = 0.0107$), meanwhile, the rate of methicillin-resistant *S. aureus* (MRSA) was stable. A significant decrease of resistance of isolates of *S. aureus* (including MRSA) was observed for erythromycin, azithromycin, clarithromycin, trimethoprim-sulfamethoxazole, clindamycin, cefoxitin, norfloxacin, moxifloxacin, gentamicin, tetracycline, rifampicin, nitrofurantoin, and teicoplanin. No *S. aureus* isolate was found to be resistant to linezolid and vancomycin. All MRSA isolates were resistant to oxacillin. These results are depicted in Table IV and Table S-V. The resistance rates of MRSA to 15 antimicrobial agents were higher than that of methicillin-susceptible *S. aureus* (MSSA) ($p < 0.05$) (Table S-VI).

During the study period, the detection rate of *P. aeruginosa* was stable. A significant decrease of resistance was observed for gentamicin, tobramycin, and polymyxin B from 52.78% to 50.58%, from 53.7% to 44.4%, and from 20.37% to 6.56%, respectively. In addition, a marked increase was seen for meropenem from 44.44% in 2011 to 49.81% in 2016 (Table V).

During the study period, the detection rate of *A. baumannii* showed an increasing tendency ($\chi^2 = 7.8954$, $p < 0.0001$). A significant increase of resistance of the isolates was observed for ceftriaxone, gentamicin, ciprofloxacin, ceftazidime, trimethoprim-sulfamethoxazole, cefepime, levofloxacin, piperacillin-tazobactam, and amikacin (Table VI).

Discussion

This study provided data about detection rates and resistance patterns of five dominant bacteria isolated in a general hospital in Zhengzhou, Henan province, China, between 2011 and 2016. Overall, the detection rates of these bacteria showed a slowly increasing trend. In addition, Gram-negative bacteria seemed to be the main cause of infection. The possible explanation of these phenomena could be the overrepresentation of some types of the samples (sputum and urine), or a double-membrane structure and the occurrence of efficient efflux pumps in Gram-negative bacteria (Blair et al. 2014). Several studies have reported similar findings. The data from CHINET surveillance between 2005 and 2014 showed that the five selected species, including *E. coli*, *K. pneumoniae*, *P. aeruginosa*, *A. baumannii*, and *S. aureus* accounted for 51.9 to 60.3%

Table IV
The resistance rates of *S. aureus* to 18 antimicrobial agents in the years 2011 to 2016.

Antimicrobial agent	MIC breakpoints	2011	2012	2013	2014	2015	2016	Total	χ^2	*p*
	I (μg/ml)	n = 96	n = 248	n = 219	n = 213	n = 254	n = 400	n = 1430		
Penicillin	0.25	92.71	93.55	94.06	95.77	88.19	89.00	91.68	–2.759	0.0058
Erythromycin	1–4	95.83	87.10	80.82	80.28	82.28	81.00	83.15	–3.0012	0.0027
Azithromycin	4	90.63	86.29	80.37	81.22	77.95	76.50	80.70	–3.8879	0.0001
Clarithromycin	4	90.63	83.87	79.45	79.81	70.08	69.00	76.43	–6.0151	< 0.0001
Trimethoprim--sulfamethoxazole	4/76	85.42	91.13	62.56	69.95	73.62	51.25	68.95	–9.9209	< 0.0001
Clindamycin	1–2	67.71	65.73	59.36	56.34	55.12	58.25	59.51	–2.4495	0.0143
Cefoxitin	8	69.79	72.18	71.23	58.69	44.49	41.50	56.36	–9.6125	< 0.0001
Norfloxacin	8	70.83	64.11	63.01	59.62	52.36	43.75	55.94	–6.6063	< 0.0001
Levofloxacin	2	67.71	61.29	57.99	56.34	48.43	36.25	51.19	–7.6331	< 0.0001
Moxifloxacin	1	63.54	56.45	52.51	53.99	48.03	34.50	48.32	–6.5328	< 0.0001
Gentamicin	8	64.58	64.11	46.12	45.54	35.83	35.00	45.45	–8.242	< 0.0001
Tetracycline	8	58.33	57.26	47.49	47.42	38.98	37.00	45.45	–5.9025	< 0.0001
Oxacillin	4	53.13	42.74	33.79	43.66	45.67	42.25	42.59	–0.6128	0.8283
Rifampicin	2	40.63	30.65	25.57	21.60	17.32	10.00	21.19	–8.1147	< 0.0001
Nitrofurantoin	64	26.04	15.73	16.44	9.86	5.91	8.00	11.75	–5.7483	< 0.0001
Teicoplanin	16	11.46	12.10	5.02	4.23	0.79	1.75	4.90	–6.6928	< 0.0001
Linezolid	8	0	0	0	0	0	0	0		
Vancomycin	4–8	0	0	0	0	0	0	0		

Table V
The resistance rates of *P. aeruginosa* to 13 antimicrobial agents in the years 2011 to 2016.

Antimicrobial agent	MIC breakpoints	2011	2012	2013	2014	2015	2016	Total	χ^2	*p*
	I (μg/ml)	n = 108	n = 236	n = 168	n = 248	n = 259	n = 259	n = 1278		
Ticarcillin	32–64	70.37	74.58	76.79	76.21	75.29	76.45	75.35	0.9182	0.3585
Piperacillin	32–64	57.41	63.14	54.76	56.45	61.00	61.39	59.47	0.3942	0.6934
Imipenem	4	50.00	52.97	60.71	53.63	62.16	57.92	56.73	1.8507	0.0642
Aztreonam	16	50.93	48.31	54.76	50.00	52.90	54.83	51.96	1.1464	0.2516
Gentamicin	8	52.78	61.02	55.36	43.95	49.42	50.58	51.80	–2.2516	0.0243
Ceftazidime	16	43.52	52.54	54.76	49.19	51.74	53.28	51.41	0.8686	0.3851
Tobramycin	8	53.70	58.90	52.38	39.11	49.81	44.40	48.98	–3.0892	0.0020
Piperacillin-tazobactam	32/4–64/4	43.52	51.27	42.86	41.94	52.90	53.28	48.44	1.6789	0.0932
Norfloxacin	8	50.93	54.24	47.02	39.92	48.26	48.26	47.81	–1.2309	0.2183
Meropenem	4	44.44	41.95	45.24	45.16	54.44	49.81	47.34	2.4052	0.0162
Cefepime	16	42.59	46.19	50.60	37.90	49.81	51.74	46.71	1.5010	0.1334
Ciprofloxacin	2	48.15	52.97	45.83	41.53	45.56	44.02	46.09	–1.7609	0.0783
Levofloxacin	4	45.37	47.88	40.48	37.90	45.95	45.95	43.97	–0.0615	0.9510
Amikacin	32	36.11	40.68	37.50	29.03	35.52	36.29	35.68	–0.9114	0.3621
Polymyxin B	4	20.37	19.49	14.29	9.68	13.51	6.56	13.15	–4.5199	< 0.0001

Table VI
The resistance rates of *A. baumannii* to 13 antimicrobial agents in the years 2011 to 2016.

Antimicrobial agent	MIC breakpoints	2011	2012	2013	2014	2015	2016	Total	χ^2	*p*
	I (μg/ml)	n = 68	n = 114	n = 114	n = 224	n = 292	n = 296	n = 1108		
Ceftriaxone	16–32	32.35	64.04	72.81	72.77	79.11	80.74	73.19	7.4412	< 0.0001
Ampicillin-sulbactam	16/8	41.18	64.91	81.58	76.79	73.63	64.53	69.77	1.5591	0.1190
Gentamicin	8	44.12	67.54	64.04	74.55	68.15	75.68	69.49	4.0867	< 0.0001
Ciprofloxacin	2	39.71	57.89	64.04	73.66	69.52	75.34	68.32	5.6165	< 0.0001
Ceftazidime	16	39.71	52.63	64.04	66.07	62.67	72.64	63.72	5.0871	< 0.0001
Trimethoprim--sulfamethoxazole	4/76	39.71	63.16	60.53	60.27	66.78	64.86	62.27	3.0414	0.0024
Cefepime	16	35.29	50.00	56.14	62.05	61.99	70.95	60.92	5.8829	< 0.0001
Levofloxacin	4	41.18	53.51	64.04	65.18	59.93	64.53	60.83	2.9341	0.0033
Piperacillin-tazobactam	32/4–64/4	29.41	50.00	57.02	58.04	64.38	68.24	59.75	6.0938	< 0.0001
Amikacin	32	33.82	60.53	56.14	62.50	57.53	62.84	58.66	2.8410	0.0045
Meropenem	4	19.12	46.49	57.89	54.02	47.95	47.64	48.19	1.9045	0.0568
Imipenem	4	20.59	48.25	61.40	59.38	45.55	37.16	46.48	–1.0354	0.3005
Polymyxin B	4	10.29	21.93	15.79	19.64	13.63	18.24	16.88	0.0504	0.9598

of all isolates (Hu et al. 2016). In a four-year study in Italy, researchers found that Gram-negative bacteria appeared to be the major causes of infection (Reale et al. 2017). Thus, in terms of quantity and proportion, Gram-negative bacteria have become a major threat in nosocomial infections.

During the study period, the situation with these multi-resistant isolates was complicated. For *K. pneumoniae* and *A. baumannii*, the rates of multi-resistant isolates were increasing. For *E. coli*, *P. aeruginosa*, and *S. aureus*, the rates were decreasing. From these results, one can get directions for making recommendations by some government policies, such as separation the clinic from the pharmacy, hospital surveillance and preventive measures. All these recommendations may have played a role in combating antibiotic resistance. But more importantly, a problem demanding prompt solution is how to prevent the spread of multi-drug

resistant isolates and how to optimize the use of the existing antibiotics.

Overall, among the Enterobacteriaceae, 14.34% of *K. pneumoniae* isolates and 50.18% of *E. coli* isolates were ESBL producers. A marked decrease in the detection rates was seen for ESBL-*K. pneumoniae* and ESBL-*E. coli*. In addition, the resistance rates of ESBL-positive isolates to multiple antibiotics (mainly cephalosporin antibiotics) were higher than that of ESBL-negative isolates. This might be related to the extensive use of cephalosporin in clinical practice, especially the third generation cephalosporin (Pathak et al. 2013; Tang et al. 2018). But the resistance rate of ESBL-positive isolates to cefoxitin was lower than that of ESBL-negative isolates. Also, the resistance rate of these isolates to cefoxitin was lower than that to the third generation cephalosporin. In the absence of details about the resistance genes of these isolates, we could not infer that this was related to *AmpC*. Moreover, the ESBL-positive isolates were not only resistant to cephalosporin antibiotics, but also resistant to fluoroquinolones. As observed in this study, the resistance rate of ESBL-*K. pneumoniae* and ESBL-*E. coli* to levofloxacin was 37.22% and 79.10%, with a marked increase, respectively. This has led to growing utilization of carbapenems. Fortunately, the majority of *K. pneumoniae* and *E. coli* were sensitive to carbapenems (Hu et al. 2016; Khan et al. 2017; Yang et al. 2017).

Although the resistance rate of *S. aureus* to most antibiotics was declining, the resistance rate of the isolates was still above 40%. This indicated the severity of multidrug resistance in *S. aureus*. This phenomenon was more pronounced in MRSA. During the study period, the detection rate of MRSA was 42.38%. The data from CHINET surveillance showed a marked decrease of MRSA from 69% in 2005 to 44.6% in 2014 (Hu et al. 2016). The resistance rate of MRSA to antibiotics was apparently higher than that of MSSA, except linezolid and vancomycin. This was associated with SCC*mec* elements. The SCC*mec* element is a mobile genetic element that carries a variety of antibiotic resistance genes, such as drug-resistance genes against mercury, cadmium, kanamycin, bleomycin, erythromycin, spectinomycin, and fusidic acid (Ito et al. 2001; Holden et al. 2004). Currently, vancomycin is still an ideal antibiotic to treat *S. aureus*-related infections, but vancomycin-resistant *S. aureus* has been reported (Panesso et al. 2015; Walters et al. 2015; Olufunmiso et al. 2017).

In this study, besides polymyxin B, *P. aeruginosa* showed high resistance to other antibiotics. The emergence of multidrug-resistant *P. aeruginosa* posed a difficult problem for clinical treatment (Vincent 2003). Compared with the data from CHINET, the resistance rate of *P. aeruginosa* to nine antibiotics (imipenem, meropenem, gentamicin, ceftazidime, tobramycin, piperacillin-tazobactam, cefepime, ciprofloxacin, levofloxacin, and amikacin) in this study were higher than in the surveillance data, which might be related to differences among the surveillance area (Hu et al. 2016). Aminoglycosides are recognized for their efficacy against *P. aeruginosa* (Holbrook and Garneau-Tsodikova, 2018). Although the resistance rate of *P. aeruginosa* to aminoglycoside antibiotics was decreasing, the strains showed high levels of resistance. For example, the antibiotic with the lowest resistance rate was amikacin, which resistance rate was 35.68%. Meanwhile, *P. aeruginosa* also showed high resistance to carbapenems, which might be related to the high use of these antibiotics in clinics.

A similar trend was observed for *A. baumannii*, and more seriously, the detection rate of isolates and the resistance rate of isolates to the majority of antibiotics were increasing. These were consistent with other studies (Peneș et al. 2017). This was mainly due to the membrane impermeability of *A. baumannii*, which leads to difficulty in traversing the membrane and reaching their targets by antibiotics (Sugawara and Nikaido 2012; Zgurskaya et al. 2015). Carbapenem antibiotics are important for the treatment the *A. baumannii* infection, but reports have shown that the rate of carbapenems-resistant *A. baumannii* was increasing (Agodi et al. 2015; Hu et al. 2016). Research had shown that the increasing use of carbapenems was associated with the increasing rate of carbapenem-resistant *A. baumannii* (Tan et al. 2015). This showed the importance of rational use of antibiotics. Rigatto et al. (2015) had shown a benefit of combination monotherapy with polymyxin B for severe extensively drug-resistant *A. baumannii* or *P. aeruginosa* infections. Resistance to polymyxin B would increase the difficulty of treating multi-drug resistant *A. baumannii* and *P. aeruginosa*. Chung et al. (2016) have developed a new combination therapy using minimal concentrations of polymyxin B.

Conclusions

In conclusion, Gram-negative bacteria appeared to be the main cause of infection in this study. The resistance rates of five species of the bacteria to most antibiotics were decreasing, but the isolates showed high levels of resistance and multiple-drug resistance, especially *P. aeruginosa* and *A. baumannii*. Methods such as the combination of antibiotics to optimize the use of antibiotics may help to solve the problem. Simultaneously, this study showed that some antibiotics continue to be active against these isolates, such as meropenem and imipenem for ESBL-*K. pneumoniae* and ESBL-*E. coli*, linezolid and vancomycin for MRSA and polymyxin B for *P. aeruginosa,* and *A. baumannii*. The mobility of modern society is unprecedented. Geographical boundaries cannot stop the spread of drug-resistant bacteria.

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Limitation

Our study has several limitations. First, we do not know the use of antibiotics in patients from whom the bacteria were isolated, nor their outcomes. Second, we did not track the changes of these strains at the genetic level in the laboratory.

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Conflict of interest

The authors do not report any financial or personal connections with other persons or organizations, which might negatively affect the contents of this publication and/or claim authorship rights to this publication.

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