doi.org/10.36721/PJPS.2023.36.3.REG.723-730.1

Surveillance and analysis of bacterial resistance in a comprehensive teaching hospital from 2015 to 2017

Yang Junlin, LI Lingzhu, LUO Guangying, Meng Huaqing and ZHA Zhuhong
Department of Nosocomial Infection Management, The Affiliated Hospital of Guizhou Medical University, Guiyang, China

Abstract: To understand the changes of resistance of major clinical isolates to commonly used antibiotics in a comprehensive teaching hospital from 2015 to 2017 and to provide a basis for rational clinical use of antibiotics in the hospital. Antimicrobial susceptibility testing of all clinical isolates from 2015 to 2017 was carried out according to a unified protocol using Kirby-Bauer method or automated systems according to the unified plan. A total of 28715 non-repetitive clinical isolates were collected from 2015 to 2017. *Escherichia coli*, *Klebsiella pneumoniae* and *Acinetobacter baumannii* were the top three most common isolates for three consecutive years. *Escherichia coli* is still highly sensitive to carbapenems, with the drug resistance rate less than 1%. *Klebsiella pneumoniae*'s resistance to carbapenems increases year by year, reaching about 18% in 2017. The resistance rate of *Acinetobacter baumannii* to meropenem was above 70%, and that of *Pseudomonas aeruginosa* to meropenem was about 30%. *Staphylococcus* is more sensitive to linezolid and vancomycin. *Enterococcus faecalis* had lower drug resistance to most tested antibiotics (except tetracycline) than *Enterococcus faecalis*, and both were sensitive to linezolid and vancomycin. Bacterial resistance to commonly used antibiotics is still on the rise. We should strengthen the management of clinical use of antimicrobial agents and maintain good practice in surveillance of bacterial resistance.

Keywords: Bacterial resistance surveillance, antimicrobial susceptibility testing, carbapenem-resistant gram-negative bacterium, carbapenem-resistant *Klebsiella pneumoniae.*

INTRODUCTION

Many aspects of modern medicine rely on the treatment or prophylactic use of antibiotics. With the clinical overuse of antibiotics, the activity of antibacterial drugs decreased with the increase of the number of drug-resistant strains and the increase of natural drug-resistant microbial infections and the detection rate of multi-drug resistant bacteria in clinical practice also increased year by year, bacterial antibiotic resistance has developed into a major problem in the field of global public health (WHO, 2012). The increasing number of multi-drug resistant strains and pan-drug resistant strains has brought great challenges to clinical anti-infection treatment, significantly prolonged the hospital stay of patients and increased the economic burden of society (Lim et al., 2015; Smith and Coast, 2013). The evolution and spread of antibiotic resistance among pathogens is outpacing the development of new antibiotics, and the search for alternative antibiotics is often limited (Dickey et al., 2017; CDC, 2013). Rational use of antibiotics can slow this trend, and perhaps reverse it. To achieve this goal, it is necessary to pay attention to the epidemiological information of drug-resistant bacteria, improve the surveillance level of bacterial resistance, and better guide the rational use of drugs in clinic. The surveillance of bacterial resistance can provide the basis of rational drug use for clinical practice, improve the level of anti-infection treatment, prevent the occurrence and development of bacterial resistance, and control the spread and outbreak of drug-resistant bacteria in hospitals (Lõme et al., 2018). There are regional differences in the distribution and drug resistance of pathogenic bacteria, and dynamic monitoring of bacterial drug resistance is of great significance to accurately grasp the characteristics of bacterial resistance to antimicrobial drugs and the changes of drug resistance, as well as to guide clinical drug selection and empirical treatment (Johnson, 2015). In response to the call of the national action plan for curbing bacterial resistance issued by the National health commission of the People's Republic of China, and better understand the distribution of nosocomial bacteria and the characteristics of drug resistance in pathogenic bacteria, this study retrospectively analyzed the drug susceptibility results of all isolated bacteria in clinical practice from 2015 to 2017 and conducted drug resistance analysis to provide a basis for the hospital clinical anti-infection treatment and the control of bacterial drug resistance transmission.

MATERIALS AND METHODS

Strain source

All clinical bacteria were isolated in the hospital from January 1, 2015 to December 31, 2017 and the repeated strains from the same patient were removed.

Antimicrobial susceptibility test

Kirby-Bauer method or automated systems was adopted. The quality control bacteria were *Escherichia coli* 25922 and *Staphylococcus aureus* 29213. The drug susceptibility

*Corresponding author: e-mail: 794787045@qq.com

test results were judged according to the latest CLSI standards of the year of surveillance. If the results of vancomycin and linezolid with Kirby-Bauer method or automated systems were non-sensitive strains, the MIC value of vancomycin and linezolid E strip was determined for confirmation.

STATISTICAL ANALYSIS

WHONET 5.6 software was used to process and analyze the data, and the distribution of pathogenic bacteria, type of pathogen specimens and drug resistance rate of commonly used animicrobial agents were counted.

ETHICAL APPROVAL

The surveillance of bacterial resistance has been approved by the Ethics Committee of Affiliated Hospital of Guizhou Medical University and patients.

RESULTS

Source of pathogen specimens

In the distribution of specimens for three consecutive years, the proportion is from high to low in the order of respiratory specimens, blood specimens and urine specimens, sputum specimens account for more than 40%, blood specimens fall to less than 20% in 2017, other sterile body fluids are about 5%, cerebrospinal fluid is about 4%, as shown in table 1.

Distribution of pathogenic bacteria

Among 28715 non-repetitive clinical isolates, *Escherichia coli*, *Klebsiella pneumoniae* and *Acinetobacter baumannii* are the most common gram-negative bacteria, all of which are more than 10%. *Staphylococcus aureus* is the most common gram-positive bacteria, accounting for about 6%, as shown in table 2.

Resistance of Enterobacteriaceae strains to animicrobial agents

The antibiotic resistance rate of *Escherichia coli* and *Klebsiella pneumoniae* to ampicillin is more than 90%, to the other three kinds of β-lactamase inhibitor compound preparations is less than 30% except for ampicillin-sulbactam, to cefazolin and cefuroxime is more than 55%, to ceftazidime is about 30%, to ceftriaxone and cefotaxime is about 30% to cefepime was more than 50%. *Escherichia coli* had low antibiotic resistance to cefoxitin, amikacin and nitrofurantoin and was still highly sensitive to carbapenem antibiotics, with the antibiotic resistance rate less than 1%.

Resistance of non-fermentative gram-negative bacilli to antimicrobial agents

The antibiotic resistance rate of *Acinetobacter baumannii* to meropenem is more than 70%, to other tested drugs is more than 60%. The antibiotic resistance rate of *Pseudomonas aeruginosa* to meropenem is about 30%, to aminoglycosides is about 20%, among which the drug resistance rate to amikacin is relatively low, and the antibiotic resistance rate to other test drugs is mostly about 30%. All the non-fermentative gram-negative bacilli were 100% resistant to nitrofurantoin, as shown in table 4.

Resistance of Staphylococcus to antimicrobial agents

Staphylococcus has a high resistance rate to penicillin, almost no resistance to linezolid and vancomycin, and a relatively stable resistance rate to nitrofurantoin and quinopudine-dafoprotin from 2015 to 2017, all of which remain below 2%. The drug resistance rate of *staphylococcus aureus* to ampicillin-sulbactam and trimethoprim-sulfamethoxazole was less than 7% and the drug resistance rate to erythromycin was more than 50%, but the resistance level to other antibiotics was less than 30%, which was relatively stable. The resistance rate of *Staphylococcus epidermidis* to ceftriaxone, trimethoprim-sulfamethoxazole and erythromycin was over 55%, to moxifloxacin was about 25%, to ciprofloxacin and levofloxacin was over 50% and to amoxicillin-clavulanic acid and ampicillin-sulbactam was low. The resistance rate of *Staphylococcus haemolyticus* to ampicillin-sulbactam, rifampicin and tetracycline is about 30%~50%, which is increasing year by year, as shown in table 5.

Resistance of Enterococcus to antimicrobial agents

The resistance rate of *Enterococcus* to oxacillin was 100%, and it was still most sensitive to linezolid and vancomycin. The resistance rates of *Enterococcus faecium* to penicillin, ampicillin-sulbactam, ceftriaxone and aminoglycoside antibiotics were all over 90%, to tetracycline and rifampicin were all over 60%, to nitrofurantoin and quinopudine-dafoprotin were all under 15%. *Enterococcus faecalis* was more than 80% resistant to ceftriaxone and tetracycline, less than 3% resistant to penicillin, ampicillin-sulbactam and Nitrofurantoin, and less than 20% resistant to aminoglycoside antibiotics. The resistance rate of *Enterococcus* to high concentration of streptomycin is about 30%, and the resistance rate to high concentration of gentamicin is decreasing year by year, as shown in table 6.

DISCUSSION

The monitoring results of bacterial resistance from 2015 to 2017 showed: (1) In the distribution of specimens for three consecutive years, the proportion is from high to low in the order of respiratory specimens, blood specimens and urine specimens, sputum specimens account for more than 40%, blood specimens fall to less than 20% in 2017, other sterile body fluids are about 5%, cerebrospinal fluid is about 4%, wound pus less than 1%, and CHINET monitoring results in 2016 (HU *et al.*, 2017).

Table 1: The specimen type of bacterial resistance monitoring in 2015~2017

Specimen type	2015		2016		2017	
	No. of strains	(%)	No. of strains	(%)	No. of strains	(%)
Respiratory tract	14545	42.95	18887	41.37	22808	41.88
Blood	7231	21.35	9864	21.61	10040	18.43
Urine	3603	10.64	5317	11.65	7432	13.65
Other sterile body fluids	1721	5.08	2756	6.04	2764	5.07
Cerebrospinal fluid	1266	3.74	1542	3.38	2305	4.23
Wound pus	299	0.88	389	0.85	278	0.51
Others	5201	15.36	6899	15.11	8838	16.23
Total	33866	100.00	45654	100.00	54465	100.00

Table 2: The distribution of bacterial species in 2015~2017`

Organism	2015		2016		2017	
	No. of strains	%	No. of strains	%	No. of strains	%
Escherichia coli	1721	18.04	1979	19.67	1821	19.96
Klebsiella pneumoniae	1152	12.08	1478	14.69	1419	15.55
Acinetobacter baumannii	959	10.05	1000	9.94	1206	13.22
Pseudomonas aeruginosa	712	7.46	937	9.31	876	9.60
Enterobacter cloacae	274	2.87	339	3.37	299	3.28
Staphylococcus aureus	520	5.45	670	6.66	619	6.78
Staphylococcus epidermidis	281	2.95	366	3.64	238	2.61
Staphylococcus haemolyticus	296	3.10	281	2.79	278	3.05
Enterococcus faecium	233	2.44	429	4.26	343	3.76
Enterococcus faecalis	132	1.38	236	2.35	89	0.98
Others	3260	34.17	2346	23.32	1936	21.22
Total	9540	100.00	10061	100.00	9124	100.00

Showed slight differences in respiratory tract specimens (41.6%), urine (19.1%), blood (13.3%), wound pus (7.3%), cerebrospinal fluid (CSF) and other sterile body fluids (7.0%). Notably, blood samples dropped below 20% in 2017, while blood culture plays an important role in the diagnosis of bloodstream infections (Wilinger and Haase, 2013), it reminds us that the hospital should strengthen the training on the collection and examination of clinical microbial specimens. (2) A total of 28715 non-repetitive strains were isolated for 3 consecutive years, and the top five strains were *Escherichia coli*, *Klebsiella pneumoniae*, *Acinetobacter baumannii*, *Pseudomonas aeruginosa* and *Staphylococcus aureus*, similar to what Liu reported that gram-negative bacteria were the most commom pathogenic bacteria from 874 strains in the department of neurology (Liu, 2018). The CHINET monitoring results in 2016 (HU *et al.*, 2017) showed in slightly different order that the top five were *Escherichia coli, Klebsiella, Acinetobacter baumannii, Staphylococcus aureus* and *Pseudomonas aeruginosa*. (3) *Escherichia coli*, a member of the *Enterobacteriaceae* family, remains highly sensitive to carbapenems, with a drug resistance rate of less than 1% for three years. In 2017, the drug resistance rate of *Klebsiella pneumoniae* to ertabenem, meropenem and imipenem reached 18%, which was lower than the drug resistance rate of *Klebsiella pneumoniae* to carbapenems in a newly-built hospital in Shanghai > 40.00% (HE *et al.*, 2018), and higher than the drug resistance rate of *Klebsiella pneumoniae* to carbapenems reported by CHINET in 2016, which was 15% (HU *et al.*, 2017). (4) The resistance rate of *Acinetobacter baumannii* to meropenem was more than 70%, and to other tested drugs was more than 60%, the resistance rate of *Pseudomonas aeruginosa* to meropenem is about 30%, similar to what CHINET reported in 2016 the resistance rates of *Pseudomonas aeruginosa* and *Acinetobacter baumannii* to carbapenems were close to 30% and 70%, respectively (HU *et al.*, 2017). (5) *Staphylococcus* is more sensitive to linezolid and vancomycin, and the overall drug resistance of *Staphylococcus haemolyticus* is higher than that of *Staphylococcus epidermidis* and *Staphylococcus aureus*. (6) The resistance rate of *Enterococcus faecalis* in *Enterococcus* to most tested antibiotics (except tetracycline) was lower than that of *Enterococcus faecalis*, and both were more sensitive to linezolid and vancomycin.

In the past, carbapenem antibiotics such as imipenem and meropenem were considered as the last line of defense in the treatment of gram-negative bacilli infection (Papp-Wallace, *et al.*, 2011). However, in recent years, with the excessive use and irregular use of carbapenem antibiotics, carbapenem-resistant gram-negative bacteria appeared, especially the detection rate of carbapenem-resistant *Klebsiella pneumoniae* and *Acinetobacter baumannii* increased, the bacterial resistance of gram-negative bacteria has become a difficult problem in clinical anti infection treatment (QIN, *et al.,* 2014).

Table 3: Resistant of Enterobacteriaceae strains to animicrobial agents` in 2015~2017`

Antibacterial agent	*Escherichia coli*									*Klebsiella pneumoniae*								
	2015 (n=1721)			2016 (n=1979)			2017 (n=1821)			2015 (n=1152)			2016 (n=1478)			2017 (n=1419)		
	(R%)	(I%)	(S%)	(R%)	(I%)	(S%)	(R%)	(I%)	(S%)	(R%)	(I%)	(S%)	(R%)	(I%)	(S%)	(R%)	(I%)	(S%)
Ampicillin	94.4	0.0	5.6	93.0	0.3	6.7	91.4	0.2	8.4	93.8	9.4	27.6	88.6	8.7	2.7	89.0	8.8	2.3
Piperacillin	92.7	0.4	7.0	90.2	0.8	9.0	90.3	0.8	8.9	63.1	17.6	61.9	60.6	6.2	33.3	56.0	6.6	37.4
Amoxicillin- Clavulanic acid	10.0	27.8	62.3	12.1	22.0	66.0	8.6	21.8	69.7	20.6	16.6	20.2	31.1	11.9	57.0	28.7	11.7	59.7
Ampicillin-Sulbactam	77.8	11.7	10.5	62.9	22.9	14.2	51.4	28.5	20.2	63.3	14.1	58.6	72.5	6.9	20.7	57.7	5.6	36.7
Ticarcillin- Clavulanic acid	11.6	25.3	63.1	13.6	20.7	65.8	10.9	20.9	68.3	27.3	4.8	81.4	35.3	10.1	54.6	28.9	12.8	58.4
Piperacillin -Tazobactam	7.0	5.3	87.7	9.5	4.2	86.4	6.2	5.8	88.0	13.9	0.6	42.2	29.3	4.1	66.7	27.1	3.6	69.3
Cefazolin	76.6	1.2	22.2	77.0	1.3	21.7	73.2	1.0	25.9	57.2	3.0	39.0	57.5	0.7	41.9	53.2	0.6	46.2
Cefuroxime	73.9	1.4	24.7	73.8	1.7	24.5	71.0	1.4	27.7	58.1	3.4	66.0	57.0	2.6	40.4	54.1	3.7	42.3
Ceftazidime	32.0	7.9	60.1	32.0	7.8	60.3	26.4	9.9	63.7	30.7	1.1	44.5	37.7	4.1	58.2	33.5	4.4	62.1
Cefatriaxone	73.2	0.5	26.3	72.8	0.9	26.4	69.4	0.5	30.2	54.4	1.5	44.0	53.8	1.0	45.2	49.4	1.1	49.6
Cefotaxime	73.1	0.6	26.4	72.0	0.9	27.1	69.3	0.5	30.3	54.5	2.0	47.1	53.2	1.9	44.9	49.2	1.5	49.4
Cefepime	70.2	1.5	28.3	68.6	2.5	28.9	65.1	1.9	33.0	50.9	6.2	81.3	49.1	2.3	48.6	44.7	2.2	53.1
Cefoxitin	7.7	9.7	82.7	11.4	10.8	77.9	7.4	9.2	83.4	12.6	3.2	57.8	25.8	6.3	67.9	26.5	5.2	68.3
Aztreonam	61.9	5.0	33.1	55.3	6.8	37.9	51.6	7.2	41.2	39.1	1.0	95.4	44.7	3.7	51.6	39.5	3.3	57.2
Ertapenem	0.6	0.3	99.1	1.0	1.1	97.9	0.9	0.6	98.5	3.7	0.3	90.1	17.5	0.7	81.9	18.4	0.6	81.1
Imipenem	0.6	0.1	99.3	0.7	0.1	99.3	0.7	0.2	99.1	9.7	0.0	89.9	16.5	0.4	83.2	17.9	0.3	81.8
Meropenem	0.4	0.1	99.5	0.7	0.0	99.3	0.7	0.0	99.3	10.1	0.4	88.3	16.6	0.2	83.2	18.0	0.2	81.9
Amikacin	3.2	1.3	95.5	1.8	1.2	97.0	1.9	0.8	97.3	11.4	0.3	54.8	15.9	0.6	83.5	18.6	0.4	81.0
Gentamicin	47.7	1.0	51.3	50.2	0.7	49.1	41.0	0.9	58.2	45.0	11.3	56.1	43.1	0.5	56.4	37.8	0.7	61.5
Tobramycin	38.1	11.4	50.5	37.4	15.4	47.2	31.1	11.7	57.2	32.6	6.4	61.1	34.8	7.7	57.5	28.3	8.0	63.7
Ciprofloxacin	55.3	1.0	43.7	59.1	1.8	39.2	50.5	1.0	48.5	32.5	4.6	74.1	36.3	4.6	59.1	32.1	4.4	63.6
Levofloxacin	51.1	2.5	46.5	56.5	2.5	41.1	47.0	3.0	50.0	21.3	0.0	51.7	26.4	6.1	67.6	26.3	3.6	70.1
Trimethoprim-sulfamethoxazole	67.1	0.0	32.9	63.6	0.0	36.4	57.1	0.0	42.9	48.4	28.7	19.9	50.7	0.0	49.3	44.3	0.0	55.8
Nitrofurantoin	3.4	5.5	91.1	4.0	5.1	90.9	4.2	5.2	90.6	51.5	4.3	55.7	58.8	19.6	21.6	51.8	23.8	24.5
Tetracycline	72.7	0.2	27.1	73.4	0.2	26.4	65.2	0.6	34.2	40.0	9.4	27.6	38.2	2.0	59.8	40.6	2.0	57.4

Table 4: Resistance of non-fermentative gram-negative bacilli to antimicrobial agents

Antibacterial agent	*Acinetobacter baumannii*									*Pseudomonas aeruginosa*								
	2015 (n=959)			2016 (n=1000)			2017 (n=1199)			2015 (n=712)			2016 (n=937)			2017 (n=862)		
	(R%)	(I%)	(S%)	(R%)	(I%)	(S%)	(R%)	(I%)	(S%)	(R%)	(I%)	(S%)	(R%)	(I%)	(S%)	(R%)	(I%)	(S%)
Piperacillin	71.0	4.3	24.7	81.9	3.6	14.5	83.9	3.0	13.1	31.0	0.0	69.1	39.9	0.0	60.1	28.9	0.0	71.1
Ampicillin-Sulbactam	73.4	0.0	26.6	80.0	0.0	20.0	94.8	2.6	2.6	-	-	-	-	-	-	-	-	-
Ticarcillin-Clavulanic acid	75.0	1.4	23.7	80.6	2.1	17.4	83.1	0.8	16.1	41.2	0.0	73.0	49.7	0.0	65.4	38.8	0.0	75.7
Ceftazidime	74.7	0.0	0.0	80.1	0.4	19.5	83.9	0.3	15.8	32.2	0.0	0.0	33.0	0.1	0.1	24.2	0.0	0.0
Cefatriaxone	75.0	10.3	0.8	79.9	3.2	16.9	83.5	3.3	13.2	-	-	-	-	-	-	-	-	-
Cefotaxime	74.5	0.4	24.9	80.3	5.2	14.5	83.8	5.6	10.6	-	-	-	-	-	-	-	-	-
Cefepime	75.3	4.4	20.7	80.4	2.1	17.5	83.2	1.4	15.5	21.4	19.4	59.2	24.1	20.1	55.8	18.0	15.4	66.7
Meropenem	72.3	7.4	18.1	77.0	1.3	21.7	81.8	1.7	16.6	22.2	0.2	0.0	32.3	0.6	2.1	23.7	0.2	0.4
Amikacin	67.3	1.1	23.6	62.5	1.4	36.1	78.9	0.1	21.1	2.7	17.2	49.1	5.5	15.7	43.8	4.0	14.1	54.0
Gentamicin	75.2	1.1	0.3	75.8	3.5	20.7	82.2	1.1	16.7	17.6	3.4	69.3	22.9	4.5	61.3	14.5	4.2	69.0
Tobramycin	69.0	1.5	26.3	65.1	0.8	34.1	79.5	0.3	20.2	15.0	6.7	71.2	22.8	4.1	63.7	12.9	4.0	72.3
Ciprofloxacin	74.0	0.3	32.4	80.0	0.2	19.9	83.9	0.1	16.1	20.2	5.3	92.1	30.1	2.4	92.2	17.8	2.8	93.3
Levofloxacin	69.6	0.3	24.6	76.3	2.9	20.8	78.6	5.2	16.2	19.0	10.9	71.5	30.7	6.1	71.1	17.7	9.2	76.3
Trimethoprim-sulfamethoxazole	34.7	0.3	30.7	60.6	0.0	39.5	69.5	0.0	30.5	-	-	-	-	-	-	-	-	-
Nitrofurantoin	100.0	0.5	25.6	100.0	0.0	0.0	100.0	0.0	0.0	100.0	4.1	75.7	100.0	3.4	66.6	99.6	2.6	79.6
Tetracycline	75.3	3.9	26.6	78.7	1.9	19.4	83.2	0.6	16.2	-	-	-	-	-	-	-	-	-

NA' not available or not tested

Table 5: Resistant of Staphylococcus spp. to antimicrobial agents

Antibacterial agent	*Staphylococcus aureus*									*Staphylococcus epidermidis*									*Staphylococcus haemolyticus*								
	2015 (n=520)			2016 (n=670)			2017 (n=619)			2015 (n=218)			2016 (n=366)			2017 (n=238)			2015 (n=296)			2016 (n=281)			2017 (n=278)		
	(R%)	(I%)	(S%)	(R%)	(I%)	(S%)	(R%)	(I%)	(S%)	(R%)	(I%)	(S%)	(R%)	(I%)	(S%)	(R%)	(I%)	(S%)	(R%)	(I%)	(S%)	(R%)	(I%)	(S%)	(R%)	(I%)	(S%)
Penicillin	93.7	0.0	6.3	94.4	0.0	5.7	94.1	0.0	6.0	96.9	0.5	2.6	95.6	0.0	4.5	97.4	0.0	2.7	97.7	0.0	2.3	98.2	0.0	1.8	97.7	0.0	2.3
Oxacillin	27.9	0.0	72.1	31.9	0.0	68.2	29.6	0.0	70.4	87.6	0.0	12.5	85.7	0.0	14.3	88.2	0.0	11.8	96.0	0.0	4.1	94.7	0.0	5.3	94.6	0.0	5.4
Amoxicillin-clavulinic acid	12.8	0.0	87.2	12.5	0.0	87.5	10.0	0.0	90.0	13.2	0.0	86.8	11.1	0.0	88.9	10.9	0.0	89.1	75.1	0.0	25.0	72.6	0.0	27.4	77.9	0.0	22.1
Ampicillin-sulbactam	1.5	8.5	90.0	1.9	10.6	87.6	2.2	6.6	91.3	0.0	1.5	98.6	0.8	3.0	96.2	1.5	3.6	95.0	32.0	38.7	29.4	38.2	31.8	30.0	51.2	36.4	12.5
Ceftriaxone	29.6	0.8	69.6	32.6	0.8	66.6	31.0	0.6	68.4	57.6	0.0	42.5	86.0	0.0	14.0	88.2	0.0	11.8	96.0	0.0	4.1	94.7	0.0	5.3	90.8	0.0	9.2
Gentamicin	18.8	0.3	80.9	16.5	0.8	82.7	15.0	2.2	82.8	45.2	1.2	53.7	38.8	2.2	59.0	35.9	3.0	61.1	80.9	4.1	15.1	80.8	2.8	16.3	67.5	2.9	29.7
Rifampicin	10.9	0.9	88.2	9.2	1.4	89.5	5.3	0.9	93.8	12.4	0.4	87.2	8.1	0.6	91.4	12.6	0.0	87.4	33.1	0.6	66.3	32.6	0.0	67.4	50.5	0.6	48.9
Ciprofloxacin	21.2	5.8	73.1	17.0	5.7	77.4	16.8	4.8	78.4	55.6	1.3	43.1	50.3	1.9	47.8	55.3	0.9	43.9	89.8	2.3	7.9	88.8	0.7	10.5	88.2	1.7	10.1
Levofloxacin	19.6	0.8	79.6	16.4	0.3	83.4	14.4	1.3	84.4	51.9	1.2	47.0	51.1	0.8	48.1	53.5	1.2	45.4	90.6	0.9	8.5	88.8	0.3	10.9	86.7	0.4	12.9
Moxifloxacin	17.7	2.5	79.8	14.5	2.6	83.0	13.9	6.3	79.8	23.6	29.5	47.0	25.1	26.4	48.6	26.1	29.2	44.8	87.1	2.3	10.7	79.7	8.7	11.6	77.3	5.2	17.5
Trimethoprim-sulfamethoxazole	1.0	0.0	99.0	6.5	0.0	93.5	3.8	0.0	96.2	68.9	0.0	31.1	66.5	0.0	33.5	61.2	0.0	38.8	54.8	0.0	45.3	49.5	0.0	50.5	51.4	0.0	48.7
Erythrocin	62.8	1.1	36.2	56.6	1.0	42.4	53.7	0.5	45.9	77.8	1.2	21.0	75.6	0.6	23.8	77.6	0.7	21.7	92.3	1.4	6.3	92.7	0.4	6.9	95.5	0.6	3.9
Nitrofurantoin	0.4	0.3	99.3	0.7	0.9	98.5	0.7	0.7	98.7	0.0	0.9	99.2	0.2	1.1	98.7	0.4	0.4	99.2	0.0	2.5	97.6	1.1	3.5	95.4	1.7	1.9	96.4
Linezolid	0.0	0.0	100.0	0.2	0.0	99.8	0.0	0.0	100.0	0.0	0.0	100.0	0.0	0.0	100.0	0.0	0.0	100.0	0.0	0.0	100.0	0.0	0.0	100.0	0.0	0.0	100.0
Vancomycin	0.0	0.0	100.0	0.0	0.0	100.0	0.0	0.6	99.4	0.0	0.0	100.0	0.0	0.0	100.0	0.0	0.0	100.0	0.0	0.0	100.0	0.0	0.0	100.0	0.0	0.0	100.0
Quinopudine-dafoprotin	0.6	0.0	99.4	1.9	1.1	97.0	1.9	1.0	97.2	0.9	0.6	98.6	1.9	0.0	98.2	1.8	0.0	98.3	0.0	3.6	96.4	0.7	2.5	96.8	1.2	2.1	96.8
Tetracycline	33.0	3.7	63.4	34.5	3.8	61.7	36.2	3.3	60.5	36.4	2.0	61.6	38.6	0.6	60.8	37.5	0.7	61.9	34.8	1.7	63.5	36.7	1.8	61.5	43.8	1.2	55.0

Table 6: Resistant of Enterococcus faecalis and Enterococcus faecium to antimicrobial agents

Antibacterial agent	*Enterococcus faecium*									*Enterococcus faecalis*								
	2015 (n=233)			2016 (n=429)			2017 (n=343)			2015 (n=132)			2016 (n=236)			2017 (n=89)		
	(R%)	(I%)	(S%)	(R%)	(I%)	(S%)	(R%)	(I%)	(S%)	(R%)	(I%)	(S%)	(R%)	(I%)	(S%)	(R%)	(I%)	(S%)
Penicillin	96.2	0.0	3.8	95.6	0.0	4.4	96.1	0.0	3.9	0.0	0.0	100.0	2.4	0.0	97.6	2.3	0.0	97.8
Oxacillin	100.0	0.0	4.8	100.0	0.0	5.8	100.0	0.0	5.3	100.0	0.0	100.0	100.0	0.0	0.0	100.0	0.0	0.0
Ampicillin/sulbactam	94.3	0.0	0.0	94.0	0.0	0.0	94.5	0.0	0.0	0.0	0.0	0.0	2.8	0.4	96.8	1.1	1.1	97.9
Ceftriaxone	99.0	1.8	3.9	99.8	0.2	5.7	99.6	0.4	5.1	93.8	2.1	4.2	96.2	2.9	0.9	99.0	1.1	0.0
High concentration of gentamicin	67.9	0.0	1.0	59.9	0.2	0.0	47.2	0.4	0.0	41.0	0.0	59.1	40.5	0.0	59.6	36.7	0.0	63.3
High concentration streptomycin	27.7	0.0	32.1	40.5	0.0	40.2	33.0	0.0	52.8	23.1	0.0	77.0	25.9	0.0	74.2	23.2	0.0	76.9
Rifampicin	71.3	0.0	72.4	75.0	0.0	59.5	75.2	0.0	67.0	37.3	25.7	37.0	40.6	24.0	35.4	39.5	23.2	37.4
Ciprofloxacin	94.6	16.5	12.2	95.9	14.1	10.9	95.0	15.9	8.9	17.4	10.1	72.5	21.0	11.6	67.5	19.4	14.1	66.6
Levofloxacin	91.1	2.2	3.3	91.1	0.9	3.2	91.1	1.6	3.5	13.0	3.6	83.4	19.3	4.6	76.1	17.3	3.3	79.5
Moxifloxacin	98.1	4.3	4.6	96.8	5.7	3.2	95.0	3.8	5.2	16.9	5.4	77.8	19.3	3.0	77.7	17.3	4.3	78.5
Erythrocin	94.5	2.0	0.0	92.6	0.5	2.7	93.2	1.2	3.9	62.7	18.3	19.0	68.0	12.9	19.2	65.4	14.8	19.8
Nitrofurantoin	15.8	4.0	1.5	15.5	4.8	2.6	14.7	4.6	2.2	2.1	2.1	95.9	0.4	1.5	98.1	2.3	3.5	94.3
Linezolid	0.0	62.5	21.8	0.2	60.8	23.8	0.0	64.7	20.6	0.0	6.9	93.1	1.4	2.1	96.5	0.0	2.5	97.6
Vancomycin	0.0	0.0	100.0	0.3	1.1	98.7	0.0	0.6	99.4	0.0	0.0	100.0	0.0	0.0	100.0	0.0	0.0	100.0
Quinopudine-dafoprotin	7.5	0.0	100.0	9.6	0.0	99.8	12.4	0.0	100.0	-	-	-	-	-	-	-	-	-
Tetracycline	69.1	10.6	81.9	63.7	14.0	76.5	65.0	5.6	82.0	83.0	0.7	16.3	84.7	0.6	14.7	81.3	0.0	18.8

NA' not available or not tested

Infection caused by carbapenem-resistant *Enterobacteriaceae* (CRE) has high morbidity and mortality, over the past decade, more and more CRE related infections have been reported worldwide, such as in Asia, the United States, Israel and Lebanon (ZHOU, *et al.*, 2013; Pollett, *et al.*, 2014; Schwaber, *et al.*, 2011; El-Herte, *et al.*, 2012; XU, *et al.*, 2015). A previously published meta-analysis study on the epidemiology of CRE showed that the epidemiology of CRE in Asia showed a steady upward trend from 2000 to 2012 (XU, *et al.*, 2015). The results of bacterial resistance monitoring in China showed that the resistance rates of *Klebsiella pneumoniae* to imipenem and meropenem were 2.9% and 2.8% in 2005, 9.3% and 9.4% respectively in 2011 (HU, *et al.*, 2013) and by 2016, the resistance rates of *Klebsiella pneumoniae* to carbapenems were more than 15% (HU *et al.*, 2017). Monitoring data in London, UK show that the isolation rate of CRE increased from 2.2% in 2009-2010 to 11.5% in 2011-2012 (Freeman, *et al.*, 2015). The rapid spread of CRE strains has become a severe challenge for the whole world. It has been shown that the main resistance mechanism of CRE is producing carbapenemase, the mutation of AmpC binding portein, producing extended spectrum β-lactamases, the decrease of permeability of carbapenem antibiotics or the change of target position of antibiotics (DAI, *et al.*, 2013). CRE is highly resistant to most commonly used antibiotics in clinical practice and there are strains resistant to both polymyxomycin and tegacycline, which should be paid great attention in clinical practice. Since there is no specific drug of CRE in clinical practice, antibacterials should be combined to reduce the death rate of infected patients. It is very important to strengthen the surveillance of drug resistance of this kind of bacteria, guide the rational use of drugs in clinical practice, and take good prevention and control measures. (Zhu *et al*., 2016; Bi *et al*., 2017).

The resistance rate of *Acinetobacter baumannii* to meropenem was more than 70%, and to other tested drugs was more than 60%, the situation of drug resistance is serious, which may be related to the strong clonal transmission ability of *Acinetobacter baumannii* and its easy to produce acquired drug resistance, as a result, it is more difficult for clinicians to treat their infection. The microbiology laboratory should take the initiative to communicate with the clinical medical staff to increase the detection of drug resistance of some antibacterial drugs that may be effective against the severely resistant strains, such as tigacycline (Qureshi *et al*., 2012; Li *et al*., 2017). The resistance rate of *Pseudomonas aeruginosa* to meropenem is about 30%. Clinical experience medication can use amikacin, or with cefepime and other antibacterial drugs (Wang *et al*., 2018).

Enterococcus is a common conditional pathogen in hospital infection. It is resistant to many kinds of antibiotics naturally, and the available antibiotics are limited. Therefore, long-term and dynamic monitoring of *Enterococcus* resistance is of great significance to guide the rational use of antibiotics in clinical practice (YANG, *et al.*, 2016), our results showed that *Enterococcus* was sensitive to linezolid and vancomycin, and the resistance rate of *Enterococcus faecium* to most antibacterial drugs is higher than that of *Enterococcus faecalis*. MRSA is easy to implant in patients nasopharynx, is one of the important pathogens of hospital infection, with the wide application of β-lactam antibiotics in clinic, the proportion of MRSA in *Staphylococcus aureus* is increasing year by year, and the drug resistance is different in different periods and regions (HU *et al.*, 2016), our monitoring results showed that *Staphylococcus aureus* was more sensitive to nitrofurantoin, quinopudine-dafopudine, linezolid and vancomycin, so these drugs could be selected to treat staphylococcus aureus infection.

CONCLUSION

The antibiotic resistance rate of *Klebsiella pneumoniae* to carbapenems is on the rise. Since there are no specific CRE drugs in clinical practice, it is necessary to strengthen the prevention and control measures of nosocomial infection and the management of clinical application of antibacterial drugs and stick to the monitoring of bacterial resistance, so as to effectively curb the spread of drug-resistant bacteria.

Funding
Thanks to the research fund of infection prevention and control of Chinese Geriatric Society for funding this project. Project number: GRYJ-KLB2018028.

REFERENCES

Centers for Disease Control and Prevention (2013). Antibiotic resistance threats in the United States. *https://www.cdc.gov/drug resistance/threat-report-2013/ index.html.*

Dai Wei, Sun Shan, Yang Ping, Huang Shifeng, Zhang Xiaojiao and ZHANG Liping (2013). Characterization of carbapenemases, extended spectrum β-lactamases and molecular epidemiology of carbapenem-non-susceptible Enterobacter cloacae in a Chinese hospital in Chongqing. *Infect. Genet. Evol.*, **14**: 1-7.

Dickey SW, Cheung GYC and Otto M (2017). Different drugs for bad bugs: Antivirulence strategies in the age of antibiotic resistance. *Nat. Rev. Drug Discov.*, **16**(7): 457-471.

El-Herte RI, Kanj SS, Matar GM and Araj GF (2012). The threat of carbapenem-resistant Enterobacteriaceae in Lebanon: An update on the regional and local epidemiology. *J. Infect. Public Heal.*, **5**(3): 233-243.

Freeman R, Moore LSP, Charlett A, Donaldson H and Holmes AH (2015). Exploring the epidemiology of carbapenem-resistant negative bacteria in west London

and the utility of riutinely collected hospital microbiogy data. *J. Antimicrob. Chemo.*, **70**(4): 1212-1218.

HE Lihua, GUO Jian, ZHOU Aiping, Ni Lijun and WU Wenjuan (2018). Antimicrobial resistance surveillance of a newly hospital in Shanghai in 2016. *Chinese Journal of Nosocomiology*, **28**(12): 1774-1778.

Hu Fupin, Guo Yan, Zhu Demei, Wang Fu, Jiang Xiaofei, Xu Yingchun, Zhang Xiaojiang, Zhang Zhaoxia, Ji Ping, Xie Yi, Kang Mei, Wang Chuanqing, Wang Aimin, Xu Yuanhong, Shen Jilu, Sun Ziyong, Chen Zhongju, Ni Yuxing, Sun Jingyong, Chu Yunzhuo, Tian Sufei, Hu Zhidong, Li Jin, Yu Yunsong, Lin Jie, Shan Bin, Du Yan, Guo Sufang, Wei Lianhua, Zou Fengmei, Zhang Hong, Wang Chun, Hu Yunjian, Ai Xiaoman, Zhuo Chao, Su Danhong, Wang Ruizhong, Fang Hua, Yu Bixia, Zhao Yong, Gong Ping, Guo Dawen, Zhao Jinying, Liu Wenen, Li Yanming, Jin Yan, Shao Chunhong, Wen Kaizhen, Zhang Yirong, Xu Xuesong, Yan Chao, Yu Hua, Huang Xiangning, Wang Shanmei, Chu Yafei, Zhang Lixia, Ma Juan, Zhou Shuping, Zhou Yan, Zhu Lei and Meng Jinhua (2017). CHINET surveillance of bacterial resistance across China: Report of the results in 2016. *Chin. J. Infect Chemother.*, **17**(5): 481-491.

Hu Fupin, Zhu Demei, Wang Fu, Jiang Xiaofei, Xu Yingchun, Zhang Xiaojiang, Zhang Zhaoxia, Ji Ping, Xie Yi, Kang Mei, Wang Chuanqing, Wang Aimin, Xu Yuanhong, Shen Jilu, Sun Ziyong, Chen Zhongju, Ni Yuxing, Sun Jingyong, Chu Yunzhuo, Tian Sufei, Hu Zhidong, Li Jin, Yu Yunsong, Lin Jie, Shan Bin, Du Yan, Guo Sufang, Wei Lianhua, Wu Ling, Zhang Hong, Wang Chun, Hu Yunjian, Ai Xiaoman, Zhuo Chao, Su Danhong, Wang Ruizhong, Fang Hua, Yu Bixia, Zhao Yong and Gong Ping (2016). Report of CHINET Antimicrobial Resistance Surveillance Program in 2015. *Chin. J. Infect Chemother*, **16**(6): 685-694.

HU Fupin, ZHU Demei, Wang Fu, Jiang Xiaofei, Yang Qing, Huang Wenxiang, JIA Bei, XU Yuanhong, SHEN Jilu, XU Yingchun, Zhang Xiaojiang, HU Yunjian, AI Xiaoman, Zhang Zhaoxia, JI Ping, SHAN Bin, DU Yan, Zhuo Chao, SU Danghong, WANG Chuanqing, WANG Aimin, NI Yuxing, SUN Jingyong, SUN Ziyong, CHEN Zhongju, WEI Lianhua, WU Ling, Zhang Hong and Kong Jing (2013). CHINET surveillance of distribution and susceptibility of carbapenemresistant Enterobacteriaceae isolates in 2010. *Chin. J. Infect Chemother.*, **13**(1): 1-7.

Johnson AP (2015). Surveillance of antibiotic resistance. *Phil. Trans.*, **370**: 1670-1682.

Li Yinhuan, Liu Xiaoyan, Lin Xiaohui, Xian Cuiyao, Wang Faxia, Liu Xianglian And Zhou Weihong (2017). Current status of distribution and drug resistance of multidrug-resistant organisms isolated from a tertiary hospital in 2015. *Chinese Journal of Nosocomiology*, **27**(5): 976-979.

Lim TP, Cai Y and Hong Y (2015). *In vitro* pharmacodynamics of various antibiotics in combination against extensively drug-resistant Klebsiella pneumoniae. *Antimicrob Agents Chemother.*, **59**(5): 2515-2524.

Liu Xiaohua, Huang Wei and Gao Yanxiang (2018). Antibiotics use and drug resistance analysis of neurology patients' infection. *Pak. J. Pharm. Sci.*, **31**(5): 2235-2240.

Lôme V, Brunel JM, Pagès JM and Bolla JM (2018). Multiparametric profiling for identification of chemosensitizers against gram-negative bacteria. *J. Front Microbio*, **9**: 204.

Papp-Wallace KM, Endimiani A, Taracila MA and Bonomo RA (2011). Carbapenems: Past, present and future. *Antimicrob. Agents Chemother.*, **55**(11): 4943-4960.

Pollett S, Miller S, Hindler J, Uslan D, Carvalho M and Humphries RM (2014). Phenotypic and molecular characteristics of carbapenem-resistant Enterobacteriaceae in a health care system in Los Angeles, California, from 2011 to 2013. *J. Clin. Microbiol.*, **52**(11): 4003-4009.

Qin Xiaohua, yang Yang, HU Fupin and Zhu Demei (2014). Hospital clonal dissemination of Enterobacter aerogenes producing carbapenemase KPC-2 in a Chinese teaching hospital. *J. Med. Microbiol.*, **63**(2): 222-228.

Qureshi ZA, Paterson DL, Potoski BA, Kilayko MC, Sandovsky D, Sordillo E, Polsky B, Adams-Haduch JM and Doi Y (2012). Treatment outcome of bacteremia due to KPC-producing *Klebsiella pneumoniae*: Superiority of combination antimicrobial regimens . *Antimicrob Agents Chemother*., **56**(4): 2108-2113.

Schwaber MJ, Lev B, Israeli A, Solter E, Smollan G, Rubinovitch B, Shalit I and Carmeli Y (2011). Containment of a country-wide outbreak of carbapenem-resistant *Klebsiella pneumoniae* in Israeli hospitals via a nationally implemented intervention. *Clin. Infect. Dis.*, **52**(7): 848-855.

Smith R and Coast J (2013). The true cost of antimicrobial resistance. *BMJ.*, **346**: f1493.

WANG Liangmin, JI Kun, SHI Liqing, HU Hairong, XU Bing, TIAN Yajuan, DUAN Xueguang and WU Yajing (2018). Dynamic analysis of distribution characteristics and drug resistance of clinical isolates in the hospital from 2015 to 2017. *Chinese Journal of Nosocomiology*, **28**(24):67-70+83.

Wilinger B and Haase G (2013). State of the art procedures and quality management in diagnostic medical. *Curr. Fungal Infect. Rep.*, **7**(3): 260-272.

World Health Organisation (2012). The evolving threat of antimicrobial resistance: options for action. http://www.who.int/patientsafety/implementation/amr/publication/en/.

XU Yanling, Gu Bing, Huang Mao, LIU Haiyan, XIA Wenying and Wang Tong (2015). Epidemiology of

carbapenem resistant Enterobacteriaceae (CRE) during 2000-2012 in Asia. *J. Thorac. Dis.*, **7**(3): 376-385.

Yang Qing, Yu Yunsong, Lin Jie, Ni Yuxing, Sun Jingyong, Xu Yingchun, Zhang Xiaojiang, Sun Ziyong, Chen Zhongju, Wang Fu, Zhu Demei, Hu Fupin, Jiang Xiaofei, Wang Chuanqing, Wang Aimin, Zhuo Chao, Su Danhong, Hu Yunjian, Ai Xiaoman, Huang Wenxiang, Jia Bei, Zhang Zhaoxia, Ji Ping, Zhang Hong, Kong Jing, Wei Lianhua, Wu Ling, Xu Yuanhong, Shen Jilu, Shan Bin, Du Yan, Hu Zhidong, Li Jin, Xie Yi, Kang Mei, Han Yanqiu, Guo Sufang, Chu Yunzhuo and Tian Sufei (2016). Resistance profile of Enterococcus in hospitals across China: results of CHINET Antimicrobial Resistance Surveillance Program, 2005-2014. *Chin. J. Infect Chemother.*, **16**(2): 146-152.

Zhou Tieli, Zhang Xiaolei, Guo Meiyan, Ye Jianbo, Lu Yamin, Bao Qiyu and Chi Wenjie (2013). Phenotypic and molecular characteristics of carbapenem-non-susceptible Enterobacteriaceae from a teaching hospital in Wenzhou, southern China. *Jpn. J. Infect. Dis.*, **66**: 96-102.