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Bacterial susceptibility in bloodstream infections: Results from China Antimicrobial Resistance Surveillance Trial (CARST) Program, 2015–2016

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ABSTRACT

Objectives: The aim of this study was to monitor the trends in antimicrobial resistance from the blood samples isolated from the Chinese mainland.
Methods: All clinical isolates were collected from 18 hospitals. The minimal inhibitory concentrations (MICs) were tested in a central laboratory using the agar dilution method recommended by the Clinical and Laboratory Standards Institute. The susceptibilities of isolates to antimicrobial agents were determined by using Clinical and Laboratory Standards Institute or European Committee on Antimicrobial Susceptibility Testing (EUCAST) 2017 guidelines.
Results: A total of 1758 strains of various types with the sum ≥ 30 were isolated from blood specimens in 2015–2016. The detection rates of extended-spectrum β-lactamases (ESBLs) among *Escherichia coli* were 55.6%, whereas those in *Klebsiella pneumoniae* were 22.4%. Carbapenems, moxalactam, tigecycline, and amikacin displayed desirable antibacterial activity against Enterobacteriaceae, but a significant increase in *Klebsiella pneumoniae* to carbapenems was noted. Nonfermenters were highly resistant to carbapenems, especially in *Acinetobacter Baumannii* isolates, >70 of which were resistant. The prevalence of methicillin-resistant *Staphylococcus aureus* (MRSA) and methicillin-resistant *Staphylococcus epidermidis* (MRSE) reached 36.1% and 90.4%, respectively. *Staphylococcus aureus* had 100% susceptibility to vancomycin. *Enterococcus faecium* isolates showed significantly higher resistant rates to most of the tested antimicrobial agents than *Enterococcus faecalis* isolates. While vancomycin-resistant *Enterococcus* (VRE) was 3.28%, the non-susceptible rate of linezolid to *Enterococcus faecalis* was 6.8%.
Conclusions: This study revealed the major bacterial pathogens' antibiotic susceptibility patterns involved with bloodstream infection in mainland China.

1. Introduction

Antimicrobial resistance in bacterial bloodstream infection is a serious problem; it is often associated with increased length of hospital stay, significant healthcare costs, and can cause morbidity and mortality in many patients [1]. The widespread use of modern medical technology, irrational use of a large number of antibiotics, and mutual transmission of hospital patients has led to serious infectious diseases and frequently occurring new antibiotic-resistant bacteria. The production and spread of antibiotic resistance in Gram-positive bacteria have been a major problem in the treatment of bloodstream infections; the rising resistance rate of Gram-negative bacteria is a problem faced by the whole world [2]. Therefore, it is particularly important for clinicians and infection control practitioners to regularly monitor bacterial resistance, especially the countries and regions misusing antimicrobial agents.

This study collected various types of strains with the sum ≥ 30 isolated from blood specimens from China Antimicrobial Resistance Surveillance Trial (CARST) Program in 2015–2016 to understand the resistance of the Chinese mainland's bloodstream infected pathogens to clinical common agents.

2. Materials and methods

2.1. Antimicrobials

Penicillin, cefazolin, tazobactam, cefazolin, cefoxitin, cefuroxime, cefotaxime, ceftriaxone, ceftazidime, cefoperazone, amikacin,

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tetracycline, minocycline, erythromycin, azithromycin, chloramphenicol, nitrofurantoin, and streptomycin were purchased from the National Institute for Food and Drug Control. Ampicillin, gentamicin and rifampicin were purchased from INALCO Company. Fosfomycin was purchased from Shanxi C&Y Pharmaceutical Group Company. Cefepime was purchased from Bristol-Myers Squibb (Shanghai, China). Aztreonam was purchased from Shanghai Xinya Pharmaceutical Company. Moxalactam was from Hainan Hai Ling Chemical Pharmaceutical Company. Flomoxef was provided by Shionogi. Imipenem and ertapenem were purchased from Merck (Elkton, VA, USA). Meropenem was the product of Sumitomo Pharmaceuticals (Su Zhou). Biapenem was purchased from Nanjing Xianshengdongyuan Pharmaceutical Company. Clavulanic acid and ticarcillin were the products of GlaxoSmithKline. Tigecycline, linezolid and sulbactam were purchased from Pfizer (Dalian, China). Ciprofloxacin was purchased from Shangyujing new Pharmaceutical Company. Levofloxacin was purchased from Daiichi Sankyo Company Limited (Shang Hai). Moxifloxacin was the product of Hangzhou Yangyangkang Biological Technology Company. Nemonoxacin was purchased from Zhejiang Medicine Company, Xinchang Pharmaceutical Factory. Clindamycin was purchased from Guangzhou yipinhong Pharmaceutical Company. Vancomycin was the product of Eli Lilly. Teicoplanin was purchased from Sainuofeian Aventis Company. Sulfamethoxazole (SMZ) and colistin were the products of Sigma. Trimethoprim (TMP) was from China Shandong Xinda Pharma Co. And daptomycin was purchased from AstraZeneca plc.

Cefoperazone/sulbactam were in a ratio of 2:1; SMZ/TMP was 19:1. The concentration of tazobactam in piperacillin/tazobactam was constant at 4 mg/L.

2.2. Experimental strains

Quality control strains included *Staphylococcus aureus* (*S. aureus*) ATCC29213, *Enterococcus faecalis* (*E. faecalis*) ATCC29212, *Streptococcus pneumoniae* (*S. pneumoniae*) ATCC49619, *Pseudomonas aeruginosa* (*P. aeruginosa*) ATCC 27853, and *Escherichia coli* (*E. coli*) ATCC 25922 and ATCC 35218.

All isolates obtained from blood samples were collected from 18 tertiary hospitals in mainland China between July 2015 and June 2016, and were then sent to the Institute of Clinical Pharmacology, Peking University First Hospital. These participating tertiary hospitals are located in 15 different provinces in China. One isolate per species per patient was collected to avoid repetitive counts. Every strain to be tested was recovered and purified before the experiment to ensure viability and purity of the bacteria.

2.3. Susceptibility test

The standard two-fold agar dilution method: bacterial suspensions were obtained by inoculation with 10^4 CFU of each bacterium via a multipoint inoculator. The two-fold broth microdilution method: the final concentration of bacteria was 5×10^5 CFU/mL, the reaction volume was 100 μL. Daptomycin was tested by the two-fold broth microdilution method, and the others with the two-fold agar dilution method.

2.4. Data collection and statistical analysis

This surveillance trial was supported by the Institute of Clinical Pharmacology of Peking University First Hospital (surveillance centre).

Table 1
Antibacterial activity (mg/L) of antimicrobial agents against *Escherichia coli*.

Agents	*E. coli (338)*				*ESBLs- E. coli (150)*				*ESBLs+ E. coli (188)*			
	MIC_{50}	MIC_{90}	S%	R%	MIC_{50}	MIC_{90}	S%	R%	MIC_{50}	MIC_{90}	S%	R%
Piperacillin	256	>256	16.9	71.3	64	>256	38	37.3	>256	>256	0	98.4
P/T	2	16	92.3	4.4	2	8	90.7	7.3	2	16	93.6	2.1
Cefazolin	>256	>256	36.4	63.6	2	>256	82	18	>256	>256	0	100
Cefoxitin	4	32	76.9	14.8	4	128	80	16	8	32	74.5	13.8
Cefuroxime	>256	>256	34.6	62.7	8	128	78	16	>256	>256	0	100
Cefotaxime	64	>256	37.6	61.5	0.062	16	84.7	13.3	256	>256	0	100
Ceftriaxone	128	>256	37.6	62.1	0.062	32	84.7	14.7	256	>256	0	100
Ceftazidime	2	128	60.9	32.8	0.125	32	85.3	12	8	128	41.5	49.5
Cefoperazone	128	>256	40.2	57.7	1	32	89.3	10	16	>256	1.1	95.7
CSL	8	32	76.3	9.8	0.5	8	91.3	6	16	64	64.4	12.8
Cefepime	4	64	47.3	34.6	0.031	0.5	91.3	7.3	16	128	12.2	56.4
Aztreonam	8	128	49.1	41.4	0.125	4	90	9.3	32	256	16.5	67
Moxalactam	0.25	2	94.7	2.7	0.125	2	93.3	6	0.25	2	95.7	0
Flomoxef	0.125	2	94.1	5	0.062	16	89.3	9.3	0.125	1	97.9	1.6
Imipenem	0.125	0.25	97.6	2.4	0.125	0.25	94.7	5.3	0.125	0.125	100	0
Meropenem	0.016	0.031	97.9	2.1	0.016	0.031	95.3	4.7	0.016	0.031	100	0
Biapenem	0.031	0.062	—	—	0.031	0.062	—	—	0.031	0.062	—	—
Ertapenem	0.016	0.25	95.6	4.1	0.008	0.125	94.7	5.3	0.031	0.25	96.3	3.2
Gentamicin	2	128	52.4	47.3	1	128	60	39.3	32	128	46.3	53.7
Amikacin	2	8	97.9	2.1	2	4	98	2	2	8	97.9	2.1
Tetracycline	128	256	31.7	67.5	128	256	35.3	63.3	128	256	28.7	70.7
Minocycline	2	16	72.5	15.7	2	16	72.7	13.3	2	16	72.3	17.6
Tigecycline	0.25	0.5	100	0	0.25	0.5	100	0	0.25	0.5	100	0
Ciprofloxacin	8	128	45.9	53.6	0.25	32	67.3	32	32	128	28.7	70.7
Levofloxacin	4	32	46.7	49.1	0.5	16	68	28	8	32	29.8	66
Nitrofurantoin	16	32	90.2	2.4	16	32	92.7	0.7	16	64	88.3	3.7
Fosfomycin	0.25	8	94.1	3.8	0.25	2	96.7	2	0.5	64	92	5.3
SXT	128	128	37.6	62.4	64	128	44.7	55.3	128	128	31.9	68.1
Colistin	0.5	1	98.2	1.8	0.5	1	98	2	0.5	1	98.4	1.6

Abbreviations: MIC, minimal inhibitory concentration; S, Susceptible; R, Resistant; P/T, Piperacillin/tazobactam; CSL, cefoperazone/sulbactam; SXT, trimethoprim-sulfamethoxazole; —, no breakpoint; *E. coli*, *Escherichia coli*; ESBLs, extended-spectrum β-lactamases; EUCAST, European Committee on Antimicrobial Susceptibility Testing; FDA, Food and Drug Administration.
The breakpoint of cefoperazone was used for cefoperazone/sulbactam (S: ≤ 16 mg/L; R: ≥ 64 mg/L).
Interpretive criteria of BD company's susceptibility disk as used for flomoxef (S: ≤ 8 mg/L; R: ≥ 32 mg/L).
USA-FDA breakpoint was applied for tigecycline (S: ≤ 2 mg/L; R: ≥ 8 mg/L).
Colistin was based on EUCAST (S: ≤ 2 mg/L; R: ≥ 4 mg/L).

The surveillance centre provides the culture preservation tubes for the cooperative hospitals, then they send the strains to the surveillance centre, and the surveillance centre uniformly measures the MICs.

Statistical tests were analysed by Statistical Package for the Social Sciences 20.0 software (SPSS, Inc., Chicago, IL, USA), calculating the MIC_{50} and MIC_{90}. The susceptibilities of isolates to antimicrobial agents were determined by using Clinical and Laboratory Standards Institute 2017 guidelines. See the notes after the tables about the agents that were not criterial (refer to European Committee on Antimicrobial Susceptibility Testing (EUCAST) 2017), or similar drugs, or were not calculated.

3. Results

3.1. Antibacterial activity of antimicrobial agents against Enterobacteriaceae

The detection rates of extended-spectrum β-lactamases (ESBLs) among *E. coli* and *Klebsiella pneumoniae* (*K. pneumoniae*) were 55.6% and 22.4%, respectively. Carbapenem antibiotics, moxalactam and tigecycline were still the most effective drugs against Enterobacteriaceae. Amikacin had a high antibacterial activity against Enterobacteriaceae, except that the resistance rate of *K. pneumoniae* was 12.4%, and the sensitivity rate of other strains was >97.2%. The incidence of ESBLs in *K. pneumoniae* was significantly lower than that in *E. coli*, and the sensitivity to penicillin, first- to fourth-generation cephalosporins, aztreonam, gentamicin, tetracycline, and TMP/SMZ was higher than *E. coli*. The resistance rates of *K. pneumoniae* to carbapenems were 16.2–17.4%. Salmonella spp. was very sensitive to third-generation cephalosporins; bacterial resistance rates were <7.5%. Quinolones, fosfomycin and SMZ-TMP were more effective against Serratia spp. (Tables 1–3).

3.2. Antibacterial activity of antimicrobial agents against non-fermentative Gram-negative bacilli

The resistance rates of *P. aeruginosa* to all tested agents were <20%; the highest resistance rate was to aztreonam at 19.2%, and the lowest was for fosfomycin at 3.8%. Thirty-six of all *P. aeruginosa* were unsusceptible to imipenem, and the resistance rates of these strains to the tested agents ranged 11.1–63.9%. The resistance rates of imipenem-sensitive *P. aeruginosa* to the tested agents were mostly <10% (Table 4).

The sensitive rates of *Acinetobacter baumannii* (*A. baumannii*) to most of the tested agents were ≤ 30%. The sensitive rates >30% were for amikacin, minocycline and tigecycline, which were 33.8%, 49.4% and 91.3%, respectively. The resistance rate of the compound containing sulbactam was slightly different, but the sensitive rate was not significantly different. There were 119 imipenem-insensitive strains in *A. baumannii*, accounting for 74.4% of all of them, and the resistance trend of *A. baumannii* was serious (Table 5).

3.3. Antibacterial activity of antimicrobial agents against Staphylococcus

The prevalence of methicillin-resistant *Staphylococcus aureus* (MRSA) and methicillin-resistant *Staphylococcus epidermidis* (MRSE) reached 36.1% and 90.4%, respectively. Vancomycin, linezolid, teicoplanin, tigecycline and minocycline showed strong

Table 2
Antibacterial activity (mg/L) of antimicrobial agents against *Klebsiella pneumoniae*.

Agents	*K. pneumoniae (241)*				*ESBLs- K. pneumoniae (187)*				*ESBLs+ K. pneumoniae (54)*			
	MIC_{50}	MIC_{90}	S%	R%	MIC_{50}	MIC_{90}	S%	R%	MIC_{50}	MIC_{90}	S%	R%
Piperacillin	16	>256	53.1	41.5	8	>256	67.9	25.7	>256	>256	1.9	96.3
P/T	4	>256	76.8	21.6	4	>256	77.5	21.4	8	>256	74.1	22.2
Cefazolin	2	>256	60.2	39.8	2	>256	75.9	24.1	>256	>256	5.6	94.4
Cefoxitin	4	256	73.9	22	4	256	73.3	24.6	4	32	75.9	13
Cefuroxime	8	>256	56	40.7	4	>256	72.2	23.5	>256	>256	0	100
Cefotaxime	0.062	>256	60.2	39.4	0.062	>256	77.5	22.5	128	>256	0	98.1
Ceftriaxone	0.125	>256	60.6	39.4	0.062	>256	78.1	21.9	256	>256	0	100
Ceftazidime	0.25	256	65.1	32	0.25	>256	77	21.9	16	128	24.1	66.7
Cefoperazone	0.5	>256	60.6	38.2	0.25	>256	77.5	21.9	>256	>256	1.9	94.4
CSL	0.5	>256	71.8	23.2	0.25	>256	79.1	19.8	32	128	46.3	35.2
Cefepime	0.062	128	66	25.3	0.062	128	79.7	19.3	8	128	18.5	46.3
Aztreonam	0.125	>256	65.1	34.9	0.062	>256	79.1	20.9	64	256	16.7	83.3
Moxalactam	0.25	256	83.8	15.8	0.125	>256	79.7	20.3	0.5	2	98.1	0
Flomoxef	0.062	>256	82.2	16.2	0.062	>256	78.6	20.9	0.125	4	94.4	0
Imipenem	0.125	64	82.6	17.4	0.125	64	79.7	20.3	0.125	0.75	92.6	7.4
Meropenem	0.031	128	83.4	16.2	0.031	128	80.2	19.8	0.031	0.062	94.4	3.7
Biapenem	0.062	64	—	—	0.062	128	—	—	0.062	0.25	—	—
Ertapenem	0.016	256	82.2	17	0.016	>256	79.1	20.3	0.062	0.5	92.6	5.6
Gentamicin	1	>256	71	28.2	0.5	>256	79.1	20.3	32	256	42.6	55.6
Amikacin	1	>256	86.3	12.4	1	>256	86.1	13.9	2	32	87	9.3
Tetracycline	4	256	53.1	39	4	256	63.6	26.7	256	>256	16.7	81.5
Minocycline	4	16	66.8	19.9	4	16	73.8	15	8	128	42.6	37
Tigecycline	0.5	2	93.8	2.9	0.5	2	94.1	2.7	1	2	92.6	3.7
Ciprofloxacin	0.062	64	67.2	30.3	0.031	64	76.5	20.9	8	256	35.2	63
Levofloxacin	0.125	32	71.8	24.9	0.062	32	80.2	19.8	4	64	42.6	42.6
Nitrofurantoin	128	256	18.3	58.1	128	256	19.8	55.6	128	256	13	66.7
Fosfomycin	4	64	90.5	9.5	4	256	89.3	10.7	4	16	94.4	5.6
SXT	0.25	128	64.3	35.7	0.125	128	79.1	20.9	128	128	13	87
Colistin	1	2	97.5	2.5	1	2	98.4	1.6	1	2	94.4	5.6

Abbreviations: MIC, minimal inhibitory concentration; S, Susceptible; R, Resistant; P/T, piperacillin/tazobactam; CSL, cefoperazone/sulbactam; SXT, trimethoprim-sulfamethoxazole; —, no breakpoint; *K. pneumoniae, Klebsiella pneumoniae*; ESBLs, extended-spectrum β-lactamases; EUCAST, European Committee on Antimicrobial Susceptibility Testing; FDA, Food and Drug Administration.
The breakpoint of cefoperazone was used for cefoperazone/sulbactam (S: ≤ 16 mg/L; R: ≥ 64 mg/L).
Interpretive criteria of BD company's susceptibility disk as used for flomoxef (S: ≤ 8 mg/L; R: ≥ 32 mg/L).
USA-FDA breakpoint was applied for tigecycline (S: ≤ 2 mg/L; R: ≥ 8 mg/L).
Colistin was based on EUCAST (S: ≤ 2 mg/L; R: ≥ 4 mg/L).

Table 3
Antibacterial activity (mg/L) of antimicrobial agents against other Enterobacteriaceae.

Agents	*Serratia spp. (42)*				*Salmonella spp. (53)*				*E. cloacae (71)*			
	MIC_{50}	MIC_{90}	S%	R%	MIC_{50}	MIC_{90}	S%	R%	MIC_{50}	MIC_{90}	S%	R%
Piperacillin	2	256	81	16.7	0.5	>256	54.7	39.6	8	>256	60.6	26.8
P/T	2	8	90.5	0	2	8	94.3	1.9	4	128	77.5	15.5
Cefoxitin	16	64	19	35.7	2	4	92.5	1.9	ND	ND	ND	ND
Cefuroxime	256	>256	2.4	95.2	8	16	83	7.5	64	>256	21.1	62
Cefotaxime	0.5	64	78.6	19	0.125	0.25	94.3	5.7	1	>256	52.1	12.3
Ceftriaxone	0.25	256	81	19	0.062	0.25	94.3	5.7	0.016	2	53.5	40.8
Ceftazidime	0.125	4	92.9	2.4	0.25	0.5	94.3	5.7	1	256	66.2	32.4
Cefoperazone	1	256	81	16.7	1	32	86.8	7.5	2	>256	67.6	29.6
CSL	2	32	81	9.5	0.5	16	92.5	1.9	1	64	76.1	14.1
Cefepime	0.125	16	83.3	14.3	0.062	0.125	94.3	5.7	0.25	32	76.1	12.7
Aztreonam	0.125	32	83.3	16.7	0.062	0.25	94.3	5.7	0.25	256	62	36.6
Moxalactam	0.5	4	97.6	0	0.125	0.25	100	0	0.25	32	77.5	9.9
Flomoxef	1	4	92.9	0	0.062	0.062	98.1	0	ND	ND	ND	ND
Imipenem	0.5	1	90.5	7.1	0.125	0.125	100	0	0.25	1	93	7
Meropenem	0.062	0.125	92.9	4.8	0.016	0.031	100	0	0.031	0.5	94.4	5.6
Biapenem	0.25	0.5	—	—	0.062	0.062	—	—	0.062	0.25	—	—
Ertapenem	0.062	0.25	90.5	7.1	0.008	0.016	100	0	0.062	2	80.3	12.7
Gentamicin	1	32	88.1	11.9	0.5	1	96.2	3.8	0.5	16	87.3	11.3
Amikacin	2	4	100	0	1	2	100	0	1	4	97.2	1.4
Tetracycline	64	128	2.4	90.5	2	128	83	17	4	256	54.9	28.2
Minocycline	8	8	42.9	4.8	2	8	83	7.5	4	32	54.9	19.7
Tigecycline	1	2	92.9	7.1	0.5	0.5	100	0	1	4	88.7	2.8
Ciprofloxacin	0.125	4	88.1	11.9	0.125	0.5	30.2	9.4	0.031	4	85.9	11.3
Levofloxacin	0.25	4	88.1	7.1	0.5	1	22.6	0	0.125	2	91.5	7
Nitrofurantoin	256	256	0	100	32	128	67.9	17	128	256	7	73.2
Fosfomycin	8	64	90.5	7.1	0.25	32	98.1	0	8	64	90.1	7
SXT	0.125	0.5	95.2	4.8	0.125	1	92.5	7.5	0.125	128	80.3	19.7

Abbreviations: MIC, minimal inhibitory concentration; S, Susceptible; R, Resistant; P/T, piperacillin/tazobactam; CSL, cefoperazone/sulbactam; SXT, trimethoprim-sulfamethoxazole; —, no breakpoint; *E. cloacae, Enterobacter cloacae*; spp., species; EUCAST, European Committee on Antimicrobial Susceptibility Testing; FDA, Food and Drug Administration.
The breakpoint of cefoperazone was used for cefoperazone/sulbactam (S: ≤ 16 mg/L; R: ≥ 64 mg/L).
Interpretive criteria of BD company's susceptibility disk as used for flomoxef (S: ≤ 8 mg/L; R: ≥ 32 mg/L).
USA-FDA breakpoint was applied for tigecycline (S: ≤ 2 mg/L; R: ≥ 8 mg/L).
Colistin was based on EUCAST (S: ≤ 2 mg/L; R: ≥ 4 mg/L).

in vitro activity against *Staphylococcus*; >95% of the isolates were susceptible.

In addition, daptomycin, fosfomycin, chloramphenicol, amikacin and rifampicin showed better antibacterial activity, which was >80%. The effect of SMZ-TMP on *S. aureus* was superior to that of coagulase-negative staphylococci, while amikacin and tetracycline showed slightly better antibacterial activity against coagulase-negative staphylococci. No vancomycin-resistant staphylococci were found. The sensitive rate of linezolid and teicoplanin to *S. aureus* was 100%, while coagulase-negative staphylococci were resistant or insensitive to test drugs other than vancomycin (Tables 6 and 7).

Table 4
Antibacterial activity (mg/L) of antimicrobial agents against *Pseudomonas aeruginosa.*

Agents	*P. aeruginosa (130)*				*IMP-S P. aeruginosa (94)*		*IMP-NS P. aeruginosa (36)*	
	MIC_{50}	MIC_{90}	S%	R%	S%	R%	S%	R%
Piperacillin	8	128	75.4	11.5	80.9	6.4	61.1	25
P/T	4	64	80	10	87.2	4.3	61.1	25
Ceftazidime	2	32	84.6	11.5	90.4	6.4	69.4	25
Cefoperazone	8	128	76.9	15.4	83	9.6	61.6	30.6
CSL	8	64	80.8	12.3	90.4	5.3	55.6	30.6
Cefepime	2	16	86.9	7.7	95.7	2.1	63.9	22.2
Aztreonam	8	32	69.2	19.2	76.6	11.7	50	38.9
Moxalactam	32	256	—	—	—	—	—	—
Imipenem	2	16	72.3	17.7	100	0	0	63.9
Meropenem	0.5	16	80.8	13.1	96.8	2.1	38.9	41.7
Biapenem	0.5	16	—	—	—	—	—	—
Gentamicin	2	8	86.2	8.5	94.7	3.2	63.9	22.2
Amikacin	2	8	94.6	5.4	97.9	2.1	86.1	13.9
Ciprofloxacin	0.25	2	86.9	9.2	95.7	2.1	63.9	27.8
Levofloxacin	1	8	82.3	11.5	93.6	3.2	52.8	33.3
Fosfomycin	32	64	92.3	3.8	95.7	0	83.3	13.9
Colistin	2	2	90.8	9.2	91.5	8.5	88.9	11.1

Abbreviations: S, Susceptible; R, Resistant; IPM-S, imipenem-susceptibility; IPM-NS, imipenem-nonsusceptibility; *P. aeruginosa, Pseudomonas aeruginosa*; P/T, piperacillin/tazobactam; CSL, cefoperazone/sulbactam; MIC, minimal inhibitory concentration; —, no breakpoint.
The breakpoint of cefoperazone for Enterobacteriaceae was used here for cefoperazone/sulbactam (S: ≤ 16 mg/L; R: ≥ 64 mg/L).
The breakpoint of fosfomycin for Enterobacteriaceae was used here (S: ≤ 64 mg/L; R: ≥ 256 mg/L).

Table 5
Antibacterial activity (mg/L) of antimicrobial agents against *Acinetobacter baumannii*.

Agents	*A. baumannii (160)*				*IMP-S A. baumannii (41)*		*IMP-NS A. baumannii (119)*	
	MIC_{50}	MIC_{90}	*S%*	*R%*	*S%*	*R%*	*S%*	*R%*
Piperacillin	>256	>256	11.3	76.9	43.9	12.2	0	99.2
P/T	>256	>256	23.1	76.2	87.8	9.8	0.8	99.2
Ampicillin/sulbactam	64	128	23.8	71.9	90.2	7.3	0.8	94.1
Cefotaxime	>256	>256	12.5	76.2	48.8	12.2	0	98.3
Ceftriaxone	>256	>256	5.6	76.9	22	12.2	0	99.2
Ceftazidime	128	>256	24.4	75	87.8	12.2	2.5	96.6
CSL	64	128	26.3	58.1	90.2	4.9	4.2	76.5
sulbactam	32	64	—	—	—	—	—	—
Cefepime	64	256	22.5	75	87.8	7.3	0	98.3
Moxalactam	128	>256	—	—	—	—	—	—
Imipenem	32	64	25.6	73.1	100	0	0	98.3
Meropenem	32	64	26.3	73.7	100	0	0.8	99.2
Biapenem	32	64	—	—	—	—	—	—
Gentamicin	>256	>256	25.6	71.9	85.4	12.2	5	92.4
Amikacin	>256	>256	33.8	66.2	87.8	12.2	15.1	84.9
Tetracycline	>256	>256	15	75.6	58.5	17.1	0	95.8
Minocycline	8	16	49.4	23.1	97.6	0	32.8	31.1
Tigecycline	2	2	91.3	5	100	0	88.2	6.7
Ciprofloxacin	64	128	23.8	76.2	87.8	12.2	1.7	98.3
Levofloxacin	8	32	24.4	62.5	90.2	9.8	1.7	80.7
SXT	16	128	43.8	56.2	85.4	14.6	29.4	70.6
Fosfomycin	128	128	6.3	5.6	9.8	12.2	5	3.4
Colistin	1	2	98.1	1.9	97.6	2.4	98.3	1.7

Abbreviations: S, Susceptible; R, Resistant; *A. baumannii*, *Acinetobacter baumannii*; IPM-S, imipenem-susceptibility; IPM-NS, imipenem-nonsusceptibility; P/T, piperacillin/tazobactam; CSL, cefoperazone/sulbactam; SXT, trimethoprim-sulfamethoxazole; FDA, Food and Drug Administration.
USA-FDA breakpoint was applied for tigecycline (S: ≤ 2 mg/L; R: ≥ 8 mg/L).

3.4. Antibacterial activity of antimicrobial agents against Enterococcus

Enterococcus faecalis isolates showed significantly lower resistant rates to most of the tested antimicrobial agents than the *E. faecium* isolates. The susceptive rates of *E. faecalis* and *Enterococcus faecium* (*E. faecium*) to ampicillin were 89.2% and 8.3%, respectively. Tigecycline, vancomycin, teicoplanin, and daptomycin showed perfect in vitro activity against Enterococcus spp. and the bacterial susceptibility was >95%. Ampicillin, linezolid, nitrofurantoin, and

Table 6
Antibacterial activity (mg/L) of antimicrobial agents against Staphylococcus spp.

Agents	*S. aureus (208)*				*S. epidermidis (94)*				*S. haemolyticus (46)*				*Other staphylococcus spp. (102)*			
	MIC_{50}	MIC_{90}	*S%*	*R%*	MIC_{50}	MIC_{90}	*S%*	*R%*	MIC_{50}	MIC_{90}	*S%*	*R%*	MIC_{50}	MIC_{90}	*S%*	*R%*
Penicillin	4	32	8.2	91.8	2	32	2.1	97.9	128	>256	4.3	95.7	16	64	7.8	92.2
Oxacillin	1	>256	66.3	33.7	4	128	9.6	90.4	>256	>256	4.3	95.7	64	>256	10.8	90.2
Cefoxitin	4	256	65.4	34.6	16	256	—	—	>256	>256	—	—	64	>256	—	—
Flomoxef	0.5	128	77.9	19.7	4	64	85.1	10.6	16	64	37	41.3	8	64	51	33.3
Biapenem	0.125	64	—	—	1	64	—	—	128	256	—	—	4	64	—	—
Gentamicin	0.25	64	68.8	28.8	0.5	128	52.1	41.5	32	128	28.3	69.6	8	64	45.1	35.3
Amikacin	2	64	84.1	12	2	64	87.2	10.6	4	8	95.7	0	1	16	94.1	3.9
Erythromycin	256	>256	38	60.1	128	>256	18.1	81.9	128	>256	4.3	95.7	256	>256	12.7	87.3
Azithromycin	256	>256	37.5	62	128	>256	18.1	81.9	128	>256	4.3	95.7	256	>256	12.7	87.3
Clindamycin	0.125	>256	61.5	38	0.125	>256	64.9	34	0.125	>256	58.7	41.3	0.25	>256	55.9	42.2
Tetracycline	0.5	32	58.2	38	1	64	77.7	19.1	2	128	80.4	19.6	1	128	60.8	39.2
Minocycline	0.125	2	95.7	1.4	0.25	0.5	100	0	0.25	0.5	100	0	0.25	0.5	98	1
Tigecycline	0.25	0.5	97.1	2.9[a]	0.125	0.5	100	0.0	0.125	0.25	100	0.0[a]	0.062	0.125	100	0.0[a]
Ciprofloxacin	0.5	64	66.8	26.9	2	32	44.7	45.7	32	64	15.2	80.4	8	64	43.1	53.9
Levofloxacin	0.5	32	73.1	26.9	1	8	51.1	47.9	16	32	19.6	80.4	4	256	44.1	53.9
Moxifloxacin	0.125	8	73.6	26	0.25	4	53.2	19.1	4	8	21.7	78.3	1	32	47.1	48
Nemonoxacin	0.062	1	92.8	7.2[a]	0.062	0.5	—	—	0.5	1	—	—	0.25	2	—	—
Linezolid	1	1	100	0	0.5	1	100	0	1	1	100	0	1	1	97.1	2.9
Vancomycin	1	1	100	0	0.5	1	100	0	0.5	1	100	0	0.5	0.5	100	0
Teicoplanin	1	2	100	0	4	8	97.9	0	4	8	100	0	0.5	4	95.1	0
Rifampicin	0.016	16	86.5	11.5	0.008	128	86.2	13.8	0.016	>256	71.7	28.3	0.016	2	88.2	7.8
SXT	0.031	0.5	98.6	1.4	2	4	74.5	25.5	1	64	69.6	30.4	1	16	61.8	39.2
Chloramphenicol	4	8	91.8	7.7	4	64	84	16	4	64	87	10.9	4	64	86.3	13.7
Fosfomycin	0.5	64	88	12	0.5	16	94.7	5.3	8	16	97.8	2.2	32	>256	80.4	19.6
Daptomycin	0.5	1	98.1	1.9[a]	0.5	1	95.7	4.3[a]	1	2	78.3	21.7[a]	0.5	2	83.3	16.7[a]

Abbreviations: S, Susceptible; R, Resistant; *S. aureus*; *Staphylococcus aureus*; *S. epidermidis*, *Staphylococcus epidermidis*; *S. haemolyticus*, *Staphylococcus haemolyticus*; SXT, trimethoprim/sulfamethoxazole; MIC, minimum inhibitory concentration; —, no breakpoint; EUCAST, European Committee on Antimicrobial Susceptibility Testing; FDA, Food and Drug Administration.
Interpretive criteria of BD company's susceptibility disk as used for flomoxef (S: ≤ 8 mg/L; R: ≥ 32 mg/L).
Interpretive criteria of FDA as used for tigecycline (S: ≤ 0.5 mg/L).
Interpretive criteria of Taijiexin introduction as used for nemonoxacin (S: ≤ 1 mg/L).
EUCAST as used for Fosfomycin (S: ≤ 32 mg/L; R: ≥ 64 mg/L).
[a] Non-susceptibility.

high-concentration streptomycin showed good in vitro activity against *E. faecalis*, and the bacterial susceptibility was >85%. The antibacterial activity of high-concentration streptomycin and chloramphenicol to *E. faecium* was 100% and 85.3%, respectively, which was better than that of *E. faecalis*. There were six strains of vancomycin-resistant *Enterococcus* (VRE), the VRE detection rate was 3.28%, and one of them was *E. faecalis*. *Enterococcus* spp. had 100% susceptibility to daptomycin, and there were seven strains of linezolid-nonsusceptive isolates (Table 8).

3.5. Antibacterial activity of antimicrobial agents against Streptococcus

Except for the higher (≥63%) resistance rate of *β-haemolytic streptococcus* to macrolides and clindamycin, the other tested agents had overall susceptibility (>95%); the susceptibility of quinolones, rifampicin and chloramphenicol was 55.6–92.6%.

Penicillin susceptibility was identified in 71.9% of the *Streptococcus viridans* isolates, resulting in a lower susceptibility to the entire β-lactam agents compared with *β-haemolytic streptococcus*. The sensitivity rates to macrolide were 33.3–38.6%, which was about 15 percentage points higher than that of *β-haemolytic streptococcus*. No imipenem, tigecycline, linezolid, vancomycin, teicoplanin and daptomycin resistant strains were found (Table 9).

4. Discussion

This study aimed to evaluate the antimicrobial resistance profiles of bloodstream infected pathogens against antimicrobial agents that are commonly used clinically.

The detection rate of ESBL-producing *E. coli* was 55.6%, which was 10.4% less than the monitoring data of the CARST Program, 2013–2014, but higher than the results of an American survey over the same period [3,4]. The detection rates of ESBLs of *K. pneumoniae* decreased from 38.7% to 22.4% [3]. Ceftazidime's moderate antibacterial activity (41.5%) against ESBLs-positive *E. coli* indicated that CTX-M type is still the prevalent ESBLs type in China. The CTX-M genotype is associated with the ability to hydrolyse cefotaxime and ceftriaxone [5,6]. ESBLs-negative *K. pneumoniae* means phenotypically negative strains, which were subdivided into carbapenem sensitive and nonsensitive. Thirty-nine (20.9%) of the ESBLs-negative *K. pneumoniae* were insensitive to carbapenems, the resistance rates of these strains to the tested drugs were mostly >70% (tables not show). In this study, some antibiotics, including tigecycline and polymyxins, were found to be effective alternative treatments against carbapenem-resistant Enterobacteriaceae (CRE); they have a much higher in vitro efficacy than other antimicrobial agents.

In non-fermentative bacteria, the resistance rates of different strains showed significant difference, and the resistance rate of *P. aeruginosa* was lower than *A. baumannii*, but for *P. aeruginosa*, the specimens from the sputum were more resistant than the ones from the blood strains [7]. The resistances rate of *A. baumannii* to the majority of tested agents was high, the rate of imipenem-resistant *A. baumannii* was 73.1%; the proportion of multidrug resistant was 78.8% [8], which was lower than that of the Middle East, Europe, Latin America, and Africa but higher than North America [9]. Carbapenems are the main antibacterial agents used to treat serious infections, especially multidrug-resistant infections. The increasing rate of resistance to carbapenems has raised great concern; in most cases, samples that are resistant to carbapenems are also resistant to many other types of antibiotics, which cause difficulties in clinical therapy and infection control [10]. Otherwise, tigecycline has a strong antibacterial effect against Gram-positive and Gram-negative bacteria, but there was still 5% of *A. baumannii* resistant to it.

Gram-positive bacteria also pose a serious threat because their morbidity in bloodstream infections is steadily increasing globally [11]. The detection rates of MRSA have continued to decline over the past decade, from 54.1% in 2007–2008 [2] to 36.1% in this study, decreasing by nearly 20%. The trend is similar to that in the United States [12]. The current study found vancomycin to be highly effective against all *Staphylococcus* and *Streptococcus* strains; and there was no resistant strain. The proportion of VRE was 3.28%, lower than foreign countries [13]. Teicoplanin-insensitive coagulase-negative

Table 7
Antibacterial activity (mg/L) of antimicrobial agents against methicillin-susceptibility and resistant staphylococci.

Agents	*MSSA (133)*		*MRSA (75)*		*MSSE (9)*		*MRSE (85)*	
	S%	*R%*	*S%*	*R%*	*S%*	*R%*	*S%*	*R%*
Penicillin	12.8	87.2	0	100	22.2	77.8	0	100
Oxacillin	100	0	6.7	93.3	100	0	0	100
Cefoxitin	100	0	4	96	—	—	—	—
Flomoxef	100	0	38.7	54.7	100	0	83.5	11.8
Gentamicin	77.4	20.3	53.3	44	66.7	22.2	50.6	43.5
Amikacin	100	0	56	33.3	100	0	85.9	11.8
Erythromycin	47.4	52.6	21.3	73.3	33.3	66.7	16.5	83.5
Azithromycin	47.4	52.6	20	78.7	33.3	66.7	16.5	83.5
Clindamycin	72.9	27.1	41.3	57.3	100	0	61.2	37.6
Tetracycline	72.2	24.8	33.3	61.3	88.9	11.1	76.5	20
Minocycline	99.2	0	89.3	4	100	0	100	0
Tigecycline	100	0.0[a]	92	8.0[a]	100	0.0[a]	100	0.0[a]
Ciprofloxacin	81.2	12	41.3	53.3	77.8	22.2	41.2	48.2
Levofloxacin	88.7	11.3	45.3	54.7	77.8	22.2	48.2	50.6
Moxifloxacin	88.7	10.5	46.7	53.3	77.8	11.1	50.6	20
Nemonoxacin	100	—	80	20.0[a]	—	—	—	—
Linezolid	100	0	100	0	100	0	100	0
Vancomycin	100	0	100	0	100	0	100	0
Teicoplanin	100	0	78.7	21.3	100	0	88.2	11.8
Rifampicin	98.5	0	65.3	32	100	0	84.7	15.3
SXT	100	0	96	4	100	0	71.8	28.2
Chloramphenicol	93.2	6	89.3	10.7	77.8	22.2	84.7	15.3
Fosfomycin	100	0	66.7	33.3	88.9	11.1	95.3	4.7
Daptomycin	100	0.0[a]	94.7	5.3[a]	88.9	11.1[a]	96.5	3.5[a]

Abbreviations: S, Susceptible; R, Resistant; MSSA, methicillin-susceptible *Staphylococcus aureus*; MRSA, methicillin-resistant *Staphylococcus aureus*; MSSE methicillin-susceptible *Staphylococcus epidermidis*; MRSE, methicillin-resistant *Staphylococcus epidermidis*; SXT, trimethoprim/sulfamethoxazole.
[a] Non-susceptibility.

Table 8
Antibacterial activity (mg/L) of antimicrobial agents against Enterococcus spp.

Agents	*E. faecalis (74)*				*E. faecium (109)*			
	MIC_{50}	MIC_{90}	*S%*	*R%*	MIC_{50}	MIC_{90}	*S%*	*R%*
Ampicillin	0.5	32	89.2	10.8	128	>256	8.3	91.7
Erythromycin	256	>256	10.8	59.5	>256	>256	3.7	85.3
Tetracycline	64	128	28.4	71.6	1	128	54.1	45.9
Minocycline	8	32	33.8	48.6	0.125	32	59.6	31.2
Tigecycline	0.062	0.125	100	0	0.062	0.125	100	0
Ciprofloxacin	1	64	54.1	35.1	64	>256	6.4	92.7
Levofloxacin	1	64	66.2	32.4	64	128	5.5	89
Moxifloxacin	0.5	16	67.6	29.7	16	64	6.4	89.9
Linezolid	2	2	93.2	1.4	1	2	98.2	0.9
Vancomycin	1	2	98.6	0	1	2	95.4	3.7
Teicoplanin	0.5	1	100	0	1	2	99.1	0
Rifampicin	8	16	12.2	68.9	8	32	10.1	83.5
Chloramphenicol	8	64	77	21.6	8	16	85.3	2.8
Fosfomycin	32	64	100	0	64	64	92.7	0.9
Nitrofurantoin	8	32	91.9	1.4	128	128	26.6	53.2
HLGM	—	—	74.3	25.7	—	—	50.5	49.5
HLSTR	—	—	86.5	13.5	—	—	100	0
Daptomycin	2	4	100	—	2	2	100	—

Abbreviations: S, Susceptible; R, Resistant; *E. faecalis*, *Enterococcus faecalis*; *E. faecium*, *Enterococcus faecium*; HLGM, high-concentration gentamicin; HLSTR, high-concentration streptomycin; FDA, Food and Drug Administration.
Interpretive criteria of FDA as used for tigecycline (S: ≤ 0.25 mg/L).
The breakpoint of moxifloxacin against *Streptococcus pneumonia* was used here (S: ≤ 1 mg/L; R: ≥ 4 mg/L); —, no breakpoint.

Table 9
Antibacterial activity (mg/L) of antimicrobial agents against Streptococcus spp.

Agents	*β-haemolytic group (30)*				*Streptococcus virdans group (60)*			
	MIC_{50}	MIC_{90}	S%	R%	MIC_{50}	MIC_{90}	S%	R%
Penicillin (iv)	0.031	0.062	96.3	3.7[a]	0.062	1	71.9	5.3
Amoxicillin	0.031	0.062	—	—	0.062	1	87.7	7
Cefuroxime	0.016	0.062	—	—	0.125	1	87.7	12.3
Ceftriaxone	0.031	0.062	100	—	0.062	0.5	91.2	5.3
Cefepime	0.031	0.062	100	—	0.125	2	87.7	7
Flomoxef	0.125	0.5	100	0	0.5	16	89.5	3.5
Imipenem	0.008	0.031	—	—	0.031	0.25	100	0
Meropenem	0.016	0.031	100	—	0.031	0.25	94.7	5.3[a]
Biapenem	0.016	0.031	—	—	0.031	0.5	—	—
Ertapenem	0.016	0.031	100	—	0.125	1	93	7[a]
Erythromycin	256	>256	22.2	74.1	2	256	33.3	63.2
Azithromycin	256	>256	22.2	74.1	2	256	38.6	56.1
Clindamycin	128	256	33.3	63	0.062	128	54.4	43.9
Tigecycline	0.062	0.25	100	—	0.031	0.062	100	—
Ciprofloxacin	0.5	32	—	—	1	4	—	—
Levofloxacin	0.5	32	66.7	29.6	0.5	2	94.7	5.3
Moxifloxacin	0.125	4	66.7	33.3	0.125	0.25	—	—
Nemonoxacin	0.062	1	—	—	0.062	0.125	—	—
Linezolid	1	1	100	—	0.5	1	100	—
Vancomycin	0.25	0.5	100	—	0.5	0.5	100	—
Teicoplanin	0.125	0.25	100	0	0.125	0.25	100	0
Rifampicin	0.062	0.125	55.6	0	0.062	0.125	—	—
SXT	0.062	0.125	100	0	0.25	2	—	—
Chloramphenicol	2	4	92.6	3.7	2	4	96.5	1.8
Fosfomycin	16	64	—	—	32	64	—	—
Daptomycin	0.125	0.25	100	—	0.125	0.5	100	—

Abbreviations: MIC, minimum inhibitory concentration; SXT, trimethoprim/sulfamethoxazole; —, no breakpoint; EUCAST, European Committee on Antimicrobial Susceptibility Testing; FDA, Food and Drug Administration; S, Susceptible; R, Resistant.
Interpretive criteria of BD company's susceptibility disk as used for flomoxef (S: ≤ 8 mg/L; R: ≥ 32 mg/L).
Interpretive criteria of FDA as used for tigecycline (S: ≤ 0.25 mg/L).
EUCAST as used for teicoplanin (S: ≤ 2 mg/L; R: ≥ 4 mg/Lβ-haemolytic group).
EUCAST as used for moxifloxacin (S: ≤ 0.5 mg/L; R: ≥ 1 mg/L).
EUCAST as used for rifampicin (S: ≤ 0.062 mg/L; R: ≥ 1 mg/L).
EUCAST as used for SXT (S: ≤ 1 mg/L; R: ≥ 4 mg/L).
Streptococcus viridans group: EUCAST as used foramoxicilin (S: ≤ 0.5 mg/L; R: ≥ 4 mg/L).
EUCAST as used for cefuroxime (S: ≤ 0.5 mg/L; R: ≥1 mg/L).
EUCAST as used for imipenem (S: ≤ 2 mg/L; R: ≥ 4 mg/L).
[a] Non-susceptibility.

staphylococci were detected but had reduced since 2011–2012 compared with the surveillance of mainland China [14,15]. The non-susceptible rate of linezolid to enterococci was 3.8%, which was significantly higher than the LEADER result of 0.3% [16]. However, similar surveillance of bloodstream infection 5 years ago did not find enterococci resistance to linezolid [17]; this shows that linezolid resistance to enterococci has a trend of increasing.

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