Original Article

Trends in Antimicrobial Resistance against Enterobacteriaceae Strains Isolated from Blood: A 10-year Epidemiological Study in Mainland China (2004–2014)

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Abstract

Background: Antimicrobial resistance is a serious problem that compromises the empirical treatment of infections, resulting in a lack of effective antibiotics and high medical expenses. Here, we aimed to monitor the trends in antimicrobial resistance among Enterobacteriaceae isolated from blood samples in mainland China.

Methods: A total of 2240 Enterobacteriaceae isolates from blood were collected from hospitalized patients at 19 tertiary hospitals between October 2004 and June 2014. The minimum inhibitory concentrations of all isolates were determined using the agar dilution method according to the Clinical and Laboratory Standards Institute 2016 guidelines.

Results: The most commonly isolated bacteria were *Escherichia coli*, compromising 47.0% (1053/2240) of the total isolates, followed by *Klebsiella* spp. (26.3%), *Salmonella* spp. (10.4%), and *Enterobacter* spp. (9.2%). The detection rates of extended-spectrum β-lactamases (ESBLs) among *E. coli* were 68.9% (2004–2005), 73.2% (2007–2008), 67.9% (2009–2010), 72.6% (2011–2012), and 58.4% (2013–2014), whereas those in ESBL-producing *Klebsiella pneumoniae* were slightly decreased (75.9%, 50.0%, 41.4%, 40.2%, and 43.0%, respectively). Carbapenems were the most potent agents against the Enterobacteriaceae isolates, followed by moxalactam, tigecycline, and amikacin. However, there was a decrease in the susceptibility rates for carbapenems in all species, particularly *K. pneumoniae* (decreased by 10.6% for imipenem) and *Enterobacter aerogenes* (decreased by 21.1% for imipenem). Reviving antibiotics (tigecycline and polymyxins) showed good *in vitro* activity against Enterobacteriaceae.

Conclusions: The activity of antibiotics against Enterobacteriaceae isolated from blood was decreased overall. Large proportions of ESBL-producing isolates were identified among *E. coli* and *Klebsiella* spp. Carbapenem-resistant isolates have become a major challenge in the treatment of infections.

Key words: Antimicrobial Resistance Trend; Blood Sample; Enterobacteriaceae; *In vitro* Activity; Susceptibility

Introduction

Enterobacteriaceae pathogens are the most commonly isolated Gram-negative bacteria identified in human blood samples. Once bloodstream infection occurs, these pathogens often result in major health problems, requiring a lengthy hospital stay, multiple antibiotic use, high medical expenses, and even death. A previous study[1] showed that patients with Gram-negative bloodstream infections have more severe inflammatory reactions and clinical symptoms than patients with Gram-positive bloodstream infections. Due to poor regulations and inappropriate use of antibiotics, antimicrobial resistance (AMR) has become a major challenge, particularly within the last decade.

In this study, we evaluated the antimicrobial susceptibility profiles of Enterobacteriaceae from blood samples with the goal of controlling AMR and improving the efficient utilization of antibiotics.

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Methods

Ethical approval

Ethics committee approval was not required because we did not collect patient identifying information.

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Clinical isolates

All isolates obtained from blood samples were collected biennially from a cumulative total of 19 tertiary hospitals in mainland China over five consecutive 1-year periods between October 2004 and June 2014 (2004–2005, 2007–2008, 2009–2010, 2011–2012, and 2013–2014) 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, and only one isolate per species per patient was collected to avoid repetitive counts in this study. Every strain to be tested was recovered and purified before the experiment to ensure the viability and purity of the bacteria. Bacterial suspensions were obtained by inoculation with 10^4 CFU of each bacterium via a multipoint inoculator. All isolates were identified by standard methods used in clinical microbiology laboratories. All organisms were deemed clinically significant by local participant criteria.

Susceptibility testing

In vitro susceptibilities to antimicrobial agents were identified by the agar dilution method, and susceptibility profiles were identified by the minimum inhibitory concentration (MIC) interpretative breakpoint criteria according to Clinical and Laboratory Standards Institute 2016 guidelines (CLSI 2016)[2] or EUCAST 2016[3] if CLSI 2016 did not provide the specific breakpoint. The double-disk synergy test was performed to identify ESBL-producing isolates among *Escherichia coli* and *Klebsiella pneumoniae*, as recommended by CLSI 2016.

Quality control

Quality control was performed using the reference strains *E. coli* ATCC 25922 and *E. coli* ATCC 35218 according to CLSI 2016. The following antibiotics were included: amoxicillin, amoxicillin-clavulanic acid (AMC), piperacillin, piperacillin-tazobactam (TZP), mezlocillin, mezlocillin-sulbactam (MSU), cefazolin, cefuroxime, ceftriaxone, cefotaxime, ceftazidime, cefoperazone, cefoperazone-sulbactam (CSL), cefepime, aztreonam, moxalactam, imipenem, meropenem, panipenem, ertapenem, gentamycin, amikacin, tetracycline, minocycline, tigecycline, ciprofloxacin, levofloxacin, nitrofurantoin, fosfomycin, polymyxin B, and colistin.

Statistical analysis

Statistical tests were analyzed by Statistical Package for the Social Sciences 20.0 software (SPSS, Inc., Chicago, IL, USA). Enumeration data were presented as percentage values. Differences in susceptibility to antibiotics between groups were analyzed by Fisher's exact tests and Chi-square tests. Results with $P < 0.05$ were considered statistically significant using two-tailed tests.

Results

Distribution of Enterobacteriaceae pathogens

Over five consecutive 1-year studies, a total of 2240 Enterobacteriaceae pathogens isolated from blood samples from 19 participating hospitals nationwide were collected. There were no significant changes in the ratio of targeted species among all studied isolates. *E. coli* (47%, $n = 1053$), *K. pneumoniae* (23.4%, $n = 524$), *Salmonella* spp. (10.4%, $n = 233$), and *Enterobacter cloacae* (6.8%, $n = 152$) were the most commonly detected species in blood samples. Notably, the average prevalence rate of *Salmonella* spp. was higher than that of *E. cloacae*, in contrast to other reports.[4-7] However, over the entire study period, the number of *Salmonella* spp. declined gradually, whereas that of *E. cloacae* increased continually, accounting for a much larger proportion of the yearly total isolates [Table 1].

Escherichia coli

The nonsusceptibility rates of third- and fourth-generation cephalosporins (except for ceftazidime, CSL, and cefepime) and fluoroquinolones remained high among *E. coli* isolates, although some fluctuations were observed for some antibiotics, with the yearly resistance rates ranging from 53.3% to 81.4%. However, the susceptibility rates of cefazolin, ceftazidime, CSL, and cefepime decreased dramatically >10% over the 10-year study. Beta-lactamase inhibitor-based combination therapy (including AMC, TZP, MSU, and CSL) showed significantly greater *in vitro* activity than monotherapy ($P < 0.01$). The same activity was observed for *K. pneumoniae*, albeit to a lesser degree. Carbapenems, moxalactam, tigecycline, and fosfomycin maintained excellent *in vitro* activity against the *E. coli* isolates, with susceptibility rates ranging from 95% to 100% over the 10-year study. Moreover, the nonsusceptibility rate of carbapenems only increased by 0.7–1.3% [Figure 1].

The detection rates of ESBL-positive *E. coli* isolates were extremely high and reached a plateau at 58.4–76.3% of all *E. coli* isolates. Compared with cefotaxime and ceftriaxone, ceftazidime maintained better activity against ESBL-positive isolates. However, there was a sharp decrease in the

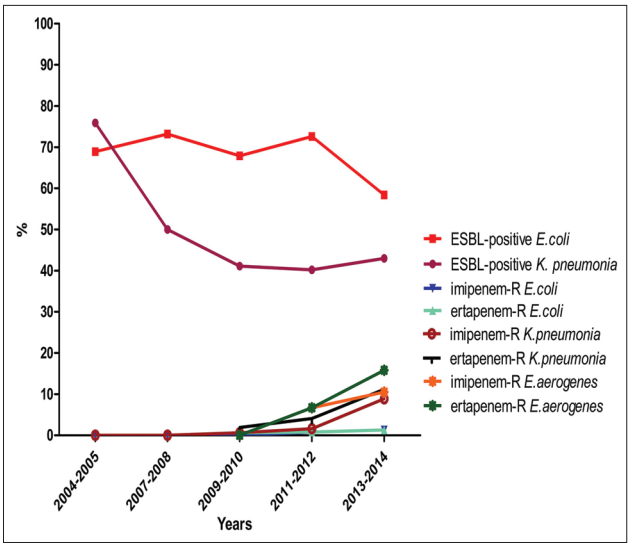

Figure 1: Rates of β-lactamase-producing *Escherichia coli* and *Klebsiella pneumoniae*, imipenem-resistant Gram-negative bacteria from blood during the period 2004–2014.

susceptibility rate for ceftazidime from 48.4% to 25.7% over the 10-year study. Moreover, CSL showed decreased efficacy against ESBL-positive *E. coli* isolates, with fluctuations during 2011–2012, and the susceptibility rate dropped from 83.9% to 62.6% over 10 years. Carbapenems, moxalactam, amikacin, and tigecycline maintained excellent *in vitro* efficacy against ESBL-positive *E. coli* isolates [Figures 1 and 2].

Klebsiella spp.

The antimicrobial profiles of *Klebsiella* spp. were similar to those of *E. coli*; however, *Klebsiella* spp. isolates displayed higher susceptibility rates to β-lactam agents than *E. coli* isolates. Notably, over the 10-year period, susceptibility rates to ceftazidime, TZP, and CSL decreased dramatically by 12.8%, 16.2%, and 22.7%, respectively, among *K. pneumoniae* isolates. Among all tested agents, >90% of *K. pneumoniae* isolates were susceptible to moxalactam, carbapenems (except ertapenem 88.3% susceptible during 2013–2014), tigecycline, fosfomycin, and polymyxin. Importantly, the frequency of occurrence of carbapenem-resistant *K. pneumoniae* increases significantly from 0% in 2004 to 8.9% in 2014, which is higher than the nationwide level for the same period [6.4% in 2014;[8] Figure 1].

The detection rates of ESBL-producing *K. pneumoniae* isolates were lower than those of *E. coli* isolates, with a yearly average rate of 44.1% [Figure 1]. There was a pronounced decrease in the *in vitro* activity of CSL over the study period, with susceptibility rates decreasing from 90.9% in 2004 to 51.9% in 2014. Over the 10-year study period, carbapenems showed good activity against ESBL-producing *K. pneumoniae* (>90.9% susceptible). Amikacin showed increased *in vitro* activity against these isolates, with susceptibility rates increasing from 77.3% in 2004 to 90.9% in 2014. Compared with *E. coli*, imipenem, amikacin, and tigecycline showed relatively lower *in vitro* activity against *K. pneumoniae*, whereas fluoroquinolones displayed much better efficacy against *K. pneumoniae* than *E. coli*. Moxalactam and polymyxins maintained good potency against *K. pneumoniae*, inhibiting >90% of ESBL-producing isolates. The antimicrobial patterns of *Klebsiella oxytoca* were similar to those of *K. pneumoniae* [data not shown and Figure 3].

Enterobacter spp.

During the study period, the total isolation rate of *E. cloacae* was much higher than that of *Enterobacter aerogenes* (6.8% versus 2.4%). Due to the low number (<10 strains) of tested isolates, the antimicrobial profiles were not

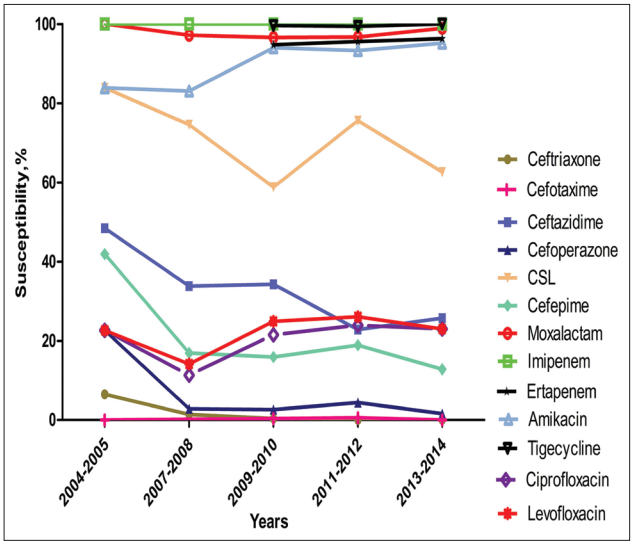

Figure 2: Susceptibility rates of extended-spectrum β-lactamase-producing *Escherichia coli* isolates to tested antimicrobial agents from blood during the period of 2004–2014.

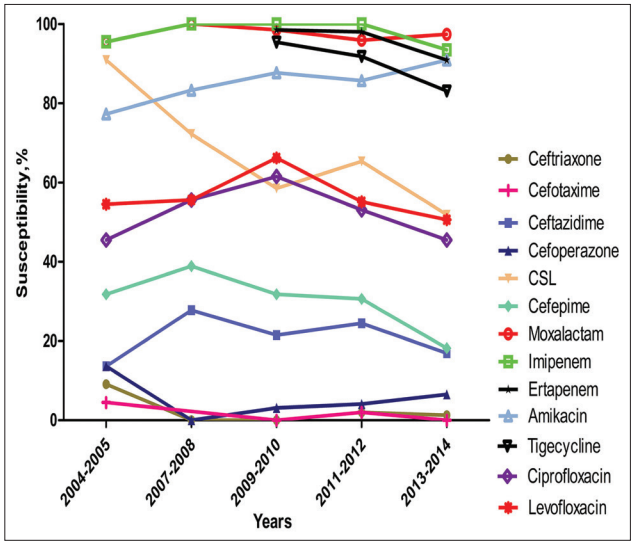

Figure 3: Susceptibility rates of extended-spectrum β-lactamase-producing *Klebsiella pneumoniae* isolates to tested antimicrobial agents from blood during the period of 2004–2014.

Table 1: Distribution and proportion of 2240 Enterobacteriaceae isolates from patients (2004–2014), *n* (%)

Microorganism	2004–2005 (*n* = 144)	2007–2008 (*n* = 218)	2009–2010 (*n* = 626)	2011–2012 (*n* = 488)	2013–2014 (*n* = 764)	2004–2014 (*n* = 2240)
E. coli	45 (31.3)	97 (44.5)	343 (54.8)	248 (50.8)	320 (41.9)	1053 (47.0)
Klebsiella spp.	32 (22.2)	42 (19.3)	165 (26.4)	131 (26.8)	218 (28.5)	588 (26.3)
E. cloacae	9 (6.3)	12 (5.5)	40 (6.4)	29 (5.9)	62 (8.1)	152 (6.8)
E. aerogenes	3 (2.1)	3 (1.4)	14 (2.2)	15 (3.1)	19 (2.5)	54 (2.4)
Salmonella spp.	46 (31.9)	54 (24.8)	40 (6.4)	39 (8.0)	54 (7.1)	233 (10.4)
Other	9 (6.3)	10 (4.9)	24 (3.8)	26 (5.3)	91 (11.9)	160 (7.1)

E. aerogenes: *Enterobacter aerogenes*; *E. cloacae*: *Enterobacter cloacae*; *E. coli*: *Escherichia coli*.

determined for both 2004–2005 and 2007–2008. Annual susceptibility rates to tested antimicrobial agents for *E. cloacae* were generally lower than those for *E. aerogenes* during 2009–2010 and 2011–2012, similar to other previous studies in China.[9] Over the three 1-year consecutive periods (2009–2010, 2011–2012, and 2013–2014), high resistance rates for β-lactam agents (except for carbapenems) were uniformly observed in *E. cloacae* and *E. aerogenes*. Carbapenems, moxalactam, amikacin, tigecycline, and fosfomycin displayed acceptable *in vitro* activity against *E. cloacae* and *E. aerogenes*, with the susceptibility rates of >75%. Notably, resistance to carbapenems tended to increase in *E. aerogenes*, particularly for ertapenem (from 0% in 2009–2010 to 15.8% in 2013–2014), with MIC_{90} increased from 0.25 to 4 mg/L. The same trend was observed for *E. cloacae*, but to a lesser degree. During 2013–2014, polymyxins (including polymyxin B and colistin) exhibited prominent *in vitro* activity against *E. aerogenes* isolates, with susceptibility rates of >90%. In contrast, polymyxins showed much lower *in vitro* activity against *E. cloacae* (<68.3% susceptible).

Salmonella spp.

Salmonella spp. were the third most commonly isolated organisms. Unlike other species within the Enterobacteriaceae family, most tested antimicrobial agents exhibited strong *in vitro* activity against *Salmonella* spp. Among β-lactam agents, >90% of the isolates were susceptible to TZP, CSL, ceftazidime, cefepime, moxalactam, and carbapenems. Amikacin, tigecycline, and fosfomycin showed strong *in vitro* activity against *Salmonella* spp. Over the 10-year study, only one strain was found to be resistant to carbapenems, and no tigecycline-resistant *Salmonella* spp. were found. Interestingly, there were no significant changes in the resistance rates for fluoroquinolones (<10% throughout the collection period); however, a large proportion of *Salmonella* spp. (48.7–83.3%) showed intermediate resistance to fluoroquinolones.

Citrobacter spp., *Serratia* spp., *Morganella* spp., and *Proteus* spp.

There were low isolation rates of *Citrobacter* spp., *Serratia* spp., *Morganella* spp., and *Proteus* spp. in this study. The antimicrobial profiles of these species to tested antibiotics are shown in Supplementary Tables 1-6. The third- and fourth-generation cephalosporins showed good *in vitro* activity against *Serratia* spp. and *Morganella* spp., acceptable *in vitro* activity against *Proteus* spp., and low *in vitro* activity against *Citrobacter* spp. The differences in susceptibility to other antibiotics were typically large. Moxalactam and carbapenems showed relatively superior *in vitro* potency compared with other tested antibiotics.

Discussion

Over the collection periods (2004–2005, 2007–2008, 2009–2010, 2011–2012, 2013–2014), Enterobacteriaceae isolates exhibited distinctively different antimicrobial susceptibilities to tested antibiotics. In this study, β-lactam antibiotics (except for carbapenems) displayed extremely poor *in vitro* activity against the Enterobacteriaceae family with the exception of *Salmonella* spp. Third-generation cephalosporin-resistant isolates were often found to be resistant to fluoroquinolones and aminoglycosides (gentamycin and amikacin) simultaneously. In this 10-year study, 2.1–6.3% of the 2240 Enterobacteriaceae isolates were resistant to these three types of antibiotics (data not shown), corresponding to the results of a European survey over the same period (1.4–19.7%).[10]

The detection rates of ESBL-producing *E. coli* and *K. pneumoniae* isolates were almost unchanged and remained consistently high over the 10-year study, with yearly total rates of 66.7% (702/1053) and 44.1% (231/524), respectively; these rates were much higher than those of other countries.[10,11] ESBL production is the main reason for treatment failure of β-lactam antibiotics. According to a previous survey, the CTX-M genotype, associated with the hydrolysis of cefotaxime and ceftriaxone, is the main genotype of ESBLs.[12,13] This could explain why cefotaxime and ceftriaxone showed much lower *in vitro* efficacy than ceftazidime against ESBLs.

Throughout the study,[7] a trend toward increased nonsusceptibility rates for carbapenems was observed, especially for *K. pneumoniae* and *E. aerogenes*. During 2013–2014, the nonsusceptibility rates of *K. pneumoniae* and *E. aerogenes* to ertapenem reached up to 11.7% and 21.1%, respectively. Furthermore, carbapenem resistance was generally caused by the production of carbapenemases carried by plasmids, which could be transmitted within species or even from species to species. However, the genes encoding carbapenemases often carry some other resistance factors at the same time, leading to extensively drug-resistant bacteria.[14] Thus, the problem of carbapenem-resistant Enterobacteriaceae (CRE) has become a major challenge to public health worldwide, resulting in higher mortality rates caused by infections and a lack of reliable treatment.[15-18]

In this study, some reviving antibiotics, including fosfomycin and polymyxins, were found to be effective alternative treatments against CRE. Polymyxins displayed strong activity against Enterobacteriaceae, with susceptibility rates of >90%, except for *E. cloacae* (66.7% susceptible). However, colistin-resistant isolates have emerged globally within the last few years.[19,20] Recently, a mobile colistin-resistance gene, called *mcr-1*, has been reported in Enterobacteriaceae isolated both from livestock and humans; this gene may compromise treatment with last resort antimicrobial agents (colistin), thereby posing a major threat to public health.[21,22] According to a survey in Europe, the resistance rate for polymyxins among carbapenem-resistant *K. pneumoniae* isolates is as high as 43%.[23] In this study, only 6.25% (1/16) of carbapenem-resistant *K. pneumoniae* isolates were found to be resistant to polymyxin B, whereas no isolates were resistant to colistin. This finding may be associated with the rare clinical use of polymyxins in China.

Given the severe condition of AMR among Enterobacteriaceae isolated from blood, precautions must be taken to control the presence of drug-resistance bacteria. A previous study[24] showed that β-lactamase-producing Gram-negative bacteria are associated with antibiotic use in healthcare settings, antibiotic use in animals, hand hygiene, environmental contamination with antibiotic-resistant bacteria, and travel. Thus, only interdisciplinary collaboration will be able to overcome the latent threat of AMR.

Several approaches could be helpful in this regard. First, professional training and public education should be strengthened. For example, leaflets, posters, and educational courses are needed to emphasize the urgency and seriousness of reducing AMR. Second, antimicrobial prescriptions must be optimized;[25] the use, misuse, and overuse of antibiotics are major determinants of AMR,[24] and promoting rational prescribing and proper use of existing antibiotics will be important. Third, governments should implement regulations to contain AMR, such as bans on the use of antibiotic growth promoters in livestock and agriculture. Fourth, better use of surveillance data, including development of comprehensive nationwide surveillance networks and monitoring of trends in AMR, is essential. Finally, the development of new drugs as powerful antimicrobial agents, particularly those that are active against ESBL producers and multidrug-resistant bacteria, is urgently needed to replace ineffective drugs; however, antibiotics show little opportunity compared with other therapeutic categories owing to the development bottleneck in new scientific breakthroughs and lack of economic incentives.[26]

In conclusion, the control of AMR requires interdisciplinary cooperation of medical microbiologists, veterinarians, hospital doctors, microbiology laboratories, and government officials. The increasing AMR in Enterobacteriaceae strains isolated from the blood is still a major problem that should be monitored closely worldwide.

Supplementary information is linked to the online version of the paper on the Chinese Medical Journal website.

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Conflicts of interest

There are no conflicts of interest.

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Supplementary Table 1: Antimicrobial susceptibility profiles of *E. coli* from blood in mainland China during the period 2004–2014

Antibiotics	2004–2005 (*n* = 45)				2007–2008 (*n* = 97)				2009–2010 (*n* = 343)			
	MIC_{50}	MIC_{90}	S	R	MIC_{50}	MIC_{90}	S	R	MIC_{50}	MIC_{90}	S	R
Amoxicillin*	>256	>256	11.1	88.9	>256	>256	7.2	90.7	>256	>256	8.2	91.5
AMC	16	32	35.6	26.7	16	32	27.8	38.1	>256	>256	68.2	13.4
Piperacillin	>256	>256	15.6	82.2	>256	>256	11.3	78.4	>256	>256	14.3	74.1
TZP	4	16	95.6	0.0	8	32	87.6	3.1	8	32	93.6	5.0
Mezlocillin†	ND	ND	ND	ND	ND	ND	ND	ND	256	>256	16.6	72.3
MSU†	ND	ND	ND	ND	ND	ND	ND	ND	32	128	42.0	11.7
Cefazolin	>256	>256	28.9	68.9	>256	>256	16.5	81.4	256	>256	20.1	76.4
Cefuroxime	>256	>256	25.1	71.1	>256	>256	21.6	74.2	>256	>256	19.2	72.9
Ceftriaxone	4	16	31.1	68.9	64	>256	23.7	74.2	>256	>256	27.4	72.0
Cefotaxime	16	256	26.7	71.1	ND	ND	ND	ND	1	8	27.7	72.0
Ceftazidime	1	32	73.3	15.6	2	32	72.2	23.7	32	>256	65.3	30.9
Cefoperazone‡	64	>256	42.2	53.3	128	>256	23.7	72.2	64	>256	29.2	65.3
CSL	4	32	88.9	4.4	8	32	76.3	0.0	1	64	69.1	11.7
Cefepime	1	32	55.6	24.4	8	64	35.1	35.1	128	>256	40.2	32.4
Aztreonam	ND	ND	ND	ND	ND	ND	ND	ND	16	64	52.2	38.8
Moxalactam	0.125	2	97.8	2.2	0.25	1	95.9	2.1	4	64	95.0	0.0
Imipenem	0.062	0.125	100.0	0.0	0.062	0.125	100.0	0.0	4	128	100.0	0.0
Meropenem	ND	ND	ND	ND	ND	ND	ND	ND	0.25	1	99.4	0.3
Panipenem§	ND	ND	ND	ND	ND	ND	ND	ND	0.125	0.125	99.1	0.6
Ertapenem	ND	ND	ND	ND	ND	ND	ND	ND	0.62	0.125	95.6	2.3
Gentamycin	32	128	31.1	64.4	64	256	35.1	63.9	0.031	0.031	37.0	62.4
Amikacin	1	32	86.7	8.9	2	64	85.6	11.3	0.16	0.25	94.2	4.1
Tetracycline	ND	ND	ND	ND	ND	ND	ND	ND	32	128	18.4	80.8
Tigecycline‖	ND	ND	ND	ND	ND	ND	ND	ND	128	256	99.7	0.3
Ciprofloxacin	16	64	31.1	66.7	32	128	17.5	82.5	4	16	31.5	67.9
Levofloxacin	8	32	33.3	55.6	16	32	19.6	72.2	0.25	0.5	34.1	61.2
Nitrofurantoin	ND	ND	ND	ND	ND	ND	ND	ND	128	256	90.4	4.1
Fosfomycin	ND	ND	ND	ND	ND	ND	ND	ND	8	32	93.3	4.7
Polymyxin B¶	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
Colistin¶	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND

Antibiotics	2011–2012 (*n* = 248)				2013–2014 (*n* = 320)			
	MIC_{50}	MIC_{90}	S	R	MIC_{50}	MIC_{90}	S	R
Amoxicillin*	ND	ND	ND	ND	ND	ND	ND	ND
AMC	ND	ND	ND	ND	ND	ND	ND	ND
Piperacillin	256	>256	12.5	74.6	>256	>256	15.6	72.8
TZP	2	16	90.3	5.6	2	16	90.3	5.6
Mezlocillin†	256	>256	14.4	71.8	>256	>256	15.3	74.7
MSU†	16	64	50.8	8.1	32	128	48.8	11.3
Cefazolin	>256	>256	18.1	78.2	>256	>256	18.8	70.6
Cefuroxime	>256	>256	22.6	76.6	>256	>256	34.4	64.4
Ceftriaxone	64	>256	23.0	76.6	128	>256	37.2	62.8
Cefotaxime	64	>256	23.8	75.8	64	>256	37.2	62.8
Ceftazidime	4	64	52.4	38.7	1	64	61.3	34.1
Cefoperazone‡	128	>256	26.2	64.1	128	>256	38.1	60.3
CSL	4	16	90.3	5.2	8	32	75.0	9.4
Cefepime	4	32	24.6	42.7	4	64	45.9	37.8
Aztreonam	16	128	41.5	52.0	8	256	47.8	44.4
Moxalactam	0.25	1	95.6	0.8	0.25	2	96.3	1.3
Imipenem	0.062	0.125	99.2	0.8	0.125	0.125	98.8	1.3
Meropenem	0.016	0.031	98.8	0.4	0.031	0.062	98.4	1.6
Panipenem§	0.125	0.125	98.4	0.8	0.125	0.25	98.8	1.3
Ertapenem	0.016	0.5	95.2	2.8	0.016	0.25	98.1	1.3

Contd...

Supplementary Table 1: Contd...

Antibiotics	2011–2012 (n = 248)				2013–2014 (n = 320)			
	MIC_{50}	MIC_{90}	S	R	MIC_{50}	MIC_{90}	S	R
Gentamycin	16	128	44.8	52.8	4	128	50.0	49.4
Amikacin	2	8	93.5	6.0	2	4	96.6	3.1
Tetracycline	128	256	30.2	69.8	128	256	25.0	74.1
Tigecycline‖	0.25	1	100.0	0.0	0.25	0.5	100.0	0.0
Ciprofloxacin	16	64	32.3	65.7	16	128	38.1	61.3
Levofloxacin	8	32	34.3	56.0	8	32	38.1	55.6
Nitrofurantoin	8	64	81.9	6.9	16	64	84.7	4.7
Fosfomycin	0.25	128	89.1	6.0	0.5	4	94.7	4.7
Polymyxin B¶	ND	ND	ND	ND	1	1	97.5	0.2
Colistin¶	ND	ND	ND	ND	0.5	0.5	97.5	0.2

*The breakpoint of amoxicillin is used as that of ampicillin (S≦8 mg/L; R≧32 mg/L); †The breakpoint of mezlocillin and mezlocillin/sulbactam is used as that of piperacillin (S≦16 mg/L; R≧128 mg/L); ‡The breakpoint of cefoperazone is used as that of cefoperazone-sulbactam (S≦16 mg/L; R≧64 mg/L); §The breakpoint of panipenem is used as that of imipenem (S≦1 mg/L; R≧4 mg/L); ‖The breakpoint of tigecycline is according to FDA (S≦2 mg/L; R≧8 mg/L); ¶The breakpoint of polymyxin E and colistin is according to EUCAST (S≦2 mg/L; R≧2 mg/L). ND: No detection; AMC: Amoxicillin-clavulanic acid; TZP: Piperacillin-tazobactam; MSU: Mezlocillin-sulbactam; CSL: Cefoperazone-sulbactam; FDA: Food and Drug Administration; MIC: Minimum inhibitory concentration; R: Resistance rate (%); S: Susceptibility rate (%).

Supplementary Table 2: Antimicrobial susceptibility profiles of *K. pneumoniae* from blood in mainland China during the period 2004–2014

Antibiotics	2004–2005 (n = 29)				2007–2008 (n = 36)				2009–2010 (n = 158)			
	MIC_{50}	MIC_{90}	S	R	MIC_{50}	MIC_{90}	S	R	MIC_{50}	MIC_{90}	S	R
Amoxicillin	>256	>256	0.0	100.0	>256	>256	2.8	0.0	>256	>256	0.0	100.0
AMC	16	128	34.5	27.6	16	32	47.2	16.7	4	32	72.8	14.6
Piperacillin	>256	>256	20.7	65.5	256	>256	41.7	55.6	64	>256	45.6	47.5
TZP	4	16	100.0	0.0	4	16	88.9	0.0	2	64	87.3	10.1
Mezlocillin	ND	ND	ND	ND	ND	ND	ND	ND	64	>256	45.6	47.5
MSU	ND	ND	ND	ND	ND	ND	ND	ND	16	128	65.2	13.3
Cefazolin	>256	>256	24.1	75.9	256	>256	38.9	61.1	16	>256	48.1	50.6
Cefuroxime	>256	>256	27.6	72.4	>256	>256	41.7	55.6	16	>256	49.4	48.1
Ceftriaxone	64	128	27.6	72.4	8	256	41.7	55.6	0.125	256	53.8	46.2
Cefotaxime	32	128	24.1	72.4	ND	ND	ND	ND	0.25	256	52.5	45.6
Ceftazidime	4	16	75.9	17.2	2	64	63.9	41.7	0.5	64	69.0	24.7
Cefoperazone	128	256	31.0	65.5	32	>256	44.4	50.0	1	>256	54.4	40.5
CSL	4	8	93.1	3.4	4	32	83.3	5.6	1	64	79.1	11.4
Cefepime	4	16	44.8	27.6	1	32	50.0	30.6	0.125	32	68.4	21.5
Aztreonam	ND	ND	ND	ND	ND	ND	ND	ND	0.125	128	68.4	27.8
Moxalactam	0.25	2	93.1	3.4	0.125	0.5	97.2	2.8	0.25	1	96.8	2.5
Imipenem	0.25	0.5	100.0	0.0	0.062	0.125	100.0	0.0	0.125	0.125	99.4	0.6
Meropenem	ND	ND	ND	ND	ND	ND	ND	ND	0.016	0.031	99.4	0.6
Panipenem	ND	ND	ND	ND	ND	ND	ND	ND	0.062	0.125	98.7	0.6
Ertapenem	ND	ND	ND	ND	ND	ND	ND	ND	0.012	0.25	97.5	1.9
Gentamycin	32	>256	44.8	55.2	1	32	61.1	16.7	32	128	65.8	33.5
Amikacin	1	>256	82.8	17.2	1	4	88.9	11.1	2	8	91.1	7.0
Tetracycline	ND	ND	ND	ND	ND	ND	ND	ND	128	256	57.0	38.0
Minocycline	ND	ND	ND	ND	ND	ND	ND	ND	4	32	69.0	17.7
Tigecycline	ND	ND	ND	ND	ND	ND	ND	ND	0.25	0.5	98.1	1.9
Ciprofloxacin	2	128	48.3	48.3	0.25	128	41.7	33.3	16	128	69.4	27.8
Levofloxacin	2	64	55.2	37.9	0.25	32	69.4	27.8	8	32	69.4	19.4
Nitrofurantoin	ND	ND	ND	ND	ND	ND	ND	ND	8	32	38.6	24.7
Fosfomycin	ND	ND	ND	ND	ND	ND	ND	ND	0.25	8	93.0	6.3
Polymyxin B	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
Colistin	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND

Contd...

Supplementary Table 2: Contd...

Antibiotics	2011–2012 (n = 122)				2013–2014 (n = 179)			
	MIC_{50}	MIC_{90}	S	R	MIC_{50}	MIC_{90}	S	R
Amoxicillin	ND	ND	ND	ND	ND	ND	ND	ND
AMC	ND	ND	ND	ND	ND	ND	ND	ND
Piperacillin	64	>256	45.9	48.4	256	>256	44.1	53.1
TZP	2	64	83.6	9.8	4	>256	83.8	13.4
Mezlocillin	128	>256	45.9	50.0	256	>256	44.1	53.6
MSU	16	128	57.4	14.8	16	256	57.0	21.8
Cefazolin	32	>256	46.7	51.6	128	>256	41.3	55.9
Cefuroxime	32	>256	48.4	50.8	256	>256	46.9	51.4
Ceftriaxone	0.25	256	52.5	46.7	16	>256	48.0	52.0
Cefotaxime	0.5	128	52.5	46.7	16	>256	47.5	52.0
Ceftazidime	0.5	64	73.0	22.1	1	128	63.1	35.2
Cefoperazone	4	>256	54.1	39.3	32	>256	49.7	49.2
CSL	2	32	89.3	5.7	4	256	70.4	21.2
Cefepime	0.25	32	66.4	17.2	1	64	56.4	31.3
Aztreonam	0.25	128	66.4	31.1	1	256	56.4	39.1
Moxalactam	0.125	2	94.3	0.8	0.25	8	89.9	8.9
Imipenem	0.125	0.25	98.4	1.6	0.125	2	89.4	8.9
Meropenem	0.016	0.031	96.7	3.3	0.031	1	89.9	10.1
Panipenem	0.125	0.125	95.9	3.3	0.125	2	89.4	10.1
Ertapenem	0.008	0.5	95.1	4.1	0.031	4	88.3	11.2
Gentamycin	0.5	128	67.2	31.1	1	128	66.5	33.0
Amikacin	1	2	93.4	6.6	2	4	92.2	7.8
Tetracycline	4	256	54.1	42.6	8	256	48.6	43.0
Minocycline	2	32	68.9	25.4	4	64	59.2	26.8
Tigecycline	0.5	2	91.8	3.3	1	2	91.1	4.5
Ciprofloxacin	0.031	64	73.8	24.6	0.125	32	68.7	26.3
Levofloxacin	0.062	16	77.0	22.1	0.25	16	72.6	20.7
Nitrofurantoin	64	256	44.3	40.2	128	256	15.1	71.5
Fosfomycin	4	64	90.2	6.6	8	64	92.2	5.0
Polymyxin B	ND	ND	ND	ND	1	1	98.3	1.7
Colistin	ND	ND	ND	ND	0.5	1	98.9	1.1

K.pneumoniae: *Klebsiella pneumoniae*; ND: No detection; AMC: Amoxicillin-clavulanic acid; TZP: Piperacillin-tazobactam; MSU: Mezlocillin-sulbactam; CSL: Cefoperazone-sulbactam; MIC: Minimum inhibitory concentration; R: Resistance rate (%); S: Susceptibility rate (%).

Supplementary Table 3: Antimicrobial susceptibility profiles of *E. cloacae* from blood in mainland China during the period 2004–2014

Antibiotics	2009–2010 (n = 40)				2011–2012 (n = 29)				2013–2014 (n = 62)			
	MIC_{50}	MIC_{90}	S	R	MIC_{50}	MIC_{90}	S	R	MIC_{50}	MIC_{90}	S	R
Amoxicillin	>256	>256	0.0	100.0	ND	ND	ND	ND	ND	ND	ND	ND
AMC	32	64	5.0	90.0	ND	ND	ND	ND	ND	ND	ND	ND
Piperacillin	16	>256	52.5	45.0	128	>256	24.1	65.5	8	>256	58.1	30.6
TZP	2	>256	72.5	20.0	4	256	72.4	13.8	4	128	75.8	12.9
Mezlocillin	16	>256	42.5	50.0	128	>256	27.6	62.1	8	>256	58.1	30.6
MSU	8	128	57.5	30.0	32	128	41.4	17.2	8	128	66.1	11.3
Cefazolin	256	>256	0.0	100.0	>256	>256	0.0	100.0	>256	>256	1.6	98.4
Cefuroxime	64	>256	37.5	55.0	>256	>256	17.2	75.9	64	>256	41.9	53.2
Ceftriaxone	8	256	42.5	57.5	64	256	27.6	72.4	0.5	>256	54.8	45.2
Cefotaxime	16	256	45.0	55.0	64	256	27.6	72.4	0.5	>256	56.5	43.5
Ceftazidime	8	256	47.5	47.5	32	256	31.0	69.0	0.5	256	62.9	33.9
Cefoperazone	4	>256	62.5	35.0	64	>256	41.4	55.2	2	>256	66.1	27.4
CSL	4	128	75.0	20.0	8	64	62.1	20.7	1	128	75.8	17.7
Cefepime	0.062	32	67.5	20.0	4	32	48.3	34.5	0.062	16	83.9	12.9

Contd...

Supplementary Table 3: Contd...

Antibiotics	2009–2010 (n = 40)				2011–2012 (n = 29)				2013–2014 (n = 62)			
	MIC_{50}	MIC_{90}	S	R	MIC_{50}	MIC_{90}	S	R	MIC_{50}	MIC_{90}	S	R
Aztreonam	8	>256	45.0	50.0	32	256	41.4	58.6	0.125	128	67.7	29.0
Moxalactam	0.25	32	75.0	12.5	0.25	128	79.3	13.8	0.25	32	75.8	9.7
Imipenem	0.125	0.25	100.0	0.0	0.25	1	93.1	6.9	0.5	2	88.7	4.8
Meropenem	0.031	0.062	100.0	0.0	0.031	1	93.1	6.9	0.031	1	91.9	4.8
Panipenem	0.125	0.25	100.0	0.0	0.125	4	82.8	13.8	0.5	4	85.5	11.3
Ertapenem	0.062	1	82.5	5.0	0.125	2	72.4	20.7	0.062	2	83.9	12.9
Gentamycin	1	256	62.5	37.5	0.5	128	65.5	34.5	0.5	64	87.1	12.9
Amikacin	2	16	92.5	7.5	1	8	93.1	6.9	2	4	98.4	1.6
Tetracycline	4	256	60.0	40.0	8	256	55.2	37.9	4	256	67.7	24.2
Tigecycline	0.5	2	97.5	2.5	0.5	2	93.1	3.4	1	2	95.2	1.6
Ciprofloxacin	0.125	16	47.5	22.5	0.25	16	37.9	41.4	0.062	1	56.5	17.7
Levofloxacin	0.062	4	52.5	22.5	0.5	32	34.5	27.6	0.25	2	50.0	14.5
Fosfomycin	4	32	97.5	2.5	4	32	93.1	6.9	8	32	95.2	3.2
Polymyxin B	ND	ND	ND	ND	ND	ND	ND	ND	2	>256	66.1	33.9
Colistin	ND	ND	ND	ND	ND	ND	ND	ND	1	256	67.7	32.3

E. cloacae: *Enterobacter cloacae*; ND: No detection; AMC: Amoxicillin-clavulanic acid; TZP: Piperacillin-tazobactam; MSU: Mezlocillin-sulbactam; CSL: Cefoperazone-sulbactam; MIC: Minimum inhibitory concentration; R: Resistance rate (%); S: Susceptibility rate (%).

Supplementary Table 4: Antimicrobial susceptibility profiles of *Enterobacter aerogenes* from blood in mainland China during the period 2004–2014

Antibiotics	2009–2010 (n = 14)				2011–2012 (n = 15)				2013–2014 (n = 19)			
	MIC_{50}	MIC_{90}	S	R	MIC_{50}	MIC_{90}	S	R	MIC_{50}	MIC_{90}	S	R
Amoxicillin	>256	>256	0.0	100.0	ND	ND	ND	ND	ND	ND	ND	ND
AMC	32	32	0.0	92.9	ND	ND	ND	ND	ND	ND	ND	ND
Piperacillin	16	>256	57.1	42.9	16	256	60.0	20.0	256	>256	42.1	52.6
TZP	4	8	92.9	7.1	16	128	53.3	13.3	16	>256	52.6	36.8
Mezlocillin	16	>256	50.0	42.9	16	>256	53.3	13.3	64	>256	42.1	47.4
MSU	8	128	57.1	35.7	16	64	66.7	6.7	16	256	52.6	36.8
Cefazolin	64	>256	0.0	85.7	16	>256	0.0	93.3	>256	>256	0.0	100.0
Cefuroxime	8	>256	50.0	50.0	32	>256	46.7	53.3	128	>256	36.8	57.9
Ceftriaxone	0.125	>256	50.0	50.0	0.5	256	60.0	40.0	16	>256	42.1	57.9
Cefotaxime	0.125	256	50.0	50.0	0.5	256	60.0	40.0	16	>256	47.4	52.6
Ceftazidime	0.25	16	64.3	35.7	1	64	60.0	40.0	16	128	47.4	52.6
Cefoperazone	0.25	>256	57.1	42.9	1	>256	86.7	13.3	128	>256	47.4	52.6
CSL	0.125	64	57.1	35.7	2	64	86.7	13.3	4	128	52.6	36.8
Cefepime	0.031	32	57.1	42.9	0.125	16	86.7	13.3	0.5	256	52.6	36.8
Aztreonam	0.062	64	57.1	42.9	0.5	64	60.0	40.0	16	256	42.1	52.6
Moxalactam	0.25	2	100.0	0.0	0.5	16	86.7	6.7	0.5	32	84.2	10.5
Imipenem	0.125	0.125	100.0	0.0	0.125	0.5	93.3	6.7	1	2	78.9	10.5
Meropenem	0.016	0.031	100.0	0.0	0.016	0.125	93.3	6.7	0.062	0.25	89.5	5.3
Panipenem	0.125	0.125	100.0	0.0	0.125	0.25	93.3	6.7	0.25	1	89.5	10.5
Ertapenem	0.062	0.25	100.0	0.0	0.062	1	93.3	6.7	0.25	4	78.9	15.8
Gentamycin	0.5	2	92.9	7.1	0.5	1	93.3	6.7	1	64	78.9	21.1
Amikacin	1	2	92.9	7.1	1	2	93.3	6.7	2	4	100.0	0.0
Tetracycline	2	32	78.6	14.3	4	32	73.3	20.0	2	128	84.2	15.8
Tigecycline	0.5	1	100.0	0.0	0.5	4	80.0	0.0	1	1	94.7	5.3
Ciprofloxacin	0.125	2	42.9	28.6	0.125	64	46.7	26.7	0.016	32	78.9	15.8
Levofloxacin	0.25	2	42.9	28.6	0.25	8	46.7	26.7	0.062	16	73.7	15.8
Fosfomycin	8	8	100.0	0.0	4	16	93.3	0.0	8	256	84.2	15.8
Polymyxin B	ND	ND	ND	ND	ND	ND	ND	ND	1	1	89.5	10.5
Colistin	ND	ND	ND	ND	ND	ND	ND	ND	0.5	1	94.7	5.3

ND: No detection; AMC: Amoxicillin-clavulanic acid; TZP: Piperacillin-tazobactam; MSU: Mezlocillin-sulbactam; CSL: Cefoperazone-sulbactam; MIC: Minimum inhibitory concentration; R: Resistance rate (%); S: Susceptibility rate (%).

Supplementary Table 5: Antimicrobial susceptibility profiles of *Salmonella* spp. from blood in mainland China during the period 2004–2014

Antibiotics	2004–2005 (n = 46)				2007–2008 (n = 54)				2009–2010 (n = 40)			
	MIC_{50}	MIC_{90}	S	R	MIC_{50}	MIC_{90}	S	R	MIC_{50}	MIC_{90}	S	R
Amoxicillin	1	512	84.8	15.2	1	512	59.3	0.0	4	512	60.0	40.0
AMC	1	4	93.5	4.3	1	8	90.7	0.0	4	8	97.5	0.0
Piperacillin	2	16	95.7	4.3	4	512	59.3	0.3	8	128	57.5	17.5
TZP	2	2	100.0	0.0	2	8	94.4	0.0	2	4	100.0	0.0
Mezlocillin	ND	ND	ND	ND	ND	ND	ND	ND	8	128	57.5	22.5
MSU	ND	ND	ND	ND	ND	ND	ND	ND	4	16	92.5	0.0
Cefazolin	2	2	91.3	8.7	2	64	85.2	0.1	2	2	90.0	2.5
Cefuroxime	4	8	87.0	4.3	4	16	77.8	0.1	8	8	95.0	0.0
Ceftriaxone	0.062	0.062	93.5	6.5	0.062	0.25	90.7	0.1	0.062	0.062	100.0	0.0
Cefotaxime	0.062	0.062	93.5	6.5	ND	ND	ND	ND	0.062	0.125	100.0	0.0
Ceftazidime	0.25	0.25	97.8	2.2	0.25	0.5	100.0	0.0	0.25	0.25	100.0	0.0
Cefoperazone	0.5	2	95.7	2.2	1	64	81.5	0.2	0.5	8	100.0	0.0
CSL	0.5	1	78.3	21.7	0.5	16	96.3	0.0	0.5	8	100.0	0.0
Cefepime	0.031	0.031	97.8	0.0	0.031	0.25	98.1	0.0	0.031	0.062	100.0	0.0
Aztreonam	ND	ND	ND	ND	ND	ND	ND	ND	0.031	0.125	100.0	0.0
Moxalactam	0.062	0.062	95.7	2.2	0.062	0.125	98.1	0.0	0.062	0.125	100.0	0.0
Imipenem	0.25	0.25	100.0	0.0	0.062	0.062	100.0	0.0	0.125	0.125	100.0	0.0
Meropenem	ND	ND	ND	ND	ND	ND	ND	ND	0.016	0.016	100.0	0.0
Panipenem	ND	ND	ND	ND	ND	ND	ND	ND	0.062	0.125	100.0	0.0
Ertapenem	ND	ND	ND	ND	ND	ND	ND	ND	0.031	0.008	100.0	0.0
Gentamycin	0.062	0.5	89.1	10.9	0.5	64	70.4	0.3	0.5	16	87.5	12.5
Amikacin	0.25	1	100.0	0.0	1	2	98.1	0.0	1	2	100.0	0.0
Tetracycline	ND	ND	ND	ND	ND	ND	ND	ND	4	128	75.0	25.0
Tigecycline	ND	ND	ND	ND	ND	ND	ND	ND	0.125	1	100.0	0.0
Ciprofloxacin	0.125	0.125	30.4	0.0	0.25	0.5	16.7	0.1	0.125	0.125	35.0	7.5
Levofloxacin	0.5	0.5	30.4	2.2	0.5	1	20.4	0.1	0.5	1	27.5	7.5
Nitrofurantoin	ND	ND	ND	ND	ND	ND	ND	ND	16	128	57.5	20.0
Fosfomycin	ND	ND	ND	ND	ND	ND	ND	ND	0.125	16	100.0	0.0

Antibiotics	2011–2012 (n = 39)				2013–2014 (n = 54)			
	MIC_{50}	MIC_{90}	S	R	MIC_{50}	MIC_{90}	S	R
Amoxicillin	ND	ND	ND	ND	ND	ND	ND	ND
AMC	ND	ND	ND	ND	ND	ND	ND	ND
Piperacillin	2	128	69.2	30.8	4	512	57.4	38.9
TZP	2	8	94.9	5.1	4	16	94.4	3.7
Mezlocillin	4	64	69.2	7.7	8	512	57.4	40.7
MSU	4	32	87.2	5.1	8	64	64.8	1.9
Cefazolin	2	64	87.2	12.8	2	512	70.4	22.2
Cefuroxime	8	16	87.2	12.8	8	256	75.9	16.7
Ceftriaxone	0.062	0.125	94.9	5.1	0.125	16	87.0	13.0
Cefotaxime	0.125	0.25	94.9	5.1	0.125	16	85.2	11.1
Ceftazidime	0.25	0.25	94.9	5.1	0.25	1	90.7	9.3
Cefoperazone	0.5	8	94.9	5.1	1	128	81.5	13.0
CSL	0.5	4	94.9	5.1	0.5	16	94.4	1.9
Cefepime	0.062	0.125	94.9	5.1	0.062	2	90.7	7.4
Aztreonam	0.062	0.25	94.9	5.1	0.125	4	90.7	9.3
Moxalactam	0.062	0.125	97.4	0.0	0.125	0.125	98.1	1.9
Imipenem	0.125	0.25	100.0	0.0	0.125	0.25	98.1	1.9
Meropenem	0.016	0.031	97.4	0.0	0.016	0.031	98.1	1.9
Panipenem	0.062	0.25	97.4	0.0	0.125	0.25	98.1	1.9
Ertapenem	0.016	0.016	97.4	2.6	0.008	0.016	98.1	1.9
Gentamycin	0.25	1	89.7	7.7	0.5	32	87.0	13.0
Amikacin	0.5	1	97.4	2.6	1	2	96.3	3.7

Contd...

Supplementary Table 5: Contd...

Antibiotics	2011–2012 (n = 39)				2013–2014 (n = 54)			
	MIC_{50}	MIC_{90}	S	R	MIC_{50}	MIC_{90}	S	R
Tetracycline	1	64	79.5	17.9	2	128	75.9	20.4
Tigecycline	0.5	0.5	100.0	0.0	0.5	1	100.0	0.0
Ciprofloxacin	0.125	0.25	48.7	2.6	0.125	0.5	25.9	5.6
Levofloxacin	0.25	1	38.5	2.6	0.25	1	27.8	3.7
Nitrofurantoin	16	128	64.1	10.3	64	128	40.7	31.5
Fosfomycin	4	32	100.0	0.0	0.25	64	98.1	1.9

ND: No detection; AMC: Amoxicillin-clavulanic acid; TZP: Piperacillin-tazobactam; MSU: Mezlocillin-sulbactam; CSL: Cefoperazone-sulbactam; MIC: Minimum inhibitory concentration; R: Resistance rate (%); S: Susceptibility rate (%).

Supplementary Table 6: Antimicrobial susceptibility profiles of *Citrobacter* spp., *Serratia* spp., *Morganella* spp., and *Proteus* spp. from blood in mainland China during the period 2004–2014

Antibiotics	*Citrobacter* spp. (n = 22)				*Serratia* spp. (n = 86)				*Morganella* spp. (n = 22)				*Proteus* spp. (n = 30)			
	MIC_{50}	MIC_{90}	S	R	MIC_{50}	MIC_{90}	S	R	MIC_{50}	MIC_{90}	S	R	MIC_{50}	MIC_{90}	S	R
Amoxicillin	>256	>256	0.0	100.0	64	>256	10.0	90.0	256	>256	0.0	100.0	>256	>256	14.3	85.7
AMC	64	128	33.3	66.7	64	128	20.0	80.0	128	256	0.0	100.0	4	8	85.7	0.0
Piperacillin	256	>256	22.7	63.6	4	256	74.4	23.3	2	128	77.3	13.6	2	64	75.0	3.6
TZP	4	256	77.3	13.6	2	8	96.5	3.5	0.25	0.5	100.0	0.0	0.5	1	100.0	0.0
Mezlocillin	256	>256	29.4	58.8	8	>256	74.1	21.0	4	128	73.7	21.1	8	128	54.2	25.0
MSU	64	128	41.2	17.6	4	64	79.0	12.3	2	16	100.0	0.0	4	8	100.0	0.0
Cefazolin	>256	>256	9.1	90.9	>256	>256	2.3	97.7	256	>256	0.0	90.9	128	>256	21.4	64.3
Cefuroxime	128	>256	27.3	72.7	256	>256	3.5	96.5	32	128	27.3	59.1	256	>256	35.7	64.3
Ceftriaxone	128	>256	30.0	70.0	0.5	128	69.0	28.6	0.016	2	75.0	25.0	1	256	45.8	54.2
Cefotaxime	64	256	31.8	68.2	0.5	128	70.9	27.9	0.031	8	77.3	9.1	4	>256	50.0	46.4
Ceftazidime	32	128	40.9	59.1	0.25	8	88.4	4.7	0.125	16	77.3	13.6	0.062	32	82.1	14.3
Cefoperazone	64	>256	40.9	54.5	2	256	76.7	22.1	1	32	77.3	4.5	4	128	60.7	35.7
CSL	16	32	63.6	18.2	1	32	88.4	5.8	1	4	100.0	0.0	1	4	96.4	0.0
Cefepime	0.25	8	54.5	31.8	0.125	16	76.7	16.3	0.031	0.062	100.0	0.0	1	16	64.3	14.3
Aztreonam	16	256	35.3	58.8	0.125	64	72.8	19.8	0.016	0.5	100.0	0.0	0.5	8	87.5	8.3
Moxalactam	0.5	4	72.7	13.6	0.5	4	93.0	4.7	0.125	0.125	100.0	0.0	0.125	0.25	100.0	0.0
Imipenem	0.125	0.5	90.9	9.1	0.5	1	90.7	7.0	2	4	40.9	22.7	1	2	64.3	7.1
Meropenem	0.031	0.062	88.2	11.8	0.062	0.25	93.8	6.2	0.062	0.125	100.0	0.0	0.062	0.125	100.0	0.0
Panipenem	0.125	0.5	90.0	10.0	0.5	2	88.1	8.3	1	2	65.0	10.0	1	2	79.2	4.2
Ertapenem	0.062	0.25	88.2	11.8	0.031	0.25	92.6	6.2	0.016	0.031	100.0	0.0	0.016	0.031	100.0	0.0
Gentamycin	1	2	71.4	23.8	1	128	77.9	17.4	0.5	128	54.5	27.3	8	>256	46.4	39.3
Amikacin	1	2	95.5	4.5	2	128	81.4	17.4	1	4	100.0	0.0	4	>256	85.7	14.3
Tetracycline	2	256	58.8	29.4	32	128	22.2	64.2	32	64	36.8	47.4	32	64	4.2	91.7
Tigecycline	0.25	1	100.0	0.0	2	4	87.7	0.0	2	8	57.9	15.8	2	4	62.5	8.3
Ciprofloxacin	0.125	1	68.2	31.8	0.125	4	87.2	8.1	0.5	8	81.8	13.6	4	64	39.3	60.7
Levofloxacin	0.5	16	68.2	27.3	0.25	4	86.0	8.1	1	2	90.9	9.1	4	32	39.3	46.4
Nitrofurantoin	32	128	52.9	17.6	256	>256	33.3	65.4	64	128	5.3	42.1	128	128	4.2	58.3
Fosfomycin	0.25	0.25	100.0	0.0	8	32	75.3	23.5	256	>256	26.3	57.9	8	256	66.7	29.2
Polymyxin B	2	4	81.8	18.2	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
Colistin	2	2	100.0	0.0	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND

ND: No detection; AMC: Amoxicillin-clavulanic acid; TZP: Piperacillin-tazobactam; MSU: Mezlocillin-sulbactam; CSL: Cefoperazone-sulbactam; MIC: Minimum inhibitory concentration; R: Resistance rate (%); S: Susceptibility rate (%).