Epidemiology and antimicrobial susceptibility profiles of extended-spectrum beta-lactamase-producing *Klebsiella pneumoniae* and *Escherichia coli* in China

Yan Wang¹ · Qinghua Zhang¹ · Yufen Jin² · Xin Jin³ · Jinyan Yu¹ · Ke Wang¹

Received: 20 July 2018 / Accepted: 27 February 2019 / Published online: 10 April 2019
© Sociedade Brasileira de Microbiologia 2019

Abstract

Objects The retrospective study aimed to determine the prevalence rate and antimicrobial susceptibility of extended-spectrum beta-lactamases (ESBLs)-producing *Klebsiella pneumoniae* and *Escherichia coli* in 2013–2017 at a single center in China.

Methods *Klebsiella pneumoniae* and *Escherichia coli* data were collected from the microbiological laboratory. VITEK 2 compact system was used for the identification and antimicrobial susceptibility testing. ESBL status was determined as per the Clinical and Laboratory Standards Institute (CLSI) protocols microdilution method.

Results Among a total of 2774 strains of *Klebsiella pneumoniae* and 2154 strains of *Escherichia coli*, 15.79% and 36.86% were found to be ESBL producers, respectively. In all patients infected by ESBLs-producing strains, those over 60 years accounted for the largest proportion. Infection by ESBLs-producing *Klebsiella pneumoniae* was more common in male, while that by ESBLs-producing *Escherichia coli* was more common in female. Urine and respiratory secretions were the most common sources of ESBLs-producing strains; however, ESBLs-producing strains from urine had been significantly declined. No carbapenem-resistant isolate was found, and all ESBLs-producing strains were resistant to ceftriaxone, aztreonam, and piperacillin. There were no differences in resistance rates between ESBLs-producing *Escherichia coli* and *Klebsiella pneumoniae* to ceftazidime and cefepime; however, ESBLs-producing *Klebsiella pneumoniae* showed higher resistance rates to piperacillin/tazobactam, amikacin, gentamicin, and co-trimoxazole compared with ESBLs-producing *Escherichia coli*.

Conclusion Different ESBLs-producing organisms have their own epidemiological characteristics, and the resistance of ESBLs-producing *Klebsiella pneumoniae* and *Escherichia coli* is different even to the same antibiotics. Therefore, it is important to continuously monitor the status of ESBLs-producing organisms, and an improved antimicrobial stewardship and infection control are much required.

Keywords Extended-spectrum beta-lactamases · *Klebsiella pneumoniae* · *Escherichia coli* · Prevalence · Antibiotics resistance

Introduction

Infections due to gram-negative bacteria are causing morbidity and mortality worldwide, and the production of beta-lactamase remains the most important contributor to beta-lactam resistance [1]. Extended-spectrum beta-lactamases (ESBLs), which were first identified in the early 1980s, can hydrolyze penicillins, cephalosporins, and oxymino beta-lactams (ceftazidime, cefotaxime, ceftriaxone, cefepime, and aztreonam), but are ineffective against carbapenems and cephamycin, and susceptible to clavulanate and tazobactam [2]. In recent years, most ESBLs-producing strains have also been found to be resistant to other major classes of antibiotics, such as aminoglycosides, fluoroquinolones, and sulfonamides, owing to the coexistence of associated resistant genes

Responsible Editor: Afonso Barth

✉ Ke Wang
kewangm1@hotmail.com

- ¹ Department of Respiratory Medicine, The Second Hospital of Jilin University, Changchun, Jilin Province, China
- ² Department of Clinical Laboratory, The Second Hospital of Jilin University, Changchun, China
- ³ Department of Hematology, The Second Hospital of Jilin University, Changchun, China

encoded in and transmitted by plasmids [3]. ESBLs-producing *Enterobacteriales*, especially *Klebsiella pneumoniae* (*K. pneumoniae*) and *Escherichia coli* (*E. coli*), have been found worldwide, and their resistance to many antibiotics has become a major global problem with serious consequences in the treatment of infectious diseases. In particular, the prevalence rate of ESBLs-producing *Enterobacteriales* in the Asia-Pacific region is very high, although the rates vary substantially in different regions and countries [4]. A study conducted by 21 centers in 16 Chinese cities in 2017 reported that ESBL-screen positive *E. coli* isolates showed a decreasing trend from 67.5% in 2012 to 58.9% in 2014 and the percentage of ESBL-screen positive *K. pneumoniae* isolates decreased from 40.4% in 2012 to 26.6% in 2014. Meanwhile, susceptibilities of ESBL-screen positive *E. coli* isolates in Zhang's study [5] were 96.66–98.08% to imipenem (IPM), 89.48–92.75% to amikacin (AMK), and 84.86–89.34% to piperacillin/tazobactam (TZP), and varied for ceftazidime (CAZ), levofloxacin (LVX), ciprofloxacin (CIP), cefepime (FEP), ceftriaxone (CEF), and cefotaxime (CTX) between 0 and 37.53%. ESBL-screen positive *Klebsiella pneumoniae* isolates were 80.0–87.5% to IPM and 83.82–87.06% to AMK as well as 63.53–68.38% to TZP and also varied between 0 and 52.21% for CAZ, LVX, CIP, FEP, CEF, and CTX [5]. However, the incidence and antimicrobial susceptibility trends of *E. coli* and *K. pneumoniae* isolates from Jilin Province, China, lacks an update. In the present study, we analyzed the epidemiological data for ESBLs-producing *K. pneumoniae* and *E. coli* strains, isolated from patients hospitalized at the Second Hospital of Jilin University, Jilin Province, China, between 2013 and 2017, thereby helping guide the continuous monitoring of the status, prevalence, and spread of ESBLs-producing bacteria.

Materials and methods

Sample collection

All clinical specimens were collected from the Second Hospital of Jilin University, a tertiary teaching hospital owning more than 20 medical specialties and 2500 beds in Jilin Province, China, between 2013 and 2017, and inoculated onto blood agar plates, MacConkey agar plates, and chocolate agar plates, using a sterile inoculating loop. After overnight incubation at 37 °C in aerobic condition, the gram-negative bacilli on MacConkey agar plates were subsequently identified by VITEK-2 Compact (bioMérieux Inc., Durham, NC).

Antibiotic sensitivity testing

As per the annual Clinical and Laboratory Standards Institute (CLSI) protocols [6–10], the minimum inhibitory

concentrations of *E. coli* and *K. pneumoniae* isolates for the antibiotics aztreonam (AZT), gentamicin (GEN), tobramycin (TOB), co-trimoxazole (SXT), piperacillin (PIP), meropenem (MEP), IMP, TZP, CAZ, LVX, CIP, CEF, FEP, and AMK were measured in the bioMérieux VITEK-2 compact system based on CLSI microdilution. Compared with the annual CLSI breakpoints, the obtained results were qualitatively recorded as sensitive (S), intermediate (I), or resistant (R). All tests were performed alongside the standard strain of *E. coli* ATCC25922 as the control.

ESBL confirmation test [6]

Suspensions of suspected ESBLs-producing isolates, with a dilution equivalent to the opacity of 0.5 McFarland, were prepared and inoculated on Mueller-Hinton agar medium. Cefotaxime (30 µg), cefotaxime/clavulanic acid (30 µg/10 µg), ceftazidime (30 µg), and ceftazidime/clavulanic acid (30 µg/10 µg) disks were used for confirming the production of ESBLs. The test was considered positive if the inhibition zone diameter around the ceftazidime/clavulanic acid or cefotaxime/clavulanic acid disk showed an increase of more than 5 mm compared with that of the inhibition zone around ceftazidime or cefotaxime.

Inclusion and exclusion of isolates

The hospital-acquired and community-acquired ESBL-screen positive *K. pneumoniae* and *E. coli* strains which are considered the pathogenic agents were included. The ESBLs-producing strains which are considered colonized; the ESBLs-producing strains separated from the same infected site in the same patient are excluded.

Data collection and statistical analysis

The demographic information (age, sex, sample type, and ward) of the patients and ESBLs-producing isolate information (bacterial species, number, infectious site, and antibiotic susceptibility profile) were collected from the microbiological laboratory in the hospital. Categorical variables were expressed as percentages, which were compared using the χ^2 test, as appropriate. A *P* value of ≤ 0.05 was considered statistically significant. All statistical analyses were performed using the statistical package SPSS (version 18.0).

Results

Isolating rates

Among a total of 2774 strains of *K. pneumoniae* and 2154 strains of *E. coli* collected in the past 5 years from patients at the Second

Table 1 Annual isolating rates of ESBLs-producing strains (2013–2017)

	ESBLs+ <i>K. pneumoniae</i>	All <i>K. pneumoniae</i>	Isolating rates (%)	ESBLs+ <i>E. coli</i>	All <i>E. coli</i>	Isolating rates (%)
2013	63	430	14.7	131	386	33.9
2014	66	520	12.7	159	405	39.3
2015	70	479	14.6	145	417	34.8
2016	126	642	19.6	171	448	38.2
2017	113	703	16.1	188	498	37.8

Hospital of Jilin University, 438 (15.79%) and 794 (36.86%) were confirmed to be ESBLs producers, respectively. The annual isolation rates of ESBLs-producing *K. pneumoniae* and *E. coli*, as well as the annual number of *K. pneumoniae* and *E. coli* isolates are presented in Table 1. The χ^2 values for the isolating rates of ESBLs-producing *K. pneumoniae* and *E. coli* from 2013 to 2017 were 41.73, 87.30, 49.67, 45.77, and 72.93, respectively, and $P < 0.001$ in each test. Therefore, there were significant differences in the isolating rates of ESBLs-producing *K. pneumoniae* and *E. coli* detected over the 5 years. Further, we evaluated the difference in prevalence along these years by χ^2 test. In ESBLs-producing *K. pneumoniae*, there were significant differences in the isolating rates from 2013 to 2017 ($\chi^2 = 11.76$, $P = 0.019$). However, there were no differences in prevalence in ESBLs-producing *E. coli* along these years ($\chi^2 = 3.70$, $P = 0.448$).

Age and sex distribution

The age range of the subjects was 0 to 94 years, the median age was 61 years, and the interquartile interval of age was 21 years (Q1 = 52 years, Q3 = 73 years). To determine the frequency of infection by ESBLs-producing *K. pneumoniae* and *E. coli* according to age, the subjects were classified into four age groups including < 20, 21–40, 41–60, and > 60 years, and the corresponding number or percentage of the subjects in each group was 30(2.4%), 116(9.4%), 433(35.1%), and 653(53.0%), respectively. It showed the patients over 60 years accounted for the largest proportion in all patients infected by

ESBLs-producing strains. Furthermore, there was a significant difference in the age distribution between all the patients infected by ESBLs-producing strains from 2013 to 2017 by χ^2 test ($\chi^2 = 21.46$, $P < 0.05$).

Among the 1232 ESBLs-producing samples, 261 ESBLs-producing *K. pneumoniae* and 330 ESBLs-producing *E. coli* were from male patients and 177 ESBLs-producing *K. pneumoniae* and 464 ESBLs-producing *E. coli* were from female patients. There is a statistically significant difference in sex distribution for infections by ESBLs-producing *K. pneumoniae* and ESBLs-producing *E. coli* by χ^2 test ($\chi^2 = 36.76$, $P < 0.001$). In other words, ESBLs-producing *K. pneumoniae* infections were more common in male patients, while ESBLs-producing *E. coli* infections were more common in female patients.

Further, we evaluated the incidence of urinary infection by ESBLs-producing *E. coli* in all patients infected by ESBLs-producing *E. coli*, and the rate was about 48.61% (386/794). In 464 female patients infected by ESBLs-producing *E. coli*, 57.5% (267/464) are infected in urine, 42.5% (197/464) were infected in other sites. In 330 male patients infected by ESBLs-producing *E. coli*, 36.1% (119/330) were infected in urine, 63.9% (211/330) were infected in other sites. The incidence of urinary infection by ESBLs-producing *E. coli* in the patients of different sex was evaluated by χ^2 test ($\chi^2 = 35.63$, $P < 0.01$). It prompted ESBLs-producing *E. coli* in urinary infections was more common in female.

Source of sample and division distribution

We further investigated the relationship between the sample source (respiratory tract, urine, blood, wound, drainage fluid, abscess, catheter tip, and skin) and the prevalence of ESBLs-producing strains. As shown in Fig. 1 and Table 2, urine and respiratory secretions were the most common sources of ESBLs-producing strains, and urology as well as nephrology was the department with the highest proportion of ESBL-producing strains. Seemingly, the proportion of ESBLs-producing strains from urine, skin, bloodstream, and abscess, relative to total ESBLs-producing strains, showed a changing trend in recent years according to Fig. 2. However, only the proportions of ESBLs-producing strains from urine over the last 5 years showed significant differences by χ^2 test ($\chi^2 =$

Fig. 1 The distribution of different sample sources of ESBLs-producing strains

Table 2 The distribution of the 1232 ESBLs-producing strains according to the wards

	ESBLs– <i>K. pneumoniae</i>	ESBLs– <i>E. coli</i>	Total	%
Urology	47	208	225	20.7
Nephrology	71	93	164	13.31
Intensive care unit	47	48	95	7.71
Pulmonology	67	35	102	8.28
Orthopedics	39	71	110	8.93
General surgery	37	105	142	11.53
Emergency units	19	44	63	5.11
Other departments	111	190	301	24.43

9.86, $P < 0.05$). It means the proportion of ESBLs-producing strains from urine has been significantly declined. In other types of samples, there were no significant differences between the proportions in the last 5 years.

% = the sum of ESBLs-producing strains in certain department / 1232

Antimicrobial susceptibility analysis

The resistance frequencies of ESBLs-producing *K. pneumoniae* and *E. coli* strains to antibiotics measured in the bioMérieux VITEK-2 compact system based on CLSI microdilution are summarized in Table 3. No carbapenem-resistant isolate was found, and all ESBLs-producing strains were resistant to CEF, AZT, and PIP in this study. The resistance rates to different antibiotics between ESBLs-producing *E. coli* and ESBLs-producing *K. pneumoniae* strains were evaluated by χ^2 test. There were no differences in the resistance rates between ESBLs-producing *E. coli* and ESBLs-

producing *K. pneumoniae* to CAZ ($P = 0.85$) and FEP ($P = 0.19$); however, there were significant difference in antibiotic resistance rates to TZP, CIP, LVX, GEN, TOB, AMK, and SXT (The χ^2 values are 10.57, 10.02, 20.16, 6.35, 182.13, 112.53, and 7.84, respectively; $P < 0.05$ in each test.). In other words, ESBLs-producing *K. pneumoniae* showed higher resistance rates to TZP, AMK, GEN, and SXT; and lower resistance rates to TOB, CIP, and LVX compared with ESBLs-producing *E. coli* strains statistically.

Changes in the annual resistance rate to each antibiotic are presented in Fig. 3. In the recent years, ESBLs-producing strains have maintained a low resistance rate of TZP and AMK in this hospital, especially, the resistance rate to AMK seem to be declining further. However, the resistance rates to SXT, CIP, LVX, GEN, and CAZ have exceeded 50%, with particularly high resistance rates to SXT and CIP reaching up to 80%. Further, we evaluated the 5 years' resistance rates of ESBLs-producing strains to different antibiotics by χ^2 test. The resistance rates to SXT, GEN, AMK, and FEP were all

Fig. 2 Annual proportion of ESBLs-producing strains from different types of samples relative to all ESBLs-producing strains

Tables 3 The resistance rates of ESBLs-producing strains to different antibiotics

Antibiotics	Total		ESBLs- <i>E. coli</i>		ESBLs- <i>K. pneumoniae</i>	
	<i>n</i>	%	<i>n</i>	%	<i>n</i>	%
TZP	36	2.9	14	1.8	22	5.0
CAZ	736	59.7	471	59.3	265	60.5
FEP	472	38.3	313	39.4	159	36.3
GEN	744	60.6	463	58.3	281	64.2
TOB	406	33.0	268	33.8	138	31.5
AMK	108	8.8	62	7.8	46	10.5
LVX	828	67.2	635	80.0	193	44.1
CIP	933	75.7	671	84.5	262	59.8
SXT	956	77.6	603	75.9	353	80.6

significantly different during the last 5 years (SXT, $\chi^2 = 28.13$, $P < 0.01$; GEN, $\chi^2 = 9.60$, $P < 0.05$; AMK, $\chi^2 = 14.48$, $P < 0.01$; FEP, $\chi^2 = 12.06$, $P < 0.05$).

Discussion

In this study, we revealed that the incidence of ESBL production from *E. coli* isolates was in the range of 33.9–39.3%, with lower rates detected among *K. pneumoniae* (12.7–19.6%). These rates are far lower than the national average as per data from CHINET, the China antimicrobial resistance surveillance network, indicating isolation rates of ESBLs-producing *E. coli* and *K. pneumoniae* to be 45.2–54% and 25.7–31.8%, respectively, between 2013 and 2016 [11–14]. Another investigation in China conducted during 2013–2015 indicated that the prevalence of ESBL-positive *E. coli* and *K. pneumoniae* was the highest in the Jiangsu-Zhejiang (Jiang-Zhe) area, which also

had the highest rate of carbapenem resistance in the country. Jiang-Zhe area being the most highly developed region in China, it is possible that higher incomes and more medical care may have contributed to the overuse of antimicrobials in the region, thereby imposing greater selection for resistant strains [15]. Therefore, we think the lower rates in the present study are possibly associated with a relatively poor economic status in the northeast of China.

In the present study, we found a statistically significant relationship between age groups (< 20, 20–40, 40–60, and > 60 years) and sample numbers or percentage of ESBLs producers, with the oldest group showing greater susceptibility to infection by ESBLs-producing strains. Our findings are consistent with a study conducted by Rodriguez-Bano et al. [16] showing that an age beyond 65 years is a risk factor for acquiring ESBL infection.

We also found an association between sex and infection frequency, with ESBLs-producing *K. pneumoniae* being more common in male patients and ESBLs-producing *E. coli* being more common in female patients. One of the possible explanations for the higher rate of ESBLs-producing *E. coli* in female could be related to the greater incidence of urinary infection by ESBLs-producing *E. coli* in female [16, 17]. Then, we evaluated the incidence of urinary infection by ESBLs-producing *E. coli* in all patients infected by ESBLs-producing *E. coli*. The statistical analysis prompted ESBLs-producing *E. coli* in urinary infections was more common in female. Although majority of the ESBLs-producing strains were isolated from urine meanwhile, urinary surgery and nephropathy were the most common departments reporting the isolation of ESBLs-producing strains in the present study, the percentages of ESBLs-producing isolates from urine have been declining in recent years. This implied, there was an increase of the isolation of ESBLs-producing strains in other types of samples or departments.

Fig. 3 The changes in the annual resistance rate to each antibiotic

16S rRNA methylase, aminoglycoside nucleotidyltransferases, aminoglycoside phosphotransferases, and aminoglycoside acetyltransferases have been identified in the resistance to aminoglycoside [18]. Plasmid-mediated quinolone resistance (PMQR) genes play an important role in resistance to not only quinolones but also beta-lactams and aminoglycosides [19]. Some studies have found gene *qnr*, *aac(6)-Ib-cr*, and genes encoding 16S rRNA methylases as well as extended-spectrum beta-lactamase may co-locate in the same ESBLs-producing strain to mediate multidrug resistance [20, 21]. A multicenter study conducted in France showed that the genes encoding the *aac(6)-Ib* and *aac(3)-II* were identified in 45% and 37.5% of the ESBLs-producing *Enterobacteriales* isolates, respectively, and the quinolone resistance genes *aac(6)-Ib-cr* and *qnrB* were identified in 38.5% and 19.5% of the isolates, respectively [22]. Similarly, the resistance rates to GEN, CIP, LVX, and SXT in ESBLs-producing strains in this study were very high, even surpassing those to CAZ and FEP. Considering the high resistance rates to quinolones in ESBLs-producing strains, the empirical use of quinolones to treat these infections is generally not recommended, especially for the treatment of urinary tract infections of ESBLs-producing *E. coli* [23, 24], since resistance to quinolones is increasing throughout the world.

The resistance rates to GEN have been reported to be high in recent years; however, approximately 96% of ESBLs-producing strains in our hospital were found to be still susceptible to AMK in 2017. Interestingly, the susceptibility of ESBLs-producing strains to AMK seemed to increase over the last years. A similar trend was also observed for AMK in several Monitoring Antimicrobial Resistance Trends (SMART) studies [25, 26]. These results were particularly important for ESBLs-producing organisms, because it indicated most patients infected by ESBLs-producing organisms could still receive appropriate treatment.

In general, ESBLs can hydrolyze all penicillins, the first to third generation of cephalosporins, and aztreonam. However, there were approximately 40% of the ESBLs-producing strains susceptible to CAZ in this study. We suspect that the genotype of the strains susceptible to CAZ would likely be CTX-M-14 based on the current epidemiological trends in China [27, 28]. FEP, a fourth-generation cephalosporin, is regarded as a potential therapeutic option for the treatment of ESBLs-producing strain related infections. However, in this study, the resistance rate to FEP was quite high at about 45%, and clinical data do not support its use owing to high failure rates [29]. In this study, there were no strains resistant to carbapenem; however, its overuse can lead to the emergence of more carbapenem-resistant gram-negative bacilli. Therefore, we recommend the combination of AMK plus TZP as a feasible empirical therapy for ESBLs before the carbapenem treatment.

There are some limitations in our study. Since the strains in this retrospective study were not preserved, their genotype could not be detected. On the other hand, the false negative

and false positive ESBLs-producing strains were not recorded; therefore, the limitations of phenotypic ESBL test is worth further research.

Acknowledgments We thank Yanlei Li, a doctor of the laboratory medicine in the Second Hospital of Jilin University, for her imparting knowledge in the field of microbiology and the writing assistance.

Funding information This study was financially supported by the Science and Technology Agency of Jilin Province [grant number 201603034YY].

Compliance with ethical standards

Competing interests The authors declare that they have no competing interests.

References

1. Leylabadlo HE, Kafil HS, Yousefi M, Aghazadeh M, Asgharzadeh M (2016) Persistent infection with metallo-beta-lactamase and extended spectrum beta-lactamase producer *Morganella morganii* in a patient with urinary tract infection after kidney transplantation. *J Nat Sci, Biol Med* 7(2):179–181. <https://doi.org/10.4103/0976-9668.184707>
2. Paterson DL, Bonomo RA (2005) Extended-spectrum beta-lactamases: a clinical update. *Clin Microbiol Rev* 18(4):657–65+. <https://doi.org/10.1128/Cmr.18.4.657-686.2005>
3. Mehdipour Moghaddam MJ, Mirbagheri AA, Salehi Z, Habibzade SM (2015) Prevalence of class 1 Integrons and extended spectrum beta lactamases among multi-drug resistant *Escherichia coli* isolates from north of Iran. *Iran Biomed J* 19(4):233–239
4. Jean SS, Coombs G, Ling T, Balaji V, Rodrigues C, Mikamo H, Kim MJ, Rajasekaram DG, Mendoza M, Tan TY, Kiratisin P, Ni Y, Weinman B, Xu Y, Hsueh PR Epidemiology and antimicrobial susceptibility profiles of pathogens causing urinary tract infections in the Asia-Pacific region: results from the Study for Monitoring Antimicrobial Resistance Trends (SMART), 2010-2013. *Int J Antimicrob Ag* 2016;47(4):328–334 doi: <https://doi.org/10.1016/j.ijantimicag.2016.01.008>
5. Zhang H, Yang Q, Liao K, Ni Y, Yu Y, Hu B, Sun Z, Huang W, Wang Y, Wu A, Feng X, Luo Y, Chu Y, Chen S, Cao B, Su J, Duan Q, Zhang S, Shao H, Kong H, Gui B, Hu Z, Badal R, Xu Y (2017) Update of incidence and antimicrobial susceptibility trends of *Escherichia coli* and *Klebsiella pneumoniae* isolates from Chinese intra-abdominal infection patients. *BMC Infect Dis* 17(1):776. <https://doi.org/10.1186/s12879-017-2873-z>
6. Institute CaLS. 2013 Performance standards for antimicrobial susceptibility testing; twenty-third informational supplement. CLSI document M100-S23. Wayne, PA
7. Institute CaLS. 2014 Performance standards for antimicrobial susceptibility testing; twenty-fourth informational supplement. CLSI document M100-S24. Wayne, PA
8. Institute CaLS. 2015 Performance standards for antimicrobial susceptibility testing; twenty-fifth informational supplement. CLSI document M100-S25. Wayne, PA
9. Institute CaLS. 2016 Performance standards for antimicrobial susceptibility testing, 26th Edition. CLSI document M100S. Wayne, PA
10. Institute CaLS. 2017 Performance standards for antimicrobial susceptibility testing; 27th Edition. CLSI document M100S. Wayne, PA.,

11. Fupin Hu, Demei Zhu, Fu Wang, et al. CHINET surveillance of bacterial resistance across China: report of the results in 2016. *Chin J Infect Chemother* 2016;17(5):481–491
12. Hu F, Wang F, Jiang X et al (2015) Report of CHINET antimicrobial resistance surveillance program in 2015. *Chin J Infect Chemother* 16(6):685–694
13. Hu F, Wang F, Jiang X et al (2014) CHINET 2014 surveillance of bacterial resistance in China. *Chin J Infect Chemother* 15(5):401–410
14. Hu F, Wang F, Jiang X et al (2013) CHINET 2013 surveillance of bacterial resistance in China. *Chin J Infect Chemother* 14(5):369–378
15. Zhang H, Yang Q, Liao K, Ni Y, Yu Y, Hu B, Sun Z, Huang W, Wang Y, Wu A, Feng X, Luo Y, Hu Z, Chu Y, Chen S, Cao B, Su J, Gui B, Duan Q, Zhang S, Shao H, Kong H, Badal RE, Xu Y (2016) Antimicrobial susceptibilities of aerobic and facultative gram-negative bacilli from intra-abdominal infections in patients from seven regions in China in 2012 and 2013. *Antimicrob Agents Chemother* 60(1):245–251. <https://doi.org/10.1128/AAC.00956-15>
16. Rodriguez-Bano J, Alcalá JC, Cisneros JM, et al. Community infections caused by extended-spectrum beta-lactamase-producing *Escherichia coli*. *Arch Intern Med* 2008;168(17):1897–1902 doi: DOI <https://doi.org/10.1001/archinte.168.17.1897>
17. Canton R, Novais A, Valverde A et al (2008) Prevalence and spread of extended-spectrum beta-lactamase-producing Enterobacteriaceae in Europe. *Clin Microbiol Infect: Off Publ Eur Soc Clin Microbiol Infect Dis* 14(Suppl 1):144–153. <https://doi.org/10.1111/j.1469-0691.2007.01850.x>
18. Krause KM, Serio AW, Kane TR, Connolly LE (2016) Aminoglycosides: an overview. *Cold Spring Harbor Perspect Med* 6(6). <https://doi.org/10.1101/cshperspect.a027029>
19. Eftekhari FP, Seyedpour SMM (2015) Prevalence of qnr and aac(6)-Ib-cr Genes in clinical isolates of *Klebsiella Pneumoniae* from Imam Hussein Hospital in Tehran. *Iranian J Med Sci* 40(6):515–521
20. Ho PL, Leung LM, Chow KH, Lai EL, Lo WU, Ng TK (2016) Prevalence of aminoglycoside modifying enzyme and 16S ribosomal RNA methylase genes among aminoglycoside-resistant *Escherichia coli* isolates. *J Microbiol, Immunol Infect= Wei mian yu gan ran za zhi* 49(1):123–126. <https://doi.org/10.1016/j.jmii.2014.08.012>
21. Du XD, Li DX, Hu GZ et al (2012) Tn1548-associated armA is co-located with qnrB2, aac(6)-Ib-cr and blaCTX-M-3 on an IncFII plasmid in a *Salmonella enterica* subsp. *enterica* serovar Paratyphi B strain isolated from chickens in China. *J Antimicrob Chemother* 67(1):246–248. <https://doi.org/10.1093/jac/dkr407>
22. Robin F, Beyrouthy R, Bonacorsi S, Aissa N, Bret L, Brieu N, Cattoir V, Chapuis A, Chardon H, Degand N, Doucet-Populaire F, Dubois V, Fortineau N, Grillon A, Lanotte P, Leyssene D, Patry I, Podglajen I, Recule C, Ros A, Colomb-Cotin M, Ponties V, Ploy MC, Bonnet R (2017) Inventory of extended-Spectrum-beta-lactamase-producing Enterobacteriaceae in France as assessed by a multicenter study. *Antimicrob Agents Chemother* 61(3). <https://doi.org/10.1128/AAC.01911-16>
23. Azargun R, Sadeghi MR, Soroush Barhaghi MH, Samadi Kafil H, Yeganeh F, Ahangar Oskouee M, Ghotaslou R (2018) The prevalence of plasmid-mediated quinolone resistance and ESBL-production in Enterobacteriaceae isolated from urinary tract infections. *Infect Drug Resist* 11:1007–1014. <https://doi.org/10.2147/IDR.S160720>
24. Wiener ES, ELH LMH, Kristie Johnson J (2016) Are fluoroquinolones appropriate for the treatment of extended-Spectrum β -lactamase-producing gram-negative bacilli? *J Pharm Technol* 32(1):16–21
25. Morrissey I, Hackel M, Badal R, Bouchillon S, Hawser S, Biedenbach D (2013) A review of ten years of the Study for Monitoring Antimicrobial Resistance Trends (SMART) from 2002 to 2011. *Pharmaceuticals* 6(11):1335–1346. <https://doi.org/10.3390/ph6111335>
26. Ponce-de-Leon A, Rodriguez-Noriega E, Morfin-Otero R et al (2018) Antimicrobial susceptibility of gram-negative bacilli isolated from intra-abdominal and urinary-tract infections in Mexico from 2009 to 2015: results from the Study for Monitoring Antimicrobial Resistance Trends (SMART). *PLoS One* 13(6): e0198621. <https://doi.org/10.1371/journal.pone.0198621>
27. Quan J, Zhao D, Liu L, Chen Y, Zhou J, Jiang Y, du X, Zhou Z, Akova M, Yu Y (2017) High prevalence of ESBL-producing *Escherichia coli* and *Klebsiella pneumoniae* in community-onset bloodstream infections in China. *J Antimicrob Chemother* 72(1): 273–280. <https://doi.org/10.1093/jac/dkw372>
28. Xia S, Fan X, Huang Z, Xia L, Xiao M, Chen R, Xu Y, Zhuo C (2014) Dominance of CTX-M-type extended-spectrum beta-lactamase (ESBL)-producing *Escherichia coli* isolated from patients with community-onset and hospital-onset infection in China. *PLoS One* 9(7):e100707. <https://doi.org/10.1371/journal.pone.0100707>
29. Chopra T, Marchaim D, Veltman J, Johnson P, Zhao JJ, Tansek R, Hatahet D, Chaudhry K, Pogue JM, Rahbar H, Chen TY, Truong T, Rodriguez V, Ellsworth J, Bernabela L, Bhargava A, Yousuf A, Alangaden G, Kaye KS (2012) Impact of cefepime therapy on mortality among patients with bloodstream infections caused by extended-spectrum-beta-lactamase-producing *Klebsiella pneumoniae* and *Escherichia coli*. *Antimicrob Agents Chemother* 56(7):3936–3942. <https://doi.org/10.1128/AAC.05419-11>

Publisher's note Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.