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ORIGINAL RESEARCH

Susceptibilities of Gram-negative bacilli from hospital- and community-acquired intra-abdominal and urinary tract infections: a 2016–2017 update of the Chinese SMART study

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Objectives: To update the epidemiology and susceptibility of hospital-acquired (HA) and community-acquired (CA), as well as intensive care unit (ICU) vs non-ICU-derived intra-abdominal infection (IAI) and urinary tract infection (UTI) pathogens in Chinese hospitals.
Methods: A total of 2,546 Gram-negative isolates from IAIs and 1,947 isolates from UTIs collected in 16 hospitals and 7 regions of China from 2016 to 2017 were analyzed.
Results: *E. coli* and *K. pneumoniae* were the most common pathogens identified in HA (40.7%, 21.9%) and CA (49.2%, 21.3%) IAIs and in HA (59.0%, 17.3%) and CA (64.3%, 12.7%) UTIs, respectively. The overall rates of extended-spectrum β-lactamase (ESBL)-positive strains were 48.2% for *E. coli* and 26.4% for *K. pneumoniae*. The rates of ESBL-positive *E. coli* and *K. pneumoniae* strains were significantly higher in HA than in CA IAIs (51.7% vs 42.4%, P=0.016 and 22.0% vs 20.6%, P<0.001). IAI *E. coli* ESBL-producing isolates were most susceptible to IPM (97.2%) and AMK (93.9%), and UTI-associated *E. coli* ESBL-producers were 94.74% susceptible to amikacin (AMK), 97.02% to imipenem (IPM), and 91.4% to ertapenem (ETP). IAI *K. pneumoniae* ESBL-producing isolates were most susceptible to AMK (84.43%) and IPM (82.79%), and UTI-associated *K. pneumoniae* ESBL-producers were 88.39% susceptible to AMK, 87.5% to IPM, and 82.14% to ETP. Overall, percentages of susceptible strains to ETP, IPM, AMK, and Piperacillin-Tazobactam (TZP) were in the range of 82.0% to 96.4%, to 5 cephalosporins in the range of 31.4%-69.6% and to 2 fluoroquinolones in the range of 37.8%-45.5% for *E. coli* and 65.5%-90.7%, 37.7%-75.3%, and 43.9%-73.2% for *K. pneumoniae*, respectively.
Conclusion: *E. coli* and *K. pneumoniae* continued to be the main pathogens in Chinese UTIs and IAIs with high ESBL-positive rates between 2016 and 2017. Carbapenem- or amikacin-based therapies were the most effective to combat IAI and UTI pathogens.
Keywords: IAI, UTI, ESBL, *E. coli, K. pneumoniae*

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Introduction

The availability of current resistance data, generated through ongoing antimicrobial susceptibility surveillance, is important for the medical community, antibiotic developers, and government policymakers, among other interested agencies. The aim of the present study was to satisfy this need by investigating and reporting on the susceptibility patterns of recent Gram-negative pathogens isolated from hospitalized patients with intra-abdominal infections (IAIs) and urinary tract infections (UTIs) in 7 regions

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from 16 Chinese hospitals between 2016 and 2017. Isolates were collected for the **S**tudy for **M**onitoring **A**ntimicrobial **R**esistance **T**rends (SMART) global surveillance program, which was established in China in 2002 for IAIs and in 2012 for UTIs 2008 to monitor in vitro antimicrobial susceptibility profiles of clinical isolates collected from Chinese patients with IAIs and UTIs.[1] In addition, surveillance data describing susceptibility patterns may provide guidance for accurate empirical antimicrobial therapy for selected infections and patient types (eg, ICU- and non-ICU-), and may stimulate antimicrobial stewardship efforts.[2,3] James et al reported that, during 2013–2015, Gram-negative ESKAPE pathogens (*Enterococcus faecium, Staphylococcus aureus, Klebsiella pneumoniae, Acinetobacter baumannii, Pseudomonas aeruginosa, and Enterobacter spp*.) isolated from patients in Asia–Pacific countries demonstrated reduced in vitro susceptibilities to parenterally administered advanced-generation cephalosporins (cefepime, ceftazidime, and ceftriaxone), piperacillin–tazobactam and fluoroquinolones (levofloxacin), with isolates from UTIs even less susceptible than isolates from IAIs. These findings demonstrated higher rates of antimicrobial resistance than those observed in North American and European studies, and identified the majority of pathogens isolated from ICUs in a number of Asia–Pacific countries.[3,4] Previously reported SMART epidemiological survey results revealed that IPM and ETP were effective in vitro against Enterobacteriaceae isolated from IAIs and UTIs between 2014 and 2015, but susceptibility to carbapenems for UTIs markedly decreased in 2015. Thus, global antimicrobial resistance, particularly for Gram-negative bacteria in China, as well as the variability in antibiotic susceptibility and the prevalence of extended-spectrum β-lactamase (ESBL)-producers in different hospital departments (both ICU and non-ICU) have been considered essential for guiding effective empirical therapy for clinical practice in recent years.

This report describes the epidemiology and susceptibility of pathogens (including ESBL-producers) from HA vs CA UTIs and IAIs sampled in ICUs and non-ICUs in China from 2016 to 2017 as an update of the SMART surveillance program.

Materials and methods

Isolates from IAI and UTI patients

From 2016 to 2017, the SMART surveillance survey collected 4,493 isolates of Gram-negative bacilli from patients in 16 hospitals with IAI (n=2,546) and UTI (n=1,947), including 2,254 *E. coli* and 866 *K. pneumoniae* strains from 7 regions in China (northeast, north, east, central, south, and the southwest). The majority of the intra-abdominal specimens were obtained during surgery, with some paracentesis specimens, and were derived from abscesses, appendix, colon, gall bladder, liver, pancreas, peritoneal fluid, rectum, small intestine, and stomach. The urinary tract infection isolates were obtained from clean-catch midstream urine, the urinary bladder, ureter, kidney, urethra, and the prostate gland. Isolates were identified using local site procedures and then shipped to the central clinical microbiology laboratory of the Peking Union Medical College Hospital for analyses and re-identification using MALDI-TOF MS (Vitek MS, BioMérieux, France). All duplicate isolates (the same genus and species from the same patient) were excluded from the study. Isolates were considered to be community-associated (CA) if they were recovered from a specimen taken <48 hrs after the patient was admitted to a hospital or HA if the specimen was taken ≥48 hrs after hospital admission, as previously described (Hawser et al, 2009b).

Antimicrobial susceptibility test method

Antimicrobial susceptibility testing was performed at the Peking Union Medical College Hospital center laboratory using panels purchased from ThermoFisher Scientific (Cleveland, OH, USA). Minimum inhibitory concentrations $(MIC)_{90}$/MIC_{50} were determined using susceptibility interpretations based on CLSI clinical breakpoints.[5]

Twelve antimicrobial agents commonly used to treat IAIs and UTI were tested (Ampicillin-Sulbactam (SAM), Piperacillin-Tazobactam (TZP), Ceftriaxone (CRO), Cefotaxime (CTX), Ceftazidime (CAZ), Cefoxitin (FOX), Cefepime (FEP), Ciprofloxacin (CIP), Levofloxacin (LVX), Amikacin (AMK), Imipenem (IPM), and Ertapenem (ETP)).

The above antimicrobial agents tested by the SMART global surveillance program are those recommended by the Surgical Infection Society and the Infectious Diseases Society of America in their guidelines for the diagnosis and management of complicated IAIs and UTIs.[6] Reference strains, *E. coli* ATCC (American Type Culture Collection) 25,922, *Pseudomonas aeruginosa* ATCC 27,853, and *K. pneumoniae* ATCC 700,603 (positive ESBL control), were used as quality control (QC) strains for each batch of MIC tests. The results were only included in the analysis when the corresponding quality control isolate test results were in accordance with CLSI guidelines and therefore within an acceptable range.

Detection of ESBLs

Phenotypic identification of ESBL production among *E. coli, K. pneumoniae, P. mirabilis*, and *K. oxytoca* was detected by disc diffusion. If the cefotaxime zone was ≤27 mm or the ceftazidime zone ≤22 mm, ESBL production was defined as a ≥5 mm increase in a zone diameter for 30 μg cefotaxime or ceftazidime tested in combination with 10 μg clavulanic acid per disc compared to the zone diameter of the agent when tested alone.

Statistical analysis

The susceptibility of all Gram-negative isolates combined was calculated using breakpoints appropriate for each species and assuming 0% susceptibility for species with no breakpoints for any given antibiotic. The 95% confidence intervals were calculated using the adjusted Wald method; comparison of ESBL rates was assessed using a chi-squared test. *P*-values <0.05 were considered statistically significant.

Results

The distribution of major isolates in IAIs and UTIs in 2016–2017

In 2016–2017, the major IAI and UTI pathogens were *E. coli* and *K. pneumoniae*, from which most *E. coli* were collected from UTIs (60.5%) and most *K. pneumoniae* appeared in IAIs (21.8%). Although the fermenting bacteria *Pseudomonas aeruginosa* and *Acinetobacter baumannii* were the third and fourth ranking isolates in IAIs and UTIs during 2016–2017, their total proportion (*n*=629) was only 14.0% of all isolates (*n*=4,493), and the majority of them were collected from HA infections (Table 1). In addition, from all IAI and UTI isolates, 4 ESBL-positive species, including *E. coli, K. pneumoniae, P. mirabilis*, and *K. oxytoca*, were analyzed and among them, IAI *E. coli* ESBL-positive (*n*=532) and *K. pneumoniae* ESBL-positive (*n*=120) isolates accounted for 96.9% of all ESBL-positive IAI isolates (*n*=673), whereas the ESBL-positive strains of *E. coli* (n=554) and *K. pneumoniae* (n=109) from UTIs accounted for 97.2% of all UTI ESBL-positive strains (*n*=682). In contrast to UTIs, in IAIs the percentage of ESBL-positive *E. coli* and *K. pneumoniae* strains were significantly higher (*P*=0.016; *P*<0.001) in HA than in CA infections (Table 2).

The susceptibility of ESBL-positive isolates of *E. coli* and *K. pneumoniae* in IAIs and UTIs to the 12 most commonly used antibiotics in 2016–2017

The susceptibility of *E. coli* ESBL-positive isolates from IAIs, including HA and CA, was >90% only for AMK and IPM, while the susceptibility of *E. coli* ESBL-positive isolates from UTI, including HA and CA, were >90% for AMK and IPM, but also for ETP.

For *K. pneumoniae* ESBL-positive isolates in CA and HA IAIs and UTIs, no antibiotics showed >90% susceptibility, but >80% susceptibilities were found for AMK and IPM (Table 3). Except for *E. coli and K. pneumoniae*, the other 2 ESBL-positive strains, *P. mirabilis and K. oxytoca*, accounted for only for a small portion in both IAIs and UTIs. *P. mirabilis* was only isolated from HA IAI infections and showed high susceptibilities (>90%) to AMK, FOX, CAZ, and ETP, but interestingly, only 1 of 13 strains was still susceptible to IPM. In UTIs, only AMK was effective in >90% of the isolates.

Table 1 Distribution of the IAI and UTI pathogens in China during 2016–2017

Name of pathogen (n, %)	IAI(/All)	HA	CA	UTI(/All)	HA	CA
Escherichia coli (n=2,254, 50.2)	1,076(42.3)	845(40.7)	224(49.2)	1,178(60.5)	815(59.0)	361(64.3)
Klebsiella pneumoniae (n=866, 19.3)	555(21.8)	454(21.9)	97(21.3)	311(16.0)	239(17.3)	71(12.7)
Pseudomonas aeruginosa (n=347, 7.7)	203(8.0)	178(8.6)	25(5.5)	144(7.4)	111(8.0)	33(5.9)
Acinetobacter baumannii (n=282, 6.3)	211(8.3)	182(8.8)	28(6.2)	71(3.6)	60(4.3)	11(2.0)
Enterobacter cloacae (n=196, 4.4)	143(5.6)	128(6.2)	15(3.3)	53(2.7)	37(2.7)	16(2.9)
Proteus mirabilis (n=100, 2.2)	44(1.7)	36(1.7)	8(1.8)	56(2.9)	33(2.4)	22(3.9)
Klebsiella aerogenes (n=74, 1.6)	53(2.1)	43(2.1)	9(2.0)	21(1.1)	13(0.9)	8(1.4)
Citrobacter freundii (n=49, 1.1)	32(1.3)	22(1.1)	9(2.0)	17(0.9)	10(0.7)	7(1.2)
Klebsiella oxytoca (n=49, 1.1)	37(1.5)	30(1.4)	7(1.5)	12(0.6)	8(0.6)	4(0.7)
Stenotrophomonas maltophilia (n=50, 1.1)	41(1.6)	36(1.7)	5(1.1)	9(0.5)	6(0.4)	3(0.5)
Serratia marcescens (n=44, 1.0)	25(1.0)	19(0.9)	6(1.3)	19(1.0)	14(1.0)	5(0.9)
Others (n=182, 4.1)	126(4.9)	103(5.0)	22(4.8)	56(2.9)	35(2.5)	20(3.6)
All (n=4493,100)	**2,546(56.7)**	**2,076(81.5)**	**455(17.9)**	**1,947(43.3)**	**1,381(70.9)**	**561(28.8)**

Abbreviations: HA, hospital-acquired; CA, community-acquired; IAI, intraabdominalinfection; UTI, urinary tract infection.

Table 2 Distribution of ESBL-producing strains in China during 2016–2017

	IAI (n=2,546)		UTI (n=1,947)		Total (n=4,493)	
	HA (n=2,076)	CA (n=455)*	HA (n=1,381)	CA (n=561)*	HA (n=3,457)	CA (n=1,016)*
Total ESBL + (% of HA or CA)	557 (26.8)	116 (25.5)	478 (34.6)	204 (36.4)	1035 (29.9)	320 (31.5)
E. coli	845 (40.7)	224 (49.2)	815 (59.0)	361 (64.3)	1660 (48.0)	585 (57.6)
ESBL + (% of *E. coli* HA or CA)	437(51.7)#	95 (42.4)	378 (46.4)	176 (48.8)	815 (49.1)	271 (46.3)
K. pneumoniae	454 (21.9)	97 (21.3)	239 (17.3)	71 (12.7)	693 (20.9)	168 (16.5)
ESBL + (% of *K. pneumoniae* HA or CA)	100 (22.0)&	20 (20.6)	86 (36.0)	23 (32.4)	186 (26.8)	43 (25.6)
P. mirabilis	36 (1.7)	8 (1.8)	33 (2.4)	22 (3.9)	69 (2.0)	30 (3.0)
ESBL + (% of *P. mirabilis* HA or CA)	13 (36.1)	0 (0)	10 (30.3)	5 (22.7)	23 (33.3)	5 (16.7)
K. oxytoca	30 (1.4)	7 (1.5)	8 (0.6)	4 (0.7)	38 (1.1)	11 (1.1)
ESBL + (% of *K. oxytoca* HA or CA)	7 (23.3)	1 (14.3)	4 (50)	0 (0)	11 (28.9)	1 (9.1)

Notes: *Missing isolates are those whose hospitalization was not specified. #P=0.016 (IAI HA vs CA); &P<0.001 (IAI HA vs UTI HA).
Abbreviations: HA, hospital-acquired; CA, community-acquired; IAI, intraabdominalinfection; UTI, urinary tract infection; IPM, Carbapenems: Imipenem; ETP, Ertapenem; AMK, Aminoglycoside: Amikacin; TZP, Piperacillin-Tazobactam; FOX, Cephalosporins: Cefoxitin; CAZ, Ceftazidime; CRO, Ceftriaxone; CTX, Cefotaxime; FEP, Cefepime; LVX, Fluoroquinolones: Levofloxacin; CIP, Ciprofloxacin.

From *K. oxytoca* ESBL positive HA IAI isolates <50% were still susceptible to all cephalosporins and only 71.43% and 57.14% to IPM and ETP, with the highest percentage susceptible to AMK (85.7%). (Table S1).

Susceptibilities of *E. coli* and *K. pneumoniae* ESBL-producing isolates from ICU- and non-ICU-derived strains to 12 common antibiotics

Most susceptibilities of IAI-derived *E. coli* ESBL-positive isolates in ICUs were slightly lower than that of *E. coli* ESBL-positive isolates from non-ICUs, but without significance. Also for other isolates, there was no significant difference in susceptibilities between ICU and non-ICU samples (all P>0.05). *E. coli* ESBL-producing strains acquired from IAIs and UTIs were 85.6% to 97.5% susceptible to IPM, ETP, and AMK, whereas 70% to 90.0% of *K. pneumoniae* ESBL-producing strains from IAIs and UTIs were susceptible to IPM, ETP, and AMK. Susceptibilities to TZP and FOX were intermediate, and all other tested antibiotics were only effective for 0% - 38.46% of the isolates (Table 4).

Overall susceptibilities of the major CA and HA IAI and UTI isolates *E. coli* and *K. pneumoniae* to 12 common antibiotics from 2016 to 2017

IAI and UTI *E. coli* and *K. pneumoniae* isolates from HA infections were generally less susceptible to 12 common antibiotics, compared to CA infections. The overall percentages of susceptible *E. coli* strains to ETP, IPM, AMK, and Piperacillin-Tazobactam (TZP) were in the range of 82.0% to 96.4%, to 5 cephalosporins in the range of 31.4%-69.6% and to 2 fluoroquinolones in the range of 37.8%–45.5% and 65.5%–90.7%, 37.7%–75.3%, and 43.9%–73.2% for *K. pneumoniae*, respectively (Figure 1).

Discussion

In 2016 and 2017, the major pathogens of Chinese IAIs and UTIs were *E. coli* and *K. pneumoniae*, which is in accordance with previous years and studies abroad.[7] The rate of ESBL-producing *E. coli* and *K. pneumoniae* strains was higher in HA IAIs than in CA IAIs, which is in accordance with a previous Chinese study, but the former percentages in 2010–2011 were essentially higher than in 2016–2017.[8] However, though ESBL rates have dropped in 2016–2017, compared to 2010–2011, the overall susceptibilities of IAI and UTI-derived *E. coli* and *K. pneumoniae* strains remained low to cephalosporins, especially in HA infections (Figure 1). Since cefoxitin (FOX) is also considered to be effective in ESBL-producing Enterobacteriaceae,[9] the relatively low susceptibilities of *E. coli* and *K. pneumoniae* to FOX also indicate other resistance mechanisms than ESBL production.[10] Also the low susceptibility rate of ESBL-positive *P. mirabilis* strains from HA IAI infections to IPM might be explained by alterations in penicillin-binding proteins, which has been also described for *Acinetobacter baumannii* and

Table 3 ESBL positivity and antibiotic susceptibility rates (%) for *E. coli* and *K. pneumoniae* isolates from HA vs CA IAIs & UTIs

	E. coli ESBL +(n=1,094)						*K. pneumoniae ESBL* +(n=231)					
	IAI			***UTI***			**IAI**			***UTI***		
	All **(n=538)**	**HA (n=437)**	**CA (n=95)**	***All*** **(n=556)**	**HA (n=378)**	**CA (n=176)**	***All*** **(n=122)**	**HA (n=100)**	**CA (n=20)**	***All*** **(n=109)**	**HA (n=86)**	**CA (n=23)**
IPM	97.21	97.02	97.89 ***	97.02	96.95	97.16	82.79	82	90	87.5	87.64	86.96
ETP	90.71	91.08	88.42	91.4	90.08	94.29 ***	77.05	76	85	82.14	85.39	69.57 ***
AMK	93.87	94.05	92.63 ***	94.74	94.4	95.43 **	84.43	85	85	88.39	88.76	86.96 ***
TZP	82.34	81.92	86.32	88.97	89.06	88.64	57.38	55	75	61.61	62.92	56.52
FOX	57.81	57.67	58.95	62.35	62.34	61.93	51.64	49	65	60.71	64.05	47.83
CAZ	31.97	31.58	34.74	37.19	37.91	35.43	23.77	23	30	24.11	28.09	8.7
CRO	0	0	0	1.58	1.28	2.27	0	0	0	1.79	2.25	0
CTX	0	0	0	1.05	0.76	1.71	0	0	0	2.68	3.37	0
FEP	3.35	4.12	0	3.86	3.32	5.11	3.28	3	5	2.68	3.37	0
LVX	28.44	29.29	25.26	25.09	24.94	24.57	37.7	37	45	33.93	37.08	21.74
CIP	26.95	27.92	23.16	22.94	22.9	22.16	34.43	34	40	30.36	32.58	21.74

Notes: **P<0.01; ***P<0.001, HA vs CA.

Abbreviations: HA, hospital-acquired; CA, community-acquired; IAI, intraabdominalinfection; UTI, urinary tract infection; IPM, Carbapenems: Imipenem; ETP, Ertapenem; AMK, Aminoglycoside: Amikacin; TZP, Piperacillin-Tazobactam; FOX, Cephalosporins: Cefoxitin; CAZ, Ceftazidime; CRO, Ceftriaxone; CTX, Cefotaxime; FEP, Cefepime; LVX, Fluoroquinolones: Levofloxacin; CIP, Ciprofloxacin.

Table 4 ESBL producing *E. coli* and *K. pneumoniae* susceptibility rates from Gram-negative IAI & UTI isolates obtained from ICU and non-ICU units

		IPM	ETP	AMK	TZP	FOX	CAZ	CRO	CTX	FEP	LVX	CIP
IAI-*E. coli ESBL* +(n=538)												
	ICU (n=97)	95.88	85.57	91.75	77.32	56.7	34.02	0	0	4.12	24.74	25.77
	Non-ICU (n=441)	97.50	91.84	94.33	83.45	58.05	31.52	0	0	3.17	29.25	27.21
	P-value	0.326	0.079	0.350	0.185	0.821	0.632			0.547	0.456	0.900
IAI-*K. pneumoniae ESBL* +(n=122)												
	ICU (n=20)	80.00	70.00	90.00	55.00	65.00	15.00	0.00	0.00	5.00	35.00	30.00
	Non-ICU (n=102)	83.33	78.43	83.33	57.84	49.02	25.49	0.00	0.00	2.94	38.24	35.29
	P-value	0.748	0.398	0.736	0.810	0.227	0.399			0.516	1.000	0.799
UTI-*E. coli ESBL* +(n=556)												
	ICU (n=39)	94.87	92.31	92.31	87.18	64.1	38.46	0.00	0.00	0.00	28.21	25.64
	Non-ICU (n=517)	97.18	91.34	94.92	89.10	62.22	37.10	1.69	1.13	4.14	24.86	22.74
	P-value	0.339	1.000	0.447	0.603	0.733	0.865	1.000	1.000	1.000	0.702	0.694
UTI-*K. pneumoniae ESBL* +(n=109)												
	ICU (n=13)	85.71	85.71	78.57	57.14	50.00	7.14	0.00	0.00	0.00	28.57	28.57
	Non-ICU (n=96)	87.76	81.63	89.8	62.24	62.24	26.53	2.04	3.06	3.06	34.69	30.61
	P-value	0.673	1.000	0.186	0.558	0.365	0.184	1.000	1.000	1.000	1.000	1.000

Abbreviations: ICU, intensive care unit; IAI, intraabdominalinfection; UTI, urinary tract infection; IPM, Carbapenems: Imipenem; ETP, Ertapenem; AMK, Aminoglycoside: Amikacin; TZP, Piperacillin-Tazobactam; FOX, Cephalosporins: Cefoxitin, CAZ, Ceftazidime, CRO, Ceftriaxone, CTX, Cefotaxime, FEP, Cefepime; LVX, Fluoroquinolones: Levofloxacin; CIP, Ciprofloxacin.

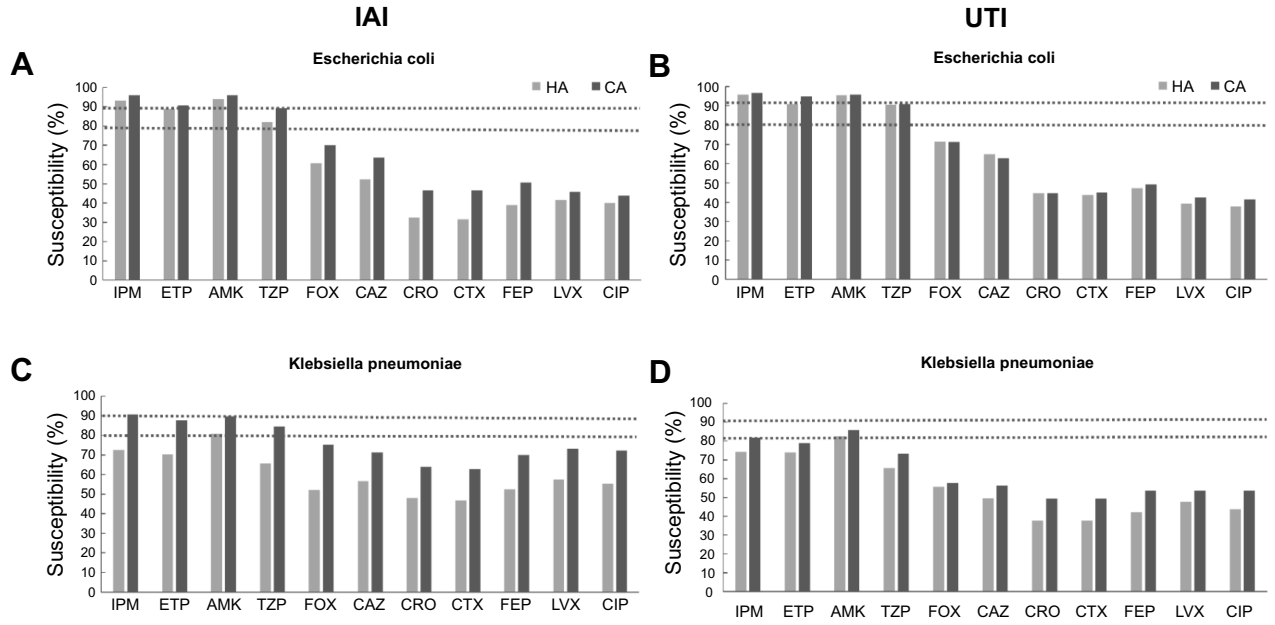

Figure 1 Susceptibilities of *E. coli* and *K. pneumonia* isolates from HA and CA IAIs and UTIs. (**A**) *E. coli* isolates from IAIs, (**B**) *E. coli* isolates from UTIs, (**C**) *K. pneumonia* isolates from IAIs, and (**D**) *K. pneumonia* isolates from UTIs.

Abbreviations: HA, hospital-acquired; CA, community-acquired; IAI, intraabdominalinfection; UTI, urinary tract infection; IPM: Carbapenems: Imipenem; ETP, Ertapenem; AMK, Aminoglycoside: Amikacin; TZP, Piperacillin-Tazobactam; FOX, Cephalosporins: Cefoxitin, CAZ, Ceftazidime, CRO, Ceftriaxone, CTX, Cefotaxime, FEP, Cefepime; LVX, Fluoroquinolones: Levofloxacin; CIP, Ciprofloxacin.

Pseudomonas aeruginosa.[11,12] In 2017 there was an obvious trend of lowered susceptibility to carbapenems in *K. pneumoniae* IAI isolates, which is in line with other studies from China.[13,14] However, there was no significant difference between susceptibilities to carbapenems in ICU and non-ICU departments, which is in contrast to a multicenter study about carbapenem-nonsusceptible GNB ICU infections in the US in 2017; however, the authors indicated that most ICU-related infections were from respiratory tracts and skin wounds, and the highest carbapenem resistance rates were found in *Acinetobacter* spp. and *P. aeruginosa*.[15] A trend toward lower susceptibilities in ICU-derived *E. coli* and *K. pneumoniae* strains was also visible in the present study, which might be explained by the fact that more frequent previous carbapenem administrations have been applied for ICU patients.[16] In addition, some susceptibilities of ESBL-positive *E. coli* strains from IAI and UTI patients to carbapenems were significantly lower in HA compared to CA infections

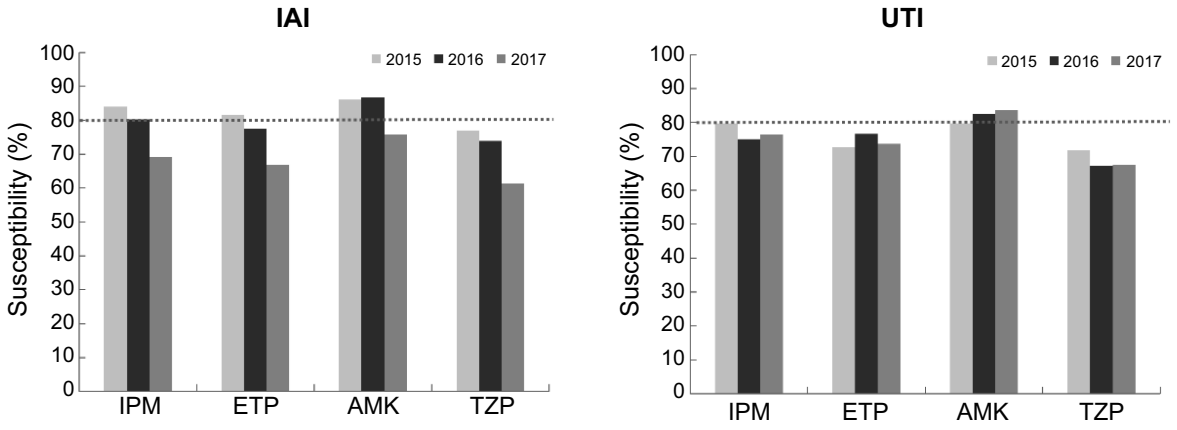

Figure 2 Percentages of susceptible *K. pneumoniae* IAI and UTI isolates to IMP, ETP, AMK, and TZP from 2015 to 2017.

Abbreviations: IAI, intraabdominalinfection; UTI, urinary tract infection; IPM: Carbapenems: Imipenem; ETP, Ertapenem; AMK, Aminoglycoside: Amikacin; TZP, Piperacillin-Tazobactam.

(Table 3), which is in line with the literature in which infection rates with carbapenem and multidrug-resistant Enterobacteriaceae were highest in long-term acute-care hospitals.[17–19] The overall susceptibilities were generally higher in CA than in HA IAIs and UTIs (Figure 1), which is in accordance with data from 2015.[20] On the other hand, susceptibilities of ESBL-producing *K. pneumoniae* strains from CA UTIs were significantly lower than HA UTIs, particularly to ETP, which needs further investigation. Comparing the overall susceptibilities of HA and CA IAI and UTI-derived *E. coli* and *K. pneumoniae* strains from 2015 with 2016/2017, susceptibilities to all cephalosporins and fluoroquinolones were far less than 80% for both bacterial species in both time periods. For *E. coli* isolates from IAIs and UTIs, susceptibilities to IPM, ETP, AMK, and TZP were in the range of 80%–94% in both time periods, without essential changes. However, overall susceptibilities to IPM, ETP, AMK, and TZP gradually dropped for *K. pneumoniae* isolates, especially from IAIs during 2015–2017 (Figure 2).

Limitations of the present study include the fact that molecular mechanisms of resistance have not been identified.

Conclusion

E. coli and *K. pneumoniae* were the main pathogens in Chinese UTIs and IAIs, with high ESBL-positive rates and low susceptibilities to cephalosporins and fluoroquinolones between 2016 and 2017, and *K. pneumoniae* showed a trend toward lower susceptibility in HA, compared to CA IAI and UTI infections. Imipenem, ertapenem, and amikacin were the most effective agents against UTIs and IAIs, but the susceptibilities of IAI-derived *K. pneumoniae* strains to these antibiotics became lower in 2017, compared to 2015 and 2016.

Ethics approval and consent to participate

The protocol has been reviewed by the human research ethics committee of the Institutional Review Board (IRB) of the Peking Union Medical College Hospital and since the project falls under the category observational study and all bacterial strains were from residual samples used in clinical diagnosis or were strains from their subcultures, it covers patient data confidentiality and compliance with the declaration of Helsinki. Since the data do not include any patient's information and demographic data it has been determined to meet the criteria for exemption. After consultation with the IRB of the Peking Union Medical College Hospital, formal ethical approval was reviewed and written informed consents from patients was not required (Ethics Approval Number: S-K238).

Availability of data and materials

The SMART database is not public and only accessible for SMART investigators, but the data that support the findings of this study are directly available from MSD China or from the authors upon reasonable request and with permission of Merck Sharp & Dohme (China) Co., Ltd.

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Author contributions

Conceptualization: HZ, AJ, QWY, YCX; data collection: HZ, AJ, GZ, YY, JJZ, DXL, SMD, QWY, YCX; data analysis: HZ, QWY, YCX; writing original draft: HZ; writing review and editing: HZ, AJ, YY, JJZ, DXL, SMD, GZ, QWY, YCX. All authors contributed to data analysis, drafting and revising the article, gave final approval of the version to be published, and agree to be accountable for all aspects of the work.

Disclosure

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Supplementary material

Table S1 ESBL positivity and antibiotic susceptibility rates (%) for *P. mirabilis* and *K. oxytoca* isolates combined in HA vs CA IAIs and UTIs

	***P. mirabilis ESBL* +(n=28)**						***K. oxytoca ESBL* +(n=23)**					
	IAI			**UTI**			**IAI**			**UTI**		
	***All* (n=13)**	**HA (n=13)**	**CA (n=0)**	***All* (n=15)**	**HA (n=10)**	**CA (n=5)**	***ALL* (n=8)**	**HA (n=7)**	**CA (n=1)**	***All* (n=4)**	**HA (n=4)**	**CA (n=0)**
IPM	7.69	7.69	NA	33.33	50	0	75	71.43	100	100	100	NA
ETP	92.31	92.31	NA	80	80	80	62.5	57.14	100	100	100	NA
AMK	92.31	92.31	NA	100	100	100	87.5	85.71	100	100	100	NA
TZP	84.62	84.62	NA	86.67	90	80	62.5	57.14	100	50	50	NA
FOX	92.31	92.31	NA	66.67	70	60	37.5	42.86	0	100	100	NA
CAZ	92.31	92.31	NA	80	80	80	12.5	14.29	0	25	25	NA
CRO	0	0	NA	6.67	10	0	0	0	0	0	0	NA
CTX	0	0	NA	6.67	10	0	0	0	0	0	0	NA
FEP	15.38	15.38	NA	6.67	10	0	12.5	0	100	0	0	NA
LVX	23.08	23.08	NA	33.33	50	0	50	57.14	0	25	25	NA
CIP	15.38	15.38	NA	13.33	20	0	50	57.14	0	25	25	NA

Abbreviations: HA, hospital-acquired; CA, community-acquired; IAI, intraabdominalinfection; UTI, urinary tract infection; IPM, Carbapenems: Imipenem; ETP, Ertapenem; AMK, Aminoglycoside: Amikacin; TZP, Piperacillin-Tazobactam; FOX, Cephalosporins: Cefoxitin; CAZ, Ceftazidime; CRO, Ceftriaxone; CTX, Cefotaxime; FEP, Cefepime; LVX, Fluoroquinolones: Levofloxacin; CIP, Ciprofloxacin; NA, not available.