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Surveillance of Antimicrobial Susceptibility of Aerobic and Facultative Gram-negative Bacilli Isolated from Patients with Urinary Tract Infections in China: 2010-2014 Study for Monitoring Antimicrobial Resistance Trends (SMART)

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Abstract

Background: To investigate the distribution and susceptibility of aerobic and facultative Gram-negative bacilli isolated from patients with urinary tract infections (UTIs) in China from 2010 to 2014.
Method: The minimum inhibitory concentrations (MICs) of 12 antibiotics for 4,332 aerobic and facultative Gram-negative bacilli from 21 hospitals in 16 cities were determined by the broth microdilution method.
Results: *Enterobacteriaceae* composed 88.5% (3,832/4,332) of the total isolates. Among the antimicrobial agents tested, the two carbapenems, ertapenem and imipenem, were the most active agents against *Enterobacteriaceae* with susceptibility rates of 92.5-96.5% and 89.9-95.2% (2010-2014) respectively, followed by amikacin (88.2-94.1%) and piperacillin-tazobactam (86.5-88.4%). The susceptibility rates of all tested third- and fourth-generation cephalosporins against *Enterobacteriaceae* were relatively low, with susceptibilities of 34.5-46.9%, 51.4-66.0%, 29.4-41.1% and 29.6-40.0% for cefepime, ceftazidime, ceftriaxone and cefotaxime, respectively. Extended spectrum beta-lactamases (ESBLs) occurrence was 62.7%, 53.5% and 39.5% in *Escherichia coli(E.Coli), Klebsiella pneumoniae (K.Pneumniae)* and *Proteus mirabilis(P.mirabilis)*, respectively, during 2010-2014. However, the ESBL rate decreased slowly over 5 years. The susceptibility of *Enterobacteriaceae* to ciprofloxacin and levofloxacin increased from 25.3-27.8% in 2010 to 44.4-48.2% in 2014. The least active agent against *Enterobacteriaceae* was ampicillin-sulbactam (16.3-24.3%).
Conclusion: *Enterobacteriaceae* were the major pathogens causing UTIs and carbapenems retained the highest susceptibility rates over the five-year study period.
Keywords: Urinary tract infections; extended spectrum beta-lactamases (ESBLs)

Introduction

The Study for Monitoring Antimicrobial Resistance Trends (SMART) study is a surveillance program designed to globally monitor susceptibilities of aerobic and facultative Gram-negative bacilli collected from intra-abdominal infections and urinary tract infections (initiated in 2002). For UTI isolates in 2009-2010 in the Asia-Pacific region, amikacin was the most effective antibiotic (susceptibility rate of 91.7%), followed by ertapenem (86.9%), imipenem (86.6%) and piperacillin-tazobactam (84.9%) [1]. In this study, we summarize the results of pathogen distributions and antimicrobial susceptibilities of UTIs in China from 2010 to 2014.

Methods

- This report summarizes the *in vitro* susceptibility of 4,332 isolates collected from patients with UTIs in 16 Chinese cities during the study period (2010-2014).
- All isolates were sent to a central laboratory in China, the clinical microbiology laboratory of Peking Union Medical College Hospital, for susceptibility or resistance testing and identification confirmation.
- Minimum inhibitory concentration (MIC) determinations were performed using dehydrated MicroScan broth microdilution panels according to the Clinical and Laboratory Standards Institute (CLSI) guidelines [2]. All antimicrobials were supplied by the panel manufacturer.
- MIC interpretive criteria followed published guidelines of the CLSI [3].
- ESBL expression was determined by CLSI phenotypic confirmatory tests. If there was at least an eightfold reduction (i.e., three doubling dilutions) of the MICs for ceftazidime or cefotaxime tested in combination with clavulanic acid *vs* their MICs when either drug was tested alone, the isolates were defined as ESBL positive [3].
- Quality controls (QC) were performed on each day of testing using appropriate ATCC control strains, following CLSI and manufacturer guidelines. Results were included in the analysis only when corresponding QC results were within the acceptable ranges [3].

Results

1. Distribution of organisms from UTIs
Enterobacteriaceae were the majority of isolates which accounted for 88.5%. Non-*Enterobacteriaceae* accounted only for 11.5% of all isolates (Table 1) .

2. *In vitro* susceptibilities of main *Enterobacteriaceae* and non-*Enterobacteriaceae* species during 2010-2014
Among the 12 analyzed antimicrobial agents susceptibility rates, *E.coli* over five years was 96.4% (2,638/2,737) and 98.7% (2,701/2,737) for ertapenem and imipenem.
In *Enterobacteriaceae*, *E. coli* and *K. pneumoniae* had the highest susceptibility to the two carbapenems, ertapenem (85-99.0%) and imipenem (89.2-99.3%) in 2010-2014, followed by amikacin (84.0-95.1%) and piperacillin-tazobactam (66.1-94.7%). The least active agent against *E. coli* and *K. pneumoniae* was ampicillin-sulbactam (14.9-37.3%) (Figure 1). Against *P. mirabilis*, imipenem was not active and ertapenem and piperacillin-tazobactam susceptibility rates were 95.7-100% and 97.9-100% in 2010-2014. For *E. cloacae*, only amikacin showed a stable susceptibility of 87% from 2010-2014, followed by ertapenem and imipenem, whose activities were > 70%.
Although Non-*Enterobacteriaceae* did not show high susceptibilities to the 12 common antibiotics, over the 5-year study period amikacin exhibited the highest *in vitro* activity against *P. aeruginosa* with an average susceptibility rate of 84.2% (Figure 1). The most active agents against *A.baumannii* were imipenem and amikacin, with average susceptibility rates of 46.9% and 46.2%, respectively, during the entire study period （Figure 1）.

3. The trend of extended spectrum beta lactamase (ESBL)–producing bacteria occurrence in UTIs from 2010 to 2014
The percentage of ESBL-positive *E. coli* isolates decreased from 68.6% in 2010 to 59.1% in 2014, while the rate decreased from 59.7% to 49.2% in *K. pneumoniae* and from 40.0% to 26.1% in *P. mirabilis* during the 5-year study period (Table 2).
The susceptibility differences to ertapenem and imipenem between ESBL and non-ESBL producing strains were generally small, but were greater for other agents particularly for the third- and fourth-generation cephalosporins ceftriaxone (1.1% vs 91.0%), ceftazidime (38.4% vs 93.5%) and cefepime (4.5% vs 96.7%) between ESBL-positive and ESBL-negative isolates

Table 1. Distribution of Chinese UTI pathogens in 2010-2014

	N (%)
Enterobacteriaceae	**3,832 (88.5%)**
Escherichia coli	2,737 (63.2%)
Klebsiella pneumoniae	529 (12.2%)
Proteus mirabilis	147 (3.4%)
Enterobacter cloacae	141 (3.3%)
Citrobacter freundii	54 (1.2%)
Klebsiella oxytoca	51 (1.2%)
Other	173 (4.0%)
Non-*Enterobacteriaceae*	**500 (11.5%)**
Pseudomonas aeruginosa	297 (6.9%)
Acinetobacter baumannii	143 (3.3%)
Other	60 (1.4%)
Total	**4,332 (100%)**

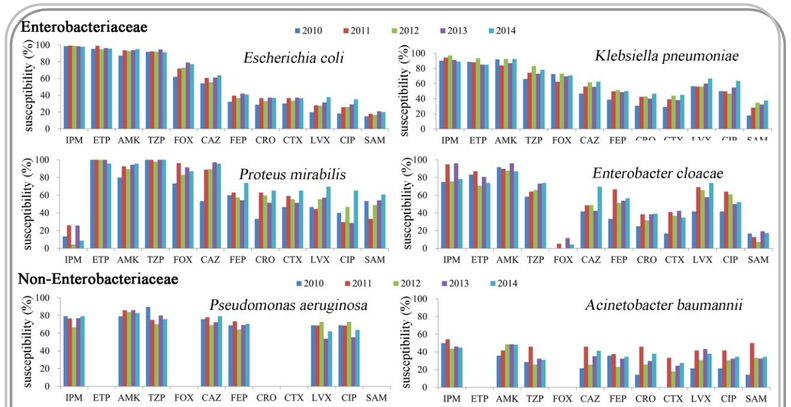

Figure 1. Trends over time in the susceptibility to antimicrobial agents* of isolates from UTIs caused by *Enterobacteriaceae* and non-*Enterobacteriaceae* in China.
*EPM, ertapenem; IPM, imipenem; AMK, amikacin; TZP, piperacillin-tazobactam; FOX, cefoxitin; FEP, cefepime; CAZ, ceftazidime; CRO, ceftriaxone; CTX, cefotaxime; LVX, levofloxacin; CIP, ciprofloxacin; SAM, ampicillin-sulbactam.

Table 2. Occurrence of ESBL-producing *Escherichia coli*, *Klebsiella pneumoniae* and *Proteus mirabilis* in 2010-2014

Organism	ESBL-producing isolates N (%)				
	2010	2011	2012	2013	2014
E. coli	249 (68.6)	423 (61.3)	410 (64.9)	346 (61.5)	289 (59.1)
K. pneumoniae	37 (59.7)	65 (52.0)	56 (52.3)	66 (57.4)	59 (49.2)
P. mirabilis	6 (40.0)	11 (40.7)	18 (38.3)	17 (48.6)	6 (26.1)

Conclusions

1.Enterobacteriaceae were the majority of isolates which accounted for 88.5%; with *E. coli* (63.2%) the most commonly isolated species, followed by *K. pneumoniae* (12.2%), *P. mirabilis* (3.4%) and *E. cloacae* (3.3%). Non-*Enterobacteriaceae* accounted only for 11.5% of all isolates; with *P. aeruginosa* (6.9%) and *A. baumanni* (3.3%).
2.Among the antimicrobial agents tested, the two carbapenems, ertapenem and imipenem, were the most active agents against *Enterobacteriaceae*.
3.The third- and fourth-generation cephalosporins, fluoroquinolones and ampicillin-sulbactam, may not be effective choices for empirical therapies of UTIs in China, even though the susceptibility of these drugs increased slightly during recent years.
4. The ESBL rate showed a decreasing trend from 2010 to 2014.

References

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