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Surveillance of the susceptibility of ESBL-producing *Escherichia coli and Klebsiella pneumoniae* isolated from patients with intra-abdominal infections in China: data from the SMART study 2012-2014

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Abstract

Background: The epidemiological susceptibility trends and incidence of Extended Spectrum Beta Lactamase producing (ESBL+) *Escherichia coli* (*E. coli*) and *Klebsiella pneumoniae* (*K. pneumoniae*) causing intra-abdominal infections (IAI) were analyzed using data from the Study for Monitoring Antimicrobial Resistance Trends (SMART) 2012-2014.
Methods: A total of 2,343 *E. coli* strains (887 strains in 2012, 772 strains in 2013 and 684 strains in 2014), which accounted respectively for 17.2%, 15.0% and 13.3% of all collected gram-negative bacilli (GNB), and 1,037 *K. pneumoniae* strains (337 in 2012, 381 in 2013 and 319 in 2014) accounting for 6.6%, 7.4% and 6.2%, respectively of all GNB isolated from patients with IAI from 2012 through 2014 in 21 centers located in 16 Chinese cities were studied. ESBL+ status and antimicrobial susceptibilities were determined at a central laboratory using CLSI broth microdilution and interpretive standards.
Results: The relative percentage of *E. coli* from IAI GNB isolates showed a decreasing trend. Similarly, ESBL+ *E. coli* isolates also showed a decreasing trend from 67.5% to 58.9% of total *E. coli* isolates from 2012 through 2014. The percentage of *K. pneumoniae* which were ESBL+ also decreased from 2012 through 2014 (40.4% to 26.7%). The susceptibility of ESBL+ *E. coli* strains was greater than 80% to imipenem (IPM), ertapenem (ETP), amikacin (AMK) and piperacillin-tazobactam (TZP), while ESBL+ *K. pneumoniae* strains were more than 70% susceptible only to ETP, IPM and AMK within the three years.
Conclusion: IMP, ETP, AMK and piperacillin-tazobactam (TZP) were the most effective antimicrobials against ESBL+ *E. coli* and *K. pneumoniae* isolates from 2012-2014 patients compared to other common antimicrobial agents, but the activity of TZP was diminished to <70% for ESBL+ *K. pneumoniae* strains. The apparent trend of declining percentages of ESBL+ *E. coli* and *K. pneumoniae* is noteworthy and will be monitored closely.
Key words: Extended spectrum beta-lactamases (ESBL); gram-negative bacilli; intra-abdominal infections

Introduction

The Study for Monitoring Antimicrobial Resistance Trends (SMART)-CHINA is a surveillance program which monitors annually *in vitro* activities of antimicrobial agents against pathogens that cause intra-abdominal infections (IAIs) and urinary tract infections (UTIs). Although it has been reported that the proportion of ESBL-positive *Enterobacteriaceae* hospital infections has significantly increased in Germany over the last 6 years [1], and was reported to have also increased from 2000 to 2010 in Japan [2], the situation in China is not clear in recent years. This study mainly focused on ESBL+ rates of IAI isolates and concomitantly on resistance rates in IAIs particularly caused by *Enterobacteriaceae* in 21 centers in 16 Chinese cities between 2012 and 2014.

Methods

❖All isolates were sent to the clinical microbiology laboratory of Peking Union Medical College Hospital, for susceptibility testing and identification confirmation.
❖Minimum inhibitory concentrations (MICs) were determined by the Clinical and Laboratory Standards Institute (CLSI)[4] broth microdilution method [3]. All antimicrobials were supplied by the panel manufacturer.
❖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 versus their MICs when either drug was tested alone, the isolates were defined as ESBL positive [4].
❖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 [4].

Results

1. From 2012 to 2014, *E. coli* and *K. pneumoniae* were the two main *Enterobacteriaceae* IAI isolates, accounting for 79.76-83.78% of infections;
2. The relative percentage of ESBL+ *E. coli* and *K. pneumoniae* strains from IAI GNB isolates showed a decreasing trend from 2012-2014;
3. Non-ESBL producing *E. coli* isolates showed an annually increasing trend from 31.0% to 41.8% of total *E.coli* isolates from 2012 through 2014;
4. The percentage of *K. pneumoniae* which were non-ESBL producing strains also increased from 2012 through 2014 (52.6% to 72.7% of all *K. pneumoniae*);
5. Susceptibilities of ESBL+ *E. coli* strains were higher than 80% to imipenem (IPM), ertapenem (ETP), amikacin (AMK) and piperacillin-tazobactam (TZP), while ESBL+*K. pneumoniae* strains were more than 70% susceptible only to ETP, IPM and AMK within the three years studied;
6. Both the susceptibility of non-ESBL producing *E. coli* and non-ESBL producing *K. pneumoniae* strains were higher than 90% to imipenem (IPM), ertapenem (ETP), amikacin (AMK) and piperacillin-tazobactam (TZP), as well as ceftazidime (CAZ), cefepime (FEP), ceftriaxone (CRO) and cefotaxime (CTX).

Table 1. Bacterial identification and epidemiological status of isolates from intra-abdominal infections in China(2012-2014)

Organism	Sum (%)	2012 (%)	2013 (%)	2014 (%)
Total	**5,160**	**1,917**	**1,665**	**1,578**
Enterobacteriaceae	**4,186 (81.1)**	**1,529 (79.8)**	**1,395 (83.8)**	**1,262 (80.0)**
Escherichia coli	2,343 (45.4)	887 (46.3)	772 (46.4)	684 (43.4)
ESBL-producing strains	1,471 (62.8)	599 (67.5)	469 (60.8)	403 (58.9)
Non-ESBL strains	829 (35.4)	275 (31.0)	275 (35.6)	279 (40.8)
Not identified	43 (1.8)	13 (1.5)	28 (3.6)	2 (0.3)
Klebsiella pneumoniae	1,037 (20.1)	337 (17.6)	381 (22.9)	319 (20.2)
ESBL-producing strains	366 (35.3)	136 (40.4)	145 (38.1)	85 (26.7)
Non-ESBL strains	639 (61.6)	194 (57.6)	213 (55.9)	232 (72.7)
Not identified	32 (3.1)	7 (2.1)	23 (6.0)	2 (0.6)
Enterobacter cloacae	266 (5.2)	101 (5.3)	85 (5.1)	80 (5.1)
Proteus mirabilis	109 (2.1)	48 (2.5)	32 (1.9)	29 (1.8)
Citrobacter freundii	95 (1.8)	33 (1.7)	30 (1.8)	32 (2.0)
Enterobacter aerogenes	91 (1.8)	37 (1.9)	23 (1.4)	31 (2.0)
Klebsiella oxytoca	70 (1.4)	21 (1.1)	18 (1.1)	31 (2.0)
Morganella morganii	63 (1.2)	15 (0.8)	24 (1.4)	24 (1.5)
Serratia marcescens	34 (0.7)	15 (0.8)	9 (0.5)	10 (0.6)
Citrobacter koseri	14 (0.3)	3 (0.2)	5 (0.3)	6 (0.4)
Proteus vulgaris	13 (0.3)	8 (0.4)	3 (0.2)	2 (0.1)
Other	51 (1.0)	24 (1.3)	13 (0.8)	14 (0.9)
Non-Enterobacteriaceae	**974 (18.9)**	**388 (20.2)**	**270 (16.2)**	**316 (20.0)**
Pseudomonas aeruginosa	505 (9.8)	207 (10.8)	141 (8.5)	157 (10.0)
Acinetobacter baumannii	345 (6.7)	139 (7.3)	94 (5.7)	112 (7.1)
Stenotrophomonas maltophilia	47 (0.9)	21 (1.1)	10 (0.6)	16 (1.0)
Aeromonas hydrophila	20 (0.4)	8 (0.4)	11 (0.7)	1 (0.1)
Other	57 (1.1)	13 (0.7)	14 (0.8)	30 (1.9)

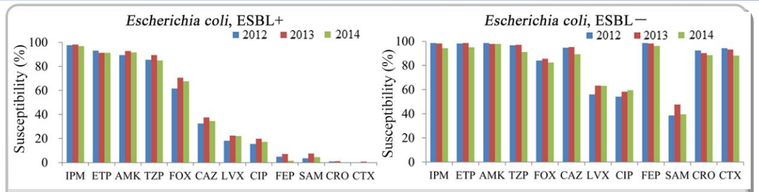

Figure 1. *In vitro* antimicrobial susceptibilities of ESBL+ or non-ESBL-producing *E. coli* strains causing IAIs between 2012-2014.

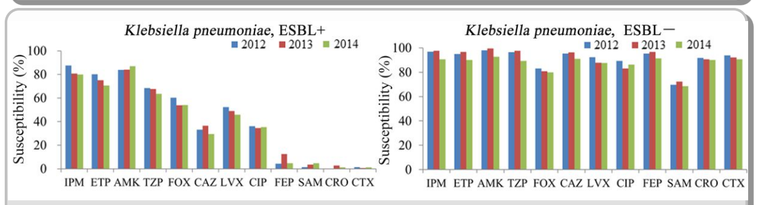

Figure 2. *In vitro* antimicrobial susceptibilities of ESBL+ or non-ESBL-producing *K. pneumoniae* strains causing IAIs between 2012-2014

Conclusions

❖In the years 2012 to 2014, from a total of 5,160 IAI isolates 81.1% were caused by *Enterobacteriaceae* and 18.9% by non-Enterobacteriaceae, with *E. coli* (45.4%) being the most common followed by *K. pneumoniae* (20.1%). The most common non-Enterobacteriaceae were *Pseudomonas aeruginosa* (9.8%) and *Acinetobacter baumannii* (6.7%).
❖The relative percentage of ESBL+ *E. coli* and K. *pneumoniae* in IAI GNB isolates showed a decreasing trend from 2012-2014.
❖Susceptibility of ESBL+ *E. coli* strains were higher than 80% to imipenem (IPM), ertapenem (ETP), amikacin (AMK) and piperacillin-tazobactam (TZP), while ESBL+ *K. pneumoniae* strains were more than 70% susceptible only to ETP, IPM and AMK 2012-2014.
❖The apparent trend of declining percentages of ESBL+ *E. coli* and *K. pneumoniae* strains is noteworthy and will be monitored closely.

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