

Revised Abstract

Background: The Study for Monitoring Antimicrobial Resistance Trends (SMART) has tracked susceptibility of intra-abdominal infection (IAI) pathogens since 2002. Globally increasing rates of multi-drug resistant, ESBL+ *E. coli* (Ec) require knowledge of local ESBL prevalence in order to optimize therapy. This report summarizes 2009 Ec data from SMART in North America. **Methods:** 777 IAI Ec from 28 sites (19 US, 9 Canada) were sent to a central lab for identification confirmation, broth microdilution susceptibility testing, and ESBL confirmation by CLSI guidelines. Drugs tested were ertapenem (Etp), imipenem (Imp), piperacillin-tazobactam (PT), ampicillin-sulbactam (AS), ceftazidime (Caz), ceftriaxone (Cax), cefepime (Cpe), amikacin (Ak), ciprofloxacin (Cp), and levofloxacin (Lvx). Susceptibility (%S) was compared for 2009 vs. 2005, and for hospital-associated (HA) vs community-associated (CA) IAI. Statistical significance was determined using Fisher's Exact Test, two-tailed. **Results:** Ec %S was ≥ 90 for 7 drugs (Imp 99.9, Etp 99.6, Ak 98.8, Cpe 94.2, PT 93.2, Caz 92.2, and Cfx 91.3); Cax and Cft were just under 90%; Cp and Lvx just above 70%; and AS was 55.1. Comparing HA to CA Ec, only Cft, Caz, and Cax had significantly lower %S in HA infection ($P < .05$). Among all IAI Ec isolates, 5 drugs (Cpe, Cft, Cax, Cp, Lvx) had significantly lower %S in 2009 than in 2005 ($P < .05$). The ESBL+ rate in 2009 was 6.9%, compared to 1.7% in 2005 ($P = .002$).

Conclusions:

- Overall, IAI Ec remain susceptible *in vitro* to many commonly-used drugs; however, fluoroquinolones inhibited only around 70% of isolates, and AS only around half.
- The *in vitro* activity of several cephalosporins and fluoroquinolones has declined significantly since 2005. *In vitro* susceptibility to fluoroquinolones was 6-fold lower in ESBL+ than in ESBL- isolates; even among ESBL- isolates the %S dropped significantly ($P < .05$) from 2005-2009.
- Only Etp, Imp, and Ak inhibited $>90\%$ of ESBL+ isolates, and the only other study drug to inhibit $>80\%$ was PT at 81.5%.
- Although the North American ESBL+ rate in Ec from IAI is lower than that reported for other regions of the world, it has nevertheless increased from 1.7% to 6.9% over the five years of this analysis. Given the much lower susceptibility rates seen in ESBL+ isolates, it is important to be aware of local ESBL+ rates when selecting empiric therapy for IAI.

Introduction

The Study for Monitoring Antimicrobial Resistance Trends (SMART) has tracked susceptibility of intra-abdominal infection (IAI) pathogens since 2002. This program and other studies have documented globally increasing rates of extended-spectrum beta-lactamase-producing (ESBL+) *E. coli*, in both hospital- and community-acquired IAI. A previous report from SMART showed an ESBL+ rate in North America of 1.7% [1]; however, given the increasing incidence of such isolates worldwide, this report summarizes *E. coli* susceptibility data and ESBL+ rates from SMART 2009 in North America (NA).

Materials & Methods

- 777 IAI *E. coli* collected in 2009 from 28 sites in North America (19 US, 2 Canada) were sent to a central lab (International Health Management Associates, Inc., Schaumburg, IL) for identification confirmation, ESBL status using Clinical and Laboratory Standards Institute (CLSI) guidelines [2, 3], and antimicrobial susceptibility testing for ertapenem (Etp), imipenem (Imp), piperacillin-tazobactam (PT), ampicillin-sulbactam (AS), ceftazidime (Caz), ceftriaxone (Cax), cefepime (Cpe), amikacin (Ak), ciprofloxacin (Cp), and levofloxacin (Lvx). Susceptibility (%S) was compared for 2009 vs. 2005, and for hospital-associated (HA) vs community-associated (CA) IAI. Statistical significance was determined using Fisher's Exact Test, two-tailed.
- Minimum inhibitory concentrations (MICs) and production of ESBL were determined using MicroScan dehydrated broth microdilution panels (Siemens Medical Solutions Diagnostics, West Sacramento, CA), following manufacturer and CLSI guidelines [3].
- Quality control was done each day of testing following CLSI guidelines [3].
- Susceptibility (%S) was compared for hospital-associated (HA) vs community-associated (CA) infection. An IAI was defined as HA if the specimen was cultured ≥ 48 hours post admission to hospital, and CA if the specimen was cultured < 48 hours post admission to hospital. Furthermore, susceptibility of ESBL+ and ESBL- isolates were compared, and overall *E. coli* 2009 susceptibility was compared to previously reported 2005 levels.
- Statistical significance was determined using Fisher's Exact Test, two-tailed.

References

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Results

Figure 1. Antimicrobial susceptibility of *E. coli* from IAI in North America in 2005 and 2009; asterisks indicate significant differences ($P < .05$).

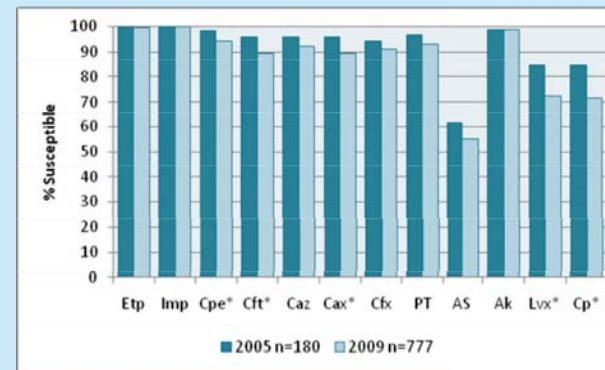
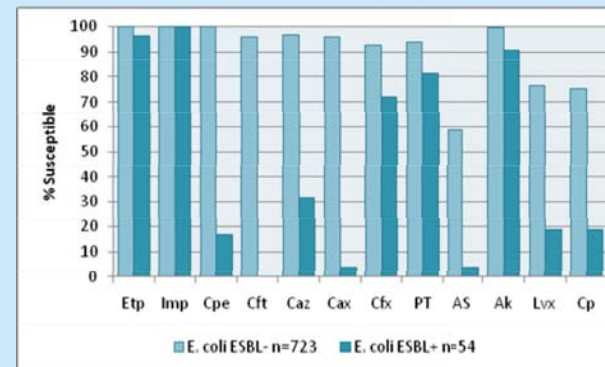


Figure 2. Antimicrobial susceptibility of ESBL+ and ESBL- *E. coli* from IAI in North America in 2009¹.



¹The ESBL rate in 2009 was 6.9% (54/777 isolates).

Figure 3. Antimicrobial susceptibility of *E. coli* isolated from hospital-acquired (HA) and community-acquired (CA) IAI in North America in 2009; asterisks indicate significant differences ($P < .05$).

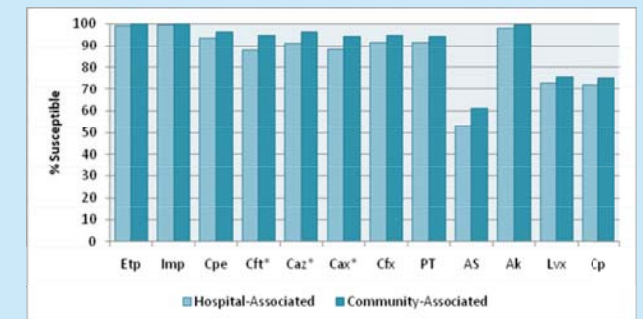
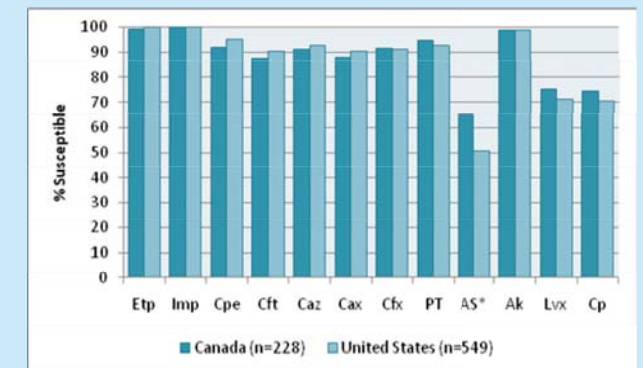


Figure 4. Antimicrobial susceptibility of *E. coli* isolated from IAI in Canada and the United States in 2009; asterisks indicate significant differences ($P < .05$).



Conclusions

- E. coli* isolated from IAI in North America remain susceptible *in vitro* to many commonly-used drugs; however, fluoroquinolones inhibited only around 70% of isolates, and ampicillin-sulbactam only around half.
- Susceptibility in Canada and the United States was not significantly different, other than for ampicillin-sulbactam where the US rate was lower.
- Nevertheless, *in vitro* activity of several cephalosporins and fluoroquinolones has declined significantly since 2005. *In vitro* susceptibility to fluoroquinolones was 6-fold lower in ESBL+ than in ESBL- isolates, and even among ESBL- isolates the %S dropped significantly from 2005-2009 ($P < .05$).
- Only ertapenem, imipenem, and amikacin inhibited $>90\%$ of ESBL+ isolates, and the only other study drug to inhibit $>80\%$ was piperacillin-tazobactam at 81.5%.
- Although the North American ESBL+ rate in *E. coli* from IAI is lower than that reported for other regions of the world, it has nevertheless increased from 1.7% to 6.9% over the five years of this analysis. Given the much lower susceptibility rates seen in ESBL+ isolates, it is important to be aware of local ESBL+ rates when selecting empiric therapy for IAI.