

More and more third generation cephalosporin-resistant enteric bacteria everywhere?

Trends of resistance among community-onset *Escherichia coli* blood isolates in the United States: an 11-year nationwide cohort study

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**Objective:** Gram-negative pathogen data on antimicrobial susceptibility to fluoroquinolones, aminoglycosides, and carbapenems have become increasingly important to guide proper empiric antimicrobial therapy for serious infections. The United States (US) Veterans Health Administration (VHA) recently established a nationwide microbiology database, which includes all microbiological results from each acute-care hospital. We report the chronological trend of susceptibility rates to fluoroquinolones, aminoglycosides, and carbapenems among community-onset *Escherichia coli* blood isolates over an 11 year period.

**Methods:** A cohort of all patients admitted to 133 VHA hospitals included all patients with community-onset *E. coli* positive blood culture (first positive culture <48 hours of admission) from 2003-2013. If the same patient had multiple positive blood cultures for *E. coli*, the only the first isolate in the calendar year was included. Antimicrobial susceptibility test results were extracted from the electronic medical record system of VHA. The isolate was considered to be non-susceptible, if not susceptible to at least one agent in an antimicrobial class. If carbapenem susceptibility test results were not available, isolates that were penicillin or cephalosporin susceptible were considered susceptible to carbapenems. Trends were assessed by the Cochran-Armitage test.

**Results:** The cohort included 21,079 community-onset *E. coli* blood isolates from 133 hospitals. Fluoroquinolone susceptibility test results were available in 20,468 isolates (97.1%), aminoglycoside in 21,039 (99.8%), and carbapenem in 21,007 (99.7%). Overall susceptibility to fluoroquinolones decreased from 88.2% in 2003 to 69.0% in 2013, and there was a rapid decline of susceptibility rates between 2003 and 2007, followed by slow decline (trend:  $p < 0.0001$ ) (See Figure). Overall susceptibility to aminoglycosides decreased from 93.7% in 2003 to 86.9% in 2013 (trend:  $p < 0.001$ ), but remained relatively high. Only 37 isolates (0.18%) were not susceptible to carbapenems in this cohort.

**Conclusion:** Fluoroquinolone susceptibility among community-onset *E. coli* blood isolates in the US declined rapidly in early 2000s, followed by a constant slow decline. Aminoglycosides showed a relatively modest decline of susceptibility rates, and carbapenem-resistant isolates were very infrequent in our cohort. The widespread use of fluoroquinolones for a broad range of indications may have contributed to increased resistance, while the relatively low use of aminoglycosides may have contributed to the preservation of this class. Further studies are needed to elucidate the factors associated with antimicrobial resistance in community-onset *E. coli* isolates, especially as plasmid-mediated carbapenem resistance in *E. coli* has been increasingly reported in the past few years.

