Trends in Antimicrobial Resistance for *Enterobacter* spp. Collected from Inpatients at a Major Canadian Tertiary Care Center: A Retrospective Analysis Over 14 Years

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BACKGROUND

Enterobacter spp. are opportunistic pathogens and a common cause of nosocomial infection.

A recent study examined susceptibility trends among 719 *Enterobacter* cloacae isolates submitted to the CANWARD surveillance program between 2007-2016 and found susceptibility to ceftazidime, ceftriaxone, ertapenem, meropenem, and co-trimoxazole decreased over time when a univariate trend test was applied.

OBJECTIVE

To evaluate the antimicrobial resistance trends among *Enterobacter* isolates collected at Sunnybrook Health Sciences Center (SHSC) and compare findings to national CANWARD trends.

METHODS

Study Design:

Retrospective observational study over a 14-year period (September 2002 to October 2016)

Study Setting:

Sunnybrook Health Sciences Centre (SHSC) Bayview Campus, Toronto, Ontario, Canada, a 627-bed acute care teaching hospital.

Data Collection:

Isolate-level susceptibility data for clinical isolates of *Enterobacter* spp. collected from inpatients during the study period were extracted from the SHSC Microbiology database.

Clinical isolates were defined as bacteria cultured from clinical specimens (i.e. specimens collected for the purpose of assisting with the diagnosis of an infection).

Antimicrobial susceptibility testing was conducted in accordance to the Clinical and Laboratory Standards Institute standards at the time of clinical sample collection.

Data Analysis:

Descriptive statistics regarding patient sex, patient location at the time of specimen collection, specimen anatomical source, type of infection (community-acquired, hospital-acquired), and *Enterobacter* spp. were determined.

Isolates were characterized as antimicrobial resistant organisms ("AROs"; non-susceptible to ≥1 antibiotic agent), multidrug resistant organisms ("MDRO"; isolate non-susceptible to antibiotic agents in ≥3 antibiotic classes), extensively drug resistant organisms ("XDROs"; only susceptible to agents in ≤2 antibiotic classes)

Longitudinal trends in *Enterobacter* isolate susceptibilities to ceftazidime, ceftriaxone, ciprofloxacin, ertapenem, gentamicin, meropenem, piperacillin-tazobactam, sulfamethoxazole-trimethoprim and tobramycin were characterized using a univariate linear regression at a significance level of 0.05.

RESULTS

Table 1. Characteristics of 3181 *Enterobacter* isolates collected from inpatients at SHSC between October 2002 and September 2016.

	n (%)
Patient Sex	
Male	1780 (56%)
Female	1401(44%)
Source	
Urine	1416 (45%)
Blood	512 (16%)
Respiratory	650 (20%)
Other	603 (19%)
Location	
Emergency Department	549 (17%)
Ward	1529 (48%)
Intensive Care Unit	1103 (35%)
Type of infection	
Community-acquired	958 (30%)
Hospital-acquired	2223 (70%)
Enterobacter spp.	
Enterobacter cloacae complex	2290 (72%)
Enterobacter aerogenes	827 (26%)
Other *Enterobacter spp.*	64 (2%)
Resistance	
ARO	2753 (87%)
MDRO	1301 (41%)
XDRO	10 (<1%)

Table 2. Linear regression of the trends in susceptibility of *Enterobacter* clinical isolates *to* antimicrobials over the 14-year study period at SHSC.

Antimicrobial agent	Trend in % of isolates susceptible per year	*P-value*
Ceftazidime Ceftriaxone	+0.2% -0.3%	Not stat. significant
Piperacillin-tazobactam	-1.0%	0.057
Ertapenem	<0.1%	Not stat. significant
Meropenem	-0.1%	**0.002***
Ciprofloxacin	+0.6%	**0.025***
Sulfamethoxazole-trimethoprim	+0.7%	0.056
Gentamicin Tobramycin	+1.0% +1.0%	**0.004*** **0.003***

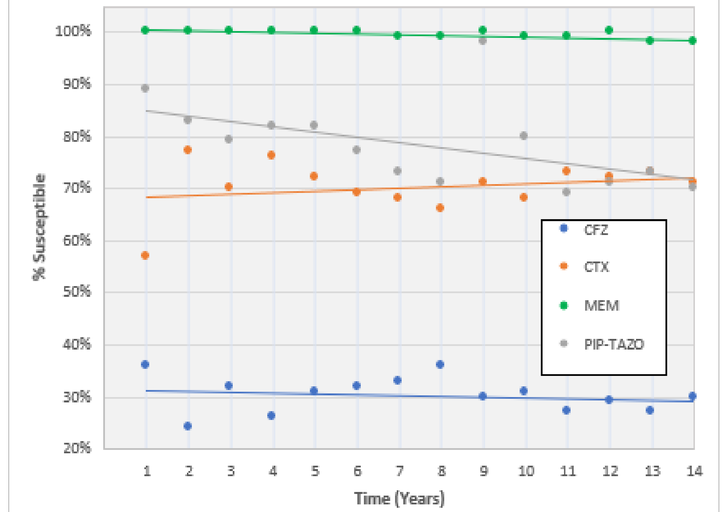

Figure 1. Susceptibility of *Enterobacter* isolates to ß-lactams each year from October 2002 to September 2016. CTX, ceftriaxone; CFZ, ceftazidime; MEM, meropenem; PIP-TAZO, piperacillin-tazobactam.

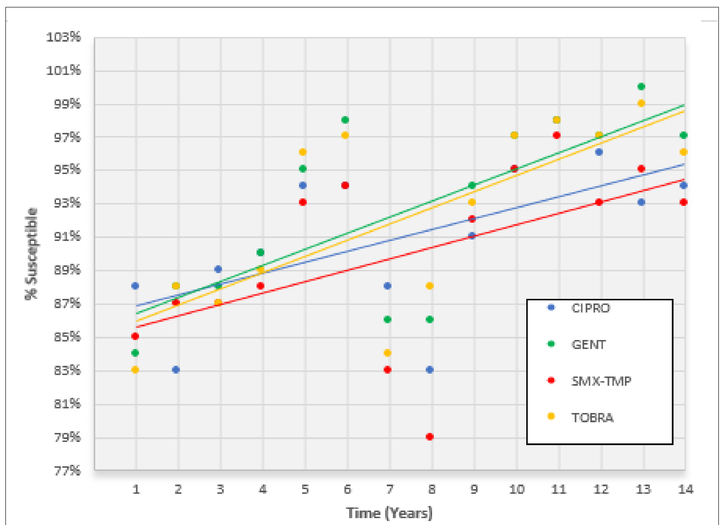

Figure 2. Susceptibility of *Enterobacter* isolates to non-ß-lactam agents each year from October 2002 to September 2016. CIPRO, ciprofloxacin; GENT, gentamicin; TOBRA, tobramycin; SMX-TMP, co-trimoxazole (sulfamethoxazole-trimethoprim).

DISCUSSION

Comparison of SHSC and CANWARD trends in *Enterobacter* resistance identified by univariable tests:

- Susceptibility of SHSC *Enterobacter* isolates to ceftriaxone and ceftazidime remained stable across the study period, discordant with the decreased susceptibility of CANWARD *E. cloacae* isolates over time.
- A signal suggesting reduced susceptibility of SHSC *Enterobacter* isolates to piperacillin-tazobactam was detected (-1.0% sensitive/year, p=0.0566), discordant with the stable susceptibility of CANWARD *E. cloacae* isolates over time.
- Susceptibility of SHSC *Enterobacter* isolates to ertapenem remained stable across the study period, discordant with the decreased susceptibility of CANWARD *E. cloacae* isolates over time.
- Susceptibility of SHSC *Enterobacter* isolates to meropenem decreased across the study period (-0.1% sensitive/year, p=0.0023), concordant with the decreased susceptibility of CANWARD *E. cloacae* isolates over time.
- Susceptibility of SHSC *Enterobacter* isolates to ciprofloxacin, gentamicin, and tobramycin increased across the study period (+0.6% ciprofloxacin-sensitive/year, p=0.0252; +1.0% gentamicin-sensitive/year, p=0.0041; +1.0% tobramycin-sensitive/year, p=0.0029; respectively), discordant with the stable susceptibility of CANWARD *E. cloacae* isolates over time.
- A signal suggesting increased susceptibility of SHSC *Enterobacter* isolates to trimethoprim-sulfamethoxazole was detected (+0.7% sensitive/year, p=0.0562), discordant with the decreased susceptibility of CANWARD *E. cloacae* isolates over time.

Limitations:

- Retrospective single centre design limits generalizability to other institutions
- Findings from univariable tests may change with multivariable analyses
- CANWARD only reported susceptibility trends for a single species, *E. cloacae*

CONCLUSION

Decreased rates of meropenem susceptibility were found for CANWARD and SHSC *Enterobacter* isolates when univariate tests were applied. However, susceptibility trends for other antimicrobials differed between the SHSC and CANWARD datasets.

Although validation with multivariate analyses is warranted, our findings suggest that knowledge of institutional susceptibilities is important as differences from national trends may exist.

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DISCLOSURES

No author has any conflict of interest related to this study.

REFERENCES

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