Patterns of Antimicrobial Resistance Among *Proteus* Isolates at Sunnybrook Health Sciences Centre: a 14-year Retrospective Observational Study

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BACKGROUND

Proteus spp. are members of the *Enterobacteriaceae* family and are common uropathogens.

Wildtype strains of *P. mirabilis* are usually susceptible to β-lactam antibiotics; however, the number of strains producing extended-spectrum β-lactamases ("ESBLs") and AmpC enzymes is on the rise.

OBJECTIVE

To investigate the antimicrobial resistance patterns among clinical isolates of *Proteus spp*. collected at Sunnybrook Health Sciences Centre (SHSC) over a 14-year study period.

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 *Proteus* 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). Isolates grown from screening swabs, surveillance swabs, or other cultures sent for infection prevention and control (IPC) purposes were excluded.

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 *Proteus* 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), and ESBL producers.

Longitudinal trends in *Proteus* isolate susceptibility to ampicillin, cefazolin, ceftazidime, ceftriaxone, ciprofloxacin, gentamicin, meropenem, piperacillin-tazobactam, sulfamethoxazole-trimethoprim and tobramycin were characterized using linear regression at a significance level of 0.05.

RESULTS

Table 1. Characteristics of 1993 Proteus isolates collected from inpatients at SHSC between October 2002 and September 2016.

	n (%)
Patient Sex	
Male	939 (47%)
Female	1054 (53%)
Source	
Urine	1483 (74%)
Blood	146 (7%)
Respiratory	108 (5%)
Other	256 (13%)
Location	
Emergency Department	724 (36%)
Ward	937 (47%)
Level 2 ICU	56 (3%)
Level 3 ICU	276 (14%)
Type of infection	
Community-acquired	1002 (50%)
Hospital-acquired	991 (50%)
Proteus spp.	
Proteus mirabilis	1850 (93%)
Proteus vulgaris	104 (5%)
Proteus penneri	39 (2%)
ESBL producer	10 (<1%)
Resistance	
ARO	1395 (70%)
MDRO	153 (8%)
XDRO	13 (<1%)

Table 2. Linear regression of the trends in susceptibility of *P. mirabilis* clinical isolates *to* selected β-lactam antimicrobials over the 14-year study period at SHSC.

Antimicrobial agent	Trend in % of isolates susceptible per year	*P-value*
Ampicillin	-0.2%	0.535
Cefazolin	-0.2%	0.319
Ceftazidime	-0.3%	**0.087***
Ceftriaxone	0.04%	0.808
Piperacillin-tazobactam	-0.3%	**<0.001**
Meropenem	-0.7%	0.438

Table 3. Linear regression of the trends in susceptibility of *P. mirabilis* clinical isolates to selected non-β-lactam antimicrobials over the 14-year study period at SHSC.

Antimicrobial agent	Trend in % of isolates susceptible per year	*P-value*
Ciprofloxacin	0.2%	0.412
Gentamicin	0.04%	0.882
Sulfamethoxazole-trimethoprim	-0.1%	0.622
Tobramycin	-0.2%	0.608

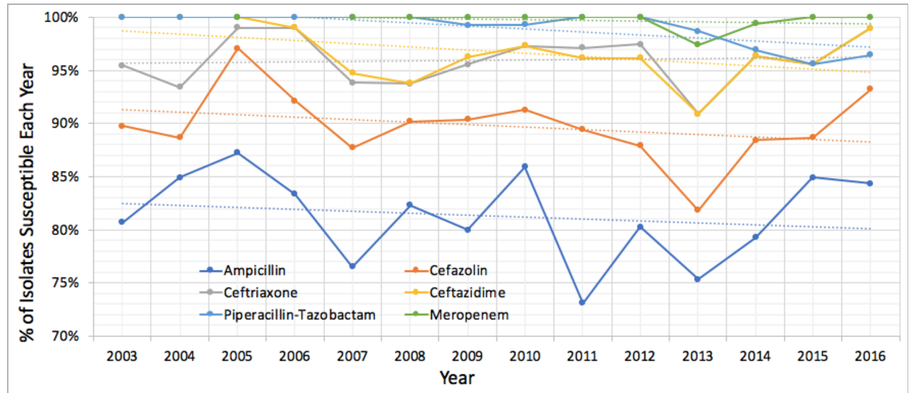

Figure 1. Susceptibility of *Proteus* isolates to ß-lactam antibiotics each year from October 2002 to September 2016.

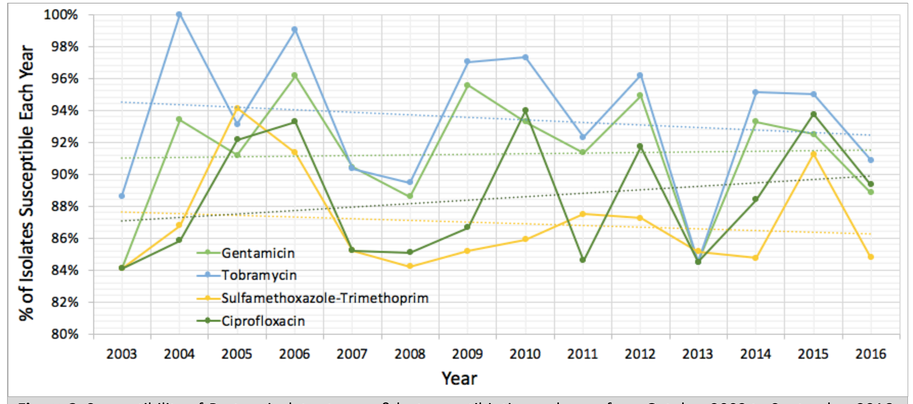

Figure 2. Susceptibility of *Proteus* isolates to non-ß-lactam antibiotics each year from October 2002 to September 2016.

DISCUSSION

A total of 1,993 unique *Proteus* isolates were identified over the 14-year study period. Most isolates exhibited resistance to ≥1 antibiotic agent (70% AROs) but few were classified as MDRO (8%). Prevalence of XDRO and ESBL producers was <1%.

Susceptibility of *P. mirabilis* to ampicillin, cefazolin, ceftriaxone, ciprofloxacin, gentamicin, meropenem, sulfamethoxazole-trimethoprim and tobramycin remained stable across the study period.

Although the proportion of isolates susceptible to piperacillin-tazobactam decreased over time (-0.3% susceptible per year; p<0.001) and a signal suggesting decreasing rates of ceftazidime susceptibility was detected (-0.3% susceptible per year; p=0.087), the overall sensitivity to piperacillin-tazobactam (~99%) and ceftazidime (~97%) remained high.

In the 14-year study period, approximately 20% of *P. mirabilis* isolates were resistant to ampicillin, suggesting that ampicillin may not be appropriate as an empiric treatment option for *P. mirabilis* infections at SHSC.

Strengths: First study examining local trends of antimicrobial susceptibility for *P. mirabilis* isolates over an extended period.

Limitations: Retrospective single centre design limits generalizability to other institutions; trends for *P. vulgaris* and *P. penneri* could not be reliably determined due to the low number of clinical isolates collected each year.

CONCLUSION

Antimicrobial resistance patterns of *P. mirabilis* at SHSC remained largely unchanged over the 14-year period assessed. All antimicrobials tested, with the exception of ampicillin, remain appropriate empiric treatment options against *P. mirabilis.*

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DISCLOSURES

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