Antimicrobial Resistance in Invasive Pneumococcal Disease in Southern Ontario, 2014-2023

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OBJECTIVES

- To describe trends in antimicrobial resistance in invasive pneumococcal disease (IPD) in south-central Ontario from 2014 to 2023.
- To determine whether non-susceptibility to fluoroquinolones and third generation cephalosporins are associated with particular patient characteristics.
- To describe the serotype (ST) distribution among isolates resistant/non-susceptible to macrolides, respiratory fluoroquinolones, and third generation cephalosporins.

METHODS

Since 1995, TIBDN has performed population-based surveillance for IPD in Metropolitan Toronto and Peel Region (population 4.6 million in 2023). IPD is defined as illness associated with a sterile site culture yielding *S. pneumoniae*. Clinical and demographic information is collected by chart review and patient/physician interview.

Isolates are submitted to a central laboratory for serotyping and antimicrobial susceptibility testing. CLSI breakpoints are used to define resistance and non-susceptibility. Multidrug resistance (MDR) is defined as resistance to ≥3 antibiotic classes (using meningeal breakpoints for penicillin and ceftriaxone). Antibiotic classes are defined as: β-lactams (penicillin, ceftriaxone), fluoroquinolones (levofloxacin, moxifloxacin), macrolides (erythromycin, clarithromycin), tetracyclines (tetracycline, doxycycline), trimethoprim–sulfamethoxazole, lincosamides (clindamycin).

Serotypes were grouped according pneumococcal conjugate vaccine (PCV) composition (Table 1).

Table 1: Serotypes included into pneumococcal conjugate vaccines.

	Serotypes																										
PCV13	4	6B	9V	14	18C	19F	23F	1	5	7F	3	6A	19A														
PCV15	4	6B	9V	14	18C	19F	23F	1	5	7F	3	6A	19A	22F	33F												
PCV20	4	6B	9V	14	18C	19F	23F	1	5	7F	3	6A	19A	22F	33F	8	10A	11A	12F	15BC							
PCV21										7F	3	6A	19A	22F	33F	8	10A	11A	12F	15BC	9N	15A	16F	17F	20	23A	23B	24F	31	35B

RESULTS

From 2014 to 2023, 3447 episodes of invasive pneumococcal disease occurred. Antimicrobial susceptibility results were available for 3210 (93%), and serotype for 3163 (92%).

Trends in antimicrobial resistance (Table 2)

- Resistance was most common to erythromycin (31%), tetracycline (16%), penicillin (meningeal breakpoints; 16%), clindamycin (12%) and TMP-SMX (11%); resistance to third generation cephalosporins and fluoroquinolones was <1%.
- From 2014 to 2023, resistance increased for oral penicillin (5.3% - 6.9%, *P*=.04), tetracycline (14.7% - 19.4%, *P*=.003), TMP-SMX (10% - 14.5%, *P*=0.04), but decreased for erythromycin (33.8% - 24.9%, *P*=.001) and ceftriaxone (3% - 0.3%, *P*=.002), and did not change for other antibiotics.
- Of 2892 isolates with susceptibility testing for all antibiotics, 397 (13.7%) were MDR, with no trend over time.

Non-susceptibility to fluoroquinolones and third generation cephalosporins (Table 3)

- Non-susceptibility to Ceftriaxone did not differ by age, diagnosis, or site of acquisition of infection, but was somewhat higher among immunocompromised patients (*P*=.09).
- Levofloxacin non-susceptibility was more common among residents of long term care homes (*P*<.001).

Table 2: Percent (%) resistances in isolates causing IPD, TIBDN, 2014-2023.

	2014	2015	2016	2017	2018	2019	2020	2021	2022	2023
Penicillin (oral)	5.3	3.7	4	2.1	4.3	2.3	4.8	7.4	5.3	6.9
Penicillin (meningeal)	16.1	17.1	19.9	14.5	13.2	14.6	17.2	16.9	14.9	13.9
Penicillin (non-meningeal)	0.3	0	0	0	0	0	0	0	0.6	0
Ceftriaxone (meningeal)	3	0.9	0.9	0.6	1	0.3	0.6	0.8	0.7	0.3
Ceftriaxone (non-meningeal)	0.3	0	0	0	0.5	0	0	0	0	0.3
Levofloxacin	1.1	0.6	2	0.3	0.5	0.8	0.6	0.9	0.8	0
Erythromycin	33.8	34.9	34	29.6	29.2	31.4	31.5	24.1	27.8	24.9
Trimethoprim-sulfamethoxazole	10	9.5	14.1	7.6	8.9	12.3	11.2	9.8	12.7	14.5
Clindamycin	14.4	11.3	14.1	10.6	11	12.9	13	11.8	12.4	8.8
Tetracycline	14.7	13.5	17.3	15.1	12.2	17.3	18	16.4	22	19.4
Multi-drug resistant	16.1	11.7	16.7	10.9	11.1	16.1	17.7	15.5	14.3	10.9

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RESULTS

Table 3: Patient characteristics and non-susceptibility to ceftriaxone and levofloxacin.

	Ceftriaxone Non-Susceptible (meningeal breakpoint)			Levofloxacin Non-Susceptible		
	Tested N	Non-S N (%)	*P*	Tested N	Non-S N (%)	*P*
Overall	3133	151 (4.8%)		3088	27 (0.9%)	
Age group						
<15 years	396	17 (4.3%)	0.84	384	1 (0.3%)	0.10
15-64 years	1402	67 (4.8%)		1381	9 (0.7%)	
≥65 years	1335	67 (5.0%)		1323	17 (1.3%)	
Diagnostic category						
Bacteremic pneumonia	1939	93 (4.8%)	0.77	1919	16 (0.8%)	0.39
Primary bacteremia	698	33 (4.7%)		693	5 (0.7%)	
Meningitis	207	8 (3.9%)		198	1 (0.5%)	
Other	289	17 (5.9%)		278	5 (1.8%)	
Source of infection						
Community	2719	127 (4.7%)	0.18	2677	19 (0.7%)	<.0001
Long term care-acquired	112	7 (6.3%)		111	7 (6.3%)	
Hospital-acquired	124	10 (8.1%)		122	1 (0.8%)	
Underlying chronic conditions						
None	1021	39 (3.8%)	0.09	1001	7 (0.7%)	0.65
≥ 1 chronic condition, but not immunocompromised	1015	50 (4.9%)		999	10 (1.0%)	
Immunocompromised	919	55 (6.0%)		910	10 (1.1%)	

Serotype distribution (Figures 2 & 3)

- The 145 isolates non-susceptible to ceftriaxone (meningeal breakpoints) included 18 STs.
  - The most common serotypes were: 35B (33%), 19A (23%) and 19F (10%).
  - 81 (56%) of isolates were of STs included in PCV20, and 104 (72%) of STs in PCV21.
- The 24 isolates non-susceptible to levofloxacin included 16 STs.
  - 11 isolates were of STs included in PCV20, 14 of STs included in PCV21.
- The 628 isolates resistant to erythromycin included 45 STs.
  - The most common were 19A (20%), 22F (19%), 23A (7%), 35B (6%).
- The 396 isolates that were MDR included 41 STs.
  - The most common were: 23A (16%), 19A (15%), 15A (9%), 3 (8%), 15BC (5%).

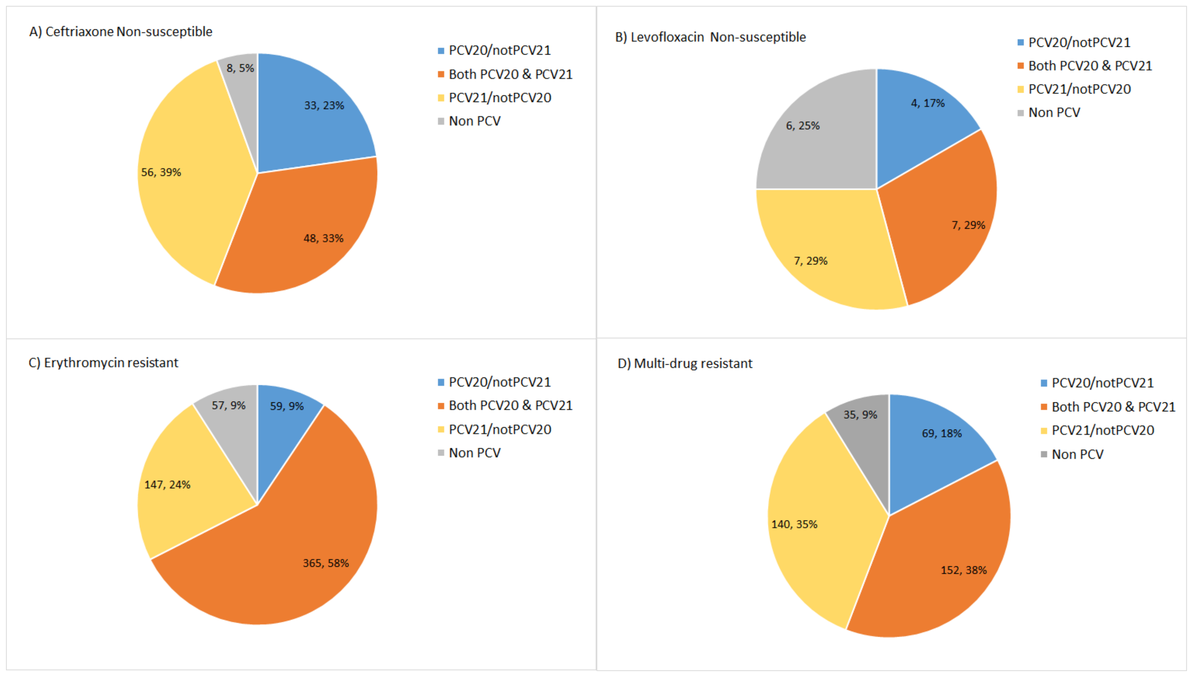

Figure 2: Distribution of vaccine-covered ST groups of isolates non-susceptible to ceftriaxone (A), levofloxacin (B), and resistant to erythromycin (C), and MDR isolates (D).

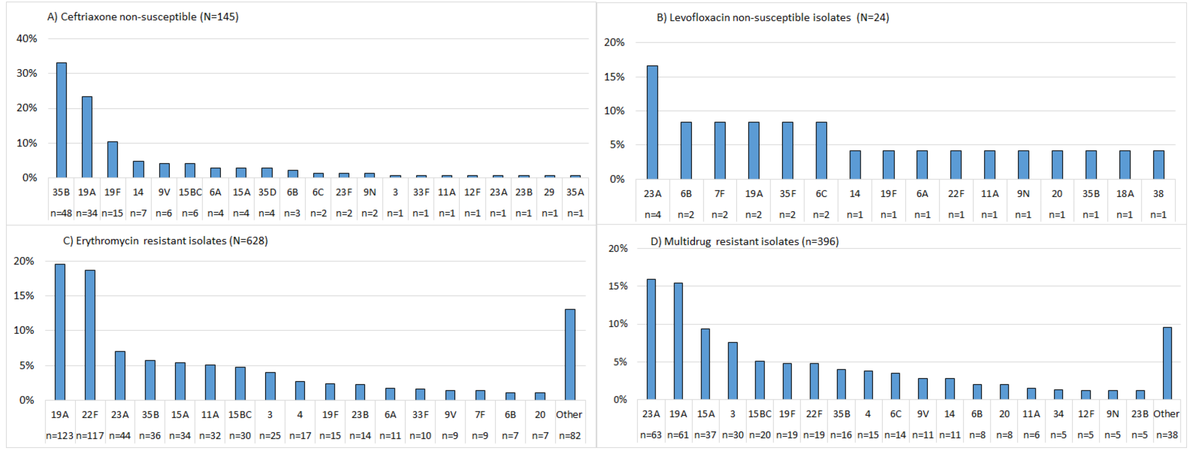

Figure 3: Serotype distribution of non-susceptible and resistant isolates.

CONCLUSION

- Antibiotic resistance among pneumococcal isolates causing IPD is generally stable, and these isolates remain susceptible to the most important antibiotic classes. Fluoroquinolone resistance is emerging in long term care.