Serotype-specific trends in population based surveillance for invasive and respiratory pneumococcal disease in adults, Toronto, 2000-2010

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Abstract

OBJECTIVES: TIBDN has performed population-based surveillance for invasive pneumococcal disease (IPD) in residents of Toronto/Peel (pop 4M) since 1995. From 2002, respiratory tract isolates have been collected and the population area expanded. PCV7 was licensed for children in Canada in 2001 and publicly-funded routine vaccination begun in January 2005.
METHODS: Serotyping and broth microdilution susceptibility testing to CLSI standards is performed on one isolate per IPD/respiratory case. Clinical data are collected from patient/physician interview and chart review.
RESULTS: From 2000 to 2010, 7993 adult (≥15 years) cases of respiratory disease (RPD) and invasive pneumococcal disease (IPD) were identified. Older adults (≥65 years) accounted for 48% of IPD (1856/3895) and 46% (1873/4098) of RPD. The rate in older adults decreased from 34 to 22/100000/y from 2002 to 2005, then increased to 26/100000/year in 2010. The rate of IPD stayed constant for adults under 65 years (5.3/100000/year in 2002 and 4.8/100000/year in 2010). From 2002 to 2010, the rate of IPD due to PCV13/nonPCV7 serotypes increased from 1.0 to 2.1/100000/year in adults <65 years and from 5.3 to 11.8/100000/year for those ≥65 years. Non-PCV13 (NPCV13) serotype disease increased from 1.2 to 2.1/100000/year in adults <65 years and from 9.9 to 11.2/100000/year in those ≥65 years. From 2002 to 2010, the proportion of disease due to PCV7 serotypes decreased from 57% to 10% for IPD and from 45% to 16% for RPD. The proportion of isolates from serotypes not in PCV7 but in PCV13 increased from 17% to 49% in IPD and 19% to 25% in RPD. The serotype distribution of IPD differs from RPD: 19F, 11A, and 23F are more likely isolated from RPD; 22F, 19A, 9V, 14 and 7F are more likely isolated from IPD. Serotype distribution also differs for nursing-home acquired (NH) and nosocomial (noso) cases. From 2005 to 2010, serotypes 19A/F, 6A, and 14 were more common in NH IPD and serotypes 11A, 34 and 17F were more common in NH RPD compared to community disease in adults ≥65years. Serotypes 35B and 6A/B are more common in noso IPD and 19F is more common in noso RPD. Isolates from noso/NH cases were also more likely antibiotic resistant (40% NH/noso IPD resistance to at least one class vs 29% for community cases; 42% vs 36% RPD isolates).
CONCLUSIONS: Since introduction of routine pediatric PCV7, the incidence of adult IPD due to PCV7 serotypes has decreased while that of PCV13 and NPCV isolates has increased. In 2010, serotypes in PCV7 comprised 10% of IPD and 16% of RPD isolates; serotypes in PCV13 comprised 59% of IPD and 41% of RPD. Serotype distribution differs for IPD and RPD and for nursing-home acquired and nosocomial cases.

Methods

From 1995 to 2010, population based surveillance for invasive pneumococcal disease was conducted in metropolitan Toronto and Peel region (popn ~4M). From 2002 to 2010, all respiratory site isolates from hospital laboratories were also collected. Serotype is determined using latex pneumococcal antisera (Statens Serum Institute, Denmark) and Quellung reaction. Population data was obtained from Statistics Canada. Demographic and clinical data were collected from review of health records and interviews with patients and attending physicians.

Results

From 2000 to 2010, 3895 cases of IPD and 4098 respiratory isolates of *S. pneumoniae* were identified in adults. Older adults (≥65 years) comprised 48% of IPD cases and 46% of respiratory isolates. 3677 (94%) isolates from IPD cases (3424 from blood, 66 from CSF, 69 from pleural fluid, 25 from synovial fluid, 22 from abscesses and 71 from other sterile sites), and 3570 (87%) of respiratory isolates (2816 sputum, 747 BAL, 7 other) were available for serotyping and antimicrobial susceptibility testing.

In 2009/10, serotypes 3, 7F and 19A were the most common serotypes causing adult IPD. Serotypes 3, 19A and 19F were most commonly identified in adult respiratory isolates. The most common non-conjugate vaccine serotypes were 11A in respiratory isolates and 22F in IPD.

Table 2: Serotype distribution by year and site for adult IPD and respiratory pneumococcal isolates, TIBDN, 2000-2010.

Serotype	Site	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010
PCV13 (%) PCV10 (%) PCV7 (%) 4	Sterile	10.6	11.3	7.3	5.2	8.0	6.7	8.0	4.9	6.6	4.7	0.8
	Respiratory			2.1	1.5	1.6	1.2	1.2	1.7	1.5	1.5	0.8
6B	Sterile	9.9	9.4	5.8	9.2	5.8	5.0	5.3	3.5	2.7	2.0	1.8
	Respiratory			9.9	7.4	4.7	4.1	5.2	3.1	1.9	2.7	2.5
9V	Sterile	5.5	4.7	6.6	6.0	4.8	5.8	6.1	5.4	3.9	1.7	2.0
	Respiratory			2.1	3.1	3.8	1.7	1.9	1.5	1.5	1.0	1.0
14	Sterile	16.06	19.53	15.6	14.9	10.3	5.6	5.8	6.0	4.1	3.2	1.8
	Respiratory			3.7	3.4	3.4	2.9	1.4	1.0	1.5	0.6	0.8
18C	Sterile	2.6	4.7	3.6	4.0	2.2	4.2	3.1	2.2	0.5	1.7	1.0
	Respiratory			2.1	0.9	3.4	2.7	2.8	2.2	1.5	0.6	1.8
19F	Sterile	4.4	5.1	7.3	5.2	6.4	4.2	3.6	3.3	2.9	2.7	2.5
	Respiratory			13.6	12.6	12.4	14.0	12.1	8.5	8.2	6.4	7.6
23F	Sterile	9.1	7.0	10.6	3.6	4.8	2.8	2.5	3.0	1.0	1.0	0.8
	Respiratory			11.6	8.6	5.6	4.6	5.5	2.9	2.2	1.9	1.3
PCV13 (%) PCV10 (%) 1	Sterile	0.73	0.39	0.0	0.0	0.3	0.6	0.3	0.5	0.2	0.0	0.5
	Respiratory			0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
5	Sterile	0.4	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
	Respiratory			0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
7F	Sterile	4.7	2.0	2.6	4.4	3.5	5.3	3.3	5.4	11.0	13.7	16.5
	Respiratory			0.8	0.3	0.7	0.5	0.7	0.7	0.7	1.5	2.8
PCV13 (%) 3	Sterile	9.9	5.9	10.6	9.6	10.6	10.8	10.5	10.6	10.0	11.0	8.7
	Respiratory			8.3	12.3	12.4	14.3	13.3	12.3	10.6	9.8	12.5
6A	Sterile	3.7	3.9	2.2	5.6	5.5	6.1	6.1	8.9	4.4	5.9	4.2
	Respiratory			7.0	6.8	7.5	5.6	7.1	8.7	5.8	6.7	3.8
19A	Sterile	1.1	0.4	1.8	2.4	3.2	3.6	6.1	8.4	11.7	13.7	19.0
	Respiratory			2.5	2.2	1.1	2.4	3.8	8.2	6.8	9.2	5.9
NPCV13	Sterile	21.5	25.8	26.2	29.7	34.6	39.4	39.3	37.9	41.1	38.7	40.7
	Respiratory			36.4	41.1	43.3	46.0	45.0	49.3	58.0	58.2	59.3

From 2002 to 2010, the rate of IPD due to serotypes included in PCV13, but not PCV7, increased from 5.3 to 11.8/100000/year in adults (≥65 years) and from 1.0 to 2.1/100000/year for those 15 to 64 years. The rate of IPD in older adults (≥65 years) decreased from 34 to 22/100000/year from 2002 to 2005 and then increased to 26/100000/year in 2010. The rate of IPD stayed constant for adults aged 15 to 64 years (5.3 in 2002 and 4.8/100000/year in 2010).

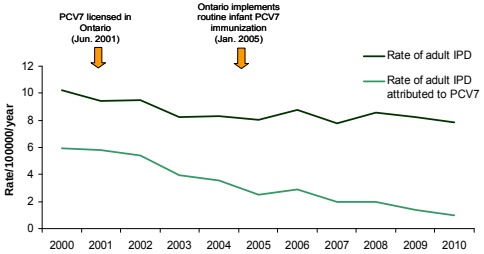

Figure 1: Rate of adult (≥15 years) IPD and adult IPD associated with serotypes covered in the PCV7 vaccine in the Toronto/Peel region, 2000 - 2010.

Results (con't)

From 2002/03 to 2009/10, the proportion of disease attributed to PCV7 serotypes decreased in both IPD and respiratory isolates. The proportion of isolates from serotypes not in PCV7 but in PCV13 increased from 19% to 47% in IPD and 20% to 26% in respiratory isolates.

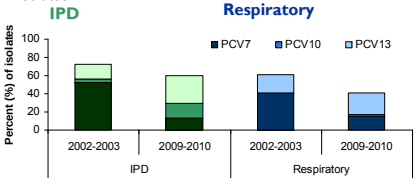

Figure 2: Percent of adult IPD and respiratory isolates associated with serotypes covered by the PCV7, PCV10, and PCV13 vaccines in the Toronto/Peel region, 2002/2003 and 2009/2010.

From 2005 to 2010, serotypes 19F, 11A, 23F and 35B were significantly ($\alpha \leq 0.05$) more likely to be isolated from respiratory isolates than isolates from IPD and serotypes 22F, 19A, 7F, 4, and 9V were more likely isolated from IPD [Fisher's exact].

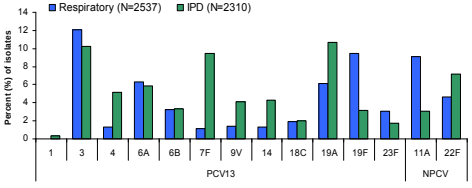

Figure 3: Percent of adult IPD and respiratory isolates for serotypes included in the PCV13 vaccine and common non-conjugate vaccine (NPCV) serotypes representing >5% of isolates in the Toronto/Peel region, 2005-2010 (Note: no isolates of ST 5 were identified).

Serotypes 19A, 19F, 6A, and 14 were more common in nursing-home associated IPD and serotypes 11A, 34 and 17F were more common in nursing-home associated respiratory isolates as compared to community disease in adults ≥ 65years. As compared to community disease/isolates, serotypes 35B, 6A and 6B were more common in nosocomial IPD, and 19F was more common in nosocomial respiratory isolates than in community disease (Figure 4).

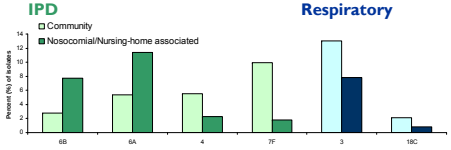

Figure 4: Percent of isolates of serotypes included in the PCV13 vaccine with a significant ($\alpha \leq 0.05$) difference between community and nosocomial/nursing-home associated adult IPD cases and respiratory isolates, 2005 to 2010 [Fisher's exact].

Results (con't)

Isolates from nosocomial/nursing-home associated cases were more likely antibiotic resistant than community associated cases (40% resistance to at least one class in NH/noso IPD cases vs 29% for community; 42% vs 36% respiratory isolates, respectively).

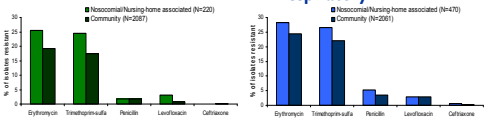

Figure 5: Percent (%) of isolates resistant to erythromycin, benzylpenicillin, trimethoprim-sulfamethoxazole, ceftriaxone, and levofloxacin from community and nosocomial/nursing-home associated adult IPD and respiratory isolates from 2005 to 2010. Broth microdilution antimicrobial susceptibility testing was interpreted to EUCAST standards (non-mening/non-pneu resistance breakpoints: penicillin>2mg/L).

Nosocomial/nursing-home associated serotypes (6A, 6B) had high levels of resistance to compared to serotypes associated with community disease (3, 4, 7F).

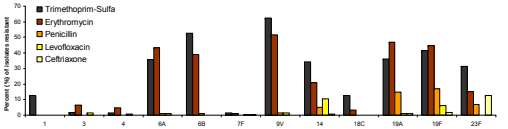

Figure 6: Percent of isolates from adult IPD/respiratory isolates resistant to erythromycin, benzylpenicillin, trimethoprim-sulfa, ceftriaxone, and levofloxacin by serotypes for serotypes included in the PCV13 vaccine***, 2005 to 2010 (non-mening/non-pneu resistance breakpoints: penicillin >2mg/L)***no isolates of serotype 5.

Conclusion

- Since the introduction of routine pediatric PCV7 vaccine, the incidence of adult IPD due to PCV7 serotypes has decreased while that due to PCV13/NonPCV7 and non-conjugate vaccine serotypes has increased.
- In 2010, serotypes included in PCV7 comprised 17% of IPD and 15% of respiratory isolates; serotypes included in PCV13 comprised 61% of IPD and 41% of respiratory isolates.
- Serotype distribution differs between sterile site and respiratory isolates, and between community, nursing home and hospital acquired disease.
- Serotypes associated with isolates acquired in nursing homes and hospitals (6A, 6B, 19F, 17F, and 34) have higher levels of antimicrobial resistance than serotypes associated with community-acquired disease.

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