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INVASIVE PNEUMOCOCCAL DISEASE TRENDS IN THOSE OLDER THAN 65 IN TORONTO, CANADA (1995-2006)

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Abstract

Background: We examined trends in the occurrence of Invasive Pneumococcal Disease (IPD) from 1995-2006 in those aged greater than 65. We compared rates of IPD and examined trends in vaccine and non-vaccine serotypes, emerging serotypes and antibiotic resistance.
Methods: Population based surveillance for invasive pneumococcal disease (IPD) in Toronto and Peel region (pop=3.9M) has been on-going since 1995. All invasive isolates are sent to a single reference laboratory where they are characterized. Clinical data was collected from patients and their physicians using a standardized collection form. We compared the five year period prior to the introduction of the PCV-7 vaccine (1997-2001) to the five year period post (2002-2006).
Results: 1800 episodes were identified. Among those age 65-74, the average incidence of IPD increased from 23.5/100,000/y to 28.2/100,000/y, while the incidence of IPD decreased from 58.3 to 42.9/100,000/y in those >=75. The proportion of nursing home acquired infection decreased from 18.4% to 11.8% (p<0.001). PCV-7 and PPV23 strains decreased from 54.6% and 86.8% of isolates to 41.0 and 80.1% respectively (p<0.001). Non-vaccine strains increased from 13.2% to 19.2% (p<0.001). Mortality declined from 36.6% to 31.1% (p<0.025). The population adjusted rates of mortality decreased for both ages 65-74 and >75 from an average of 7.1 to 5.6/100,000 and 22.9 to 16.5/100,000 respectively. There were no differences in the proportion of isolates that were high level resistant to penicillin, resistant to erythromycin, or resistant to levofloxacin between the two periods. Statistically significant increases in the relative frequency of serotypes (ST) 22F, 12F and 35 were seen concomitant with simultaneous decreases in ST 14, 19F, 4, and 20. There was no real increase in ST 19A disease.
Conclusions: Among those aged greater than 65, the incidence of IPD appears to be stable in those age 65-74 and decreasing among those aged >75. This decrease is primarily made up of PCV-7 and PPV23 ST with a concomitant increase in the rates of disease caused by non vaccine strains. Across both age categories mortality rates seem to be decreasing possibly due to a decrease in the proportion of cases arising in long term care facilities. There have been significant changes in the proportion of disease caused by various serotypes and we describe the emergence of disease caused by ST 35.

Introduction and Purpose

With the introduction of the pneumococcal conjugate vaccine in paediatric patients in 2001, there was a unique opportunity to study changes in the epidemiology of pneumococcal disease. Numerous such population based studies have been published recently.

With universal immunization provided to children in Ontario, Canada where our data was collected, we sought to analyze whether there were measurable changes, possibly related to herd immunity, in the rates of IPD in the population at large, focussing on those aged greater than 65. We also sought to characterize whether or not there were concomitant changes in the serotypes present in the community that were responsible for IPD.

Methods (see abstract)

The Toronto Invasive Bacterial Diseases Network (TIBDN) surveillance network includes all 25 licensed microbiology hospital-based laboratories that provide clinical care to area residents, and the two largest community-based laboratories serving physician offices and long term care facilities. All isolates of *S. pneumonaie* from sterile sites are sent to the central study laboratory for workup.

In the central study laboratory, all isolates are confirmed as *S. pneumoniae* by standard methodology, including confirmatory genotyping. Broth microdilution antimicrobial susceptibility testing is performed and interpreted according to the Clinical Laboratory Standards Institute (CLSI). Serotyping of all isolates is performed at the central study laboratory and the National Streptococcal Centre in Edmonton Alberta according to standard methodology.

Statistical comparisons were made using Chi-Square or the T-test as appropriate with a p-value of 0.05 representing statistical significance.

Results

Table 1 – Demographics

	1996-2001 (n=779)	2002-2006 (n=775)	P-Value
Average Age (y)	79.4	77.9	<0.001
Age 65-69 (%)	16.7	21.5	<0.008
Age 70-74 (%)	19.0	21.5	NA
Age >=75 (%)	64.3	56.9	NA
Male Gender (%)	44.3	50.1	<0.025
Nosocomial (%)	6.5	8.4	NS
Nursing Home (%)	18.4	11.8	<0.001
Received Any ABx in Past 3 months (%)	32.3	30.3	NS
Oral Abx Pre Hospital (%)	10.5	10.2	NS
ICU Admission (%)	26.4	27.7	NS
Mechanical Vent. (%)	19.1	18.9	NS
Mortality (%)	36.6	31.1	<0.026

Table 2 – Vaccine Serotypes

	1996-2001 (n=779)	2002-2006 (n=775)	P-Value
Conjugate Vaccine Serotype (%)	54.6	41.0	<0.001
Polysaccharide Vaccine Serotype (%)	86.8	80.1	<0.001
Non Vaccine (%)	13.2	19.2	<0.001

PCV7: 4,6B, 9V, 14, 18C, 19F, 23F
Polysaccharide: 1 2 3 4 5 6B 7F 8 9N 9V 10A 11A 12F 14 15B 17F 18C 19F 19A 20 22F 23F 33F

Table 3 – Top Serotypes Pre/Post Vaccine

Serotype	1996-2001 (n=667)	%
14	121	18.1
3	72	10.8
6B	63	9.4
23F	55	8.2
19F	39	5.8
22F	39	5.8
6A	38	5.7
4	37	5.5
9V	31	4.6
19A	26	3.9
18C	18	2.7
7F	16	2.4
9N	14	2.1
11A	13	1.9
38	9	1.3
23A	8	1.2
20	6	0.9
12F	5	0.7
16F	5	0.7
33F	5	0.7

Serotype	2002-2006 (n=748)	%
3	93	12.4
14	86	11.5
22F	65	8.7
6B	56	7.5
6A	46	6.1
23F	43	5.7
9V	35	4.7
19F	26	3.5
19A	26	3.5
4	23	3.1
11A	23	3.1
7F	22	2.9
18C	21	2.8
9N	19	2.5
12F	18	2.4
23A	14	1.9
35B	14	1.9
38	12	1.6
16F	8	1.1
10A	8	1.1

Table 4 – Significant Changes Post Vaccine

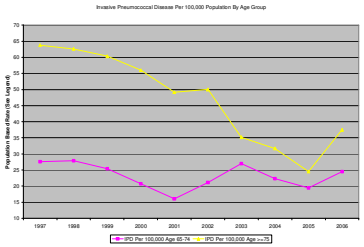
Serotype	1996-2001 (n=667)	%	2002-2006 (n=748)	%	P-Value
22F	39	5.8	65	8.7	0.051
12F	5	0.7	18	2.4	0.02
35B	1	0.1	14	1.9	<0.007
35F	0	0	7	0.9	0.02

Serotype	1996-2001 (n=667)	%	2002-2006 (n=748)	%	P-Value
14	121	18.1	86	11.5	0.0005
19F	39	5.8	26	3.5	0.045
4	37	5.5	23	3.1	0.03
20	6	0.9	0	0	0.021

Table 5 – Antibiotic Resistance

	1996-2001 (n=779)	2002-2006 (n=775)	P-Value
High Level Penicillin Resistance (%)	0.9	0.9	NS
Erythromycin Resistance (%)	9.4	12.7	NS
TMP-SMX Resistance (%)	18.1	15.9	NS
Levofloxacin Resistance (%)	2.1	1.5	NS
Moxifloxacin Resistance (%)	1	0.3	NS
Resistance to 2 or more of above (%)	9.8	11.6	NS

Figure 1 – Population Rate of IPD per 100,000



Figures 2/3 – Population Rates of Disease by vaccine type

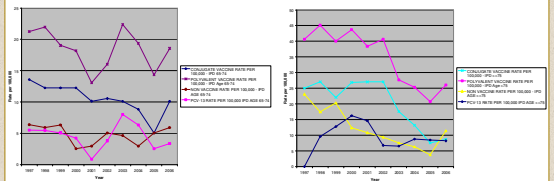
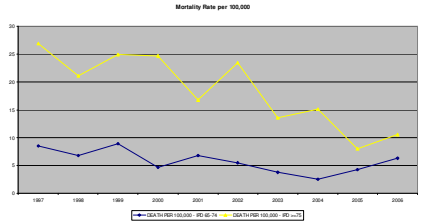


Figure 4 – Mortality



Conclusions

- The incidence of IPD in the elderly has been stable or decreasing over the 11 year interval
- With the introduction of the conjugate vaccine, there was been a statistically significant decrease in the percentage of serotypes contained in the vaccine, with a concomitant increase in non-vaccine serotypes
- Serotype 35 has emerged in our population since the introduction of the vaccine.
- There has been a decline in mortality rates from IPD in the elderly. This is most pronounced in patients over 65 and is not related to detectible changes in antibiotic resistance. However, IPD still has a significant >30% mortality rate overall in our population