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Serotype Epidemiology of Invasive Pneumococcal Disease in Swiss Adults

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Introduction and Purpose

- Vaccinal prevention of invasive pneumococcal disease (IPD) in adults is much less advanced than in infants.
- In some countries, adults have profited from indirect protection due to the use of the heptavalent pneumococcal conjugate vaccine (PCV7) in infants ('herd immunity').
- PCV7 was added to the infant vaccine schedule in Switzerland in 2005 and was replaced by the 13-valent conjugate vaccine (PCV13) in 2011
- **Objectives of the study**

  i. Characterization of adult IPD patients (age ≥ 16 years) and case fatality rates (Table 1)

  ii. Influence of PCV7 vaccination in infants on the serotype distribution of IPD in adults (2007-2010) (Table 2)

  iii. Association of serotypes/serogroups with patient's age and having comorbidities (Table 3)

Methods

- *S. pneumoniae* isolates were typified at the Swiss National Reference Centre for *S. pneumoniae* (NRCP) and data about clinical manifestations (pneumonia, sepsis, arthritis and meningitis), comorbidity and reported fatality were obtained from the Swiss Federal Office of Public Health (FOPH).
- For the logistic regression analyses of objective i), Likelihood Ratio (LR) test was used for testing significance.
- An exact *P* value was used for the Cochran-Armitage χ^2 test of trend, to examine IPD of individual *S. pneumoniae* serotypes/serogroups in Switzerland (2007-2010) (Table 2). $P<0.05$ is considered being significant.
- For the logistic regression analyses of objective iii), all other serotypes/serogroups served as defined reference groups (Table 3). Crude OR of LR test are shown (CI <1.0 or >1.0 indicate significance (i.e. $P<0.05$)).

Results

1. Adult patient characteristics with IPD in Switzerland (2007-2010)

- 4098 isolates of IPD patients (2007-2010)
- 828 (20.2%) were excluded (patients with missing clinical information or aged <16 years)
- 3270 remaining IPD patients (≥16 years) with mean age of 65.2 years (SD 17.5)
- The annual average number of adult patients with IPD was 818 (SD 107).
- The overall case fatality rate within 90 days after disease onset was 11% (Table 1).
- Older age, having ≥ 1 comorbidities, number and type of manifestation were significantly associated with death (Table 1)
- There was no significant change in the case fatality rate within 2007-2010.

Table 1: Adult patient characteristics and univariate logistic regression analysis of IPD related fatality

	Total N	Case fatality (%)	OR (95% CI)	*P*
n	3270	11.0		
Age				
16-49 years	663	4.2	1.0	Baseline
50-64 years	737	9.0	2.2 (1.4-3.5)	.001
65-69 years	327	11.0	2.8 (1.7-4.7)	<.001
70-80 years	853	12.2	3.1 (2.0-4.8)	<.001
>80 years	690	18.3	5.1 (3.3-7.7)	<.001
Sex				
Male	1840	11.1	1.0	Baseline
Female	1430	10.9	1.0 (0.8-1.2)	.9
Number of Comorbidities per patient				
0[a]	1382	6.2	1.0	Baseline
1	1133	13.1	2.3 (1.7-3.0)	<.001
2	560	15.2	2.7 (2.0-3.8)	<.001
3	162	19.8	3.8 (2.4-5.9)	<.001
4	28	28.6	6.1 (2.6-14.3)	<.001
5	5	40.0	10.2 (1.7-61.7)	.01
Number of Manifestations per patient				
0	394	4.3	1.0	Baseline
1	2082	10.4	2.6 (1.5-4.3)	<.001
2	775	15.7	4.1 (2.5-7.0)	<.001
3	19	26.3	7.9 (2.6-24.5)	<.001
Type of Manifestations				
Pneumonia	2306	10.3	1.0	Baseline
Bacteremia w/o focus[b]	1160	17.9	2.9 (2.3-3.6)	<.001
Meningitis[c]	170	15.3	1.8 (1.1-2.8)	.02

[a] This also includes patients for whom the number of comorbidities is unknown
[b] This also includes patients with additional arthritis
[c] This also includes patients with additional pneumonia and/or arthritis

2. Changing epidemiology due to the introduction of PCV7 vaccination in infants

- There was an overall rise in the number of different serotypes/serogroups (total of 37 in 2007; 44 in 2010) with 20 occurring at a frequency of >1%.
- Overall annual prevalence of the 7 serotypes included in PCV7 decreased (Table 2; $P<0.001$) but not all PCV7 serotypes to the same extend: serotype 14 and 9V most significantly ($P<0.001$) but 18C and 4 not significantly.
- Overall, non-PCV13 serotypes and non-PCV7 serotypes included in PCV13 significantly increased ($P<0.001$); the increase of non-PCV7 serotypes was mainly due to serotype 19A .
- In 2010, the highest prevalences were received for the non-PCV7 serotypes 3 (13.0%) and 7F (11.1%) but no significant increasing trend.

3. Association of the serotype epidemiology with the patient characteristics

- IPD of patients aged ≥ 65 years were more likely to be caused by serotypes 14, 6A and 23F and less likely by serotypes 1, 4 , 7F and 8 compared to all others (Table 3).
- In addition, Serotype 3 was more often in people >50 years ($p<0.05$) (not shown).
- IPD of patients with comorbidities were less likely for 1, 7F and 8 but more likely for 6B, 19F and 35 (Table 3)
- Among the patients with 3 manifestations, the serotypes 3, 7F and 14 accounted for >50% of IPD cases (not shown). However: Multi-variate logistic regression analyses adjusted for age, number of comorbidities and manifestations indicated identical results (Preliminary results; not shown)

Table 2: Proportion of serotypes/serogroups among adult IPD patients, Switzerland 2007-10

Serotype/ Serogroup[a]	Adults with IPD, N (%) 2007 (n=723)	2008 (n=861)	2009 (n=948)	2010 (n=738)	*P*[b]
14	103 (14.2)	86 (10.0)	79 (8.3)	50 (6.8)	<.001
18C	23 (3.2)	17 (2.0)	16 (1.7)	21 (2.8)	.6
19F	32 (4.4)	32 (3.7)	26 (2.7)	21 (2.8)	.05
23F	44 (6.1)	56 (6.5)	51 (5.4)	20 (2.7)	.002
4	53 (7.3)	67 (7.8)	72 (7.6)	44 (6.0)	.3
6B	25 (3.5)	18 (2.1)	19 (2.0)	15 (2.0)	.08
9V	61 (8.4)	55 (6.4)	45 (4.7)	23 (3.1)	<.001
1	24 (3.3)	30 (3.5)	38 (4.0)	34 (4.6)	.2
19A	27 (3.7)	35 (4.1)	57 (6.0)	67 (9.1)	<.001
3	86 (11.9)	113 (13.1)	138 (14.6)	96 (13.0)	.4
7F	70 (9.7)	71 (8.2)	95 (10.0)	82 (11.1)	.2
6A	29 (4.0)	28 (3.3)	36 (3.8)	24 (3.3)	.6
8	22 (3.0)	46 (5.3)	46 (4.9)	37 (5.0)	.1
9	17 (2.4)	37 (4.3)	25 (2.6)	26 (3.5)	.6
22	24 (3.3)	28 (3.3)	48 (5.1)	51 (6.9)	.0002
15	8 (1.1)	16 (1.9)	16 (1.7)	26 (3.5)	.003
11	9 (1.2)	25 (2.9)	20 (2.1)	10 (1.4)	.8
23	5 (0.7)	13 (1.5)	17 (1.8)	13 (1.8)	.08
35	6 (0.8)	8 (0.9)	13 (1.4)	14 (1.9)	.05
20	5 (0.7)	12 (1.4)	12 (1.3)	7 (0.9)	.7
others	50 (6.9)	68 (7.9)	79 (8.3)	58 (7.9)	.5

[a] Serotypes/Serogroups occurring with a frequency of <1% are grouped as 'others'. PCV7 serotypes are indicated in bold and non-PCV7 additional serotypes included in PCV13 are indicated in italics.
[b] Exact *P* values for Cochran-Armitage χ^2 test

Table 3: Univariate logistic regression analyses of pneumococcal Serotype/Serogroups associated with age ≥65 years and having comorbidities, respectively

Serogroup/ Serotype[a]	Age ≥ 65 years (vs. <65) N (%)	OR (95% CI)[b]	Comorbidities (vs. no known comorbidity) N (%)	OR (95% CI)[b]
14	201 (63.2)	**1.3 (1.0-1.7)**	172 (54.3)	0.9 (0.7-1.1)
18C	40 (52.0)	0.8 (0.5-1.3)	45 (58.4)	1.0 (0.7-1.6)
19F	65 (58.6)	1.1 (0.7-1.6)	76 (68.5)	**1.6 (1.1-2.4)**
23F	121 (70.8)	**1.9 (1.3-2.6)**	104 (60.8)	1.1 (0.8-1.6)
4	110 (46.6)	**0.6 (0.5-0.8)**	129 (54.7)	0.9 (0.7-1.1)
6B	48 (62.3)	1.3 (0.8-2.0)	58 (75.3)	**2.3 (1.4-3.8)**
9V	111 (60.3)	1.2 (0.9-1.6)	114 (62.0)	1.2 (0.9-1.6)
1	42 (33.3)	**0.4 (0.3-0.5)**	46 (36.5)	**0.4 (0.3-0.6)**
19A	116 (62.4)	1.3 (0.9-1.7)	112 (60.2	1.1 (0.8-1.5)
3	266 (61.4)	1.2 (1.0-1.5)	260 (60.0)	1.1 (0.9-1.4)
7F	149 (46.9)	**0.6 (0.5-0.8)**	136 (42.7)	**0.5 (0.4-0.7)**
6A	79 (67.5)	**1.6 (1.1-2.3)**	72 (61.5)	1.2 (0.8-1.7)
8	71 (47.0)	**0.7 (0.5-0.9)**	67 (44.4)	**0.6 (0.4-0.8)**
9	67 (63.8)	1.3 (0.9-2.0)	68 (64.8)	1.4 (0.9-2.1)
22	92 (60.9)	1.2 (0.8-1.6)	91 (60.2)	1.1 (0.8-1.6)
15	45 (68.2)	1.6 (1.0-2.7)	40 (60.6)	1.1 (0.7-1.9)
11	40 (62.5)	1.3 (0.8-2.1)	43 (67.2)	1.5 (0.9-2.6)
23	29 (60.4)	1.1 (0.6-2.1)	32 (66.7)	1.5 (0.8-2.7)
35	21 (51.2)	0.8 (0.4-1.5)	31 (75.6)	**2.3 (1.1-4.7)**
20	21 (58.3)	1.1 (0.5-2.0)	26 (72.2)	1.9 (0.9-4.0)
others	136 (53.3)	0.8 (0.7-1.1)	166 (65.1)	**1.4 (1.1-1.8)**

[a] Serotypes/Serogroups occurring with a frequency of <1% are grouped as 'others'
[b] Significant ORs received by LR are indicated in bold (i.e. $P<0.05$)

Conclusions

- Introduction of PCV7 to the infant vaccination schedule resulted in a changing epidemiology in adults in 2007-2010.
- Some serotypes are associated with IPD in elderly patients and/or patients with comorbidities.
- The continuation of monitoring the serotype epidemiology of *Streptococcus pneumoniae* on national and international level remains crucial to build up appropriate prevention i.e. vaccination strategies for the future.

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