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Characteristics of invasive pneumococcal disease in immunocompromised adults after PCV7 implementation, Toronto, Canada, 2005-2012

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BACKGROUND: Persons who are immunocompromised (IC) are at significantly higher risk of invasive pneumococcal disease (IPD). Recently, 13-valent pneumococcal conjugate vaccine (PCV13) has been recommended for IC adults in the USA and Canada. We analyzed data from population-based surveillance and describe the characteristics and outcomes of IPD in IC adults in the post-PCV7 era.

METHODS: From 2005 to 2012, TIBDN performed population-based surveillance for IPD in Toronto, Canada. Demographic and medical data were collected by chart review and patient and physician interview. Serotyping was performed at a central laboratory. Immunocompromising conditions include: HIV, solid organ or bone marrow/stem cell transplant, systemic lupus erythematosus (SLE), asplenia, sickle cell disease, hematologic malignancy, hepatic cirrhosis, chronic renal failure, or chronic receipt of immunosuppressive medications.

RESULTS: From 2005 to 2012, 3249 IPD episodes were identified among adults (>15 yrs old). Clinical information was available for 3036 (93%) episodes and 972 (32%) had at least one immunocompromising condition or was receiving immunosuppressive medication(s) **(Table 1)**.

Median age of IC adults was 61.5 years (IQR; 48-73). 567 (58%) were male. 667 (69%) presented with bacteremic pneumonia, 225 (23%) with primary bacteremia, 41 (4%) with meningitis, 19 (2%) with empyema, and 20 (2%) with other diagnoses.

Serotype (ST) was available for 919/972 (95%). Overall, among IC adults, 20% (n=184) of IPD was due to PCV7 STs, 27% (n=247) due to PCV13/notPCV7 STs, 25% (n=229) due to PPV23/notPCV STs, and 28% (n=259) due to non-vaccine STs.

The most common STs (n≥30) were 19A (n=102), 22F (76), 3 (62), 7F (44), 6C (44), 4 (38), 23A (38), 6A (37), 9V (35), 11A (35), and 33A (30). Between 2005/2006 and 2011/2012, the proportion of PCV7 STs decreased from 32.8% to 4.7% (p<0.0001), PCV13/not PCV7 increased from 18.4% o 32.6% (p=0.0006), non-vaccine STs increased from 21.2% to 35.3% (p=0.001), and PPV23/notPCV did not change in frequency. ST distribution in 2011/2012 is shown **Figure 1**.

Table 1: Immunocompromising conditions among adults with IPD (n=972)

	N (%)
Chronic renal failure	134 (13.8)
Hepatic cirrhosis	134 (13.8)
HIV	110 (11.3)
Myeloma	101 (10.4)
Lymphoma	90 (9.3)
Leukemia	81 (8.3)
Organ/bone marrow transplant	85 (8.7)
Asplenia	53 (5.5)
SLE	43 (4.4)
Sickle cell disease	5 (0.5)
Immunosuppressive therapy [1]	249 (25.6)

1 Reasons for immunosuppressive therapy included: asthma (n=24), COPD (n=33), other chronic lung condition (n=18), rheumatological conditions (n=42), current chemotherapy or radiation for solid cancer (n=98), and other (n=28).

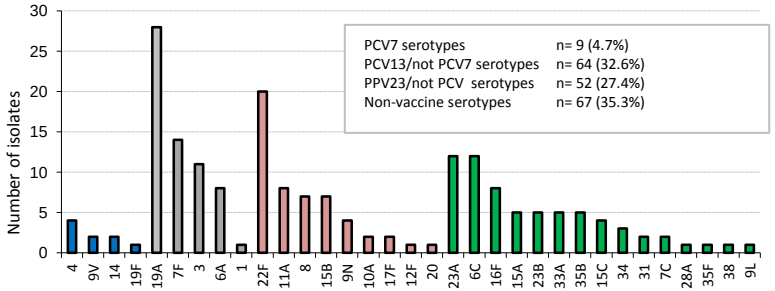

Figure 1: Distribution of serotypes in 2011/2012 (n=190)

RESULTS (continued): History of PPV23 vaccination was available for 724/919 (79%) IC adults. 289/724 (40%) were vaccinated more than 14 days prior to onset of their IPD episode. Overall, PPV23 vaccine efficacy (VE) was 12.5% (95% CI; - 21.4% to 37.0%) **(Figure 2).**

Among, IC adults, 886 (91%) required hospital admission, 316 (33%) required intensive care, and 195 (20%) died within 30 days of hospital admission.

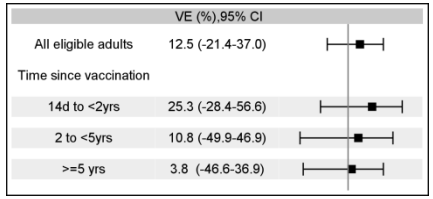

Figure 2: PPV23 VE by time since vaccination

In multivariable logistic regression, a statistically significant association was found between increased risk of death and older age, nursing home residence, primary bacteremia, underlying hepatic cirrhosis, cancer (solid organ), and illness due to serotype 3 **(Table 2)**. Patients with HIV infection were less likely to die.

Table 2: Factors associated with case fatality among IC adults with IPD

			Multivariate analysis		
	Total	N (%) died	Odds Ratio (95% CI)		p-value
Age (in decades)			1.22	(1.04, 1.42)	0.013
Year of study			1.02	(0.94, 1.12)	0.606
Gender, female (reference=male)	384	79 (20.6)	1.09	(0.74, 1.60)	0.672
Bacteremia without focus	213	55 (25.8)	1.56	(1.02, 2.40)	0.042
Nursing home resident	32	16 (50.0)	4.06	(1.76, 9.38)	0.001
IC conditions					
Chronic renal failure	128	32 (25.0)	1.91	(0.90, 4.03)	0.090
Hepatic cirrhosis	128	44 (34.4)	3.21	(1.43, 7.18)	0.005
HIV	104	4 (3.9)	0.19	(0.04, 0.90)	0.037
Myeloma	96	15 (15.6)	1.40	(0.56, 3.50)	0.478
Lymphoma	84	16 (19.1)	1.84	(0.75, 4.50)	0.180
Leukemia	73	10 (13.7)	1.50	(0.56, 4.06)	0.423
Organ/bone marrow transplant	84	8 (9.5)	0.54	(0.22, 1.36)	0.190
Asplenia	52	9 (17.3)	1.36	(0.49, 3.73)	0.556
SLE	42	3 (7.1)	0.55	(0.12, 2.60)	0.448
Immunosuppressive therapy	235	61 (26.0)	1.99	(0.87, 4.57)	0.102
Concurrent conditions					
Cancer, solid organ	127	43 (33.9)	2.26	(1.31, 3.90)	0.003
Other chronic conditions	440	98 (22.3)	0.95	(0.63, 1.42)	0.788
Serotypes					
19A	102	21 (20.6)	1.21	(0.66, 2.24)	0.539
22F	76	6 (7.9)	0.40	(0.15, 1.08)	0.070
3	62	22 (35.5)	2.02	(1.06, 3.82)	0.031
6C	44	10 (22.7)	0.86	(0.36, 2.07)	0.738
7F	44	8 (18.2)	1.07	(0.45, 2.54)	0.872
6A	38	10 (26.3)	1.67	(0.69, 4.00)	0.253
11A	35	9 (25.7)	1.37	(0.54, 3.47)	0.507
Other (Reference)	377	67 (17.8)			

CONCLUSIONS: IC adults comprise nearly one-third of all IPD episodes and rates of ICU admission and death are high. Reasons for immunocompromise are heterogeneous, which may make vaccination programs challenging to deliver. PPV23 does not appear to be effective in reducing disease. Assessing the effectiveness of PCV13 in preventing disease is warranted, although herd immunity from pediatric vaccination programs may over time reduce the benefits of adult vaccination.

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