

Abstract (updated)

**Background:** Homeless adults are at significant risk for serious pneumococcal infection, but few data are available to guide vaccine or treatment recommendations. We describe the epidemiology of invasive pneumococcal disease (IPD) in homeless adults in Toronto.

**Methods:** Prospective, population-based surveillance for IPD in Toronto (2.3M) was conducted from 1/1/2002 to 31/12/2006. Demographic and medical data are collected, all isolates were serotyped, broth microdilution susceptibility testing to CLSI standards was performed.

**Results:** Over 5 years, 69 of 1039 (6.6%) adult cases of IPD occurred in the homeless, with an incidence of 273 cases/100,000/yr (versus 91/100,000/yr in adults overall). Patients who were homeless were younger (median age 45 v 66 years, P<.001), more likely to be male (81% v 57%), to have underlying liver disease (38% v 7.9%), alcohol abuse (62% v 15%), HIV infection (25% v 8.4%), more likely to be smokers (96% v 31%) and to have received antibiotics in the previous 3 months (64% v 27%). They were less likely to have cancer (5.8% v 21%). There was no difference in clinical diagnosis (87% v 73% pneumonia, 7.2% v 15% bacteremia without focus, 2.9% v 5% meningitis), and no difference in the proportion with complicating empyema (1.5% v 3.8%), ICU admission (29% v 20%) or death (14% v 23%). Rates of resistance to common antibiotics were not different. The serotype distribution in homeless persons was different from the general population: serotypes 12F, 22F and 4 were most common; 84% of isolates had a serotype included in the 23-valent pneumococcal vaccine, v 31% in the 7-valent conjugate vaccine. 7 (12%) patients had >1 episode IPD. There was some evidence of clustering of disease in larger shelters.

**Conclusions:** Homeless persons have an elevated risk of IPD and should be targeted in prevention strategies.

Results

Incidence

Over the 5 year period, there were 69 episodes of invasive pneumococcal disease in homeless persons, and 970 episodes in residential residents. The estimated rate of invasive disease in homeless persons was 273 per 100,000 per year, 30 fold higher than the concurrent rate in housed adults (9.0 per 100,000 per year). Homeless persons comprised 6.6% of all cases of invasive pneumococcal disease, but only 0.2% of the population of Toronto.

The typical seasonal pattern of invasive pneumococcal disease in Toronto, with highest rates in the winter months, and a nadir in July and August, was not present in cases in homeless persons (Figure 1).

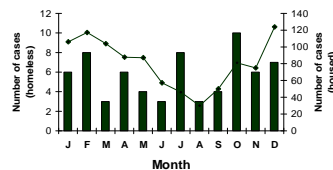
Clinical characteristics of invasive pneumococcal disease

Characteristics of invasive pneumococcal disease in homeless and housed adults are shown in Table 1. Of the 69 homeless persons with invasive disease, six (9%) had received pneumococcal vaccine prior to admission, 6 (9%) were vaccinated during or shortly after their hospitalization, 15 (22%) were known not to have been vaccinated, and data were not available for the remaining 42 (61%) patients. In contrast, a history of pneumococcal vaccination was available for 74% of patients who were not homeless, with 28% having been vaccinated prior to admission.

The 69 episodes of invasive disease in homeless persons occurred in 58 patients: 6 patients had two episodes of disease, and 1 patient had six episodes. The proportion of patients with recurrent disease was 5 fold higher in homeless (75%, 12%) than housed (24 of 943, 2.5%) patients (P<.001). One episode may have been a relapse, all other episodes occurred more than 4 months apart, and, in all cases where both isolates were available for typing, the isolates were of different serotypes. Three patients with episodes of invasive disease while they were homeless had another episode of disease during a time in which they had housing. Patients who had recurrent episodes of disease were more likely to have underlying liver disease (6/10 (60%) versus 12/48 (25%), P=0.55), but did not differ in other characteristics from patients who had only one episode of disease. The case fatality rate was 1/5 of 53 for first episodes of disease in homeless persons, and 3 of 10 for repeat episodes (P=.18).

Out of 69 homeless patients 7 (10%) were not admitted, and 7 (10%) left hospital against medical advice (AMA). In comparison, 150 (15%) of housed patients were not admitted to hospital, and 2 (0.2%) left AMA.

Figure 1: Number of cases of invasive pneumococcal disease, by month, in homeless and housed residents of Toronto, 2002-2006. Bars represent cases in homeless persons, line represents cases in housed persons. Fifteen of 69 (22%) of cases in homeless persons occurred in the summer, compared to 126 (13%) of those in housed persons (P=.06)



Outbreaks/clustering of cases

No outbreaks of pneumonia or pneumococcal disease were identified by clinicians or public health authorities in shelters in Toronto during this five year period. However, there was some evidence of clustering of episodes of illness due to particular serotypes. For instance, all five episodes due to serotype 7F (6% of isolates from homeless were of serotype 7F, compared to 2.9% of others, P=.18) occurred over an eight month period; all three episodes due to serotype 11B (3% of isolates from homeless vs 0.7% others, P=0.04) occurred over an eight month period. The first isolate of serotype 12F (20% of isolates from homeless vs 4% others, P<.001), was identified in September 2003, and all subsequent isolates occurred in residents of the largest shelter or those living on the street. In addition, all ten isolates of serotype 22F identified in homeless persons were resistant to erythromycin (MIC>=64ug/ml), compared to 14 of 79 (18%) other serotype 22F strains (P<.0001).

Results (cont'd)

Table 1: Clinical characteristics of episodes of invasive pneumococcal disease in housed and homeless adults, Toronto, 2002-2006.

Characteristic	Homeless persons	All other adults	P value
	(N=69)	(N=†)	
Median age (range)	45.7 years (27-72)	66.5 years (15 - 108 y)	<.001
Gender (% male)	56.69 (81%)	553/970 (57%)	<.001
Underlying illness			
Any*	61/69 (88%)	736/964(76%)	0.09
Diabetes mellitus	5/69 (7.3%)	182/950 (19%)	0.02
Chronic cardiac disease	12/69 (17%)	302/950 (32%)	0.02
Chronic lung disease	12/69 (17%)	193/950 (20%)	0.67
Cancer	4/69 (5.8%)	195/950 (21%)	0.005
Chronic liver disease	26/69 (38%)	75/950 (7.9%)	<.001
Chronic kidney disease	2/69 (2.9%)	69/950 (7.3%)	.22
HIV infection	17/69 (25%)	80/950 (8.4%)	<.001
Smoker	54/56 (96%)	297 (31%)	<.001
Alcohol abuse	43/69 (62%)	142 (15%)	<.001
Intravenous drug use	29/69 (42%)	35/950 (3.7%)	<.001
Recent antibiotic exposure			
Any antibiotic	21/33 (64%)	205/762 (27%)	<.001
Failing oral therapy	5/63 (7.9%)	60/848 (7.1%)	0.80
Clinical diagnosis			
Pneumonia	60/69 (87%)	692/949 (73%)	0.08
Sepsis without focus	5/69 (7.2%)	140/949 (15%)	
Meningitis	2/69 (2.9%)	47/949 (5%)	
Other	2/69 (2.9%)	70/949 (7.4%)	
Required hospitalization	60/69 (87%)	838/952 (88%)	0.94
Hospital-acquired disease	1/69 (1.4%)	49/954 (5.1%)	0.25
Hospital length of stay (median, range)	6 days (1-74 days)	8 days (1-214 days)	0.23
Outcome/complications			
Empyema	1/69 (1.5%)	36/949 (3.8%)	0.52
ICU admission	20/69 (29%)	273/951 (29%)	0.93
Recurrences	7/58 (12%)	24/943 (2.5%)	
Death	10/68 (14%)	220/959 (23%)	0.14

Isolate characteristics

Isolates were typed available for 1309 of 1383 (95%) of episodes. The most frequently identified serotypes are shown in Table 2. Overall, 32% (28/87) isolates associated with disease in homeless persons were of serotypes included in the conjugate vaccine, and 83% (72/87) isolates were of serotypes included in the 23-valent polysaccharide vaccine.

There were no differences in rates of resistance between isolates from homeless and housed adults (data not shown). Of the 87 isolates available from episodes of illness in homeless persons, 18 (21%) were resistant to erythromycin, 3 (3.5%) resistant to trimethoprim-sulfamethoxazole, 2 (2.3%) resistant to penicillin, and 1 (1.2%) resistant to levofloxacin.

Results (con't)

Table 2: Serotype distribution in patients with severe pneumococcal disease, Toronto, 2002-2006

Serotype*	Overall	Invasive disease		Non-bacteremic pneumonia	
		Housed N=943	Homeless N=62	Housed N=279	Homeless N=25
3†	1309	161 (12%)	108 (11%)	2 (3.2%)	48 (17%)
14†	112 (8.6%)	98 (10%)	3 (4.8%)	8 (2.9%)	3 (12%)
19F†	84 (6.4%)	52 (5.5%)	0	32 (11%)	0
4†	87 (6.7%)	73 (7.7%)	10 (16%)	2 (0.7%)	2 (8%)
22F‡	89 (6.8%)	63 (6.7%)	6 (9.7%)	16 (5.7%)	4 (16%)
6B†	74 (5.7%)	54 (5.7%)	0	20 (7.1%)	0
12F‡	71 (5.4%)	51 (5.4%)	16 (26%)	3 (1.1%)	1 (4.0%)
9V†	66 (5.0%)	51 (5.4%)	4 (6.5%)	10 (3.6%)	1 (4.0%)
6A	63 (4.8%)	41 (4.3%)	2 (3.2%)	20 (7.4%)	0
23F†	61 (4.7%)	44 (4.7%)	1 (1.6%)	15 (5.4%)	1 (4.0%)
7F‡	41 (2.9%)	35 (3.5%)	5 (8.1%)	3 (1.1%)	0
18C†	29 (2.4%)	21 (2.2%)	1 (1.6%)	5 (1.8%)	2 (8.0%)
11A‡	37 (2.8%)	21 (2.2%)	1 (1.6%)	15 (5.4%)	0
17F‡	12 (0.9%)	4 (0.4%)	0	6 (2.1%)	2 (8.0%)
In 7-valent conjugate vaccine	513 (39%)	393 (42%)	19 (31%)	92 (33%)	9 (36%)
In 23-valent polysaccharide vaccine	1042 (80%)	770 (82%)	52 (84%)	200 (72%)	20 (80%)

\*Serotypes listed are those which comprise >5% of isolates from any one category of disease  
 †Serotypes included in 7-valent conjugate and 23-valent polysaccharide vaccine  
 ‡Serotypes included in 23-valent polysaccharide vaccine, but not the 7-valent conjugate vaccine

Conclusions

- Homeless persons in Toronto have an exceptionally high rate of invasive pneumococcal disease, and few are vaccinated.
- Relative to disease in housed persons, disease in homeless persons is more likely to occur in the summer months, and more likely to be associated with a clinical diagnosis of pneumonia.
- 84 % episodes of invasive disease in homeless persons were caused by *S. pneumoniae* isolates of serotypes included in 23-polysaccharide vaccine, but only 31% by isolates of serotypes included in the 7-valent conjugate vaccine.
- The very high rate of disease suggests that specific vaccination programs should be developed for homeless populations.

Methods

Population-based surveillance

The Toronto Invasive Bacterial Diseases Network (TIBDN) has conducted prospective, population-based surveillance of invasive pneumococcal disease in metropolitan Toronto, Canada (population, 2.3 million), since 1 January 1995, and population based surveillance for culture confirmed non-bacteremic pneumococcal pneumonia since 1 January 2002. The surveillance network includes all hospital-based laboratories in hospitals to which residents of the population area may be admitted and the two largest private laboratories serving physician offices and nursing homes. Personnel from these laboratories telephone the central TIBDN study office at the Mount Sinai Hospital whenever *S. pneumoniae* is isolated from a sterile site or respiratory specimen. Case data are acquired by chart review, patient interview, and from patients' attending physicians. All isolates are submitted to the central study laboratory. Annual audits are conducted in each laboratory. Surveillance and associated studies are approved by the research ethics boards of all participating institutions.

For this study, population statistics were obtained from Statistics Canada. Population estimates of the adult homeless population in Toronto were obtained from the Shelter, Support and Housing Administration of the City of Toronto ( ).

Definitions

Persons were classified as homeless if they had no fixed address, or gave their address as an emergency or transitional shelter. Invasive pneumococcal disease was defined as isolation of *Streptococcus pneumoniae* from a sterile body fluid with a compatible clinical syndrome. Sterile sites included blood, CSF, peritoneal fluid, pleural fluid, or needle aspiration of a collection, but not bronchoalveolar lavage specimens. Nonbacteremic pneumococcal pneumonia was defined as: (i) a clinical presentation including symptoms (eg. cough, sputum, fever) and physical findings consistent with pneumonia; (ii) an infiltrate on chest radiograph; (iii) microscopic examination of a Gram stained sputum showing >= 20 WBC per high power field and a predominance of Gram positive cocci in pairs or chains and a sputum culture yielding *S. pneumoniae* as the only pathogen, and (iv) no positive blood cultures for *S. pneumoniae*.

Laboratory methods

All isolates were serotyped at the central study laboratory at the Mount Sinai Hospital, or the National Center for Streptococcus, Edmonton, Canada using commercial antisera (Statens Serum Institut, Copenhagen, Denmark). Antimicrobial susceptibility testing was performed by broth microdilution to CLSI (Clinical and Laboratory Standards Institute) standard. Susceptible and nonsusceptible (intermediate or resistant) isolates were defined as per the breakpoints set by CLSI.

Statistical Methods

All data was entered in duplicate and analyzed using SAS for PC. Proportions were compared using chi-square or Fisher's exact tests and odds ratios calculated with 95% confidence intervals.