Streptococcus pneumoniae Serotypes 22F and 33F Causing Invasive Pneumococcal Disease in Canada

The SAVE Study 2011-2018

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INTRODUCTION

Public vaccination schedules including pneumococcal conjugate vaccines have decreased the incidence of invasive pneumococcal disease (IPD). However, serotype replacement with non-vaccine serotypes has been observed after the introduction of PCV7 and PCV13 vaccines. New 15-valent pneumococcal conjugate vaccines will also cover serotypes 22F and 33F. These serotypes have previously been characterized as having relatively high potential for invasiveness compared to other non-PCV13 serotypes. We assessed antimicrobial susceptibility and multidrug resistance (MDR) of IPD caused by these serotypes in Canada from 2011 to 2018.

METHODS

The SAVE study is a partnership between the Canadian Antimicrobial Resistance Alliance (CARA) and the National Microbiology Laboratory (NML).

Isolates: From 2011 to 2018, eight provincial public health laboratories contributed S. pneumoniae isolated from sterile sites, along with patient demographic information. Participating provinces were categorized into West (Saskatchewan, Manitoba), Central (Ontario, Quebec), and East (New Brunswick, Nova Scotia, Prince Edward Island, Newfoundland and Labrador). Alberta and British Columbia did not submit isolates.

Serotyping, antimicrobial susceptibility testing, and statistical methods: Serotyping was performed using the Quellung reaction. Antimicrobial susceptibility testing was performed by microdilution for each isolate and interpreted by CLSI breakpoints. Whole genome sequencing was performed on select isolates. The Cochran-Armitage test was used to identify significant trends over time.

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RESULTS

Demographics and overall resistance: 11,044 isolates were included in the study. The most common source of isolate was blood (n=10,018), followed by CSF (n=399), and other (n=57). Rates of resistance are depicted in Table 2. Annual prevalence of 22F, 33F, PCV13 serotype, and all others combined are shown in Figure 1. The rate of multiresistant organisms was 6.3% overall, and 13.9% for PCV13 serotypes.

22F: 22F was the most common serotype identified in all cases of IPD, with 9.3% (1024/11,044) of isolates. There was no statistically significant trend to increased or decreased as a percentage across the study time period. It caused higher proportions of IPD in patients aged 65 and older (10.0%) and 5 years of age and under (11.0%). It caused 18.5% of IPD in patients over 65 years of age. There was a statistically significant trend to decreasing clariacin susceptibility from 2011 (80.3%) to 2018 (52.9%) (P<0.0001). This was prominent in the Central region (66.3% in 2018) and Prairie region (90.9% in 2011 to 34.4% in 2018). In the Eastern region there was overall susceptibility was higher (77.9%) and stable over the study period. Multidrug resistance was uncommon in 22F, seen in 1.5% (15/1021).

Serotype 22F was highly clonal; 96.0% of sequenced strains (n=351) were related to ST433 (see Table 1).

33F: Serotype 33F accounted for 3.8% (416/11,044) of isolates, and 7.0% (70/1,006) of isolates in children under 5 years of age. It tended to comprising an increased proportion of isolates (2.2% in 2011 to 5.1% in 2018, P=0.001). Of 33F isolates 4.8% (20/415) were MDR.

33F isolates related to ST100 increased in prevalence from 2011 (50.0%) to 2018 (84.8%, P=0.006). Clonal clusters are described in Table 1. Of isolates related to ST100 (n=139) 50% were susceptible to trimethoprim-sulfamethoxazole (SXT), and 22.3% were susceptible to clariacin.

Table 1: MLST sequence types defined by 22F and 33F (2011-2018)

<table>
<thead>
<tr>
<th>Serotype</th>
<th>Cluster</th>
<th>Sequence type</th>
<th>% of total isolates for each sequence type</th>
</tr>
</thead>
<tbody>
<tr>
<td>22F</td>
<td>ST433</td>
<td>ST433</td>
<td>64.0</td>
</tr>
<tr>
<td>33F</td>
<td>ST100</td>
<td>ST100</td>
<td>80.8</td>
</tr>
</tbody>
</table>

CONCLUSIONS

• Of 11,044 invasive S. pneumoniae isolates collected in Canada from 2011-2018, 1,024 (9.3%) were 22F, and 426 (3.8%) were 33F.
• Serotype 33F had a statistically significant trend towards increasing proportion of IPD isolates over the study period (P<0.0001). The proportion of IPD caused by serotype 22F was stable.
• Serotype 22F trended to decreasing claracin susceptibility over the study period (80.3% to 52.9%, P<0.001). It was significantly higher resistant to other antimicrobials. The rate of MDR was 1.5%.
• Serotype 33F had low susceptibility to SXT (24.6%), significant trend to decreasing susceptibility, and claracin (22.4%). The rate of MDR was 4.8%.
• 22F was highly clonal (96.0% ST433). The proportion of 33F related to ST100 rose from 50.0% to 84.8% during the study period.

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