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Seasonal Variation in Penicillin Susceptibility and Invasive Pneumococcal Disease

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Abstract

We evaluated prospectively laboratory surveillance data from Massachusetts to investigate whether seasonal variation in invasive pneumococcal disease is associated with the proportion of penicillin susceptible isolates. The proportion of penicillin susceptible isolates associated with invasive pneumococcal disease varied by season, with proportions highest in the winter and lowest in the summer, and rates of invasive disease were highest in the autumn and winter seasons and lowest in the summer.

Keywords

invasive pneumococcal disease; seasonality; penicillin susceptibility; pediatric; clinical outcome

Invasive pneumococcal disease (IPD) exhibits seasonal variation in different geographic regions.[1] Climactic factors including temperature, humidity, rainfall and windspeed have been implicated,[1, 2] as well as increased indoor air pollution during cold months,[3] potentially from wood-burning stoves. Host factors include an increase in asthma exacerbations during cold months, which is a known risk factor for IPD.[4] In children, respiratory viral infections have correlated with increased admissions with IPD.[5] Cold months have also been significantly associated with higher antimicrobial resistance rates among Jewish children with acute otitis media.[6] We hypothesized that seasonal variation in IPD in children would also be associated with differences in penicillin susceptibility rates, with higher nonsusceptibility rates in the winter season.

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Methods

Enhanced statewide surveillance for IPD has been in place in Massachusetts since 2001, and *Streptococcus pneumoniae* isolates recovered from sterile sites from children less than 18 years of age are provided by clinical laboratories to the Massachusetts Department of Public Health. We analyzed Massachusetts public health surveillance of clinical laboratory reports from 2007-2012 for all children ≤5 years of age, and compared patient demographics, clinical and microbiologic features, comorbidities and other risk factors. This encompassed the period before introduction of the 13-valent pneumococcal conjugate vaccine (pre-PCV13: 2007-2009) and after (post-PCV13: 2010-2012). IPD was defined as a positive culture for *S. pneumoniae* from a normally sterile site. We defined the seasons as: winter (January through March), spring (April through June), summer (July through September), and autumn (October through December). For statistical analysis, we used chi-squared test of proportions to compare incidence across months and seasons, Fisher's Exact test to compare penicillin susceptibility across seasons, and to compare patient characteristics. Statistical analyses were performed using SAS v. 9.3 (SAS Institute, Cary, NC), with significance set at 5%. This study was approved by the Institutional Review Boards of the University of Minnesota and the Massachusetts Department of Public Health.

Results

Between 2007-2012, 253 cases of IPD in Massachusetts children ≤ 5 years of age were documented. Penicillin susceptibility data was available for 94.5% of isolates. There was significant variation in IPD cases overall by month and by season, with autumn and winter having higher than average incidence and summer having a much lower than average incidence ($p<0.01$; Figure 1). A significant association between season and number of IPD cases was noted both pre-PCV13 ($p<0.01$) and post-PCV13 ($p=0.02$). The highest incidence occurred in December ($p<0.01$). There was no significant association between seasonality and age ($p=0.33$) nor by vaccine serotype ($p=0.92$). Penicillin nonsusceptibility was highest in the winter (15.8%) and lowest in the summer (9.1%), but the difference was overall not significant ($p=0.86$), neither for pre-PCV13 ($p=0.98$) nor post-PCV13 periods ($p=0.31$).

Discussion

The higher proportion of nonsusceptible isolates in the winter compared to the summer, although not statistically significant, is of interest. One possible explanation for the observed greater proportion of nonsusceptible isolates in the winter is the selective pressure from increased antimicrobial usage during cold months on pneumococcal carriage prevalence and density.[6, 7] Seasonal prescribing practices for otitis media in one community setting was significantly associated with seasonality in antimicrobial susceptibility; in another community where prescription practices did not vary substantially between seasons changes in susceptibility during winter season was not observed.[6]

Our analysis was based solely on penicillin susceptibility, for which we had the most complete data, rather than including other antimicrobials. As a result, since cephalosporins and azithromycin have been purported to promote the carriage and spread of nonsusceptible

S. pneumoniae based on their pharmacokinetic and pharmacodynamic characteristics,[8] we likely have an incomplete picture of seasonal variation among antimicrobials in IPD.

In conclusion, our study shows a seasonal pattern of IPD that is largely unchanged after introduction of PCV13. This is consistent with the overall seasonal carriage pattern found in children studied following the introduction of PCV13 in Massachusetts children less than 5 years of age.[9] Seasonal variation in penicillin susceptibility was also noted, although this did not reach statistical significance. Our findings suggest that seasonal variation in IPD persists and likely reflects the increased antimicrobial prescribing associated with respiratory tract infection in winter. Efforts to optimize judicious use of antimicrobials remain necessary to further reduce the prevalence of nonsusceptible pneumococci in the community.

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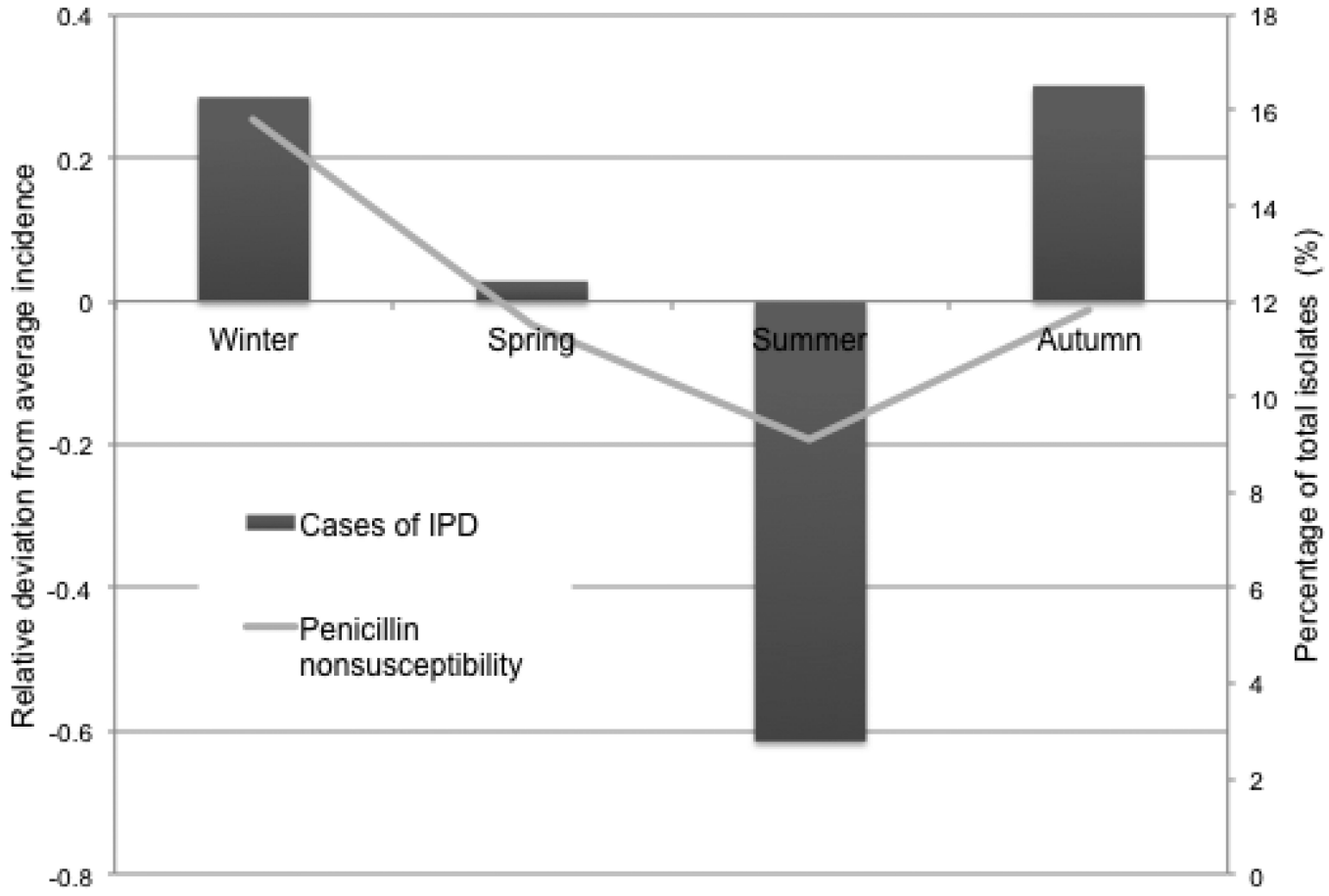

Figure 1.

Seasonal variation in proportion of penicillin nonsusceptible isolates and relative deviation from mean number of cases of invasive pneumococcal disease