

Missed Pneumococcal Vaccination Opportunities in Adults With Invasive Pneumococcal Disease in a Community Health System

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Background. Adult vaccination programs are suboptimal.

Methods. Pneumococcal vaccination history, and health-care contact were assessed in patients with invasive pneumococcal disease.

Results. Of the 229 cases, 14% were vaccinated. Observed mortality was 20.1%.

Conclusions. Numerous missed vaccination opportunities were identified.

Keywords. blood stream infection; invasive pneumococcal disease; meningitis; *Streptococcus pneumoniae*; vaccines.

Invasive pneumococcal disease (IPD) remains a significant cause of morbidity and mortality in the United States, with a case fatality rate of at least 20% in adults [1, 2]. Vaccination against *Streptococcus pneumoniae* significantly decreased the overall burden of IPD [3–12]. The Centers for Disease Control and Prevention (CDC) estimates that a significant portion of the US population remains unvaccinated despite many patients meeting the Advisory Committee on Immunization Practices (ACIP) and CDC criteria for vaccination [13, 14]. The objective of this study was to identify missed opportunities to immunize adults who developed IPD against *S pneumoniae*.

MATERIALS AND METHODS

This was a retrospective observational study in adults admitted with IPD between January 1, 2014 and June 30, 2019 at Norton Healthcare, a large community health system in Louisville, Kentucky. The primary outcome was the percentage of patients ≥ 18 years of age with IPD who received recommended

pneumococcal vaccinations. Secondary outcomes included frequency of missed opportunities for vaccination by setting, in-hospital mortality, and *S pneumoniae* serotype prevalence. IPD was defined as any patient with a cerebrospinal fluid or blood culture yielding *S pneumoniae*. Each episode of IPD was counted once. Patients' electronic medical record (EMR) were manually reviewed for risk factors for IPD and related mortality [15–19]. These included smoking, alcohol use disorder, diabetes mellitus, chronic heart disease, chronic lung disease, chronic liver disease, immunocompromising conditions, and age ≥ 65 years. Immunization status was assessed by documentation of receiving pneumococcal 13-valent conjugate vaccine (PCV13) and/or pneumococcal polysaccharide vaccine (PPSV23) any time before developing IPD. Vaccination history was obtained from the medical record and the Kentucky Immunization Registry, a nonmandatory, web-based reporting registry linking thousands of sites [20]. A missed opportunity for vaccination was defined as a visit to a Norton Healthcare outpatient office (primary care or specialist), immediate care center, emergency department, or hospital admission before developing IPD where no ACIP recommended pneumococcal vaccination was administered. Patients who had not visited any Norton Healthcare facility before developing IPD were considered to have no missed vaccination opportunities. From the entire cohort, a subset of 156 patients were randomly selected for *S pneumoniae* serotyping. Serotypes were determined utilizing the Quellung reaction and procedure previously described by Habib et al [21]. Data were evaluated using descriptive statistics.

Patient Consent Statement

This study was approved by the institutional review board at the University of Louisville with a waiver of informed consent.

RESULTS

A total of 229 cases of IPD were identified. Risk factors for IPD are described in Table 1. Ten patients met no criteria for pneumococcal vaccination. Of the 219 patients who met at least one vaccination criteria, 31 (14%) had documentation of being up to date on recommended pneumococcal vaccinations. The frequency of patients who had previously received a pneumococcal vaccine stratified by number of risk factors is listed in Table 1.

Sixty-one (26.6%) patients had no contact with our health-care system before IPD episode and therefore had no known missed opportunities for vaccination. Location of missed opportunities to administer a pneumococcal vaccine before IPD within our health system is described in Table 1. Of patients with IPD, 55.9% had at least 1 inpatient admission before IPD episode and 53.3% had at least 1 visit to an outpatient office.

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Table 1. IPD Risk Factors, Vaccination Status, and Mortality

| All IPD Patients | n = 229 | Received Correct Pneumococcal Vaccine(s) | Inpatient Mortality |
|---|------------|--|---------------------|
| IPD Risk Factor | | | |
| Smoking, n (%) | 153 (66.8) | | |
| Chronic heart disease, n (%) | 95 (41.5) | | |
| Chronic lung disease, n (%) | 95 (41.5) | | |
| Age >65 years, n (%) | 92 (40.2) | | |
| Immunocompromising condition, n (%) | 83 (36.2) | | |
| Diabetes mellitus, n (%) | 64 (27.9) | | |
| Alcohol use disorder, n (%) | 53 (23.1) | | |
| Number of Risk Factors | | | |
| 0 risk factors | 10 (4.4) | N/A | 0/10 (0.0%) |
| 1 risk factor | 40 (17.5) | 6/40 (15.0%) | 8/40 (20.0%) |
| 2 risk factors | 52 (22.7) | 7/52 (13.5%) | 12/52 (23.1%) |
| 3 risk factors | 48 (21.0) | 7/48 (14.6%) | 11/48 (22.9%) |
| 4 risk factors | 39 (17.0) | 5/39 (12.8%) | 8/39 (20.5%) |
| 5 risk factors | 29 (12.7) | 6/29 (20.7%) | 6/29 (20.7%) |
| 6 risk factors | 10 (4.4) | 0/10 (0.0%) | 1/10 (10.0%) |
| 7 risk factors | 1 (0.4) | 0/1 (0.0%) | 0/1 (0.0%) |
| Location of Missed Vaccine Opportunity | | | |
| Inpatient admission, n (%) | 128 (55.9) | | |
| Outpatient office, n (%) | 122 (53.3) | | |
| Emergency department, n (%) | 84 (36.7) | | |
| Immediate care clinic, n (%) | 16 (7.0) | | |

Abbreviations: IPD, invasive pneumococcal disease; N/A, not applicable.

NOTE: Patient could have more than 1 missed vaccination opportunity.

Mortality

In-hospital death occurred in 46 of 229 cases with an overall in-hospital mortality rate of 20.1%. There were no deaths observed in the 10 patients who had no documented risk factors for IPD. The observed in-hospital mortality by number of IPD risk factors is described in [Table 1](#).

Streptococcus pneumoniae Serotype

Pneumococcal serotyping was completed on 156 isolates; serotype information was not available for the entire cohort. The distribution of serotypes is described in [Table 2](#). The most common serotypes were 3, 22F, and 20 (12.2%, 10.3%, and 9.6%, respectively).

DISCUSSION

Only 14% of patients were vaccinated appropriately, which is notably lower than national rates. The CDC estimates that among US adults aged 19–64 with risk factors for pneumococcal disease and in adults ages ≥65, vaccination rates are 29.2% and 70.3%, respectively [13]. Over half of patients who developed IPD had a missed vaccination opportunity in the inpatient setting and or at an outpatient office visit. Missed vaccination opportunities occurred less frequently in emergency room visits without admission and at immediate care centers. This may be due to emergency room visits being infrequent rather than vaccination rates being high. Srivastav et al [22] surveyed clinicians and found that 70% self-reported that they

Table 2. Distribution of *Streptococcus pneumoniae* Serotype Prevalence

| Serotype | n = 156 |
|-----------------------------|-----------|
| 3 | 19 (12.2) |
| 22F | 16 (10.3) |
| 20 | 15 (9.6) |
| 35 | 14 (9.0) |
| 23A | 12 (7.7) |
| 33F | 9 (5.8) |
| 8 | 8 (5.1) |
| 11 | 8 (5.1) |
| 19A | 8 (5.1) |
| 9 not V | 8 (5.1) |
| 9V | 8 (5.1) |
| 7 | 6 (3.8) |
| 6B | 5 (3.2) |
| 15 | 4 (2.6) |
| 10 | 3 (1.9) |
| 12F | 3 (1.9) |
| 23F | 3 (1.9) |
| 6A | 2 (1.3) |
| 12 | 1 (0.6) |
| 12B | 1 (0.6) |
| 18F | 1 (0.6) |
| 19F | 1 (0.6) |
| 23, not otherwise specified | 1 (0.6) |

NOTES: All data described as n (%). Serotypes contained in pneumococcal 13-valent conjugate vaccine (PPV13): 1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 19A, 19F, 23F. Serotypes contained in pneumococcal polysaccharide vaccine (PPSV23): 1, 2, 3, 4, 5, 6B, 7F, 8, 9N, 9V, 10A, 11A, 12F, 14, 15B, 17F, 18C, 19A, 19F, 20, 22F, 23F, 33F [18].

routinely evaluated need for immunization. However, of these same prescribers, only 31.6% had administered an adult vaccine per state database records. Although it is possible that immunization information services provide incomplete data, this study suggests a potential gap between providers' perception of their practice regarding vaccines and reality [22].

The overwhelming majority (95.6%) of patients had risk factors for developing IPD. Although IPD did occur in 10 patients with no documented risk factors, this finding implies that the risk factors outlined in the ACIP vaccination guidelines appear to be predictive of IPD [14]. A total of 78.2% patients had multiple risk factors for IPD, which highlights the likely increased risk for developing IPD with an increasing number of risk factors [15]. None of the patients with ≥ 6 risk factors for IPD were vaccinated.

The most commonly identified *S pneumoniae* serotype was 3, which is contained in both PCV13 and PPSV23. However, serotype 3 is more challenging for vaccines to elicit a humoral response and provide adequate clinical protection [23–26]. A total of 17.9% of identified serotypes were not contained in either PCV13 or PPSV23, which demonstrates that most episodes may have been preventable through vaccines.

The observed in-hospital mortality of 20.1% is similar to inpatient mortality rates reported in other studies [1, 2, 18]. Previous data support that mortality in IPD increases as the number of risk factors increases, which is known as risk stacking; patients with ≥ 2 risk factors appear to be at higher risk for disease and mortality [16, 17]. In the present study, this risk stacking effect on mortality was not observed; however, similar mortality rates were observed with an increasing number of risk factors, in contrast to previous investigations [16].

The strengths of the study include characterizing significantly low vaccination rate and the high number of risk factors in a group of IPD patients in whom vaccination opportunities often went unfulfilled. A large portion of patients with IPD had inpatient hospitalizations before developing IPD. These data were collected after The Joint Commission changed its pneumococcal vaccination program from a core measure to a quality measure. The Joint Commission has since removed it completely due to complexity in determining vaccine eligibility [27]. At Norton Healthcare, standing orders were available for nurses to administer pneumococcal vaccinations to eligible inpatients. In addition, clinical decision support in the EMR was implemented in outpatient offices in 2016. Despite this, opportunities to vaccinate exist.

There are several limitations in this study. First, we relied on documentation of comorbidities in the EMR to identify patient risk factors for IPD rather than diagnostic criteria. This method could result in missed risk factors, particularly in conditions in which patients may not be forthcoming, such as alcohol use disorder. Second, the high prevalence of smoking in this cohort may not be generalizable to all patient populations; Kentucky has an unusually high prevalence of smoking (23.4%) relative

to the rest of the United States (13.7%) [28, 29]. In addition, we only collected in-hospital mortality data, which may not fully describe mortality associated with IPD. Finally, complete subtyping was not available on all samples, so comments on complete vaccine preventability of IPD are unknown.

Although we collected missed opportunities for vaccination, we cannot eliminate the possibility that pneumococcal vaccine was offered and refused by the patient during a visit before the development of IPD. The World Health Organization reports that vaccine hesitancy may be due to lack of confidence in the safety or efficacy of vaccines, underestimation of the risks associated with vaccine-preventable illness, or that receiving the vaccine is viewed as too inconvenient [30]. Clear communication from clinicians, including follow-up if a patient has previously declined a vaccine, may be key factors in patients' vaccine acceptance [30–32].

Future efforts should focus on adult pneumococcal immunization, especially in areas with high prevalence of risk factors. Despite cost-effectiveness evaluations of pneumococcal vaccines in adults showing significant health and societal benefits, there continues to be significant barriers to health systems including complex reimbursement models, lack of insurance coverage, and inadequate reimbursement in the United States [33–36]. Additional investment in adult vaccination services is needed to adopt a culture of vaccinating every eligible person at every point of contact with the healthcare system.

CONCLUSIONS

Invasive pneumococcal disease is a serious vaccine-preventable illness in adults, and US vaccination rates remain well below CDC goals despite demonstrated opportunities to vaccinate patients in multiple care settings. In this study, we identify missed opportunities to vaccinate adults with risk factors for IPD in multiple care settings who were subsequently hospitalized due to IPD. Highlighting the downstream consequences and missed opportunities to providers in commonly encountered health-care settings may help reinforce the importance of preventative vaccinations and highlight areas of opportunity for setting policy on vaccine reimbursement.

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