Hospitalisation Outcomes in Pneumococcal Vaccinated Versus Unvaccinated Patients with Exacerbation of COPD – Results From The HOPE COPD Study

Rajesh Venkitakrishnan, Anand Vijay, Jolsana Augustine, Divya Ramachandran, Melcy Cleetus, Aparna S Nirmal, Susan John


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ABSTRACT

Background

Infectious exacerbations are crucial events that dictate the natural course of COPD patients. Pneumococcal vaccination has shown to decrease incidence of community acquired pneumonia in COPD patients. There is paucity of data on outcomes of hospitalisation in pneumococcal vaccinated COPD patients in comparison with unvaccinated subjects.

Objectives

To evaluate the difference in hospitalisation outcomes in pneumococcal vaccinated versus unvaccinated COPD subjects hospitalized with Acute Exacerbation.

Methods

This was a prospective analytical study on 120 subjects hospitalised with acute COPD exacerbation. 60 patients with prior pneumococcal vaccination and 60 unvaccinated patients were recruited. Outcomes of hospitalisation like mortality rate, need for assisted ventilation, length of hospital stay, need for ICU care, and length of ICU stay were collected and compared between two groups with appropriate statistical tools.

Results

60% of unvaccinated patients (36 / 60) required assisted ventilation whereas only 43.3% of vaccinated subjects (26 / 60) needed assisted ventilation (p value 0.04). Most of
the secondary outcomes were better in the vaccinated group. The mean length of ICU stay in the vaccinated group was 0.67 days ($\pm$ 1.11) compared to 1.77 ($\pm$ 1.89) in the unvaccinated group. The mean length of hospital stay was 4.50 days ($\pm$ 1.64) and 5.47 days ($\pm$ 2.03) days in vaccinated and unvaccinated group respectively (p value 0.005).

Conclusions

COPD patients who have received prior pneumococcal vaccination have better outcomes when they are hospitalised for an acute exacerbation. Pneumococcal vaccination may be recommended for all patients with COPD who are at risk of hospitalisation with acute exacerbation.

KEY WORDS

Pneumococcal vaccination, acute exacerbation of COPD, hospitalisation outcomes

INTRODUCTION

Chronic obstructive pulmonary obstructive disease (COPD) is a condition characterized by persistent airflow limitation that is usually progressive and is associated with an enhanced inflammatory response in the airways and lungs to noxious particles and gases (1). The burden of COPD in India is huge. Of the total global disability adjusted life years (DALYs) due to chronic respiratory diseases in 2016, 32·0% occurred in India. The contribution of chronic respiratory diseases to the total DALYs in India increased from 4·5% (95% UI 4·0—4·9) in 1990 to 6·4% (5·8—7·0) in 2016 (2). COPD and asthma were responsible for 75·6% and 20·0% of the chronic respiratory disease DALYs, respectively, in India in 2016 (2).

The goals of COPD management include providing symptom relief, preserving lung function, ensuring acceptable quality of life etc. Exacerbations are acute events that punctuate the natural course of COPD and are associated with worsening symptoms, escalation of pulmonary and systemic inflammation, worsening functional status and mortality (3,4). Exacerbations are increasingly recognised to be crucial events that can potentially dictate the natural course and longevity of COPD patients (5). Prevention of future exacerbations can be viewed upon as a key strategy in COPD management. The
crucial role of bacterial and viral infections as exacerbation triggers have been recognised for decades. Susceptibility to infections poses a major threat in leading to exacerbations of COPD and translates to accelerated decline in pulmonary functions (3). Patients with COPD are at high risk of community-acquired pneumonia (CAP), which imposes a substantial disease burden. *Streptococcus pneumoniae* is the leading cause of CAP in India (6). In Europe, the incidence of CAP was found to be more than 20-fold higher in persons with COPD (22.4 per 1,000 person-years) than in the general population (1.07–1.2 per 1,000 person-years) with the incidence dramatically higher in persons with severe COPD (forced expiratory volume in 1 second [FEV1] < 50% of expected) (7).

Pneumococcal vaccination can substantially reduce the mortality and morbidity risks associated with pneumococcal diseases and are recommended for patients at high risk (8). Humoral response is important to help eradicate the bacteria during primary infection, although these responses are not as robust during primary infection. Anticapsular polysaccharide antibodies are believed to represent the single most important protective mechanism against invasive disease. In fact, antibodies to pneumococcal polysaccharides were the basis of serum therapy in which passively transferred, serotype-specific antipneumococcal serum was shown to reduce mortality from pneumococcal pneumonia by half (9).

Pneumococcal vaccines can be broadly divided into the polysaccharide vaccines, which are antibodies to the capsular polysaccharides, or the conjugate vaccines. Since the immunogenicity of polysaccharides are traditionally low, conjugation improves the immunogenicity and immune memory. In 1983, the 23-valent polysaccharide vaccine (PPSV23) was approved for use in the United States for adults and children older than 2 years of age. This new formulation was developed after worldwide surveillance showed a high frequency of pneumococcal bacteremia and meningitis by serotypes not covered in the previous 14-valent vaccine (10). Use of PPSV23 has repeatedly been shown to provide a significant reduction in the rates of invasive pneumococcal disease, however, sadly, without impact on overall mortality or in overall rates of pneumonia (11). Conjugate vaccines have been marketed as the 7 valent, 10 valent, 13 valent and 20 valent vaccines. (PCV 7, 10, 13 or 20). The impetus to administer conjugate vaccine in the elderly population was the robust immunogenicity data in this population. This fact, in conjunction with clinical trial results in
immunocompromised populations, was the foundation for the present substantial shift in adult immunization practice towards conjugate vaccine. This strategy appears to be well supported by the compelling results observed in CAPiTA study (12), with 45% efficacy in prevention of community-acquired pneumonia and 75% efficacy in prevention of invasive pneumococcal disease.

Pneumococcal vaccination affords protection predominantly against invasive infections like bacteremia, meningitis and pneumonia. Despite clear-cut recommendations by the Centre for Disease Control, the adherence to pneumococcal vaccine among adult subjects has been traditionally low. Published Indian evidences reveal that the uptake of pneumococcal vaccine remains low within the general public, elderly population and those with medical comorbidities (13, 14).

Most of the studies, reviews and meta-analysis on the efficacy of pneumococcal vaccination have looked at pneumococcal pneumonias or invasive pneumococcal diseases as the outcome measure (15, 16). While these may be the best outcomes to look at from a vaccine efficacy point of view, clinically relevant outcomes for COPD patient would be exacerbation rates. A randomised, non placebo control trial however showed decreased exacerbation rate in COPD patients after administration pneumococcal polyvalent vaccine (17).

Prior pneumococcal vaccination with polysaccharide vaccine has been associated with a 40%-70% reduction in risk of in-hospital death in a large cohort of hospitalised individuals with community acquired pneumonia who were admitted (18). Pneumococcal vaccine reduces bacteremic pneumococcal disease in vaccinated subjects. Pneumococcal bacteremia may translate to elevated mortality despite an adequate host immune response and appropriate antibiotic therapy because of the release of cell-wall components by killed bacteria, which results in an inflammatory cascade causing death in experimental models of pneumococcal disease (19). Mechanistically, prevention of such a “cytokine storm” would be consistent with the improved outcomes observed in this study. Extrapolation of this mechanism may operate in patients of COPD hospitalised with acute exacerbations and translate to improved outcomes, although there is a lack of evidence in this regard. Further, pneumococcal vaccinated subjects demonstrate better immunity to pneumococcal
infections as well as related organisms in experimental mice (including influenza virus) via complex overlapping mechanisms, which may be postulated to contribute to improved survival and related outcomes in hospitalised COPD patients (20).

There is a lack of data on outcomes of hospitalisation in pneumococcal vaccinated COPD patients versus the unvaccinated subjects. Further, there is paucity of Indian data on the benefits of pneumococcal vaccination in COPD patients. The present study was undertaken to explore these aspects in COPD patients.

OBJECTIVES

The present study was carried out with the following objectives.

Primary Objectives

1. To evaluate the difference in mortality rate and need for assisted ventilation in pneumococcal vaccinated (with PCV 13) versus unvaccinated COPD subjects who are hospitalized with Acute Exacerbation of COPD

Secondary Objectives

1. To evaluate the differences in other relevant clinical outcomes (occurrence of respiratory failure, length of hospital stay, need for ICU care, length of ICU stay) in pneumococcal vaccinated (with PCV 13) versus unvaccinated COPD subjects hospitalized with Acute Exacerbation of COPD

MATERIALS AND METHODS

This was a prospective analytical study conducted in the department of Pulmonary Medicine, Rajagiri Hospital, Aluva, a tertiary care institution in Central Kerala, India. The study period spanned from September 2019 to September 2021, which included a 12-month recruitment period from September 2019 to September 2020 and a further follow up period of one year after the recruitment of the last study subject. The study population comprised of patients hospitalised with an acute exacerbation of COPD within the study period.
Inclusion Criteria

The inclusion criteria for the present study was

1. Patients with a previous diagnosis of chronic obstructive pulmonary disease (COPD) as per the Global Initiative for COPD (GOLD) criteria
2. Patients hospitalised to the study centre with an acute exacerbation of COPD within the study period

Both criteria needed to be met for qualifying for inclusion into the study

Exclusion Criteria

The exclusion criteria for the present study were

1. COPD patients whose previous pneumococcal vaccination status is unclear after personal interrogation and cross checking of previous medical records
2. Patients with overlapping chronic lung diseases like asthma, interstitial lung diseases, bronchiectasis (unrelated to COPD status) etc
3. Patients with immunocompromised states including active HIV infection, active hematological or solid organ malignancies, primary immunodeficiencies, current usage of regular systemic steroids or other immunosuppressive agents etc
4. Patients who opted out of active management (like care in the ICU, assisted ventilation etc) during the hospitalisation for acute exacerbation of COPD

The presence of any one criterion led to exclusion from considering into the study.

Sample size

Being a single centre study extending for a limited time period and in the absence of previous similar studies, an arbitrary sample size of 120 was fixed with 60 patients needing to be recruited into pneumococcal vaccinated as well as unvaccinated group. Patients who
had previous administration of 13 valent pneumococcal conjugate vaccine were recruited into the vaccinated group.

Data collection and follow up

Immediately on hospitalisation, the patients were interrogated and a detailed medical history including the vaccination status was obtained. Specific attention was paid to baseline demographic factors, medical comorbidities, stage and category of COPD, severity of exacerbation etc. Focused physical examination was performed and findings were obtained. Results of investigations performed at hospitalisation (arterial blood gas analysis, chest radiograph findings and blood investigations etc) were noted down. They were managed as per standard management guidelines for acute exacerbation of COPD. Attention was paid to site of admission (respiratory ward versus intensive care unit), need for supplemental oxygen, assisted ventilation etc. Subjects were followed up on a daily basis until discharge from hospital or death. Clinical course and follow up tests etc were ascertained.

The outcome measures specifically focused include mortality, length of hospitalisation, occurrence of respiratory failure, need for assisted ventilation, need for ICU care, duration of ICU care and duration of mechanical ventilation. Comparison were made between the vaccinated versus non vaccinated subjects with regard to the outcomes.

Statistical analysis

Data was entered in Microsoft excel sheet and statistical analysis was done using SPSS software 25 version. The qualitative data were expressed as proportions or percentage and the quantitative data as mean and standard deviation. Association between qualitative data was done using chi-square test and quantitative data was done using unpaired t – test. A p value < 0.05 was considered as significant.

Ethical Approval

The study protocol was approved by the institutional ethical committee (letter no RAJH/SRC/DNB0026). It was observed that the study does not pose any ethical issues to the patient.
RESULTS

Demographic characteristics

A total of 120 patients hospitalized with acute exacerbation of COPD were recruited into our study, 60 of whom were previously pneumococcal vaccinated and 60 were unvaccinated. The mean age of the study population was 72.43 years (+/- 8.764). The youngest patient was aged 49 years and the oldest patient was 92 years old. Most of the patients (73%, 88 patients) belonged to the age group of 61-80 years. Among the study population, 91 patients were males (75.8%) and the rest 29 were females (24.2%). Comparing between the vaccinated and non vaccinated groups, the mean age of vaccinated patients was 4 years higher and the proportion of female patients was much higher in the vaccinated group. Table 1 shows the age distribution of the study patients.

Table 1 - age distribution of the study patients

<table>
<thead>
<tr>
<th>AGE IN YEARS</th>
<th>VACCINATED POPULATION</th>
<th>UNVACCINATED POPULATION</th>
</tr>
</thead>
<tbody>
<tr>
<td>45-60 YEARS</td>
<td>3 (2.5%)</td>
<td>6 (5%)</td>
</tr>
<tr>
<td>61-80 YEARS</td>
<td>42 (35%)</td>
<td>46 (767%)</td>
</tr>
<tr>
<td>&gt;80 YEARS</td>
<td>15 (12.5%)</td>
<td>8 (13.3%)</td>
</tr>
<tr>
<td>Total</td>
<td>60 (50%)</td>
<td>60 (50%)</td>
</tr>
</tbody>
</table>

Baseline characteristics

Among the 120 patients, 92 patients belonged to GOLD stage D, 21 belonged to GOLD stage C and 7 belonged to stage B. 113 out of 120 (94.2%) patients had more than 2 exacerbation episode in the previous year. The mean number of annual exacerbations in the study group was 3.17 (+/-1.16). The mean number of annual hospitalisation in the study
subjects was 1.25 (+/-0.963). Systemic hypertension, diabetes mellitus and ischemic heart disease were common medical comorbidities in the study patients being present in 57.5%, 36.6% and 42.5% patients respectively.

Comparison between the baseline characteristics including demography, smoking status, COPD severity, comorbid illness etc between the vaccinated group and unvaccinated group are showed in table 2. As previously mentioned, the mean age of vaccinated patients was 4 years higher and the proportion of female patients was much higher in the vaccinated group. The presence of medical comorbidities was much higher in the vaccinated group and these differences were statistically significant. Fever and multilobar consolidation were seen in a much higher percentage of unvaccinated patients. Among the 60 patients in the vaccinated with conjugate vaccine (PCV 13), 4 had history of receiving PPSV 23 also whereas 54 had not received PPSV 23. In contrast, as per the protocol, patients who had not received any pneumococcal vaccine were only recruited into the unvaccinated group.

Table 2: Relation between Baseline characters and Vaccination status

<table>
<thead>
<tr>
<th>PARAMETER</th>
<th>VACCINATED GROUP</th>
<th>UNVACCINATED GROUP</th>
<th>P VALUE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean age</td>
<td>74.43 (+/-8.039)</td>
<td>70.42(+/-9.060)</td>
<td>0.01*</td>
</tr>
<tr>
<td>M : F ratio</td>
<td>37:23</td>
<td>54:6</td>
<td>0.002*</td>
</tr>
<tr>
<td>Smoking habit</td>
<td>25 (41.6%)</td>
<td>25 (41.6%)</td>
<td>0.98*</td>
</tr>
<tr>
<td>Indoor biomass exposure</td>
<td>18 (30%)</td>
<td>18(30%)</td>
<td>0.96*</td>
</tr>
<tr>
<td>COPD stage D</td>
<td>46 (76.7%)</td>
<td>46 (76.7%)</td>
<td>0.19*</td>
</tr>
<tr>
<td>Systemic hypertension</td>
<td>40 (66.7%)</td>
<td>29 (48.3%)</td>
<td>0.04*</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>28(46.7%)</td>
<td>16 (26.7%)</td>
<td>0.02*</td>
</tr>
<tr>
<td>Ischemic heart disease</td>
<td>32 (53.3%)</td>
<td>19(31.7%)</td>
<td>0.01*</td>
</tr>
<tr>
<td>Chronic kidney disease</td>
<td>12 (20%)</td>
<td>5 (8.3%)</td>
<td>0.06*</td>
</tr>
<tr>
<td>Chronic respiratory failure (before)</td>
<td>7 (11.6%)</td>
<td>2 (3.3%)</td>
<td>0.08*</td>
</tr>
</tbody>
</table>
Influenza vaccination in the previous year

<table>
<thead>
<tr>
<th></th>
<th>Vaccinated</th>
<th>Unvaccinated</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>56 (93.3%)</td>
<td>54 (90%)</td>
<td></td>
<td>0.94</td>
</tr>
</tbody>
</table>

Respiratory failure (New onset at presentation)

<table>
<thead>
<tr>
<th></th>
<th>Vaccinated</th>
<th>Unvaccinated</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>33 (50%)</td>
<td>40 (66.6%)</td>
<td></td>
<td>0.13</td>
</tr>
</tbody>
</table>

Fever at presentation

<table>
<thead>
<tr>
<th></th>
<th>Vaccinated</th>
<th>Unvaccinated</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>13 (21.7%)</td>
<td>38 (63.3%)</td>
<td></td>
<td>&lt; 0.001</td>
</tr>
</tbody>
</table>

Multilobar consolidation

<table>
<thead>
<tr>
<th></th>
<th>Vaccinated</th>
<th>Unvaccinated</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>4 (6.7%)</td>
<td>36 (60%)</td>
<td></td>
<td>&lt; 0.001</td>
</tr>
</tbody>
</table>

Test of Significance Used: *- Independent student t test, #-Chisquare test

**Outcomes**

118 out of the 120 patients were discharged alive from hospital. Only 2 patients (1.7%) died during the current hospital stay. Both these patients belonged to the unvaccinated group. This difference was statistically non-significant. Persisting respiratory failure at discharge was 18.3% in the vaccinated group against 28.3% in the unvaccinated group. This difference was statistically non-significant (p value 0.13). No additional post discharge mortality was seen in either group in the first thirty days after discharge. 3 patients from vaccinated group and 4 patients from unvaccinated group needed hospitalisation for another exacerbation in the 30 days following discharge.

Assisted ventilation was required in 62 (51.7%) patients. Among this, 26 patients were vaccinated and 36 subjects were unvaccinated. 60% of unvaccinated patients (36 / 60) required assisted ventilation whereas only 43.3% of vaccinated subjects (26 / 60) needed assisted ventilation. This difference was statistically significant with a p value of 0.04. Figure 1 is a Kaplan Meier graph which shows the proportion of patients surviving without the need for assisted ventilation during the current admission.

Most of the secondary outcomes were better in the vaccinated group of COPD patients. The place of initial admission was intensive care unit in 53 patients (44.2%). 18 patients (30%) from vaccinated group needed ICU admission whereas 35 patients (58.3%) from unvaccinated group needed ICU admission. (p value 0.002). The mean length of ICU stay was 1.22 days (± 1.22) in study subjects. Figure 2 shows the percentage of patients needing ICU...
stay on each day of hospitalisation during the present admission for COPD exacerbation. The length of ICU stay in the vaccinated group was 0.67 days (± 1.11) whereas the corresponding figure was 1.77 (± 1.89) in the unvaccinated group. The mean number of days of ventilation who needed assisted ventilation is 1.47 (± 1.69) days. The mean duration of hospital stay compared between vaccinated versus non vaccinated groups was 5.39 days (± 1.68) versus 6.06 days (± 2.14). The mean length of hospital stay was 4.50 days (± 1.64) and 5.47 days (± 2.03) days in vaccinated and unvaccinated group respectively (p value 0.005). The differences in clinically relevant secondary outcomes in vaccinated as well as unvaccinated subjects are summarised in table 3 and crucial differences are depicted in figure 3.

Table 3 – Comparison of clinically relevant outcomes in vaccinated versus unvaccinated subjects

<table>
<thead>
<tr>
<th>PARAMETER</th>
<th>VACCINATED GROUP</th>
<th>UNVACCINATED GROUP</th>
<th>P VALUE</th>
</tr>
</thead>
<tbody>
<tr>
<td>In hospital mortality</td>
<td>0 (0%)</td>
<td>2 (1.7%)</td>
<td>0.13**</td>
</tr>
<tr>
<td>Need for assisted ventilation</td>
<td>26 (43.3%)</td>
<td>36 (60%)</td>
<td>0.04**</td>
</tr>
<tr>
<td>Need for ICU care</td>
<td>18 (30%)</td>
<td>35 (58.3%)</td>
<td>0.002**</td>
</tr>
<tr>
<td>Mean length of ICU stay (N = 53)</td>
<td>0.67(+/−1.11)</td>
<td>1.77(+/−1.890)</td>
<td>0.001*</td>
</tr>
<tr>
<td>Mean length of hospital stay</td>
<td>4.12 (+/−1.48) days</td>
<td>4.64 (+/−1.57) days</td>
<td>0.008*</td>
</tr>
<tr>
<td>Mean days of assisted ventilation (N=62)</td>
<td>1.15 (+/−1.52)</td>
<td>1.73(+/−1.79)</td>
<td>0.04*</td>
</tr>
<tr>
<td>No of patients with</td>
<td>11 (18.3%)</td>
<td>17 (28.3%)</td>
<td>0.13**</td>
</tr>
</tbody>
</table>
DISCUSSION

The HOPE-COPD study has examined the outcomes of hospitalisation due to COPD exacerbations in pneumococcal vaccinated versus unvaccinated patients. 120 patients hospitalised with acute exacerbation of COPD were evaluated in the present study, 60 of who had received prior pneumococcal vaccination and 60 of whom who had not.

In our study, fever, leukocytosis, multilobar pulmonary infiltrates and need for ICU care were significantly less in the vaccinated population. The occurrence of respiratory failure was higher among unvaccinated subjects, although this difference was not significant statistically. Similar results have been noted by other investigators also (21), where significant differences were observed between groups in age, some symptoms and radiological findings. Although there is no strong association between the radiographic patterns and the causative agents, consolidation is more frequently observed in pneumococcal pneumonia. Accordingly, lower rates of consolidation were observed in vaccinated persons with PCV 13, suggesting that pneumococcal conjugate vaccination may have had a strong preventive effect for pneumococcal pneumonia, or may have resulted in milder forms of radiographic presentation.

In the present study, clinical outcomes were better in the vaccinated group of patients. Prior pneumococcal vaccination decreases the incidence of bacteremic pneumonia. Our findings are consistent with the observation that polyvalent pneumococcal polysaccharide vaccine reduces bacteremic pneumococcal disease in adults and might translate to clinically relevant outcomes [22, 23]. Reports of reduction in pneumonia-related mortality among vaccinated individuals in observational studies performed in Sweden and Austria are also available. The vaccinated group had less severe disease as noticed by the decreased incidence of multilobar consolidation. This may be a manifestation of the protective efficacy of PCV 13 and would have translated to lesser ICU need and length of
hospital stay. Both cases of mortality reported occurred in the unvaccinated group. However, considering the extremely small mortality number in the study patients, meaningful comparison of outcomes could not be done and the results were not statistically significant.

Fisman et al (18) looked at 62,918 adults hospitalized with community-acquired pneumonia between 1999 and 2003 of whom 7390 (12%) had a record of prior pneumococcal vaccination. Vaccine recipients were less likely to die of any cause during hospitalization than were individuals with no record of vaccination (adjusted odds ratio 0.50; 95% confidence interval, 0.43–0.59), even after adjustment for the presence of comorbid illnesses, age, smoking, and influenza vaccination. Vaccination also lowered the risk of respiratory failure (adjusted OR, 0.67; 95% CI, 0.59–0.76) and other complications and reduced median length of stay by 2 days, compared with nonvaccinated individuals. Due to small number of subjects, the mortality rate is low in our study. A Turkish study (24) looked at the outcomes with pneumonia in patients vaccinated with pneumococcal vaccine and influenza vaccine and had contrasting observations. Although there was a trend for lower 30-day mortality and for lower rates of intensive care unit (ICU) admission, these did not reach statistical significance. A pneumonia severity index (PSI) score >/= 90, CURB-65 score >/= 3 and multilobar involvement, but not the vaccination status, were identified as independent determinants of ICU admission. The study concluded that prior vaccination does not appear to significantly affect the clinical outcomes.

In another study (25) the mortality rate and ICU admission were less among vaccinated patients. ICU admission was reduced among vaccinated patients in our study also. A population-based cohort study involving elderly hospitalized patients with pneumonia in Canada demonstrated that PPV23 immunization was associated with a reduced risk of death or further hospitalization (26). Supporting the benefits of pneumococcal vaccination, a prospective cohort study conducted by Vila-Corcoles et al (27) in Spain found that PPV23 vaccination in the elderly was associated with considerable reductions of death risk from pneumonia although the risk of overall pneumonia or hospitalization from pneumonia was unaltered. Li et al (28) in a US based study, tested the effectiveness of pneumococcal vaccination and influenza vaccination in preventing CAP. It was found that prior pneumococcal vaccination alone was not associated with shortened
length of admission, reduced risk of inpatient mortality, or risk of respiratory complications compared with no vaccination, while having had both vaccinations of pneumococcal and influenza before CAP admission was associated with a 10% reduction in length of admission. The differences in patient characteristics, treatment protocols, duration after vaccination and study protocols would have accounted for the differences in observations observed across different studies. However, majority of studies suggest benefits in clinical outcomes with the pneumococcal vaccine.

The present study is unique in the fact that it has examined the hospitalisation outcomes of COPD patients who were admitted for acute exacerbations, whereas all the above discussed studies have looked at patients admitted with community acquired pneumonia. The outcomes have been unequivocally beneficial in the prior vaccinated subjects.

**Limitations of the study**

The present study has some limitations. In the absence of a previous study of this sort in hospitalised COPD patients, the sample size has been arbitrarily chosen. All the vaccinated group in the study have received the PCV 13. Some patients in the vaccinated group have received the pneumococcal polysaccharide vaccine also, which might have an impact in the outcomes. However, only 4 patients in the vaccinated group have received PPSV 13 and this small number is unlikely to have an impact on the overall outcome. The vaccinated patients have received pneumococcal vaccination at varying times in the past. The immunity and duration of protection afforded by the polysaccharide vaccine is known to wane off with time (29), which may have an impact in patient outcomes. Studies using PCV13 conjugate vaccine have shown that immunity levels do not fall drastically beyond baseline (30). However, only the vaccination history in the last five years has been noted down and the immunity is unlikely to wane off in this period. During the course of hospitalisation and in-hospital care for acute exacerbation of COPD, the study investigators were not blinded with regard to vaccination status. Our hospital, though, follows a standardised protocol for management of COPD exacerbations that is unlikely to be biased by the prior pneumococcal vaccination status of the patient. However, the authors perceive that the impact of these limitations on the study outcomes and conclusions is minimal.
Given the similar nature of COPD patients hospitalised across various institutions, we feel that the generalisability (external validity) of this study is high. Nevertheless, prospective randomised trials with a larger sample size are encouraged to overcome the limitations of this study.

Conclusions

The HOPE-COPD study has attempted to examine the differences in clinically relevant outcomes in pneumococcal vaccinated versus unvaccinated COPD patients who are hospitalised with an acute exacerbation in pneumococcal vaccinated versus unvaccinated patients. The in-hospital and post discharge mortality rate among the study subjects has been very small and does not permit meaningful conclusions regarding any mortality benefit. COPD patients who have received prior pneumococcal vaccination have better outcomes including lesser need for ICU admissions, smaller proportion requiring assisted ventilation, shorter hospital stay, less duration of ICU stay etc. Pneumococcal vaccination is recommended for all patients with COPD who are at risk of hospitalisation with acute exacerbation as it improves hospitalisation outcomes.

SOURCE OF FUNDING

Nil

DISCLOSURES AND CONFLICTS OF INTEREST

None to declare

REFERENCES


Figure 1 - Kaplan Meier graph showing the probability of surviving without the need for assisted ventilation during the current admission

Figure 2 showing the percentage of patients needing ICU stay on each day of hospitalisation during the present admission for COPD exacerbation.

Figure 3 showing differences in crucial clinical outcomes between vaccinated and unvaccinated patients