



# Influenza Vaccination rate, Awareness and Risk of Acute Exacerbation of Chronic Obstructive Pulmonary Disease (COPD): A Tertiary Care Cross-Sectional Analysis

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The authors declare that there is no conflict to interest.

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## ABSTRACT

**Background:** Chronic Obstructive Pulmonary Disease (COPD) is one of the top four diseases causing a tremendous burden for the health care system. Recurrent exacerbations in these patients are the main problems causing significant ill health and deaths. Most of the exacerbations are caused by infections and especially the rhinoviruses. The most effective way to prevent exacerbation event is yearly influenza vaccination for all persons with COPD. The reasons for non-adherence to yearly vaccination are multifactorial; therefore evidence is needed about influenza vaccine usage among COPD patients in Pakistan.

**Objective:** This study was conducted with the aim to determine the yearly influenza vaccination rate, influencing factors, barriers and its association with acute exacerbation of COPD in patients admitted in our regional tertiary care hospital.

**Methodology:** This cross-sectional study was done on patients who were admitted with acute exacerbation of COPD at Ayub Teaching Hospital Abbottabad, Pakistan from July 2021 to June 2022. Patients were interviewed for all baseline characteristics and medical records were checked for yearly Influenza vaccination status and number of admissions with exacerbation and hospitalization during preceding year; i.e. July 2020 to June 2021.

**Results:** Mean age of the study participants was 59.1 ( $\pm 8.1$ ) years. Males were 282 (34.18%) and 543 (65.82%) were females. Illiterate patients were 714 (86.5%). Over all 162 (19.64%) participants received vaccine during the year. Among the vaccinated individuals 134 (82.71%) individuals received only influenza vaccine. The frequency of vaccination was lowest for illiterate individuals (13.3 %,  $p < 0.05$ ). Yearly Influenza vaccination reduced hospitalizations for episodes of acute exacerbation of COPD, the evidence is conclusive as 18-35% of respondents who had two or more episodes of acute exacerbation rate in last one year, the vaccination rate was quite low (0.12-0.85%). In logistic regression analysis, yearly influenza vaccination rate was associated with reduced hospitalization due to episodes of acute exacerbation of COPD with adjusted odds ratio (AOR) of 0.19 (95% CI: 0.01 - 0.07).

**Conclusion:** Yearly Influenza vaccination rate is very low in our region and is associated with a high risk of exacerbations in COPD patients. Important barrier in getting vaccine is lack of awareness about influenza vaccine.

**Key words:** Influenza Vaccine; Acute Exacerbation of COPD; Awareness

## Introduction

Chronic obstructive pulmonary disease (COPD) is the fourth leading cause of death with around 12% prevalence worldwide.<sup>1</sup> It is expected that by the year 2030, COPD will be the third leading cause of death with a significant disease burden and fifth leading cause of human disability.<sup>2</sup> Influenza infection plays a major role in triggering COPD exacerbation. Exacerbations are responsible for many complications in affected individuals. These exacerbations are also causing huge amount of burden on health care system and economy. For that very reason, universal and regional health organizations and agencies have started emphasizing universal vaccination coverage against influenza infection especially in high risk individuals.<sup>3-5</sup> Nevertheless, many countries have below target influenza vaccination coverage rates. In USA, the coverage of even very high-risk adults with influenza vaccine was less than 67%, which was below the target of 70%.<sup>5</sup> In European countries the target for influenza vaccination was 75%.<sup>3</sup>

Acute exacerbations of COPD are believed to cause significant amount of COPD-related complications and deaths. Influenza play major role amongst all respiratory infections in triggering exacerbations.<sup>6</sup> Influenza affects 5%-15% of the population each year, and is causing around 30,000 deaths annually. The affected individuals are mostly elderly and are having chronic respiratory diseases.<sup>7</sup> These exacerbations are causing greater progression of disease, deterioration in lung functions, higher rate of hospitalization and increase in total deaths.<sup>8</sup> Vaccination is considered to significantly lower the incidence rate of exacerbations, severity of disease, number of hospitalizations, and mortality.<sup>9,10</sup>

We conducted an evidence based cross-sectional study to estimate the rate of influenza vaccination in COPD patients with the aim to update and inform healthcare professionals on the current vaccination status. In addition, we aim to identify potential factors and barriers involved in the low rate of vaccination. We also wanted to evaluate whether low influenza vaccination rate has any association with increased risk of exacerbations. Through our findings we may get scientific evidence which can be utilized for the implementation of strategies in the management of COPD patients including proper vaccination across Pakistan. We will also provide an insight for the development of focused efforts to improve yearly influenza vaccination rates.

## Objective

To determine the rate of yearly influenza vaccination, influencing factors, barriers and its association with acute exacerbation of COPD in patients admitted in Department

of Pulmonology Ayub Teaching Hospital Abbottabad, Pakistan.

## Methodology

This study was carried out at the Department of Pulmonology Ayub Teaching Hospital Abbottabad, Pakistan from July 2021 to June 2022 on patients admitted with acute exacerbation of COPD. Ayub Teaching Hospital Abbottabad is the largest tertiary care hospital and referral centre in Hazara Division of Khyber Pakhtunkhwa province, Pakistan.

Patients were enrolled and interviewed after obtaining an informed consent approved by the Institutional Ethical Committee. Data was recorded about age, gender, smoking status, biomass exposure, and patients' yearly influenza vaccination status. Medical records of all study patients were checked for comorbid conditions, education level and whether influenza vaccination was advised by pulmonary medicine specialist, internal medicine specialist, general practitioners, post graduate residents or pharmacists. They were also interviewed about yearly influenza vaccination and number of admissions with exacerbation in any hospital during preceding year i.e., July 2020 to June 2021. All accumulated data was entered into a predesigned proforma for statistical analysis.

SPSS (version 21, SPSS Inc., Chicago, IL, USA) was used to analyze the data. Baseline characteristics including age, gender, education level, tobacco smoking/ biomass smoke exposure status, advice about vaccination and total duration receiving regular vaccination are presented in frequency tables and graphs. Categorical variables like education level, smoking status, gender, advice about vaccination, and total duration receiving regular vaccination and risk to low vaccination rate were examined by using the Chi square test. Continuous variables like age and duration of COPD diagnosis and vaccination rate were analyzed using t-test and p value < 0.05 was considered statistically significant. To estimate the risk of acute exacerbation associated with influenza vaccine, we performed logistic regression to derive odds ratios (ORs) and 95% confidence intervals (95%CI) and rates of acute exacerbation were compared between vaccinated and non vaccinated groups.

## Results

Among total 825 participants of mean age 59.1(SD ±8.1) years, 282(34.18%) were males and 543(65.82%) were females. In total, 162(19.64%) respondents received vaccines during the year 2021–2022. Among the vaccinated individuals, 134(82.71%) received only influenza vaccine, 4(2.47%) only pneumonia (pneumococcal) vaccine and 24(14.81%) received both influenza and pneumococcal vaccines (Figure 1 and Table

1). Vaccination rate for influenza and pneumonia (pneumococcal) vaccine was 24.11% in males while among females it was 17.31%. We distributed our study population in three groups on the basis of their education level, namely: illiterate, primary/matric and BA/BSc. Illiterate patients were 714 (86.5%), 80 (9.7%) had primary/matric education and 31(3.8%) had BA/BSc degree education. The frequency of receiving yearly vaccine was 83.9% for those who had BA/BSc degree

education, 51.3% for primary/matric education ( $p < 0.05$ ), and 13.3% among illiterate individuals ( $p < 0.05$ ) as presented in Figure 2.

Yearly Influenza vaccination reduced hospitalizations for episodes of acute exacerbation of COPD as shown in Table 2. In logistic regression analysis, yearly influenza vaccination rate was associated with reduced hospitalization due to episodes of acute exacerbation of

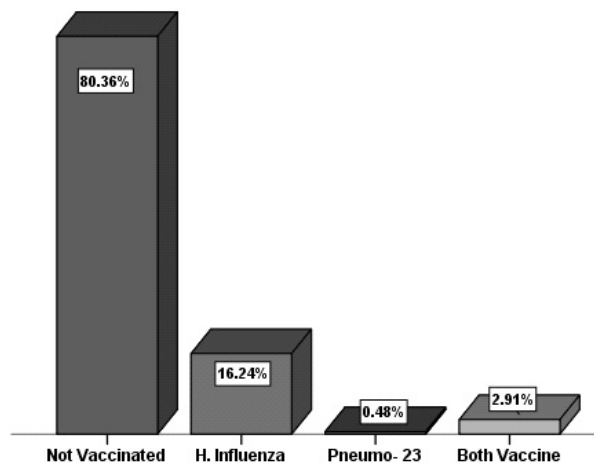


Figure 1: Vaccine status among COPD patients with acute exacerbation

Table1: Gender distribution of current Influenza vaccine status

Gender	Vaccine Status			
	Un-Vaccinated	Influenza Vaccine	Pneumonia Vaccine	Both Vaccine
Males	214 (25.9%)	56 (6.8%)	2 (0.2%)	10 (1.2%)
Females	449 (54.4%)	78 (9.5%)	2 (0.4%)	14 (1.7%)
<b>Total</b>	<b>663 (80.4%)</b>	<b>134 (16.3%)</b>	<b>4 (0.6%)</b>	<b>24 (2.9%)</b>

Figure 2: Level of education and yearly influenza vaccination status of patients

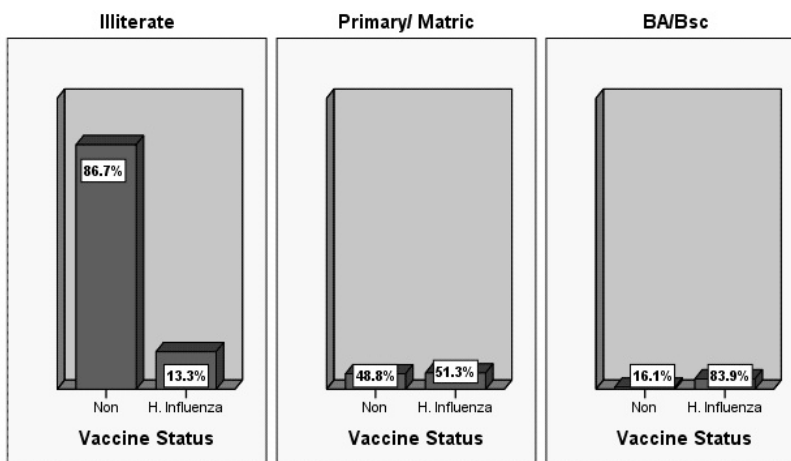


Table 2: Yearly rate of acute Exacerbation of COPD with vaccination status

Episodes of COPD Exacerbation/Year	Vaccine Status			
	Un-vaccinated	Influenza	Pneumococcal	Both Vaccine
None	90 (64.30%)	49 (35.0%)	1 (0.7%)	0 (0%)
1 episode	135 (57.2%)	74 (31.4%)	3 (1.3%)	24 (10.2%)
2 episodes	288 (96.6%)	10 (3.4%)	0 (0%)	0 (0%)
= 3 episodes	150 (99.3%)	1 (0.7%)	0 (0%)	0 (0%)
<b>Total</b>	<b>663 (80.4%)</b>	<b>134 (16.2%)</b>	<b>4 (0.5%)</b>	<b>24 (2.9%)</b>

COPD, with adjusted odds ratio of 0.19 (95% CI: 0.01 – 0.07).

Mean duration since our patients were diagnosed and were receiving regular therapy for COPD was 5 (SD ± 2.00) years and during this period, 66% of the respondents had visited pulmonary medicine specialist, 20% had visited internal medicine specialist and 14% were under treatment of general practitioner. Among those who were vaccinated, 16% were advised by pulmonary medicine specialists for yearly influenza vaccination, 4% were advised by internal medicine specialists, while those who visited general practitioners, none had been prescribed influenza vaccine.

## Discussion

The influenza vaccination rate among COPD patients in our study was 19.64%. Though global influenza vaccination rate for patients with COPD varies in different countries, the targeted vaccination rates are higher. However, few studies reported lower vaccination rates like 30% in Italian COPD patients.<sup>11</sup> A Spanish study reported the influenza vaccination rate to be 59.6% in their COPD patients, which is quite higher than in our region.<sup>12</sup> In Turkey, researchers reported 37.9% influenza vaccination rates in their COPD patients, which is also much higher than in our study.<sup>13</sup> A Korean study revealed similar vaccination among Korean population of COPD patients.<sup>14</sup> Researchers have observed that influenza vaccination rates are higher among elderly individuals and those with concomitant health disorders, but in our analysis the most vaccinated individuals were having mean age group of 45 years.<sup>15</sup> The reason might be due to differences in study settings and type of patients enrolled as we included only COPD patients with exacerbation at tertiary care hospital. This may be a limiting factor as due to the main receiving hospital in the region we barely see any proper referral mechanism to channelize our patients and almost all types of patients with variable severity present to our institution.

One of the important factors in not getting vaccinated seems to be the cost and easy availability of the vaccine. During the study period the influenza vaccine was in short supply in the country due to multiple reasons. For that

reason we recommend that influenza vaccine should be made available free of cost to the public.

A Spanish study investigated the factors which affected the yearly vaccination in their COPD patients. They demonstrated the findings that there was no effect of general practitioners' visits on the rate of vaccination in their patients.<sup>16</sup> In our study the vaccination rate was almost zero in the patients who visited general practitioner, indicating that our major health care providers in remote areas are either unaware of yearly influenza vaccination and its association to prevent the episode of acute exacerbation of COPD, or the high cost and less availability issues might have prompted them not to inform the patients. Therefore we also need to focus on this potential group of general practitioners and launch campaign for educating them and making them aware of the benefits associated with yearly influenza vaccination in COPD patients.

The most important indicator we observed for enhancing the rate of influenza vaccination was the level of education as 84% of patients having higher education with BA/BSc degree got vaccinated while only 14% patients among the illiterate were vaccinated. Some authors reported that the vaccination rate was less in highly educated elderly patients with COPD. In contrast, other studies demonstrated that yearly vaccination was improved in patients having higher education.<sup>17</sup> Hence education level influenced yearly vaccination rate that could be either due to advice of doctors or it could be learnt through media and further studies are required to address the impact of education on yearly Influenza vaccination in our country.

The researchers have studied the effect on the vaccination rates by visiting different categories of doctors. In a study by *Chiatti et al.*, it was revealed that influenza vaccination rates were higher in patients visiting chest diseases specialists.<sup>11</sup> We also observed higher rate of vaccination in patients visiting pulmonary disease specialists as compared to those who visited internal medicine specialists, i.e; 16% versus 4%. Therefore lack of advice or recommendation by a doctor was a major reason for non- vaccination in our study. The most important cause for non-vaccination in the study by Ciblak MA, et al was the lack of belief in the efficacy of the vaccines; rather the

vaccines were believed to trigger the flu and hence created unwillingness in the patients to repeat the dose.<sup>18</sup>

In our study, we noted that the lack of knowledge about the efficacy of influenza vaccine or about its usefulness was the main reason for low vaccination rate in our patients. These observations indicate that most COPD patients of our region don't know well about the efficacy of Influenza vaccination.

The difference in the acceptance level of vaccination in both genders was also studied and our study revealed that 82.69% of female patients and 75.88% among males didn't receive vaccination. Various researchers have demonstrated conflicting reports in which some advocate that gender does not affect vaccination, while others claim that vaccination rates are higher among women.<sup>19</sup>

By conducting this study we understand that the relatively low vaccination rate in the elderly Pakistani COPD patients is quite important public health concern that needs to be addressed on priority basis, and require urgent action by our health authorities and clinicians. Furthermore, it has been observed that the possible explanations for the low vaccination rate also include a lack of physicians' recommendation. We therefore concluded that improving the knowledge and awareness of health care workers regarding the effectiveness, safety, and importance of influenza vaccination would be an important strategy to improve yearly vaccination rate.<sup>20,21</sup>

We observed that the rate of acute exacerbation was reduced and the rate of hospitalization was also quite low in patients who received influenza vaccination. This fact has been investigated and reported by several researchers.<sup>16</sup> Hence it is expected that vaccines can help a lot in bringing down the rate of COPD exacerbations, resulting in reduced hospitalizations and deaths associated with COPD.

The study was conducted during covid19 pandemic and we also had no data about covid vaccination status of our patients. The covid related respiratory illness might have affected our results as many exacerbations during this period may be attributable to covid.

### Limitations and Strengths

This analysis was a simple observational study; therefore we could only demonstrate that influenza vaccination is associated with lower risk of acute exacerbations but we were unable to establish a causal relationship. Secondly, since this study is based on a survey therefore we understand that some of the patients' statements may not be accurate. Thirdly it is not a multi-centre study therefore it could not represent the data about vaccination rates among COPD patients in the whole country.

The strength of our study is that for the first time in our region we reported the association between influenza vaccination and risk of acute exacerbations of COPD.

### Conclusions

Yearly influenza vaccination coverage is very low and is associated with increased risk of acute exacerbation rate among patients with COPD in our country. The most notable cause of low vaccination rate is lack of recommendation by their doctors that could be secondary to lack of awareness about vaccination both by doctors and patients. Barriers to vaccination in the patients and health care workers can be overcome with targeted education, free of cost availability and system-wide interventions. Further research is required to attempt for improvements in vaccine status and its acceptability and identify novel targets for future vaccination.

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