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CLINICAL OUTCOMES OF ACUTE EXACERBATION OF COPD IN INFLUENZA ACCORDING TO VACCINATION STATUS IN PATIENTS ABOVE AGE 65 YEARS

Original Research

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ABSTRACT

Background: Chronic Obstructive Pulmonary Disease (COPD) is a leading cause of morbidity and mortality in the elderly, with acute exacerbations frequently triggered by respiratory infections such as influenza. Vaccination against influenza is globally recommended in this population; however, real-world evidence regarding its impact on clinical outcomes remains limited in low-resource settings.

Objective: To assess and compare clinical outcomes, particularly in-hospital mortality and length of hospital stay, in elderly patients (≥65 years) with acute exacerbation of COPD, based on their influenza vaccination status.

Methods: This descriptive study was conducted at the Department of Medicine, Khyber Teaching Hospital, Peshawar, over a 6-month period. A total of 112 patients aged 65 to 80 years, hospitalized with acute COPD exacerbation, were enrolled and divided equally into vaccinated and unvaccinated groups based on verified influenza vaccination status. Key outcomes included in-hospital mortality and prolonged hospital stay (>5 days). Data were collected prospectively and analyzed using SPSS v24, with $p \leq 0.05$ considered statistically significant.

Results: Among the vaccinated group (n=56), in-hospital mortality was 5.4% compared to 16.1% in the unvaccinated group. Prolonged hospital stays were observed in 12.5% of vaccinated patients versus 32.1% in unvaccinated patients. The mean hospital stay was significantly shorter in vaccinated individuals (4.2 ± 1.6 days) than in the unvaccinated group (6.3 ± 2.4 days), indicating a clear protective association of influenza vaccination.

Conclusion: Influenza vaccination was significantly associated with reduced mortality and shorter hospital stays in elderly COPD patients experiencing acute exacerbations. These findings reinforce the urgent need to improve vaccination coverage in high-risk elderly populations.

Keywords: Aged, Chronic Obstructive Pulmonary Disease, Hospital Mortality, Influenza Vaccines, Length of Stay, Preventive Health Services, Respiratory Tract Infections.

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INTRODUCTION

Chronic obstructive pulmonary disease (COPD) remains one of the most prevalent chronic illnesses globally and is a leading contributor to years of life lost, particularly among older adults. Characterized by irreversible airflow limitation, COPD is often complicated by recurrent episodes of acute exacerbations, which significantly contribute to the disease burden, increasing the risk of hospitalization, mortality, and deterioration in quality of life (1,2). These exacerbations are most commonly triggered by respiratory infections, with influenza being one of the most frequently implicated viral agents (3). While there is currently no definitive cure for COPD, exacerbation prevention is central to disease management, as each episode of acute worsening accelerates disease progression and adds to healthcare costs. It is estimated that up to 70% of COPD exacerbations are infectious in origin, with respiratory viruses alone accounting for nearly one-third of these cases. Among them, rhinovirus is the most commonly identified, followed closely by influenza viruses. Co-infections involving both bacterial and viral pathogens are also not uncommon, further complicating the clinical course (4-6). Influenza vaccination remains the most effective preventive strategy against virus-induced exacerbations. Patients with COPD are particularly vulnerable to severe influenza infections, which often result in hospitalization and can be fatal. Global guidelines therefore recommend annual influenza vaccination for this high-risk population (7).

However, existing evidence suggests that the immunological response to influenza vaccination may be suboptimal in COPD patients due to underlying immune dysfunction, potentially affecting vaccine effectiveness (8,9). Despite these recommendations, influenza vaccination rates among elderly COPD patients remain disappointingly low in many regions, partly due to lack of awareness and underestimation of vaccine benefits by both patients and healthcare providers (10). Although some studies have evaluated the impact of influenza vaccination on clinical outcomes in COPD, there remains a paucity of data examining these effects specifically in individuals aged 65 years and older, particularly within real-world hospital and general practice settings. Furthermore, prior studies often lack consideration of prior vaccination history or clearly defined clinical outcomes, limiting the generalizability and clinical applicability of their findings (11-13). The need for robust, contextually relevant evidence is therefore critical to support targeted vaccination strategies and improve health outcomes in this vulnerable group. In view of these gaps, this study aims to assess the clinical outcomes of acute exacerbations of COPD associated with influenza infection in individuals aged over 65 years and to compare these outcomes based on influenza vaccination status. Findings from this study are intended to guide better clinical counselling, promote vaccination uptake, and ultimately contribute to improved management of COPD in elderly patients.

METHODS

This descriptive study was conducted in the Department of Medicine at Khyber Teaching Hospital, Peshawar, over a period of six months following approval of the research synopsis by the institutional review board (IRB). The study aimed to assess clinical outcomes of acute exacerbations of COPD related to influenza in individuals aged 65 years and above, and to compare outcomes based on vaccination status. A sample size of 112 patients was calculated using the WHO sample size formula, considering an anticipated in-hospital mortality rate of 4.9% in vaccinated COPD patients (7), an absolute precision of 4%, and a 95% confidence level. Non-probability consecutive sampling was employed for patient selection. Patients aged between 65 and 80 years of either gender, admitted with acute exacerbation of COPD as per pre-defined operational criteria, were considered eligible for inclusion. Patients were excluded if they had a history of heart failure, known hypersensitivity to influenza vaccine, severe cardiopulmonary compromise, end-stage renal or hepatic disease, or active malignancy. These exclusion criteria were established to minimize confounding factors that could independently influence clinical outcomes such as mortality or duration of hospitalization (14). After obtaining written informed consent, patients meeting the inclusion criteria were enrolled from the indoor medical wards. Baseline demographic and clinical data were collected using a structured proforma. This included age, gender, height (measured using a stadiometer), weight (measured via a calibrated weighing scale), BMI (kg/m²), residence (urban/rural), monthly income, profession, socioeconomic status, educational level, and duration of COPD (in months). History of influenza vaccination within the past 12 months was verified using vaccination cards. Vaccinated individuals were defined as those who had received a 0.5 mL intramuscular dose of influenza haemagglutinin surface glycoprotein, while unvaccinated individuals had not received this vaccine in the defined time frame (15,16).

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All patients were managed according to institutional treatment protocols for acute exacerbation of COPD, which included supplemental oxygen therapy, empirical antibiotic coverage, bronchodilator therapy, and supportive care. Clinical management decisions, including discharge criteria, were made by the attending consultant physician. Patients were followed prospectively until hospital discharge or in-hospital death. Primary clinical outcomes were defined as in-hospital mortality and prolonged hospital stay (defined as more than five days), as per operational definitions. Data collection was performed directly by the principal investigator using the predesigned data collection form (Annexure 1). Collected data were entered and analyzed using IBM SPSS Statistics version 24. Descriptive statistics, including means and standard deviations (or medians with interquartile ranges for non-normally distributed data as determined by the Shapiro-Wilk test), were used for continuous variables such as age, BMI, duration of disease, and length of hospital stay. Categorical variables such as gender, residence, profession, socioeconomic status, education level, vaccination status, and clinical outcomes were reported as frequencies and percentages. Clinical outcomes were compared between vaccinated and unvaccinated groups using chi-square test or Fisher's exact test, as appropriate, with a p-value ≤0.05 considered statistically significant. Post-stratification analysis was conducted to control for potential confounding variables including age, gender, BMI, socioeconomic status, and disease duration.

RESULTS

A total of 112 patients diagnosed with acute exacerbation of COPD were included in this study, equally divided into vaccinated (n=56) and unvaccinated (n=56) groups based on their influenza vaccination status. The mean age of participants in the vaccinated group was 71.2 ± 4.1 years, while in the unvaccinated group it was 72.5 ± 3.9 years. Males constituted the majority in both groups (64.3% in vaccinated and 58.9% in unvaccinated). The mean BMI was slightly higher in the vaccinated group (25.8 ± 3.7 kg/m²) compared to the unvaccinated group (24.9 ± 4.2 kg/m²). Socioeconomic status distribution showed that the majority of vaccinated individuals belonged to the middle-income group (53.6%), while the unvaccinated group had a relatively higher proportion in the lower-income category (35.7%). Employment rates were higher among vaccinated individuals (67.9%) as compared to their unvaccinated counterparts (53.6%). Regarding area of residence, 60.7% of the vaccinated group resided in urban areas compared to an even 50% in the unvaccinated group. Educational status varied, with a higher percentage of vaccinated participants having received middle or higher education (78.6%) than the unvaccinated group (64.2%). In-hospital mortality occurred in 3 vaccinated patients (5.4%) as opposed to 9 unvaccinated patients (16.1%), indicating a notable difference in survival outcomes. Similarly, prolonged hospital stays (>5 days) were observed in only 12.5% of vaccinated patients compared to 32.1% of the unvaccinated cohort. The mean hospital stay for vaccinated individuals was 4.2 ± 1.6 days, while the unvaccinated group had a significantly longer stay of 6.3 ± 2.4 days. These findings suggest a consistent pattern in which influenza vaccination appears to be associated with reduced in-hospital mortality and shorter hospital stays among elderly patients hospitalized for acute exacerbation of COPD. The numerical differences in outcome variables between groups were substantial and support the study objective.

Table 1: Demographic

Variable	Vaccinated (n=56)	Unvaccinated (n=56)
Age (Mean ± SD)	71.2 ± 4.1	72.5 ± 3.9
Gender		
Male	36 (64.3%)	33 (58.9%)
Female	20 (35.7%)	23 (41.1%)
BMI (Mean ± SD)	25.8 ± 3.7	24.9 ± 4.2
Socioeconomic Status		
Lower	14 (25.0%)	20 (35.7%)
Middle	30 (53.6%)	25 (44.6%)
Upper	12 (21.4%)	11 (19.7%)
Occupation Status		
Employed	38 (67.9%)	30 (53.6%)
Unemployed	18 (32.1%)	26 (46.4%)
Residence		
Rural	22 (39.3%)	28 (50.0%)

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Variable	Vaccinated (n=56)	Unvaccinated (n=56)
Urban	34 (60.7%)	28 (50.0%)
Education		
Primary	12 (21.4%)	20 (35.7%)
Middle	24 (42.9%)	18 (32.1%)
Higher	20 (35.7%)	18 (32.1%)

Table 2: In-Hospital Mortality

Vaccination Status	In-Hospital Mortality (n, %)
Vaccinated	3 (5.4%)
Unvaccinated	9 (16.1%)

Table 3: Prolonged Hospital Stay

Vaccination Status	Prolonged Stay >5 days (n, %)
Vaccinated	7 (12.5%)
Unvaccinated	18 (32.1%)

Table 4: Mean Hospital Stay

Vaccination Status	Mean Hospital Stay (days)	Standard Deviation
Vaccinated	4.2	1.6
Unvaccinated	6.3	2.4

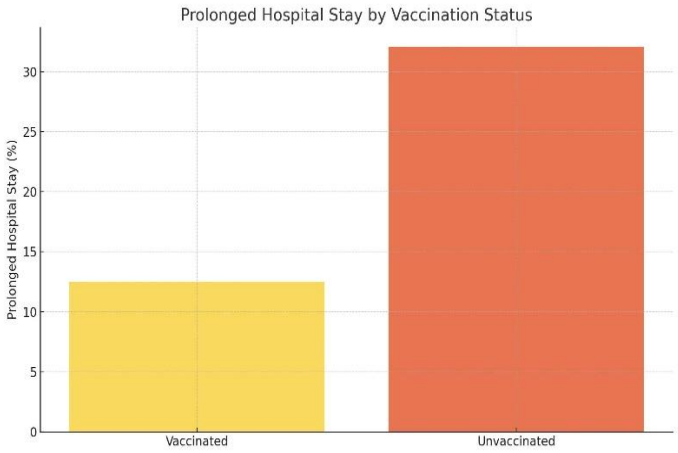

Figure 2 Prolonged Hospital Stay by Vaccination Stats

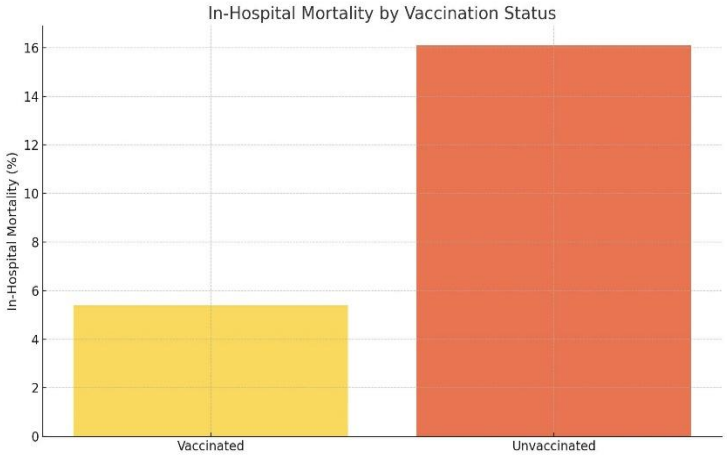

Figure 2 In-Hospital Mortality by Vaccination Status

DISCUSSION

The findings of this study demonstrated that influenza vaccination was associated with significantly better clinical outcomes in elderly patients hospitalized with acute exacerbation of chronic obstructive pulmonary disease (COPD). Specifically, the vaccinated group had lower in-hospital mortality (5.4%) and reduced frequency of prolonged hospital stays (12.5%) compared to their unvaccinated counterparts (16.1% and 32.1% respectively). These findings align with existing international evidence suggesting a protective role of influenza vaccination in elderly populations, particularly those with comorbid conditions like COPD. Several recent studies have reinforced the positive impact of influenza vaccination on reducing hospitalization and mortality rates among older adults with chronic diseases (17,18). A large-scale study conducted among elderly male veterans with COPD reported that influenza vaccination was associated with a 75% reduction in all-cause mortality and an 82% reduction in pneumonia/influenza-related mortality during peak flu

seasons (19). Similarly, a population-wide study from Northern Italy highlighted that influenza vaccination in individuals aged ≥65 years significantly reduced emergency admissions, respiratory complications, and deaths, with the greatest benefit observed in those with higher comorbidity burdens (20). The protective association observed in this study is also supported by recent Asian data. A study using Beijing hospital records found that influenza vaccination lowered in-hospital mortality among patients aged ≥60 years admitted with respiratory or cardiovascular conditions, with a 34% reduction observed among those with COPD (21). Furthermore, a comprehensive cohort study from Taiwan emphasized that even elderly individuals with disabilities, a population highly prone to complications, benefited from reduced hospitalizations and mortality due to influenza vaccination (22). These findings provide compelling support for the implementation and strengthening of annual influenza vaccination campaigns targeting high-risk elderly populations, especially those with COPD. However, the literature is not entirely unanimous. A regression discontinuity analysis conducted in the UK using data from over 7 million elderly patients found no statistically significant reduction in mortality or hospitalizations post-vaccination, suggesting that earlier observational estimates may have been influenced by confounding factors such as healthy user bias (23). This perspective encourages cautious interpretation of associations seen in non-randomized designs, including the present study.

A key strength of this study is its focus on a clearly defined, high-risk group of elderly patients with COPD and its use of objective outcome measures, such as in-hospital mortality and length of stay. The strict inclusion and exclusion criteria helped reduce confounding from severe comorbid conditions. Data collection was done prospectively and under standardized hospital protocols, minimizing variability in patient management. Nevertheless, the study is not without limitations. The use of a non-probability consecutive sampling technique may have introduced selection bias, limiting the generalizability of findings. Additionally, the observational nature of the study prevents establishing a causal relationship between vaccination and outcomes. Unmeasured confounding factors such as prior health-seeking behavior, nutritional status, and underlying frailty may have influenced results. Verification of vaccination status solely via vaccination cards may have missed undocumented or incorrectly recorded vaccinations. Another limitation is the absence of stratification based on influenza season severity or circulating strain, which are known to influence vaccine effectiveness. Moreover, the operational definition of “prolonged hospital stay” as more than five days, while clinically intuitive, lacks universal standardization and could vary across healthcare systems. Future studies should consider multicentric designs with larger sample sizes and use of propensity score matching or instrumental variable analysis to minimize bias. Evaluation of vaccine strain matching, timing of vaccination, and co-administration with pneumococcal or COVID-19 vaccines could provide further insights into optimizing protective strategies for elderly COPD patients. Randomized controlled trials, although difficult to execute ethically in vaccine studies, could offer more definitive evidence if feasible under specific conditions. In conclusion, the study findings contribute to the growing body of evidence supporting influenza vaccination as a beneficial intervention in elderly patients with COPD. Given the consistently demonstrated reductions in mortality and hospital burden, health systems should intensify efforts to improve vaccine coverage in this population, especially in low- and middle-income settings where awareness and access may remain limited.

CONCLUSION

This study demonstrated that influenza vaccination significantly reduces in-hospital mortality and shortens hospital stay among elderly patients hospitalized with acute exacerbation of COPD. These findings underscore the critical role of annual influenza immunization in improving clinical outcomes and reducing healthcare burden in this high-risk population. Strengthening vaccination coverage through targeted awareness and healthcare strategies is essential for better disease management and public health impact.

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AUTHOR CONTRIBUTION

Author	Contribution
Qaiser Wadud*	Substantial Contribution to study design, analysis, acquisition of Data Manuscript Writing Has given Final Approval of the version to be published
Zahid Mohammad Wazir	Substantial Contribution to study design, acquisition and interpretation of Data Critical Review and Manuscript Writing Has given Final Approval of the version to be published
Nayab Sami	Substantial Contribution to acquisition and interpretation of Data Has given Final Approval of the version to be published
Farid Ullah	Contributed to Data Collection and Analysis Has given Final Approval of the version to be published
Almas Khan	Contributed to Data Collection and Analysis Has given Final Approval of the version to be published
Israr Muhammad	Substantial Contribution to study design and Data Analysis Has given Final Approval of the version to be published

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