The role of influenza as a viral etiology of COPD exacerbations during the winter

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ABSTRACT

Introduction
Chronic obstructive pulmonary disease (COPD) is the fourth leading cause of mortality worldwide. COPD exacerbations produce reductions in quality of life and lung function, and are associated with accelerated progression of disease. The role of influenza as etiology of acute exacerbation of COPD during the winter season is not well defined.

The objective of this study was to describe the role of influenza as etiology of acute exacerbation of COPD during the winter season.

Methods
This was a secondary data analysis of the Assessing the Management of Hospitalized Patients with Lower Respiratory Tract Infections database. Hospitalized patients with COPD were included in the study. The Luminex x-Tag respiratory viral panel was used to detect influenza and other respiratory viruses.

Results
A total of 341 hospitalized patients with COPD were included in the study. A viral etiology was identified in 124 (36%) patients. Among those influenza virus was the most common virus identified, in 49 (40%) patients. A total of 28 (58%) patients identified with influenza virus had a history of influenza vaccine for the current season.

Conclusions
This study indicates that influenza is the most common viral etiology of COPD exacerbation during the winter months. The fact that 58% of the population was properly vaccinated for influenza emphasizes the need for more effective vaccines. The history of prior influenza vaccination should not preclude clinicians to suspect influenza viruses as etiologies of acute exacerbations of COPD.

INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is the fourth leading cause of mortality worldwide (1). In the United States it is the third ranked cause of death, killing more than 120,000 individuals each year (2).

COPD exacerbations produce reductions in quality of life and lung function, and are associated with accelerated progression of disease. Additionally, COPD causes high resource utilization including frequent hospitalizations due to acute exacerbations (3). By decreasing the number of acute exacerbations perhaps we can improve patient quality of life and lung function, slow disease progression, and reduce resource utilization.

There have been many studies regarding viral illness and COPD exacerbations. However, the role of influenza as an etiology of acute exacerbation of COPD during the winter season is not well defined. The objective of this study was to describe the role of influenza as etiology of acute exacerbation of COPD during the winter season.

MATERIALS AND METHODS

Study Design
This was a secondary data analysis of the Assessing the Management of Hospitalized Patients with Lower Respiratory Tract Infections (LRTI) database. Adult patients hospitalized with a diagnosis of LRTI were included from 9 Louisville hospitals: Baptist East Hospital, University of Louisville Hospital, Robley Rex VA Hospital, Jewish Hospital, Sts. Mary and Elizabeth Hospital, Norton Hospital, Norton Audubon Hospital, Norton Brownsboro Hospital, and Norton Women's and Kosair Hospital. Hospitalized patients with COPD were also included in the study. This study was approved by the Ethics Committee at each hospital.

Study definitions
Inclusion Criteria
- 18 years of age or older
- Patients Hospitalized ≤ 48 hours
- No new pulmonary or progressive infiltrate in chest X-ray
- Documented history of COPD
- Meet criteria for acute LRTI (see below)

LRTI was defined by the presence of the following inclusion criteria:
1) Signs of acute infection at the time of diagnosis (at least one of the following):
- Fever (>100.0°F) or hypothermia (<96.0°F) or patient subjectively reporting fever, chills or myalgia
- Changes (above or below "normal" for each respective hospital lab involved) in White Blood Cells (WBC) count (leukocytosis, leukopenia) or abnormalities in the differential count (left shift, changes in number or proportion of lymphocytes)
- Mental Status changes
2) Signs and symptoms of respiratory infection at the time of diagnosis (at least one of the following):
- New or increased cough
- Changes in quantity and quality of sputum
- Evidence of reduced oxygenation
- New auscultatory findings (rales, rhonchi, wheezing)
- New shortness of breath
- Tachypnea (Respiratory Rate ≥ 24 per minute)

Respiratory Virus Detection and Study Samples
For all patients enrolled, a nasopharyngeal swab was obtained and analyzed for influenza virus using Luminex RVP® kit. The viral etiology was defined as a positive RT-PCR for any of the following respiratory viruses: influenza, rhinovirus, respiratory syncytial virus (RSV), metapneumovirus, parainfluenza virus, adenovirus and coronavirus. Influenza viruses included Influenza A H1 (pandemic), Influenza A H3 (seasonal), and Influenza B.

RESULTS

A total of 341 hospitalized patients with COPD were included in the study. Patient characteristics are described in table 1.

Table 1 Patient Characteristics

Patient Characteristic Chart n=124	
Variable	Value
Demographics	
Age , Median(IQR)	61.5 (15.2)
Sex, n(%)	59 (47.6)
Nursing home resident, n(%)	1 (0.8)
Comorbid Conditions	
Congestive Heart Failure, n(%)	27 (21.8)
Diabetes, n(%)	42 (33.9)
HIV, n(%)	2 (1.6)
Renal Disease, n(%)	17 (13.7)
Liver Disease, n(%)	7 (5.6)
Neoplastic Disease, n(%)	12 (9.7)
Physical Exam	
Altered mental status on admission, n(%)	3 (2.4)
Respiratory Rate, Median(IQR)	20 (4)
Systolic blood pressure, Median(IQR)	138 (34.2)
Temperature (degrees Celsius),Median(IQR)	98.6 (1.4)
Heart rate, Median(IQR)	102 (24)
Lab/Radiography	
pH, Median(IQR)	7.4 (0.1)
PaO2, Median(IQR)	69.2 (22)
Blood Urea Nitrogen, Median(IQR)	14 (9)
Serum sodium, Median(IQR)	138 (5)
Serum glucose, Median(IQR)	120.5(43.8)
Hematocrit, Median(IQR)	40.8 (6.6)
Pleural effusion, Median(IQR)	0 (0)
Severity of Disease	
ICU admission, n(%)	13 (10.5)
Pneumonia Severity Index, Median(IQR)	75.5(33.8)

A viral etiology for COPD exacerbation was identified in 124 (36%) patients. Influenza virus was the most common virus identified, in 49 (40%) patients. The majority of influenza was H3 seasonal. Other viral etiologies identified included respiratory synctial virus, metapneumovirus, parainfluenza virus, and corona virus. These results are demonstrated in Table 2. Of note a total of (28) 58% of patients identified with influenza virus had a history of influenza vaccine for the current season.

Table 2 Viral etiologies

Virus	Frequency
Corona Virus	5
Corona Virus 229E	1
Corona Virus OC43	4
Influenza	49
Influenza A H1 pandemic	6
Influenza A H3	36
Influenza B	7
Metapneumovirus	12
Parainfluenza Virus	3
Parainfluenza Virus 3	1
Parainfluenza Virus 4	2
Respiratory Syncytial Virus	21
Respiratory Syncytial Virus A	11
Respiratory Syncytial Virus B	10
Respiratory Syncytial Virus B, Rhinovirus/Enterovirus	1
Rhinovirus/Enterovirus	33
Total	124

CONCLUSIONS

This study indicates that influenza is the most common viral etiology of COPD exacerbation during the winter months. Influenza viruses included Influenza A H1 pandemic, Influenza A H3 seasonal, and Influenza B . Vaccines during the study period also included these viruses.

Since influenza is a preventable disease through vaccination, encouraging COPD patients to get their immunization should help to decrease the number of acute exacerbations thus improving patient quality of life and lung function, slowing disease progression, and reducing resource utilization (4).

The fact that 58% of the study population identified with influenza were vaccinated against the virus emphasizes the need for more effective vaccines. However, Influenza vaccination should still be encouraged in all patients with COPD. Furthermore, the history of prior influenza vaccination should not preclude clinicians from suspecting influenza viruses as etiologies of acute exacerbations of COPD.

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