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Prevalence of Respiratory Viruses in Exacerbation of Chronic Obstructive Pulmonary Disease

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Abstract

Chronic Obstructive Pulmonary Disease (COPD) is a progressive disease characterized by the obstruction of airflow in the lungs, airway inflammation, and decline in lung function over time, and gradual impairment in quality of life. COPD exacerbation has significant contribution to the worldwide morbidity and mortality rate and incurs extensive expenses in the healthcare resources. Respiratory viruses are a major cause of concern for patients suffering with lung diseases, such as, Chronic Obstructive Pulmonary Disease (COPD). The main objective of the study was to characterize the viruses prevalent in COPD patients in Northern India. During the period of 2014-2015, respiratory viruses were identified in 70.9% patients. Influenza Virus was found to be most prevalent in this study, which can possibly be due to the outbreak at the time of sample collection.

Keywords: Chronic obstructive pulmonary disease; Coronavirus; Influenza

Introduction

Chronic obstructive pulmonary disease is a progressive disease contributing significantly to worldwide morbidity and mortality. It poses a severe economic burden in Asia-Pacific region, as it does to the world by incurring extensive healthcare expenses. The COPD patients are associated with symptoms such as cough, sputum, and dyspnea and progressive decline in lung function [1,2]. Globally, about 64 million people from low- and middle-income countries have COPD, with about 90% mortality rate [3]. However the true burden of the disease is hard to estimate, because it is not recognized until moderately advanced [4].

COPD exacerbations contribute significantly to the increase in mortality rate and it is estimated to be the third leading cause of death worldwide by 2030 [5]. The studies determining the prevalence of COPD in India are highly discrepant ranging from 2% - 22% in men and in women from 1.2%-19% [6,7]. The inducing factors for Acute Exacerbation of Chronic Obstructive Disease (AECOPD) include infectious (Viral and bacterial infections) and noninfectious (outdoor and indoor pollution agent) agents [5]. The effect of viral infections alters the respiratory biome in the lower respiratory tract, thereby making the patient more prone to the secondary bacterial infections. Hence respiratory viral infection is responsible for more severe AECOPD and takes a longer recovery time [8].

The main objective of this study was to identify and characterize the respiratory viruses prevalent in COPD patients in Northern India. The study will help in better understanding of viral infection in exacerbations of COPD and aid in the development of preventive and therapeutic strategies thereby severely impacting the morbidity and mortality of the disease.

Methodology

Subject recruitment

Patients of 35 years and above, with their written consent, were enrolled in the study at Vallabhbhai Patel Chest Institute (VPCI), New Delhi. The criteria of subject enrollment were that they should have characteristic symptoms like chronic cough, dyspnea, and / or a history of exposure to risk factors for the disease (tobacco smoke, smoke from biomass fuels). The study excluded the patients having any concurrent pulmonary disease and any other cause of breathlessness.

Sample collection

The samples in the form of Nasal and Throat swabs were collected from COPD patients from VPCI and transported to the Virology laboratory at the Department of Microbiology at Vallabhbhai Patel Chest Institute, University of Delhi, India for further processing.

Real-time PCR detection

RNA was isolated from the Nasal and Throat Swab samples using viral RNA isolation kit (Qiagen RNeasy Mini Kit, Qiagen, Germany, Cat No# 74106) as per manufacturer's instructions. The isolated viral RNA were subjected to multiplex real time PCR assay with the help

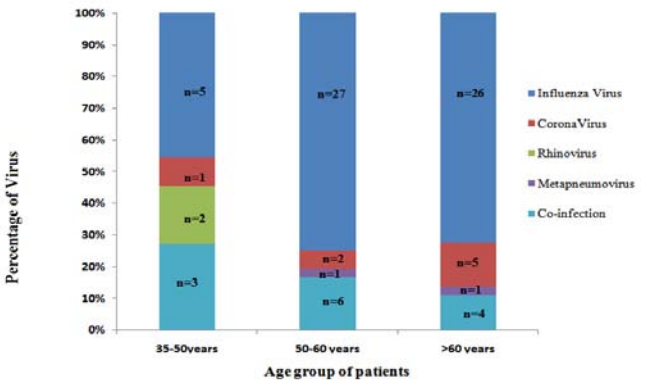

Figure 1: Total percentage of Respiratory Virus prevalent in different age groups. The prevalence of respiratory virus increased with the age in AECOPD patients. n denotes the number of patients in particular age group.

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Table 1: The table demonstrates the number of samples taken at different time intervals and the number of positive viruses detected during that time frame.

	January 2014-March 2014	April 2014-June 2014	July 2014–September 2014	October 2014–December 2014	January 2015–March 2015
Samples collected	42	8	16	21	30
Influenza	11	3	7	13	24
Coronavirus	8				
Rhinovirus				1	1
Metapneumovirus	1				
Co-infection	2	2	2		7

of Fast Track Diagnostics (FTD) Respiratory pathogens 21 plus kit (Fast Track Diagnostics, Luxembourg, FTD-2-96/12) according to manufacturer's instructions. In brief, the kit consists of five separate primers and probes), which at specific wavelength are specific for detection of respiratory viruses [rhinovirus, coronavirus influenza, parainfluenza, respiratory syncitial virus, adenovirus, human metapnemovirus] and other pathogens in the nasal swab samples by real time RT-PCR.

Results

Of the 117 COPD patients enrolled, the average age of the patients was 65.16 + 10.12 years. From January 2014 to March 2015, 34 (29.05%) were un-infected and 83 (70.9%) were found to be infected with different respiratory virus as detected by real time PCR of which 22.09 % were females and 77.10% were males. Among the infected patients, 11 (13.25%) were found to be between the age group of 35- 50 years, 36 (43.37%) were from age group 50-60 years and 36 (43.37%) were > 60 years of age.

The various respiratory viruses reported in this study were Influenza virus, coronaviruses, human metapneumovirus, parainfluenza viruses and rhinovirus. The most prevalent virus detected in the study was Influenza virus present in58 (49.57%) patients among which two (1.7%) were Influenza B positive. Coronavirus was observed in eight (6.8%) patients and Rhinovirus was observed in two (1.7%) patients. Among the other infected patients, metapneumovirus was detected in two (1.7%) patients and 13 (11.11%) were co-infected with two different types of virus as shown in Table1.Viral detection in Acute Exacerbation of COPD (AECOPD) increased with age, with about 30.76% virus detection in each 50-60 age group and >60 years (Figure 1).

Discussion

COPD exacerbations have significant contribution to the worldwide morbidity and mortality rate. It has been suggested on various occasions that viral infections are highly prevalent in AECOPD which corroborates with this study [9,10]. A number of viruses (rhinovirus, Coronavirus, influenza A and B, parainfluenza, adenovirus and respiratory syncytial virus) lead to respiratory tract infections triggering the exacerbations as shown in our results which is in accordance with the other published literature [10]. The epidemiology of viral infections was evaluated and a high rate (70.9%) of respiratory virus infections was detected. More common occurrence of COPD exacerbations during extreme temperature conditions- both heat and cold, further provides evidence for induction of respiratory COPD exacerbation [11].

In our study the overall prevalence of Influenza A virus was found to be significantly high (47.8%) as shown previously by Zakharkina et al. [12] and Tan et al. [13]. This could be because there was outbreak of influenza A (January-March 2015, as shown in Table 1) in India during the time period of sample collection and the patients were not vaccinated. In the present study, Coronaviruses was observed 6.8% of the patients which is higher than previously reported data [14]. In accordance with the present data Ko et al. reported that the most prevalent viruses detected during acute exacerbations of COPD in Hong Kong were influenza A virus and coronavirus [15].

Apart from the mortality rate, COPD causes severe economic losses to the country in which about 84% cost is associated with the hospitalization [16]. This is mainly because of lack of awareness and poor diagnosis. In the country like India, it is more economical to prevent the development of COPD than the treatment. For this, it is important to understand the inducing factors that lead to and their contribution to AECOPD especially in Indian scenario.

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