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Study of Prevalence and Pattern of Infections in Acute Exacerbations of Obstructive Airway Disease

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Abstract

Objectives: To study the prevalence and pattern of infections causing exacerbations of obstructive airway diseases.

Methods: A prospective cross sectional study which included 126 consecutive obstructive airway disease patients were enrolled for the study. All the included patients were subjected to detailed history, clinical examination and routine investigations including sputum Gram's stain and aerobic culture after obtaining a written informed consent. Pharyngeal swab was collected and sent in Viral Transport Medium (VTM, Himedia) within 24 hrs to Regional Medical Research Centre (ICMR), Bhubaneswar for detection of respiratory viruses. Samples were tested by Real Time reverse-transcription polymerase chain reaction (RT-PCR).

Results: Among patients with COPD, Flu A/H3N2 (9.375%) was found in highest number of patients followed by rhinovirus (7.3%). In bronchial asthma patients,virus was isolated only in 3 cases (13.6%). No virus was detected in bronchiectasis patients. Isolated bacterial infection was detected in 26 cases (20.63%). *Acinetobacter baumanii* and *Klesiella pneumoniae* were most common bacterial pathogens detected. Bacterial pathogens were commonly isolated among COPD patients.Co-infection with both bacteria and virus was detected in 12 patients (9.52%) of which 11 were diagnosed with COPD. Only 1 case of bronchial asthma reported a co-infection. Among cases with co-infection with both bacteria and virus, *Acinetobacter baumanii* and *Pseudomonas aeruginosa* were found to be most common bacterial pathogens. There was no typical pattern in viral infection among the cases throughout the year.

Conclusion: The risk of exacerbation due to viral etiology is perennial but might be self limiting. Recovery from exacerbation takes a long time and patients with exacerbations have an impaired quality of life, diminished exercise capacity and loss of lung function.

Key words: Obstructive airway disease, Exacerbation, COPD, bronchiectasis.

Introduction

Obstructive airway disease encompasses chronic obstructive pulmonary disease (COPD), bronchial asthma, bronchiectasis, cystic fibrosis and small airway disease.

COPD has been defined as a "common preventable, treatable disease that is characterized by persistent respiratory symptoms and airflow limitation that is due to airway and/or alveolar abnormalities usually caused by significant exposure to noxious particles or gases".[1] Asthma is a heterogeneous disease usually characterized by chronic airway inflammation. It is defined by the history of respiratory symptoms such as wheeze, shortness of breath, chest tightness and cough that vary over time and in intensity together with variable expiratory airflow limitation.[2] Bronchiectasis is defined by dilation or ectasia of the airways or bronchus.[3]

COPD is an umbrella term for various clinical entities with multiple causes resulting in airflow limitation that is not fully reversible.[4,5,6] COPD is a clinical syndrome characterised by chronic respiratory symptoms, structural pulmonary abnormalities, lung function impairment, or any combination of these.[7] It is the 3rd leading cause of death worldwide; COPD led to 3.2 million deaths in 2017, a toll that is expected to reach 4.4 million yearly by 2040.[8,9] A COPD exacerbation is defined as "an increase in dyspnoea, cough, or sputum production with or without symptoms of upper respiratory infection".

Infection is an important cause of acute exacerbation and progression of COPD.[10,11] Approximately 40–60% of exacerbations are due to upper respiratory tract infections and/or viral infections;[12,13] 30 to 50% of exacerbations have a bacterial cause (*Haemophilus influenza*, *Streptococcus pneumonia*, *Moraxella catarrhalis*, and *Chlamydia pneumoniae*) and viruses such as influenza virus and rhinoviruses are involved in up to 30% cases.[14]

Respiratory viral infections and infections with atypical bacteria such as *Mycoplasma* and/or *Chlamydia* have been implicated in the development of asthma. Asthma exacerbations are largely responsible for the overall disease burden, leading to hospitalizations, decline in lung function, and sometimes death. Triggers described by adult asthma patient are either allergic (pollen, dust, mold, animal dander, cockroaches, food allergens) or non-allergic. Non-allergic triggers include respiratory infections, exercise, cold air, air pollution, medications and other factors.

Identification of infectious triggers can be useful in guiding treatment of acute asthma exacerbations as well as predicting resolution of symptoms. Differentiating between true viral infection and colonization (epiphenomenon) is only one of the challenges in establishing the clear role of viral infection in exacerbations.[15]

Bronchiectasis is a major contributor to chronic respiratory morbidity and mortality globally, and a few randomised controlled trials are available to guide management.[16] An exacerbation in bronchiectasis is defined as an increase in sputum volume or purulence, increased cough frequency or a change type of cough (dry to wet) for atleast 3 consecutive days.[17] The role of antibiotics in the management of exacerbations of any severity has also been questioned by some experts, who have suggested that exacerbations triggered by viruses might be self limiting.[18]

There is scanty report on the study of viral etiology of exacerbations of obstructive airway disease from eastern India. This study aimed to find the prevalence and pattern of infections among patients with obstructive airway disease.

Materials and Methods

Study Population

A total of 126 consecutive obstructive airway disease patients admitted with exacerbations in the wards and intensive care units in KIMS, Bhubaneswar from July 2018 to December 2019 were enrolled for the study.

Study Design

It was a prospective cross sectional observational study.

Inclusion Criteria

Acute exacerbation of chronic COPD, asthma, bronchiectasis on medications suffering from exacerbations were included.

Exclusion Criteria

1. Patients with new onset respiratory illness.
2. Patients with diffuse parenchymal lung disease.
3. Patients with pulmonary tuberculosis.
4. Patients with suspected malignancy.

Procedure

All the included patients were subjected to detail history, clinical examination, chest X-ray, HRCT thorax (whenever necessary) and laboratory investigations like CBC, sputum gram stain and aerobic culture for detection of bacteria after obtaining a written informed consent from them or the attendant. Pharyngeal swab was collected and sent in Viral Transport Medium (VTM, Himedia) within 24 hrs to Regional Medical Research Centre (ICMR), Bhubaneswar for detection of respiratory viruses. Samples were tested by Real Time reverse-transcription polymerase chain reaction (RT-PCR). The test was done by using recommended commercial kit (FTD, UK) following manufactures instruction on ABI-7500 equipment (ABI, USA).

Observation

1. Distribution of pathogens in acute exacerbation of obstructive airway disease

The total number of patients (N = 126) enrolled for the study were classified as COPD (76.19%), bronchial asthma (17.46%) and bronchiectasis (6.35%) based on their history, clinical findings and radiology. Among patients with COPD, Flu A/H3N2 (9.375%) was found in highest number of patients followed by rhinovirus (7.3%). Virus was isolated only in 3 cases (13.6%). No virus was detected in bronchiectasis patients (Table 1).

Isolated bacterial infection was detected in 26 cases (20.63%). *Acinetobacter baumanii* and *Klesiella pneumoniae* were most common bacterial pathogens detected. Bacterial pathogens were commonly isolated among COPD patients (Table 2).

Co-infection with both bacteria and virus was detected in 12 patients (9.52%) of which 11 were diagnosed with COPD. Only 1 case of bronchial asthma reported a co-infection (Table 3). Among cases with co-infection with both bacteria and virus, *Acinetobacter baumanii* and *Pseudomonas aeruginosa* were found to be most common bacterial pathogens (Table 4).

There was no typical pattern in viral infection among the cases throughout the year. Flu A (H3N2) was observed in 10 cases for whom sample was collected between March to Sept. followed by Rhinovirus in 8 cases. Other viruses detected throughout the year in low prevalence (Table 5).

2. Demographic, clinical and radiological comparison in various types of infection

Majority of the patients belonged to the age group of greater than or equal to 60 years (34.126%) followed by patients in the age group of 40–59 years (11.11%). Males predominated in all groups with a M:F ratio of 2.1:1. The clinical presentations did not differ significantly in all groups. Hyperinflation was the commonest finding in all groups on Chest X ray examination. Patients had recovered within 7 days in majority of cases among the viral and co-infection categories, which

Table 1. **Viruses detected amongst the enrolled patients**

List of viruses	COPD (n = 96)	%	Bronchial asthma (n = 22)	%	Bronchiectasis (n = 8)	%
Flu-A(H3N2)	9	9.375	1	4.54	0	0
Flu-A/PDM 09	3	3.125	0	0	0	0
Flu-B	4	4.17	0	0	0	0
RSV-A	2	2.08	0	0	0	0
RSV-B	5	5.2	0	0	0	0
Hmpv	3	3.125	1	4.54	0	0
PIV-1	0	0	0	0	0	0
PIV-2	0	0	0	0	0	0
PIV-3	2	2.08	0	0	0	0
PIV-4	0	0	0	0	0	0
Rhinovirus	7	7.29	1	4.54	0	0
Adenovirus	2	2.08	0	0	0	0
Total	37	38.54	3	13.6	0	0

Table 2. **Bacteria detected as isolated cause among patients (*N* = 126)**

Name of bacteria	COPD (*n* = 96)	%	Bronchial asthma (*n* = 22)	%	Bronchiectasis (*n* = 8)	%	Total
Acinetobacter baumanii	4	4.17	1	4.54	0	0	5
Pseudomans putida	1	1.04	0	0	0	0	1
Staphylococcus aureus	2	2.08	0	0	0	0	2
Enterobacter aerogens	2	2.08	0	0	0	0	2
Klebsiella pneumoniae	2	2.08	1	4.54	2	25	5
E. coli	3	3.125	0	0	0	0	3
Burkholderia cepacia	1	1.04	0	0	0	0	1
Enterobacter cloacae complex	2	2.08	1	4.54	0	0	3
Pseudomonas aeruginosa	1	1.04	1	4.54	1	12.5	3
Serratia marcescens	1	1.04	0	0	0	0	1
Total	19	19.79	4	18.18	3	37.5	26

Table 3. **Bacterial, viral infection and co-infection as a cause of acute exacerbation of obstructive airway disease**

Disease	Total no. of cases	Cases positive for only viral infection	Cases positive for only bacterial infection	Cases with co-infection (bacteria and virus)
COPD	96	20	18	11
Br. asthma	22	2	4	1
Bronchiectasis	8	0	3	0

Table 4. **Distribution of bacteria in co-infection cases**

Bacteria	No. of cases with co-infection	%
Acinetobacter baumanii	4	33.3
Klebsiella pneumonia	2	16.7
Streptococcus pneumoniae	1	8.3
E.coli	1	8.3
Pseudomonas aeruginosa	4	33.3
Total	12	

speaks of early convalescence. Renal failure and dyselectrolytemia were more common in patients with bacterial infection indicating the severity of the illness while leucocytosis was noticed in all groups. Patients with co-infection had respiratory failure predominantly with requirement for mechanical ventilation (50%).

Discussion

The natural course of obstructive airway disease is interrupted by episodes of respiratory symptom worsening, termed exacerbations. Exacerbations are important events in COPD and are major determinants of health status, independent predictors of mortality. This exacerbation also drives disease progression, with approximately 25% decline in lung function.[19]

Over the past two decades, increasing evidence has shown that in patients with chronic airway disease, viral infection is a common cause of exacerbation especially in asthma and bronchiectasis.[20,21] In our study a high prevalence of 31.7% was observed with viral etiology. A systematic review by Mohan et al. found that viruses were detected in 34.1% of exacerbations.[22]

In our study 25% of cases were infected with influenza A virus with a subtype of H3N2 where as Flu B was observed in 10% of cases. Parvaiz et al. reported 44% of H3N2 among influenza positives with a history of COPD followed by 26% infections with Flu B.[23] Human rhino virus was commonly associated with exacerbations. Viruses can be identified in up to 69% exacerbations among all viral isolates.[24]

Bacteria may be present in lower airway as coloniser in stable cases. The presence of gram negative bacteria as secondary invaders or opportunistic pathogens causing exacerbations still needs to be defined. In 11 out of 96 COPD cases in our series there was bacterial and viral co-infection. It is likely that viral infection predisposes the susceptible host to secondary bacterial co-infection and vice versa.[25]

Bacteria play a diverse and complex role in asthma pathogenesis and acute and chronic exposure can precipitate exacerbation and persistence of asthma. Advances in bacterial identification and efforts to sample the airway directly led to the recognition that bacteria are critical in asthma pathogenesis. *Mycoplasma pneumonia*e, *Chlamydia pneumoniae*, *Chlamydia trachomatis*, *Staphylococcus aureus* and *Hemophilus influenza* have been identified as causes of asthma.[26]

In our series, we had gram negative bacteria as an etiology of exacerbation in obstructive airway disease which could be due to underlying immunocompromised state. Thus viral or bacterial infections were observed in 31.81% asthma exacerbations. However Likura M, Hojo M, Koketsu R et al. reported such infections in 70% of adult patients with an asthma exacerbations.[27] Clinical studies report that asthma onset after an

Table 5. **Month-wise distribution of pathogenic viruses (*N* = 126)**

	Jul-18	Aug-18	Sep-18	Oct-18	Nov-18	Dec-18	Jan-19	Feb-19	Mar-19	April-19	May-19	Jun-19	Jul-19	Aug-19	Sep-19	Oct-19	Total
Flu-A (H3N2)	0	0	0	0	0	0	0	0	2	1	1	1	3	1	1	0	10 (25%)
Flu-A/PDM 09	0	0	0	0	0	0	1	2	0	0	0	0	0	0	0	0	3
Flu-B	0	1	3	0	0	0	0	0	0	0	0	0	0	0	0	0	4
RSV-A	0	0	0	1	0	0	1	0	0	0	0	0	0	0	0	0	2
RSV-B	0	1	2	1	0	0	1	0	0	0	0	0	0	0	0	0	5
hMPV	0	0	1	0	0	0	0	2	0	0	0	0	0	0	0	1	4
PIV-1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
PIV-2	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
PIV-3	1	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	2
PIV-4	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Rhino virus	1	0	0	0	1	0	1	1	0	0	0	0	1	0	0	3	8
Adeno virus	0	0	0	0	0	0	0	2	0	0	0	0	0	0	0	0	2
Total	2	2	6	2	1	0	4	8	2	1	1	1	4	1	1	4	40

acute respiratory illness is exceedingly common in adult-onset asthma cases.[28]

Radiologically diagnosed pneumonia was witnessed in 7 out of 59 cases, indicating the extent of microbes in causation of acute exacerbations. 19 cases out of 59 (32.20%) required ICU admission for mechanical ventilation which corroborated with gram negative microbes.

Environmental pollution accounts for cases in which no microbe could be isolated.

Conclusion

The risk of exacerbation due to viral etiology is perennial but might be self limiting. Recovery from exacerbation takes a long time and patients with exacerbations have an impaired quality of life, diminished exercise capacity and loss of lung function.[29] It is imperative to identify the etiological agent of exacerbations of obstructive airway diseases and to treat bacterial infections judiciously in order to prevent decline in lung function. At the same time antibiotic stewardship has to be kept in mind as antimicrobial resistance is of global concern.

Ethical Clearance

The study was approved by the Institutional Ethics Committee, Kalinga Institute of Medical Sciences, KIIT deemed-to-be University, Bhubaneswar.

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Conflicts of Interest

None.

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