International Journal of Science and Research (IJSR)
ISSN (Online): 2319-7064
Index Copernicus Value (2016): 79.57 | Impact Factor (2015): 6.391

Association of Severity of Chronic Obstructive Pulmonary Disease with Sputum Bacterial Isolation

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Abstract: ***Background: Chronic Obstructive Pulmonary Disease is a frequent respiratory disease seen in chronic smokers. These patients suffer from episodes of exacerbations, commonly caused by bacterial infection. The study aimed at finding association of COPD severity with the bacteria isolated. Methods: The study was conducted in Silchar Medical College, Assam in 114 patients. Sputum samples were sent for culture testing. Spirometry was performed to grade the severity. Results: A significant association was found between increasing severity and greater isolation of Gram Negative bacteria (p-value< 0.05). Conclusion: Gram Negative bacteria are a common cause of exacerbations in more severe cases of COPD.***

Keywords: Chronic Obstructive Pulmonary Disease, Exacerbation, Sputum, Bacteria

1. Introduction

Chronic obstructive pulmonary disease (COPD) constitutes about 30% of all the cases seen in chest clinics and accounts for 1- 2.5% of all hospital admissions in India.[1] As per W.H.O, It is the third leading cause of death worldwide behind ischemic heart disease and stroke.[2]India contributes a significant percentage of COPD mortality which is estimated to be amongst the highest in the world, with about 556,000 (>20%) out of a world total of 2,748,000 annually.[3]

COPD is defined by the Global Initiative for Chronic Obstructive Lung Disease (GOLD) as 'a common preventable and treatable disease, characterized by persistent airflow limitation that is usually progressive and associated with an enhanced chronic inflammatory response in the airways and the lung to noxious particles or gases with exacerbations and comorbidities contributing to the overall severity in individual patients'.[4]

Established risk factors for development of COPD include tobacco smoking, environmental tobacco smoke, hyper-responsiveness to various exogenous stimuli, occupational coal dust exposure, prolonged exposure to smoke produced by biomass combustion and alpha-1-antitrypsin deficiency.[5]

Acute Exacerbations of COPD (AECOPD) are a prominent feature of the natural history of COPD. Exacerbations are defined as -"An acute event characterized by a worsening of the patient's respiratory symptoms that is beyond normal day to day variations and leads to a change in medication".[4]

The clinical severity of an AECOPD varies widely. It may be managed in the out-patient setting or may be severe enough to require hospitalization. If complicated by respiratory failure, intensive care including non-invasive or invasive ventilator support, may be required.[6]

Ball et al reported that AECOPD contributes considerably to the morbidity and the diminished quality of life of people afflicted with COPD. Patients who suffer the most exacerbations have significantly lower health status.[7] Kanner et al showed that exacerbation frequency predicts an accelerated decline in lung function.[8]An increase in in-hospital and future mortality is seen in frequent exacerbations of COPD.[9]AECOPD episodes have been associated with diminished physical activity and increase in cardiovascular risk, osteoporosis and neuropsychiatric complications.[6]Exacerbations of COPD have considerable impact on health care system at both primary and tertiary care levels as they are the major reason for antibiotic use and admissions. Additionally, such episodes lead to indirect costs because of days lost from work.[10]

Bacterial infection stands as one of the main precipitants of AECOPD.[11]Older studies implicated the following bacteria as a cause of the exacerbation- Moraxella catarrhalis, Hemophilus influenzae, Streptococcus pneumonia.[7] However, in the recent studies there has been noted a shift from the older isolates to different ones, namely- Enterobacteriaceae and Pseudomonas aeruginosa.[6]Atypical organisms, such as Mycoplasma pneumoniae and Chlamydia pneumoniae have been isolated rarely.[12]

2. Materials and Methods

All the patients with clinical features suggestive of COPD, such as progressive dyspnea, chronic cough, chronic sputum production with history of exposure to risk factors or a family history of COPD, were assessed. Out of these, the patients fulfilling the criteria for Acute Exacerbation of COPD were enrolled. AECOPD was diagnosed as per the criteria put forth by Anthonisen et al.:[13]

Presence of any two of the following symptoms:
-Increased cough
-Increased purulence and / or volume of expectorations and
-Increased severity of dyspnoea.

These patients were treated and stabilized. Informed and written consent was obtained from the patients.A detailed clinical history was taken and complete physical examination was done in all cases. A spirometry was performed on all patients, along with bronchodilator reversibility testing. A post-bronchodilator FEV_1/FVC of <0.7 confirmed the diagnosis of COPD as per the GOLD 2015 guidelines.[4]Severity of COPD was assessed using FEV_1% predicted values.[4]Routine investigations, Chest Radiograph, and ECG were done in all the patients.

The data of such patients fulfilling the inclusion and exclusion criteria were collected on a structured preformat. Sputum samples were collected from all eligible patients for sputum culture and sensitivity testing. Processing and examination of the samples was done in the Department of Microbiology.

Study setting:
The present study was conducted in the Department of Medicine, Silchar Medical College and Hospital, Silchar, Assam.

Period of study:
The present study was conducted from 1st August 2016 to 31st July 2017 for a period of one year.

Sample Size:
A total of 114 patients from the OPD and IPD of the Department of Medicine were included randomly for the study, after fulfilment of inclusion and exclusion criteria

Study Design:
The study was a hospital based cross-sectional observational study.

Inclusion Criteria:
All patients above 18 years of age, diagnosed with COPD, as per GOLD criteria[5] presenting with acute exacerbation, were included in the study.

Exclusion Criteria:
1) Patients treated with antibiotics in the past 48 hours
2) Known cases of malignancy or immunosuppression
3) Tuberculosis
4) Heart Failure
5) Pneumonia
6) Asthma
7) Unwilling patients

Ethical Clearance:
Ethical clearance for the study was taken from the Ethical Committee of Silchar Medical College and Hospital, Silchar, Assam (Date of approval- 13th February 2015)

Statistical analysis:
The data collected, were compiled, tabulated and analysed in terms of descriptive statistics using SPSS version 17.0 software. Continuous variables were presented as mean ± SD and categorical variables were expressed as frequencies and percentages. Categorical data between the groups were compared using Chi square test. A p-value < 0.05 was considered as statistically significant. Graphical and diagrammatic representations were made wherever felt necessary.

3. Results

Out of the 114 cases, maximum number of cases were seen in the age groups of 56-65 years (42%). The next commonest age group was 66-75 years, with 20% of the cases. As many as 19% of the patients were between the ages of 46-55 years. Other 13% cases were above the age of 75 years. Mean age was 62.9 ±10.7 years.

There were 88/114 (77.2%) males and 26/114 (22.8%) females. The Male: Female ratio was 3.4:1.

There were 58/114 (50.9%) farmers, 29/114 (25.4%) day labourers, 13/114 (11.4%) shopkeepers and 14/114 (12.3%) housewives.

All patients (100%) had dyspnoea on presentation. The next frequent presenting symptom was cough (95.6%). Increased sputum volume was seen in 68.4% patients. Chest pain was seen in 34.2% and fever in 34.5% of the cases.

Out of the 114 patients, bacteria were detected in 80 patients on microscopy. Out of these 80 patients, Gram positive bacteria were seen in 32.5% cases whereas Gramnegative bacteria were seen in 67.5% cases.

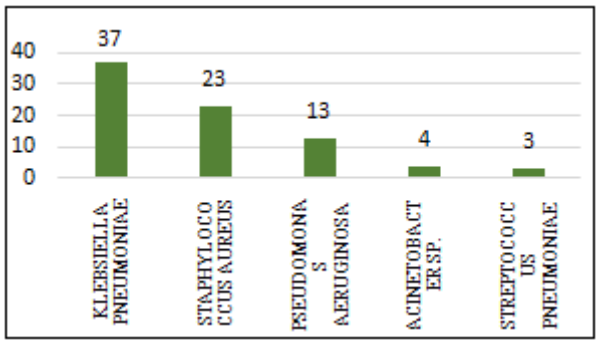

Figure 1: Bar diagram showing the bacteriological profile

Table 1: Association between nature of sputum and frequency of isolation of bacteria

Nature of Sputum	Sputum Culture (No. of cases)		Total	P-value
	Sterile	Bacteria grown		
Mucoid	22 (61.1%)	14 (38.9%)	36 100%	
Mucopurulent / Purulent	12 (15.4%)	66 (84.6%)	78 100%	
Total	34 (29.8%)	80 (70.2%)	114 100%	<0.0001

There was a statistically significant association between nature of sputum and frequency of isolation of bacteria (p-value < 0.05).

Out of 114 patients, there were 41.2% patients with stage 4 GOLD severity, 31.6% patients with stage 3 GOLD severity and 27.2% patients with stage 2 GOLD severity. There were no patients with GOLD stage 1 in this study. The mean FEV_1% was 39.60 ± 19.560.

Table 2: Association of FEV_1% predicted with sputum culture.

	Sputum Culture and Staining Results			Total	
	Sterile	Gram Positive	Gram Negative		
50% </= FEV_1<80% predicted	11 32.4%	12 46.2%	8 14.8%	31 27.2%	P-value
30% </= FEV_1<50% predicted	11 32.4%	8 30.8%	17 31.5%	36 31.6%	
FEV_1<30% predicted	12 35.3%	6 23.1%	29 53.7%	47 41.2%	
Total	34 100%	26 100%	54 100%	114 100%	0.024

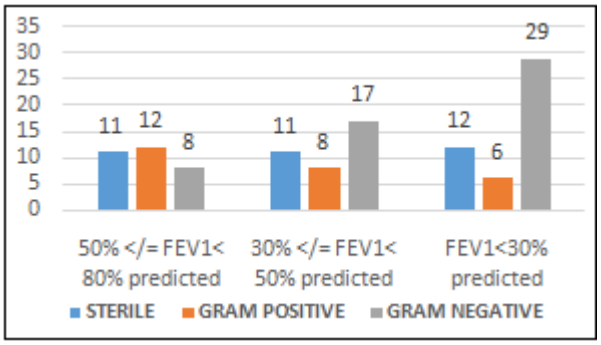

Figure 2: Bar diagram showing association of FEV_1% predicted with sputum culture.

4. Discussion

Socio-demographic data:

1) Age

Age is often considered as among the risk factors of COPD. But whether healthy ageing by itself leads to COPD or it reflects the sum of cumulative exposures throughout life, is a debated issue. [4] In the study conducted by Saikat Basu et al, which similar to this study, majority of patients (33.33%) were in the ages between 55-65 and 65-75.[13] In the other study, as many as 40.19% were also in the age group of 55-65.[14]Mean age in the study by Shahanawaz et al was 59.42 + 10.59 years.[15]

2) Sex

A male preponderance, similar to the present study has been noted in other studies. In a study conducted in Kolkata, there were reported 76.2% male and 23.8% female cases. The ratio of male:female in that study was 3.2 : 1.[13] There were also around 79 % male cases and 21 % female cases that recorded in the other study [16]. Miravitlles et al noted 81 % males and 19% females in their study.[17]. The higher number of males in the study may be a result of a higher number of males engaging in tobacco smoking as compared to females. The Global Adult Tobacco Survey revealed that 47.9% Indian males and 20.3 % Indian females smoke tobacco.[18]. The higher male prevalence in this study could also be a result of the greater financial independence, better disease awareness and the earlier seeking of medical attention of males in this part of the country.

3) Occupation

The greater number of farmers in this study could be because this part of North-Eastern India primarily has agriculture-based population.

Spirometric data:

A majority of the patients had 'very severe' i.e. GOLD 4 (FEV_1% <30%) and 'severe' i.e. GOLD 3 (30%</= FEV_1% <50%) COPD.[4]

This institute being a tertiary referral centre, caters to a large number of patients with severe forms of disease. A large proportion of the cases having a severe / very severe grade of COPD, could be a result of this.

Bacteriological data:

1) Frequency of isolation of bacteria

Bacterial growth was present in 70.2 % cases. In 29.8% cases there was no growth seen (sterile). Aleemullah et al in 2016, reported that 73.65% of samples in their study showed bacterial growth.[19] Kumar Surindar et alin 2012, reportedly found bacterial isolates in 67.14% in their study.[20]These studies correlate with the frequency of isolation noted in the present study.

2) Differentiation based on gram staining

The greater frequency of isolation of Gram negative bacteria has been reported in other studies, such as those conducted by Narayangowda et al (55%), Kumar Surinder et al (57.7%), Aleemulah et al (71.42%), and Madhavi et al (75%).[14,16,19,20]

3) Bacteriological profile

The current study thus correlates with the studies of Saikat Basu et al, Dalvi et al, Narayangowda et al, Madhavi S et al and Sharan et al, which showed Klebsiella pneumonia as the most common isolated organism overall.[13-16]

Associations:

1) Association between nature of sputum and frequency of isolation of bacteria.

In this study, 31.6% (36/114) patients produced mucoid sputum, whereas 68.4% (78/114) patients produced mucopurulent / purulent sputum. Out of the mucoid sputum samples, cultures of 38.89 % (14/36) samples showed bacterial growth. Out of the mucopurulent / purulent samples, cultures of 84.61 % (66/78) samples showed bacterial growth. Thus, the frequency of colonization by bacteria was found to be higher in those patients that have increased purulence of sputum. This finding is statistically significant ($p < 0.0001$)

Other studies report similar findings. The frequencies of isolation of bacteria in mucoid sputum as reported in a few other studies were as follows: Arora et al- 25%, Aleemullah et al- 41.67%, and Patel et al- 68.97%. In these studies, the frequencies of isolating bacteria from mucopurulent / purulent sputum samples were as follows: Arora et al- 85%, Aleemullah et al- 83.93% and Patel et al- 100%.[1,19,21]Thus, frequency of isolating bacteria increased with purulent sputum compared to mucoid.

2) Association between lung function and isolation of Gram negative and positive isolates.
Frequencies of isolating Gram negative bacteria were 14.8%, 31.5% and 53.7% in patients with FEV_1% predicted: 50% - <80%, 30% - <50 % and < 30% respectively. This suggests a higher frequency of isolating Gram negative bacteria at low FEV_1% predicted.

Frequencies of isolating Gram positive bacteria were 46.2%, 30.8% and 23.1% and frequencies of not obtaining any growth on culture were 32.4%, 32.4% and 35.3% in patients with FEV_1% predicted: 50% - <80%, 30% - <50 % and < 30% respectively.

There was a statistically significant ($p < 0.05$) association between the FEV_1 % predicted and group of bacteria isolated. Similar to the present study, Eller et al in their 1998 study titled 'Infective exacerbations of chronic bronchitis: relation between bacteriologic etiology and lung function'showed that a lower predicted FEV1% was associated with more frequent colonization with Gram negative bacteria (Enterobacteriaceae and Pseudomonas sp.).[22]

Similar findings were also noted in the studies, by Miravitlles et al in 2000, and Levent Erkan et al in 2008where a low FEV1% was associated with greater frequency of isolation of Gram negative bacteria.[17,23]

5. Conclusion

Worsening COPD is associated with greater frequency of colonization with Gram Negative bacteria. Antibiotics used to treat exacerbations in severe and very severe cases of COPD should provide coverage of Gram Negative bacteria.

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