Identifying Risk Factors for Acute Exacerbations of Chronic Obstructive Pulmonary Disease

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Abstract

COPD (Chronic Obstructive Pulmonary Disease) is a chronic progressive disease with airflow obstruction. Exacerbations of COPD are a significant cause of hospital admission and readmission and an important determinant of health related quality of life. Identifying risk factors associated with exacerbations would help prevent deterioration in respiratory function. In our study, a total of 100 patients admitted with acute exacerbations of COPD in a tertiary care hospital were investigated using routine blood investigations and sputum study. Critically ill patients admitted in ICU, immunecompromised patients, those who were not compliant with prescribed home based bronchodilator treatment and in patients with sudden breathlessness due to cause other than AECOPD (Acute Exacerbations of COPD) were excluded from the study. Upon admission, a detailed history including history of previous exacerbations, smoking history, prior recent spirometry results were obtained. The data collected from each patient was analyzed using SPSS for windows, version 20.0. In our study, p value less than 0.05 was taken as significant. We found that 60 cases out of 100 had sputum sample positive for bacterial growth. Pseudomonas was the most common organism followed by H. influenza. We also found that not only respiratory infections are a major cause of exacerbations, but they also lead to higher hospital stay and mortality. Smokers had higher frequency of exacerbations.

Index terms—

1 I. Introduction

OPD is projected to become third leading cause of death by 2020. 1 It is the only chronic disease with increasing mortality. 2 Exacerbations are important, not only because they impact an individual's life, but also because of their long term effects on health status, morbidity and mortality. Reducing the frequency of exacerbations would help an individual to live a stable healthy life without significant decline in respiratory capacity. This will also reduce health expenditure of frequent hospitalizations. Exacerbations are usually defined as increased sputum volume and/or purulence which necessitate a change or increased dose of routine medication. Anthonisen et al 3 . Divided exacerbations into three types. Type 1 was defined as increased breathlessness, sputum volume and sputum purulence. Type 2 was presence of 2 of the above three, type 3 by 1 of above in addition to upper respiratory infection in preceding 5 days, fever without other cause, increase heart rate or respiratory rate by 20%. In 1996 a study of survival following hospital admission for acute exacerbations reported in hospital mortality rate of 11% and 1 year mortality rate of 43%. 4 Published data suggest that 50-70% of exacerbations are due to respiratory infections 5 (including bacteria, respiratory viruses and atypical organism), 10% are due to environmental pollution (depending on season and geographical placement) 6 , and upto 30% are of unknown etiology. 4 Identifying risk factors in a particular geographical location by examining and investigating patients of AECOPD would help in reducing the future episodes and lead to better quality of life.

2 II. Methods

The study was conducted in a tertiary care hospital in Ahmedabad, Gujarat. This study was approved by institutional review board. It was a prospective observational study from August 2015 -December 2017.

3 a) Selection Criteria

4 i. Inclusion

? Age more than 18 years. ? Patients who were diagnosed with COPD previously and came with acute exacerbation.

ii. Exclusion

? Patients admitted with breathlessness but with a different cause such as heart failure, pneumothorax or pulmonary thromboembolism).

? Patients who were not compliant with baseline home based COPD prescribed treatment. ? Immunocompromised patients (HIV, malignancy or immunosuppressive therapy). ? Critically ill patients admitted in intensive care units.

Upon admission to the hospital with suspected AECOPD and having ruled out other possible causes of breathlessness, a complete clinical history with demographic factors, history of hospitalizations and prior exacerbations in recent years as well as history of contact with family member having respiratory infection was obtained.

Previous treatment records and latest spirometry results were also collected. F investigation including complete blood count, liver and renal function test, as well as blood gas analysis was done. Sputum was collected from each patient before starting antibiotic treatment. Sputum was cultured only if it was considered adequate. (<10 epithelial cells and >25 polymorphonuclear leukocytes).

Patients were kept on routine follow up after discharge from hospital and monitored for treatment adherence, any future episode of exacerbation or other adverse outcome during the follow up period between August 2015 -December 2017.

The data were collected in a Microsoft access database and analyzed using SPSS for windows, version 20.0 (IBM Corporation, Armonk, NY).

Comparison between means were performed using student's t test for independent samples or the Mann-Whitney U test for variables that did not meet the criteria for normality. For comparison between proportions, Chi square or Fischer's test was used. P value <0.05 was taken for statistical significance.

5 III. Results

We prospectively studied 100 patients who were admitted with a diagnosis of AECOPD in department of general medicine of a tertiary care hospital, Gujarat, between August 2015 to December 2017.

The following observations were made based on data analysis of these patients.

No. of Patients (Out of 100) In the present study, sputum culture turned out to be positive for bacterial etiology in 60 patients out of 100. Remaining 40 patients had sputum culture result negative.

6 IV. Discussion

This prospective observational study of 100 patients admitted with AECOPD in department of general medicine of a tertiary care hospital, Ahmedabad included a 2-year follow up period and was intended to identify risk factors for acute exacerbations in patients with COPD.

Overall, tobacco accounts for around 80-90% risk of developing COPD. 8 In our study, 77% of patients were smokers, none of which had quit smoking. Shumail Bashir et al 9 found 80% smokers in his study also. Our study also showed that smoking was associated with higher frequency of exacerbations in patients with COPD. This is due to the fact that smoking leads to decrease in mucociliary clearance and innate immunity 10 .

On admission, according to anthonisen 2 criteria, all patients were divided into types of exacerbation (type 1/2/3). It showed that patients with more severe exacerbation had higher mortality. 71.42% patients with type 1 exacerbations whereas only 02.43% patients with type 3 exacerbation died during follow up. This data was statistically significant with p value <0.05, however there was no statistically significant difference between outcome for type 2 and type 3 exacerbations (p=0.269). N. A. Dewan et al 11 study also showed significant difference between type 1 and type 3 exacerbations (22% v/s 07.1%; p=0.037) and non significant difference between type 2 and 3 exacerbations (22% v/s 12.4%; p=0.081).

In our study, 60% of patients had sputum culture positive for different bacteria. Most common bacteria isolated was Pseudomonas aeruginosa (43.3%) followed by H. influenza (26.6.%) and Moraxella catarrhalis (13.3%). Other bacteria isolated were streptococcus pneumonia, staphylococcus aureus and E. coli. In the remaining 40% of patients with AECOPD, sputum culture was negative. Kolarov et al 12 study also found Pseudomonas aeuruginosa (38.9%) as the most common bacteria to be isolated in hospitalized patients followed by H. influenza (26.59%). Another study by Ramon Boixeda et al 13 showed 28.03% bacterial, 10.6% viral and 61.37% non infective etiology as a cause for We obtained chest x-ray from each of the total 100 patients out of which 50 had unilateral and 13 had bilateral interstitial infiltrates. Bilateral infiltrates on chest x-say was associated with

a poor outcome, which was statistically significant (p value <0.05). All 37 patients with normal x-ray finding survived. Similar to the study by Lieberman et al. 14 , the presence of infiltrates was associated with higher rate of isolation of organisms, an increased incidence of complications, increased morbidity and mortality. This may be indicative of higher level of lung damage or poor individual immune response against respiratory pathogens and hence worse outcome in terms of survival.

In our study, 26.66% of sputum positive patients expired compared to only 7.5% of sputum negative patients. This data was statistically significant. This is suggestive that infective etiology for acute exacerbation of COPD had higher mortality as compared to non-infective etiology. Duration of hospital stay was also higher for patients with infective etiology. Karin H et al 15 study also showed mortality in 8.22% (mean) but only 7.5% had sputum culture negative Whereas 9.09% had sputum positive result.

7 V. Study Limitation

Unfortunately, we could not obtain samples for virological evaluation of sputum or other respiratory secretions. In our study, number of sputum negative result may be containing virus as a possible cause of exacerbation which was missed. Though sputum was also sent for antibiotic sensitivity, the information obtained from a very few positive samples is difficult to analyze as a whole. The sample population studied belonged to in-hospital patients admitted with AECOPD only. Those who were treated on OPD basis were not included. Lastly the sample size was not big enough to extrapolate the result for a given locality.

Nonetheless our study provides important information regarding cause of frequent exacerbations in patients with COPD and other prognostic markers, these will help in prevention as well as prompt treatment in future to reduce burden of AECOPD on health care system.

8 VI. Conclusion

With the above study, we conclude that respiratory infections are a major cause of acute exacerbation in patients with COPD. Smoking is found as a major risk factor in COPD patients which contributes to exacerbations. We also report increased mortality in AECOPD patients with prior history of frequent exacerbations (2 or more per year). 29.62% of patients with frequent exacerbations expired compared to only 6.52% of patients without prior exacerbations. This data was statistically significant. Naresh A Dewan et al 11 study also reported increased risk of failure with increase in the number of exacerbations. His study reported that risk of atleast one failure increased to 100% with history of four or more exacerbations in past 24 months.

9 Comparison with Previous Study for Commonly Isolated

Organisms.

1

All routine

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Figure 1: Table 1 :

2

History of Smoking (Atleast Ten Pack Years)	History of Frequent Exacerbations (2 or More per Year) Present	Absent
Present (N=77)	51 (66.23%)	26 (33.76%)
Absent (N=23)	03 (13.04%)	20 (86.95%)
	Total = 54	Total = 46
	P Value = 0.000007 (<0.05)	

Figure 2: Table 2 :

3

Severity of Exacerbation	Outcome Survived (N=81)	Expired (N=19)	P Value
Type 1 (N=21)	06 (28.57%)	15 (71.42%)	P = <0.00001 (<0.05)
Type 2 (N=38) Type 3 (N=41)	35 (92.10%) 40 (97.56%)	03 (07.89%) 01 (02.43%)	P = 0.2693 (> 0.05)

Figure 3: Table 3 :

4

Etiology	
Bacterial	60 (60%)
Pseudomonas Aeruginosa	26 (43.3%)
Haemophilus Influenza	16 (26.6%)
Moraxella Catarrhalis	8 (13.3%)
Streptococcus Pneumoniae	5 (08.3%)
Staphylococcus Aureus	3 (05.0%)
E. Coli	2 (03.3%)
Unknown	40 (40%)
Total	100 (100%)

Figure 4: Table 4 :

5

Outcome of Patients (Total Patients N=100)	Bilateral Infiltrates (N=13)	Unilateral Infiltrates (N=50)	Normal (N=37)
Survived (N=81)	-	44	37 (100%)
Expired (N=19)	13 (68.42%)	6 (31.50%)	-

Figure 5: Table 5 :

6

Outcome	Sputum Culture Positive (N=60)		Sputum Culture Negative (N=40)		No. of Patients		P Value
Survive Expired	44 (73.33%) (26.66%)	16	37 (92.5%)	3 (07.5%)	81 (81%) (19%)	19	0.0166
Hospital Stay	7.27 ± 3.08		6.02 ± 2.35		100 (100%)		0.0318

Figure 6: Table 6 :

7

Prior History of Exacerbation (2 or More per Year)	Outcome Survived (N=81)	Expired (N=19)
Present (N=54)	38 (70.37%)	16 (29.62%)
Absent (N=46)	43 (93.47%)	03 (06.52%)
	Total = 81	Total = 19
	P Value = 0.0033 (<0.05)	

Figure 7: Table 7 :

Isolated Organism	Present Study (%)	
Psedumonas Aeruginosa	43.3	38.92
H.Influenza	26.6	26.59
Moraxella Catarrhalis	13.3	03.19
Streptococcus Pneumonia	08.3	17.02

Figure 8:

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