

## Original Research Article

# A prospective study of the predictors of mortality in acute exacerbation of COPD: an Indian perspective

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### ABSTRACT

**Background:** Chronic obstructive pulmonary disease (COPD) is a leading cause of morbidity and mortality worldwide. In 2011, COPD was the third leading cause of death. The prevalence and burden of COPD are projected to increase over the coming decades due to continued exposure to COPD risk factors. Thus prevention, early detection and prompt treatment of COPD and its exacerbations may have an impact on the clinical progression and the risk of hospitalization. This is a prospective study to determine the predictors of mortality in COPD patients hospitalized for an acute exacerbation.

**Methods:** This was a prospective study of 94 patients admitted for acute exacerbation of COPD in a tertiary care hospital over a period of 18 months. After a detailed medical history and physical examination, patient's blood sample was sent for Arterial Blood Gas (ABG) analysis, a complete hemogram, blood sugar levels, serum albumin levels, blood urea nitrogen levels (BUN), serum creatinin levels, SGPT, SGOT and serum sodium and potassium levels. We then compared these parameters in patients who died with those who survived to determine the mortality predictors.

**Results:** A statistically significant relation was obtained between male gender, smoking history (odd ratio of 1.5), number of pack years ( $p = 0.029$ ), history of prior admission (odds ratio of 2), longer duration of illness ( $p = 0.045$ ), elevated blood sugar levels ( $p = 0.035$ ), hypoalbuminaemia (0.001), hyponatremia (0.001), respiratory acidosis (0.003), elevated partial pressure of  $\text{CO}_2$  (0.001) and mortality.

**Conclusions:** We found a male preponderance, with increase in mortality with the increase in the number of smoking pack years. Longer duration of illness was also an important predictor of mortality. Respiratory acidosis, hyponatremia, elevated blood sugar levels and hypoalbuminemia at the time of presentation were other important predictors of mortality in patients hospitalized for acute exacerbation of COPD.

**Keywords:** Acute exacerbation, COPD, Mortality

### INTRODUCTION

Chronic Obstructive pulmonary disease (COPD) is a leading cause of mortality and morbidity worldwide.<sup>1</sup> The prevalence of COPD is directly related to the prevalence of tobacco smoking, although in many countries outdoor, occupational and indoor air pollution resulting from

burning of wood and other biogas fuels are major COPD risk factors.<sup>2</sup>

The prevalence and mortality due to COPD are projected to increase over the coming decades due to continued exposure to COPD risk factors. In 2011, COPD was the third leading cause of death in the United States. Globally

there are around three million deaths annually due to COPD.<sup>3</sup> It is estimated that by 2030 there may be over 4.5 million deaths annually from COPD.<sup>4</sup> COPD exacerbations affect the quality of life and prognosis of patients. Older age, decreased lung functions, lower health status, diabetes mellitus and prior hospital admission are important risk factors for mortality. COPD is associated with significant economic burden. COPD exacerbations account for the greatest proportion of the total COPD burden on the health care system. Hospitalization and ambulatory oxygen cost soar with increasing COPD severity.

Treatment cost for those who require intensive care admission is the highest. It is important to identify at the time of admission, patients who are likely to have a poor outcome, so that such patients can be managed aggressively. Many prognostic factors have been devised for the same. These help to segregate patients who are likely to die from those who will have better outcome. The present study was planned to determine the predictors of mortality in acute exacerbation of COPD admitted to a tertiary care hospital.

## METHODS

This was a prospective study of 94 patients admitted for Acute Exacerbation of COPD in a tertiary care hospital over a period of 18 months. A COPD exacerbation was defined by the presence of an increase in at least two of the following three symptoms of dyspnoea, cough and sputum purulence, severe enough to warrant hospitalization.<sup>5</sup> All patients were documented cases of COPD as per GOLD guidelines with prior spirometry confirmation of irreversible obstructive airway disease.<sup>5</sup> A detailed history and demography of all patients was taken including history of smoking, exposure to occupational dust, biomass fuel gas and exposure to other obnoxious gases.

History of hospitalization in the previous year, ICU stay, history of concomitant illnesses and previous history of pulmonary tuberculosis were noted. All patients were then subjected to a detailed clinical examination. Temperature, pulse, blood pressure and oxygen saturation by pulse oximetry were noted. At the time of admission, blood was sent for a complete hemogram, blood sugar levels, serum proteins, SGPT, SGOT, serum creatinin, and serum sodium and potassium levels.

Patients were also subjected to a chest radiograph, electrocardiogram and a 2-dimensional echocardiography. We did not include patients with hemodynamic instability requiring ICU admission, patients with other life threatening conditions and patients who refused to give consent.

The patients were managed as per GOLD guidelines for the management of severe but not life threatening exacerbations.<sup>5</sup> Patients were administered nasal oxygen through a venturi mask where-ever needed. They were given nebulized salbutamol and ipratropium, oral prednisolone in the dose of 40 mg once daily, and intravenous antibiotics when signs of bacterial infection were present.

The fluid balance was monitored and managed in all patients, and any concomitant illness was managed according to the respective guidelines. The patients were followed up either till discharge or death.

## RESULTS

A total of 94 patients were enrolled over 18 months. The patients were aged between 45-76 years, with a mean age of 60.5 years, with majority patients between 51-70 years. The male: female ratio was 74:20. Out of 94 patients, 64 (68.1%) patients were either smokers or ex-smokers with smoking index of more than 200 and 30 (31.9%) were non-smokers. Out of 94 patients, 78 (83%) were discharged while 16 (17%) died of which 14 (87.5%) were males and 2 (12.5%) were females (Table 1).

**Table 1: Sex distribution and mortality relation amongst patients admitted for acute exacerbation of COPD.**

Status	Male	Female	Total
Discharged	60 (77%)	18 (23%)	78 (100%)
Expired	14 (87.5%)	2 (12.5%)	16 (100%)
<b>Total</b>	<b>74</b>	<b>20</b>	<b>94</b>

**Table 2: Relation between smoking and mortality in patients admitted for acute exacerbation of COPD.**

	Survived	Expired	Total	Odd ratio
Smoker	52 (67%)	12 (75%)	64	1.5
Non-smoker	26 (33%)	4 (25%)	30	
<b>Total</b>	<b>78 (100%)</b>	<b>16 (100%)</b>	<b>94</b>	

**Table 3: Relation between smoking in pack years and mortality in patients admitted for acute exacerbation of COPD.**

Status	Number	Mean (pack years)	Standard deviation (±)	Standard error mean	P-value
Pack year	Survived	52	18.21	1.170	0.029
	Expired	12	23.83	1.218	

**Table 4: Relation between prior hospital admission for COPD exacerbation in previous year and mortality.**

Status	Prior hospitalization for COPD exacerbation		Total	Odd's ratio
	Present	Absent		
Survived	46 (59%)	32 (41%)	78 (100%)	2
Expired	12 (75%)	4 (25%)	16 (100%)	
<b>Total</b>	<b>58</b>	<b>36</b>		

**Table 5: Relation between total duration of illness and mortality in patients admitted for acute exacerbation of COPD.**

Variable	Status	Number	Mean (years)	Standard deviation ( $\pm$ )	Standard error mean	P-value
Total duration of illness	Survived	78	13.51	5.519	0.625	0.045
	Expired	16	16.62	5.909	1.477	

**Table 6: Relation between laboratory parameters and mortality in patients admitted for acute exacerbation of COPD.**

Variable	Status	Number of patients	Mean	Standard deviation	Standard error mean	P-value
Haemoglobin	Survived	58	13.297 gm%	2.7129	0.3562	0.716
	Expired	16	13.640 gm%	2.9497	0.9328	
Total leucocyte count	Survived	78	13140	3997.478	452.625	0.138
	Expired	16	15340	9822.695	2455.674	
Serum albumin	Survived	74	3.392 gm%	0.33699	0.03917	0.001
	Expired	16	3.0519 gm%	0.37872	0.09468	
Blood urea	Survived	78	63.04 mg%	36.693	4.155	0.542
	Expired	14	69.29 mg%	24.228	6.475	
Serum creatinin	Survived	78	1.4590 mg%	0.62987	0.07132	0.870
	Expired	14	1.4700 mg%	0.47390	0.12666	
Serum sodium	Survived	74	135.92 mEq/dl	6.221	0.723	0.001
	Expired	14	123.43 mEq/dl	10.825	2.893	
Serum potassium	Survived	74	4.451 mEq/dl	1.1233	0.1306	0.410
	Expired	14	4.186 mEq/dl	0.9566	0.2557	
Random blood sugar	Survived	76	167.13 mg%	94.214	10.807	0.035
	Expired	16	231.64 mg%	165.893	41.473	
PaO <sub>2</sub> in ABG	Survived	76	56.80 mmHg	17.206	1.974	0.845
	Expired	16	55.88 mmHg	16.705	4.176	
PaCO <sub>2</sub> in ABG	Survived	76	53.182 mmHg	15.4171	1.7685	0.001
	Expired	16	72.088 mmHg	33.4712	8.3678	
pH in ABG	Survived	76	7.39889	0.070122	0.008044	0.003
	Expired	16	7.30350	0.107542	0.026886	
Serum HCO <sub>3</sub>	Survived	76	32.245 mEq/dl	8.9514	1.0268	0.385
	Expired	16	34.712 mEq/dl	12.8490	3.2123	

Among the patients who survived, 67% were smokers and among the patients who expired during hospital stay, 75% were smokers. So mortality was more common among smokers with an odds ratio of 1.5 (Table 2).

Among the patients who survived (78), 52 were smokers with a mean pack years of 18.21, and among those who died (16), 12 were smokers with a mean pack years of 23.83 (Table 3). This difference was statistically

significant (p value is 0.029), thus demonstrating a strong relation between the number of cigarettes smoked and mortality.

Of the 16 patients who died, 12 (75%) had history of prior admissions for COPD exacerbation in the previous one year (Table 4). Patients with longer duration of illness (mean duration of 16.62 years) had greater mortality (p value = 0.045) (Table 5).

Patients with increased blood sugar levels (mean random blood sugar levels of 231.62 mg%), lower serum albumin levels (mean serum albumin levels of 3.0519 mg%) and lower serum sodium levels (mean serum sodium levels of 123.43 mEq/dl) had an increased mortality which was statistically significant. Statistically higher mortality was observed when the ABG at the time of admission showed an acidic PH (mean pH of 7.3035) and a higher PaCO<sub>2</sub> levels (mean PaCO<sub>2</sub> of 72.088 mmHg) (Table 6).

## DISCUSSION

The main objective of the study was to evaluate the predictors of mortality in acute exacerbation of COPD. Patient characteristics related to an increased mortality rate were analysed. Out of 94 patients admitted, 16 (17%) died during hospital stay. This observation was supported by study done by Connors et al who reported an in-hospital mortality of 11% and Fuso et al who reported an in-hospital mortality rate of 14.4%.<sup>6,7</sup>

In this study, of the 16 patients who died, 2 were females (12.5%) and 14 were males (87.5%) (Table 1). This may be due to the fact that smoking habits are more common in males and they seek medical help more often in our country.

We observed that the mortality was 1.5 times higher among smokers than non-smokers (odd ratio 1.5) (Table 2). Smokers who died had a mean pack year of 23.83 against those who survived (mean pack years was 18.21). Thus this concludes that the total number of cigarettes smoked was an independent predictor of mortality in patients with acute exacerbation of COPD (Table 3).

In our study out of the 16 patients who died, 12 (75%) patients gave history of hospitalization for acute exacerbation of COPD in the previous year (Table 4). Several studies have shown that prior admission to hospital increases mortality in COPD exacerbation.<sup>6,8</sup>

There is a high incidence of mortality in patients with a longer duration of illness (Table 5). The mean total duration of COPD in the survived group was 13.51 years and in the patients who died it was 16.62 years. The long duration of illness implies a more severe disease due to gradual decline in lung functions with passing years. Thus duration of illness is also an important predictor of mortality in patients admitted with COPD exacerbation.

On comparing the ABG of the two groups of patients in our study, it was seen that patients who died had a low partial pressure of oxygen compared to those patients who survived, though this difference was not statistically significant. This finding is supported by Karin H Groenewegen et al, but was contrary to observations made by Almagro et al.<sup>5,6</sup> The patients who died had a higher level of partial pressure of carbon dioxide (72.088 mmHg) as compared to the survivors

(53.182 mmHg). This difference was statistically significant.<sup>6,9</sup>

In our study mean pH of patients who died was 7.30350 as compared to the survivors (7.39889) which were statistically significant. The acidosis was predominantly respiratory with elevated PaCO<sub>2</sub>. Acidosis at the time of acute presentation is thus an important predictor of mortality.

An elevated HCO<sub>3</sub> levels were seen in both the groups of patients. The difference was not statistically significant.<sup>10</sup> The increase in HCO<sub>3</sub> levels is a compensatory mechanism to counter the respiratory acidosis. Acute respiratory acidosis which is not compensated is a risk factor for mortality in patients of acute exacerbation of COPD.

It was observed in our study that the difference in the Blood Urea Nitrogen and serum creatinin levels in the two groups were not significant and thus did not predict mortality, a similar finding found in several studies.<sup>10,11</sup> This was however contrary to a study which showed serum creatinin to be an independent predictor of mortality.<sup>12</sup>

Also in our study, patients with hyponatremia had a higher mortality as compared with patients with normal serum sodium levels (p = 0.001) as documented in literature.<sup>12</sup>

We did not observe a significant difference in the haemoglobin levels and the total leucocyte count in both the groups. In both the groups, the total leucocyte count was elevated which indicates infection as the cause of exacerbation in our patients.

Our study shows hyperglycemia at the time of admission as one of the predictors of mortality in acute exacerbation of COPD. The mean random blood sugar of patients who died was 231.62 mg/dl compared to 167.13 mg/dl in the survivors. Previous studies have not commented on a random blood sugar levels at the time of admission as mortality factor. Diabetes is an important co-morbidity in patients with COPD. Previous studies have shown that COPD patients with hyperglycemia are more prone for getting secondary infection. Patients with hyperglycemia and COPD also have a higher incidence of coronary artery disease which is again an important cause of mortality in COPD patients.<sup>13,14</sup>

In our study a low serum albumin levels at the time of admission was an important predictor of mortality, with the difference in the two groups being statistically significant. This observation is supported by a study which concluded that serum albumin levels in the first 24 hours of admission is an independent predictor of mortality in patients with acute exacerbation of COPD.<sup>15,16</sup>

## CONCLUSION

In this prospective study of hospitalized patients with acute exacerbation of COPD, we summarize the predictors of mortality. We found a male preponderance, with increase in mortality with increase in the number of smoking pack years. Longer duration of illness was also an important predictor of mortality. Respiratory acidosis (with decrease in pH and an increase in PaCO<sub>2</sub>), hyponatremia, elevated blood sugar levels and hypoalbuminemia at the time of presentation were other important predictors of mortality in patients hospitalized for acute exacerbation of COPD.

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