Predictors of mortality in acute exacerbation of chronic obstructive pulmonary disease

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Abstract
Introduction: Chronic obstructive pulmonary disease (COPD) is a major cause of chronic morbidity and mortality throughout the world. Many people suffer from this disease for years and die prematurely from it or its complication. COPD is the fourth leading cause of death in the world, and further increase in its prevalence and mortality can be predicted in coming decades. The aim of this work is to study and evaluate predictors of mortality in patients of acute exacerbation of COPD. **Materials and Methods:** We prospectively included in the study all patients who had been attended for an acute exacerbation of COPD in patient department of TB and respiratory diseases, UNS ASMC,Jaunpur during oct 2021 to 2 feb 2022. An exacerbation was defined by the presence of an increase in at least two of the three following symptoms: dysponea, cough, and sputum purulence severe enough to warrant hospital admission. All patients were documented cases of COPD with prior pulmonary function test conformation (FEV1/FVC<0.7) with irreversible airway obstruction and had been receiving a combination of various bronchodilators. During hospital admission, patients were treated with a standard protocol consisting of the IV administration of corticosteroids (in a standardized dosage of 0.5 mg/kg), theophylline, and nebulised salbutamol and ipratropium bromide as bronchodilating agents, O2 was titrated according to the results of blood gas analyses. **Results:** 92 patients taken in study out of which 80 survived and 12 were expired during hospital stay. So in this study mortality rate of acute Exacerbation of COPD was 13.04% during hospital stay. Out of 92 patients taken in study, only 8 patients (8.6%) were smoker as well had other risk factor while 58 (63.04%) smoker did not have any other risk factor. 16 patients (17.4%) who were non smoker, had other non smoking risk factors like post tuberculosis bronchlectasis, biomass fuel, Occupational exposer, etc. **Conclusion:** Predictor of mortality in acute exacerbation of chronic obstructive pulmonary disease at the time of admission are age of patient at the time of admission is mortality predictor in patients of acute exacerbation of COPD. Higher the age of patient, more is the risk of mortality during hospital stay. Amount of smoking in pack years is predictor of mortality. Higher the pack year of smoking more is the risk of mortality during hospital stay. Total duration of illness is a predictor of mortality in patients with acute exacerbation of COPD. More the chronic disease more is mortality.
Key Words: Chronic obstructive pulmonary disease, theophylline, Salbutamol.

Introduction
Chronic obstructive pulmonary disease (COPD) is a major cause of chronic morbidity and mortality throughout the world. Many people suffer from this disease for years and die prematurely from it or its complication. COPD is the fourth leading cause of death in the world, and further increase in its prevalence and mortality can be predicted in coming decades[1].
Global initiative for chronic obstructive lung disease (GOLD) defines COPD as a preventable and treatable disease with some significant extra pulmonary effect that may contribute to the severity in individual patients[2]. Its pulmonary component is characterized by airflow limitation that is not fully reversible. The airflow limitation is usually progressive and associated with abnormal inflammatory response of the lung to noxious particle or gases[3].
COPD is generally a progressive disease, especially if patient's exposure to noxious agents continues. In patients with COPD there is rapid decline of FEV1 which lead to insidious loss of ventilator reserve. Most of the patients remain asymptomatic with mild disease. With progression of disease comes progressive exercise limitation[4]. This is due to increased work of breathing and dynamic hyperinflation. With further progression of total per capita health care costs for COPD are account for by exacerbations alone. Severe exacerbations requiring hospitalizations are responsible for a large share of these costs and among these, treatment costs for those who require intensive care unit (ICU) is admission is highest.

In most of the third world countries, large number of ICU beds is occupied by patients with critical illness secondary to various infectious diseases, most of which are reversible. Thus prevention, early detection, and prompt treatment of exacerbations may impact their clinical progression by ameliorating the effect on quality of life and minimizing the risk of hospitalization[6].
It is important to identify the patients at the time of admission who are likely to have poor outcome, so that such patients can be managed aggressively. Many prognostic factors have been devised for the same purpose[7]. These factors help to segregate patients who are the sickest and are likely to die from those who are expected to have better outcome and survive. Most of the scoring systems have been devised for a broad range of critically ill patients. The present study was planned to determine the predictors of mortality in patients with exacerbation of COPD admitted to general ward. An attempt was made to develop a scoring system using the predictors of mortality that would help to identify patients at high risk of dying.

Materials and methods
This study was conducted in deptt. of pulmonary medicine UNS ASNC Jaunpur The hospital serves as tertiary care center for patients coming from sorrounding distt of Jaunpur like Azamgarh, Sant Ravi Das nagar, Pratapgarh, Sultaanpur. Patients selected from those attending department of tuberculosis and respiratory diseases.

Aim of the study
The aim of this work is to study and evaluate predictors of mortality in patients of acute exacerbation of COPD.

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Patient Selection

We prospectively included in the study all patients who had been attended for an acute exacerbation of COPD in patient department of TB and respiratory UNS ASMC Jaunpur during oct 2021 to feb 2022. An exacerbation was defined by the presence of an increase in at least two of the three following symptoms: dysponea, cough, and sputum purulence severe enough to warrant hospital admission. All patients were documented cases of COPD with prior pulmonary function test conformation (FEV1/FVC<0.7) with irreversible airway obstruction and had been receiving a combination of various bronchodilators. During hospital admission, patients were treated with a standard protocol consisting of the IV administration of corticosteroids (in a standardized dosage of 0.5 mg/kg), theophylline, and nebulised salbutamol and ipratropium bromide as bronchodilating agents, O2 was titrated according to the results of blood gas analyses.

Study size

There was of 92 patients of acute exacerbation of COPD.

Exclusion Criteria

1. Patients who are presented with exacerbation not due to COPD but because of other diseases like bronchial asthma, bronchiectasis etc.
2. Patients who were associated with other chronic disease like diabetes, hypertension, renal disease, hepatic disease, neurological disease, coronary artery disease etc.
3. Patients with multiple organ failure.
4. Haemodynamic instability.
5. Those patients who are not giving consent.

Materials

a. BPL's pulse oxymeter to take oxygen saturation.

b. Dispovan 2 ml syringe (preheparinised) used to take blood for arterial blood gas analysis.
c. ABG analyser machine.
d. Auto analyzer machine for liver function test, renal function test, complete blood count, random blood sugar.

Data collection

Based on out come after hospital stay, patients were devided into two groups.

Group-1: This group includes those patients who died during hospital stay.

Group-2: This group includes all those patients who survived during hospital stay and discharged to home.

Prospectively following data were collected: a) ABG-pO2, pCO2, pH, A-a gradient, b)Total leucocyte count, c)S.Albumin SGPT, SGOT d) B.Urea, S.Creatinine e) S.Electrolytes, f)RBS.

Statistical Methods

All data were analyzed by using software SPSS statistical software package. All calculation also done by using same software. Discrete data were analyzed by cross tables by using descriptive method. Continuous data were analyzed by Univariate analysis. Means of both group patients (survived group and expired group) were analyzed by Independent student's t test. Multiple variables were analyzed by multivariate analysis differences with p valueless than 0.05 were considered as statistically significant.

Results

92 patients taken in study out of which 80 survived and 12 were expired during hospital stay. So in this study mortality rate of acute Exacerbation of COPD was 13.04% during hospital stay.

Table 1: Descriptive statistics of all patients

Total Patients	Survived	Expired
92	80(86.9%)	12 (13.01%)

Table 2: Descriptive statistics of all patients

	N	Min (years)	Max (years)	Mean	Std. Deviation
AGE	92	45	76	62.00	8.096

In our study of 92 patients of acute Exacerbation of COPD youngest patient was 45 year old and the oldest one was 76 year old. Mean age of the patients was 62 years (SD±8.096).

Mean age of patients who survived was 61.24 years with standard deviation was 8.228 and mean age of patients who expired during hospital stay was 65.62 years with (SD ±5.830). This difference in both groups was significant statistically (P value 0.046).

Table 3: Mean age of both group- (student independent t test)

Status	N	Mean (Years)	SD	St. error mean	P Value
Survived	80	61.24	8.228	0.932	0.046
Non survived	12	65.62	5.830	1.457	

Table 4: Gender Distribution

Status	Male	Female	Total
Survived	62(77.5%)	18 (22.5%)	80 (100%)
Expired	10 (83.3%)	2 (16.7%)	12 (100%)
Total	72	20	92

There were 20 female and 72 male participants in this study. Male outnumber female by almost four times. It may be partly because of the fact, smoking is more prevalent in males and women present late in the course of the disease.

Table 5: Risk factors for COPD.

	Other risk factors		Total	Odd Ratio
	Present	Absent		
Smoker	8 (12.5%)	56 (87.5%)	64 (68%)	
Non smoker	16 (57.14%)	12 (42.85%)	28 (32%)	10.5
Total	24 (26%)	68 (74%)	92 (100%)	

Out of 92 patients taken in study, only 8 patients (8.5%) were smoker as well had other risk factor while 56 (87.5%) smoker did not have any other risk factor. 16 patients (19.56%) who were non smoker, had other non smoking risk factors like post tuberculosis bronchlectasis, biomass fuel, Occupational exposer, etc.

Table 6: Prior hospital Admission

Status	Prior history of hospitalization		Total	Odd Ratio
	Present	Absent		
Survived	48 (60%)	32 (40%)	80 (100%)	
Expired	10 (83.4%)	2 (16.6%)	16 (100%)	
Total	58	34		2

Patients those who were survived, 48 patients (60%) had history of prior hospitalization and patients those who were expired, 10 patients (83.4%) had prior history of hospitalization for indication of acute exacerbation of COPD. So patients with history of prior hospitalization have more mortality rate.

Table 7: Total Duration of Illness

Sex	N	Mean TDI (years)	SD	Std. error mean	P value
Male	72	14.34	5.679	0.660	
Female	20	12.95	5.680	1.270	0.97

Mean total duration of illness in male patients was more than that of female. It could be due to female are not seeking medical attention earlier while male come earlier to hospital once he gets symptoms. The difference in both groups is not significant statistically (p 0.97).

Table 8: Partial pressure of oxygen in arterial blood (PaO2)

	Status	N	Mean (mm Hg)	SD	Std.error. mean	P Value
PaO2	Survived	80	57.80	17.206	1.974	0.845
	Expired	12	54.88	16.705	4.176	

Patients those who had survived had mean PaO2 58.80 mmHg and those had expired had mean PaO2 54.88 mmHg which is less than that of those patients who survived but this difference is not statistically significant (p value -0.845).

Table 9: Partial Pressure of carbon di Oxide in arterial blood.

	Status	N	Mean (mm Hg)	SD	Std.error. mean	P Value
PaCO2	Survived	80	55.182	15.41	1.7685	0.001
	Expired	12	74.088	33.47	8.3678	

Groups of survived had mean paCO2 55.182 mmHg and group of expired patients had mean PaCO2 74.088 mmHg. This difference between these two groups is statistically significant (p value 0.001).

Tablet 10: pH

	Status	N	Mean (mm Hg)	SD	Std.error. mean	P Value
pH	Survived	80	7.39	0.070	0.008	0.003
	Expired	12	7.30	0.010	0.026	

Group of survived patient had mean pH 7.3588 and group of expired patients had mean pH 7.2935 which is more acidic than that of survived patient group and this difference is statistically significant (P Value-0.003).

Table 11: Blood urea

	Status	N	Mean (mm Hg)	SD	Std.error. mean	P Value
Urea	Survived	80	65.04	36.69	4.155	0.542
	Expired	12	70.29	24.28	6.475	

Those patients who survived had mean urea level 65.04 mg/dl and those had expired had mean urea level 70.29 mg/dl but this difference was not statistically significant.

Table 12: Serum creatinine

	Status	N	Mean (mm Hg)	SD	Std.error. mean	P Value
Creatinine	Survived	80	1.43	0.62	0.071	0.870
	Expired	12	1.49	0.47	0.126	

Patients of survived group had mean serum creatinine 1.43 mg/dl and patients of expired group had mean serum creatinine level 1.49 mg/dl and this difference these two group was not statistically significant.

Table 13: Serum Sodium

	Status	N	Mean (mm Hg)	SD	Std.error. mean	P Value
Sodium	Survived	80	135.92	6.221	0.723	0.001
	Expired	12	123.43	10.825	2.893	

In group of survived patients mean sodium was 135.92 mEq/dl and in group of expired patients mean sodium was 123.43mEq/dl. This difference in both groups was statistically significant.

Table 14: Serum Albumin

	Status	N	Mean (mm Hg)	SD	Std.error. mean	P Value
Albumin	Survived	80	3.87	0.33	0.039	0.001
	Expired	12	3.08	0.37	0.09	

In patients of survived group had mean albumin 3.87gr% and in patients of expired group had mean albumin 3.08 gr%. This difference in both groups was statistically significant (p value 0.001).

Discussion

The main objective of this study was to evaluate predictors of mortality in acute exacerbations of COPD. Patient characteristics related to an increased mortality rate were analyzed.

92 patients of COPD (diagnosed based on old spirometry reports) who presented in hospital with acute exacerbation were enrolled in this study. Out of 92 patients 12 patients (14%) expired during hospital stay and 80 patients were discharged at the end of hospital stay. In all in-hospital cases of mortality, progressive respiratory

failure was the primary cause of death. This observation were partially supported by the study done by Connors et al who reported an in-hospital mortality of 11% and Fuso et al who reported an in-hospital mortality of 14.4%. In the study done by Karin H. Groenwegen et al (2000), mortality rate were 8% during hospital stay which increases to 16% by 3 months follow up, it was 18% in 6 month follow up and it was 23% after 1 year. In our study mortality rate was higher this is probably due to poor treatment facility and selection criteria of admission in hospital[8].

In our study majority of the patients who expired during hospital stay were in age group of 56-70 years (81%) and patients who survived were in age group of 51-70 years (76.4%).

In this study mean age of patients who survived was 51.24 (SD±8.228) and mean age of patients who expired during hospital stay was 65.62 (SD ±5.830). These differences in both groups were significantly (p value 0.046). So age has been proven to be an important determinant of survival in COPD patients. Age also has been associated with an accelerated decline in lung function. It is important to find out and treat the symptoms of COPD at an earlier stage in order to prevent this decline. This is in accordance with the observation made by Connors AF et al (1995), traver GA et al (1979), Anthonisen NR et al (1986), Inealzi RA et al (1997) and Hansen et al (1999)[9].

In this study, among the expired patients 2 were females (16.7%) and 10 were males (83.3%) and in the survival group 18 (22.5%) were females and 62(77.5%) were males, in the study population there is a male predominance. This may be partly because of the fact, smoking habits are more common in male and they seek medical help more often and early.

Among 92 patients, 62 patients were smoker. Those patients who survived, 67% were smokers and patients those who expired during hospital stay, 75% were smokers. So mortality was 1.5 times higher among smoker than non smokers.

In our study among the 92 patients with acute exacerbation of COPD, 56(59.5%) had smoking as the only risk factor while 8 patents had other risk factors along with smoking. In the study population 18(19.2%) patients had identifiable non smoking risk factors for COPD while in 12(12.8%) patients the risk factor is not known, hence more research needs to be done to identify these factors and their association with pathogenesis of COPD. Risk factor other than smoking also play a major role in developing COPD, when a person who has no history of smoking get exposed to other risk factors like Post TB bronchiectasis, biomass Fuel exposure, occupational exposure etc, will have 10.5 times more chance of developing COPD. This observation is supported by Kunzli et al (1997) who told exposure to outdoor and indoor air pollutants increases the prevalence of COPD by an estimated 2% for each 10g/m3 increase in particulate matter, this observation is also supported by Halbert et al, (2003) who told that the use of biomass fuels increases the risk of COPD by three to four times, contributing significantly to COPD prevalence, especially in rural regions[10].

Our study shows that mean total protein in survived patients group was 5.95 gm/dl and mean total protein in group of expired group was 5.65 gm/dl. This difference these two groups was not significant statistically (P value 0.079).

In our study albumin was also found as predictor of mortality. Mean albumin level of albumin in patients of survived group was 3.37 gm/dl while mean serum level of albumin in patients of expired group was 3.08 gm/dl. This difference was significant statistically (P value 0.001). This observation was supported by GC Khilani et al (2004) who conclude serum albumin in the first 24 hour of admission is independent predictor of mortality in patients of acute exacerbation of COPD. Albumin has a long half life of approximately 18 days and because of this fact it is unlikely to change with development of acute respiratory failure in patients with COPD. On the other hand albumin is known to reflect the underlying nutritional status and to be affected by the severity of chronic illness. These factors are of obvious significance in deciding the outcome of these patients.

Conclusion

Predictor of mortality in acute exacerbation of chronic obstructive pulmonary disease at the time of admission are age of patient at the time of admission is mortality predictor in patients of acute exacerbation of COPD. Higher the age of patient, more is the risk of mortality during hospital stay. Amount of smoking in pack years is predictor of mortality. Higher the pack year of smoking more is the risk of mortality during hospital stay. Total duration of illness is a predictor of mortality in patients with acute exacerbation of COPD. More the chronic disease more is mortality. Partial pressure of carbon dioxide in arterial blood (PaCO2) is predictor of mortality in patients with acute exacerbation of COPD. P^{H} of arterial blood at the time of admission is predictor of mortality in patients of acute exacerbation of COPD. Serum Sodium level at the time of admission is predictor of mortality in patients of acute exacerbation of COPD.

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