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RESEARCH ARTICLE

Acute Exacerbation of Chronic Obstructive Pulmonary Disease – Clinical Presentation and Predictors of Outcome

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ABSTRACT

Background and Objectives: Chronic Obstructive Pulmonary Disease (COPD) is a common, costly and preventable disease and is at present the fourth leading cause of death globally. To study the outcome of patients with acute exacerbation of COPD and to analyse the risk factors predicting adverse outcomes in patients with acute exacerbation of COPD.

Patients and Methods: A Prospective study was conducted over a period of one year, from December 2021 to December 2022, Minimum of 50 patients, both male and female with AECOPD getting admitted to a Tertiary care centre were included in this study.

Results: Of the 50 patients studied, 42 were males; all of them were smokers (84%). The mean age was 64.34 ± 10.47 years. The mean duration of the disease was 10.04±6 years. All patients presented with cough, recent worsening of Dyspnea and increased sputum purulence/volume. 70% patients had one or more associated co-morbid illness, majority had hypertension (40%). Of 32 patients with Respiratory failure on admission 17(53.12%) patients had Type II and 15(46.28%) had Type I failure. 44 patients received medical management and 6 patients required invasive mechanical ventilation (IMV). Overall mortality was 5 (10%). 20 variables were compared between survivors and non-survivors. Univariate sensitivity analysis revealed that presence of altered sensorium (P=0.001), Hypotension (P=0.02), cyanosis (P=0.00463), pedal edema (P=0.02), presence of infection (P=0.024) Severe Acidosis (P=0.012), Hypercapnia (P=0.016), cor pulmonale (P=0.04), at the time of admission and need for invasive mechanical ventilation (P<0.001) as predictors of mortality.

Conclusions: 64% of AECOPD presented with respiratory failure, majority were type II. Overall mortality was 10%. Altered Sensorium, pedal edema, presence of infection, cyanosis, hypotension, severe acidosis, hypercapnia and presence of cor pulmonale at the time of admission predict adverse outcome. Those who need invasive mechanical ventilation had high mortality. Survivors had less hospital stay.

Keywords: COPD, Cor pulmonale, Respiratory failure, Mechanical ventilation.

Introduction:

Chronic Obstructive Pulmonary Disease (COPD) is a common, costly and preventable disease and is at present the fourth leading cause of death globally.[1] In the Global Burden of Disease Study carried out by the World Health Organization (WHO) and the World Bank[2], the worldwide prevalence of COPD in 1990 was estimated to be 9.34/1000 in men and 7.33/1000 in women,but the estimate in 2002 suggests an increase in the worldwide prevalence of COPD to 11.6/1000 in men and 8.77/1000 in women.[3] However, these estimates included all age groups and may therefore be underestimating the actual burden of COPD, which is predominantly a disease of the aged. Internationally, there is a substantial variation in death rate due to COPD possibly reflecting smoking behavior, type and processing of tobacco, pollution, climate, respiratory management and genetic factors.[4,5] The economic and social burden of COPD is enormous. According to the estimate of the Global Burden of Disease Study,[2,3] by the year 2020, COPD is likely to become the fifth leading cause of disability adjusted life years (DALYS; the sum of the years lost because of premature mortality and years of life lived with disability, adjusted for the severity of disability), behind ischemic heart disease, major depression, traffic accidents and cerebrovascular disease moving ahead from the twelth position it occupied in 1990.

The prevalence of COPD is more in countries where smoking is highly prevalent while the prevalence is low in countries with a low prevalence of smoking. Sadly, smoking is turning out to be a menace on the rise in India. It has been estimated that 2500 Indians die every day from smoking related diseases - one in every 40 seconds.[6,7] In India, it has been estimated that 65%. Of all men use some form of tobacco, (about 35% smoke, 22% use smokeless tobacco and 8% use both). Overall prevalence of beedi and cigarette smoking among women has been estimated to be about 3%.[6,7] While reliable epidemiological data about COPD are lacking from India, given the fact that there is an increasing tendency to abuse tobacco, prevalence of COPD isexpected to increase in the years to come.

Acute exacerbation of COPD (AE COPD) is a common cause of emergency room (ER) visits and is a major cause of morbidity and mortality. Following an acute exacerbation, majority of the patients experience a temporary or permanent decrease in the quality of life. Moreover, more than half the patients discharged with AE COPD often require readmission in the subsequent six months.[8] Thus, the economic and social burdens of AE COPD are extremely high.[5] The great variability in the course of AE COPD even in patients with similar degree of pulmonary impairment renders the prediction of the outcome in a given patient is very difficult. Most studies have tried to correlate impairment in both respiratory and non- respiratory physiology with the course and progression of the AE COPD with inconclusive results.

Though AE COPD is a common reason for ER Visits, very little has been documented about this problem from India. Furthermore, very little data are available from India regarding the prevalence, precipitating factors andprognostic factors in patients with AECOPD. Even from the developed world, while there are many published studies regarding the prognostic factors among patients with AE COPD who are ambulatory, few studies have examined the prognostic factors in patients with severe AECOPD who visit the ER and very little is known regarding the long term prognosis of patients with AECOPD.[9] Keeping these factors in mind, the present study was designed to prospectively study the clinical presentation, arterial blood gas and other laboratory abnormalities and predictors of outcome in the patients with AECOPD.

Patients and Methods:

Source of Data: Prospective study was conducted over a period of one year, from December 2021 to December 2022, 50 patients, both male and female with AECOPD getting admitted to Tertiary care centre were included in this study.

Study design: A prospective study.

Study period: December 2021 to December 2022,

Statistical method: Descriptive analysis was used to compute percentages, to calculate mean and standard deviation. Univariate regression analysis was used to compare variables to determine the predictors of outcome.

Inclusion criteria:

- All patients with acute exacerbation of COPD.
- COPD diagnosed earlier by premorbid pulmonary function testing when available.
- COPD based on the clinical criteria, clinical history with compatible clinical findings and evidence of COPD changes on chest radiograph will be used.

Exclusion criteria:

• Patients with Bronchial asthma, Bronchiectasis and Interstitial lung disease.

• Patients not willing to participate in the study.

Methods:

An institutional-based prospective study, Written and informed consent was taken from the patients. Complete clinical history, thorough clinical examination, detailed investigations Haematological profile- Hb%, TLC, DLC, Platelet count, ESR, renal parameters-Blood urea, serum creatinine, RBS, serum Electrolytes, LFT, ABG analysis, ECG, Chest x-ray, Sputum for gram stain and AFB were done.

Results: The present study entitled "Acute exacerbation of chronic obstructive pulmonary disease – clinical presentation and predictors of outcome" was conducted in the Department of Pulmonary Medicine, at a tertiary care centre from December 2021 to December 2022. 50 patients, both male and female with AECOPD getting admitted in Hospital were included in the study.

TABLE 1. AGE DISTRIBUTION

Age (yrs)	No. of cases	Percentage
< 60	17	34.0
60 & above	33	66.0
Total	**50**	**100.0**

Among the total of 50 patients studied majority were more than 60 yearsof (66%). Mean age was 64.34 ± 10.47 years. In our study male constituted (84%) of the total patients and rest ofthem were females (16%).

TABLE 2. DURATION OF COPD.

Duration of COPD (years)	No. of cases	Percentage
5 and Below	12	24.0
6 - 10	23	46.0
11 - 15	7	14.0
> 16	8	16.0
Total	**50**	**100.0**

20% of the patients had duration of COPD of >10 years. Rest of themwere below 10 years.

TABLE 3. SMOKING HISTORY

Smoking history	Male	Female
Smoker	42	0
Non-smoker	0	8

TABLE – 4. TYPE OF SMOKER

Type	No.of cases	Percentage
Cigarette	21	42.0
Beedi	21	42.0
Non smoker	8	16.0
Total	**50**	**100.0**

Out of 50 patients studied 21 (42%) were Cigarette and 21(42%) were Beedi smokers rest of the 8 were non-smokers. All the non-smokers were females.

Clinical Presentation:

TABLE 5. SYMPTOMS

Symptoms	No. of cases	Percentage
Cough	50	100
Increased Sputum Volume/purulence	50	100
Worsening dyspnoea	50	100
Fever	26	52
Inability to Complete sentences	25	50
Altered sensorium	13	26

All patients presented with cough, recent worsening of dyspnoea and either increased sputum purulence or sputum volume. More than 50% had history of fever; altered sensorium was seen in 26% of the cases.

All the patients manifested with wheeze, other predominant signs were tachypnoea, tachycardia, 36% of the patients had cyanosis and more than 30% of the patients presented with signs of cor pulmonale, hypotension was seen in16% of the cases.

TABLE 6. CO-MORBIDITY

Co-morbidity	No.of cases	Percentage
Diabetes	5	10
Hypertension	20	40
IHD	6	12
TB in past	8	16
CRF	1	2
Other	2	4

70% of the patients had one or more co-morbid conditions, among which hypertension was the most common (40%) followed by IHD and Diabetes.16% of the patients had past history of tuberculosis.

TABLE 7. LABORATORY ABNORMALITIES

Laboratory abnormalities	No.of cases	Percentage
Anaemia (<10%)	5	10
Leukocytosis	32	61
Neutrophilia	40	80
Low S Proteins	19	38
pH (<7.3)	22	44
PaO2(<60)	32	64
PaCO2(>45)	17	34

At the time of admission leukocytosis and neutrophilia were seen in more than 60% of the cases, 44% of the cases had pH of <7.3. In our study 5 organisms were isolated from 12 patients among which streptococcus (6 cases) was most common isolate. No growth was seen in 38 cases.

Out of 50 patients 44 patients were managed conservatively, 6 required ventilatory support out of which 5 patients died.

Predictors of Outcome:

In our study out of 50 patients 6 patients required invasive mechanical ventilation of which 5 patients died. A total of 20 variables were compared with patients who died in the hospital. Univariate sensitivity analysis revealed that presence of infection (P =0.024), inability to complete sentences (P=0.05), presence of edema (P=0.02), Altered sensorium (P=0.001), hypotension (P=0.02), cyanosis (P=0.004), cor pulmonale (0.04), low pH (P= 0.012), PaCO2(P= 0.016), need for invasive mechanical ventilation (P= 0.0001) as the predictors of death. Patients who survived the episode had a shorter hospital stay compared to those who died.

TABLE 8. PREDICTOR OF OUTCOME

Sl No	Variable	patients	Death	Recovered	P value
1	Subject	50	5	45	
2	Age (> 60 yrs)	33	5	28	0.152
3	Male gender	42	4	38	1.00
4	Duration of COPD (> 10 yrs)	38	4	34	0.309
5	Previous hospitalization	29	5	24	0.06
6	Altered sensorium	13	5	8	0.001
7	Hypotension	8	3	5	0.024
8	Cyanosis	18	5	13	0.004
9	Raised JVP	16	4	12	0.031
10	Pedal edema	15	4	11	0.02
11	leukocytosis	32	4	28	0.368
12	Raised liver enzymes	3	1	2	0.276
13	pH(<7.3)	22	5	17	0.012
14	PaO2(low)	34	5	29	1.000
15	PaCO2 (high)	23	5	18	0.016
16	Need for IMV	6	5	1	0.0001
17	Infection	8	3	8	0.024
18	Inability to complete sentences	25	5	20	0.05
19	LTOT	3	1	2	0.276
20	Cor pulmonale	17	4	13	0.04

TABLE 9. PREDICTORS OF OUTCOME

Sl No	Variable	Death	Discharged	P value
1	Altered sensorium	5	8	0.001
2	Hypotension	3	5	0.024
3	Cyanosis	5	13	0.004
4	Raised JVP	4	12	0.031
5	Pedal edema	4	11	0.02
6	pH(<7.3)	5	17	0.012
7	PaCO2 increased	5	18	0.016
8	Need for IMV	5	1	0.0001
9	Infection	3	8	0.024
10	Inability to completesentences	5	20	0.05
11	Cor pulmonale	4	13	0.04

Discussion:

Fifty patients of COPD with acute exacerbation who were admitted to the hospital and satisfied the inclusion criteria were included in the study. All cases were examined, investigated according to the pre-designed proforma after taking consent. In the present study the mean age of the patients was 64.34 ± 10.47 years most of the patients were more than 60 years of age [33 (66%)]. CM Robert et al[76] (2002) studied 1342 patients and observed mean age was 72 years, more than 75% were old age. H Gunen et al[89] (2005) in their study of factors affecting survival of 205 patients with AECOPD quoted the mean age was 64.8+/- 9.3 and 65 % were more than 65 years of age. As seen in above studies, COPD is a disease of the aged. In our study most of the patients were of elderly age group, which co-relates with other studies. In Indian setup the onset of the disease may be earlier due to smokingat younger age, excessive beedi smoking which is unfiltered, poor socio-economic status. Poor nutritional status, low BMI, delay in seeking early medical care, increased exposure to domestic smoke both in men and women.

In present study 42(84%) patients were male and 8 (16%) were females. N. Arora et al[36] (2001) in their observation of 58 patients with AECOPD, 67.24% were males and 32.76% were females CM Robert et al[76] (2002) studies showed that 54% were males and 46 % were females. Pedro Almagro et al[87] had 91.2% as male patients and 8.85 as female patients in their study. In another study by H Gunen et al[89] 87.84 % were males and 12.16% females. In a study done by Ramkrishna et al[83] in Hyderabad had 87.5% males and 12.5% females. Thus our study also co-relates with the other studies suggesting that most of the patients are males who suffer from COPD, due to the higher prevalence of smoking in the male population, females with COPD had history of exposure to domestic fuel i.e. firewood used for cooking, heating water, presence of poorly ventilated kitchen which might be the cause of increased exposure to smoke fumes and can increase the risk of disease in them.

In the present study the duration of the disease was more than 10 years in 15 patients (20%). Rest of them had duration of less than 10 years. In a study by Ramkrishna et al[83] had studied 48 patients where 28 patients had COPD for < 10 years (58.33%), 14 patients had more than 10 years. In the present study 42 (84%) patients were smokers and all were males. None of the females were smokers but gave a history of exposure to domestic fuel. In H Gunen et al[89] out of 205 patients a total of 86.82 % had smoking history. This co relates very closely with our study. Thus, the associationbetween smoking and COPD is more than 80 % as in various literatures.

In our study all patients had history of recent worsening of cough, dyspnoea and increased sputum volume or purulence, more than half (52%) of patients had history of fever prior to the episode of exacerbation. 26% of patients had altered sensorium at the time of presentation, with more than 30% of the patients had cyanosis, pedal edema and raised JVP. All the patients had wheeze at the time of presentation. Connor et al[9] and Seneff et al[77] had similar clinical findings in their study of 1016 and 365 patients respectively, admitted with AECOPD. The observation that considerable number of patients had fever andaltered sensorium at the time of presentation indicating that infection being the major trigger for exacerbation and altered sensorium being secondary to CO2 retention.

In our study more than 60 % had leukocytosis and Neutrophilia, 38 % of the patients had hypoalbumenia, around 12 % had hyponatremia. Our study has similar findings with Ramkrishna et al[83] where 48 patients were studied of which 60% had leukocytosis, 30% had hypoalbumenia, 10 % had hyponatremia. Similar results were sought in study done by Connor et al[9]. In our study out of 50 patients 35 (70%) patients had one or more co morbid illness, out of which hypertension in 20 patients, was the most common co-morbid illness in COPD patients followed by IHD in 7 patients and diabetesin 5 patients. In Ramkrishna et al[83] 33 (68%) patients had co morbid illness, in which Hypertension (n=16) was the most common followed by IHD (n=7) and Diabetes (n=6). In JJ Soler et al[88] studied 304 patients out of which 159 (52.4%) patients had one or more co-morbid illness.

Antonelli et al[92] observed 72.59% of patients had co-morbid illness,most common was hypertension (28%) followed by diabetes and IHD. Thus smoking could be attributable to the increased incidence of hypertension in patients with COPD. Our study findings co-related with other studies co-morbid conditions can be confusing factor when assessing a patient with AECOPD as they themselves can cause respiratory symptoms[16] further more co-morbid conditions can trigger AECOPD and their presence has been considered to be predictors of poor outcome in several studies.[9,85]

In our study out of 50 patients causative organism were isolated in 12 patients (24%). The organisms were Streptococci species, Klebsiella, anaerobicorganisms, Staphylococcus, Acinitobacter species. Fagon et al[32], Monso et al[31], Soler et al[30] in their studies isolated organisms in 50% of patients with AECOPD, with most common being Hemophilus, streptococci followed by Klebsiella Arora et al[36] studied 58 patients with AECOPD established etiology in 72% of cases. Ramkrishna et al[83] (2006) had a lower isolate of 25%. The reason for low results could be due to the use of antibiotics prior to the investigation and limitations in the availability of various serological tests for atypical organisms and virological diagnostic methods which could have aided in higher diagnostic yield and higher microbial isolate. In our study out of 50 patients 32 patients (64%) had respiratory failure,in which 17(53%) patients had type II respiratory failure and 15(47) had type I failure at the time of admission. In study by Ramkrishna et al[83] out of 48 patients, 66.6% of patients had respiratory failure and 20 patients had type II failure rest had type I failure.

In our study out of 50 patients 42 patients had signs suggestive of COPD changes, 8 patients had signs of old healed TB, 9 patients(18%) had new infiltrates on Chest x-ray, 8 x-rays appeared

normal. In three separate studies by Sherman S et al (1989)[93], Tsai TW et al (1993)[94] and Emerman et al (1933)[95], 16 to 21% of the cases had new infiltratesin the chest x-ray at the time of admission. In our study out of 50 patients 20 had Peaked P waves in lead II suggestive of overt cor pulmonale. Patients with IHD had well-formed Q wavesin the respective leads. Patients with hypertension had signs of left ventricular hypertrophy. 16 patients had sighs of right ventricular hypertrophy and pulmonary arterial hypertension as 2D ECHO findings.

In our study out of 50 patients 44 patients were managed conservatively and 6 patients received invasive mechanical ventilation. Out of 50 patients 45 patients (90%) recovered and got discharged and 5 patients on invasive ventilation expired (10%). The patients who recovered had a shorter hospital stay as compared to patients who died. The overall mortality rate in AECOPD with respiratory failure is around 10%.[28] In our study noninvasive ventilation was not used because of disease severity, altered sensorium, and patient's poor compliance. Similar results were seen in Ramkrishna et al[83] which showed 10.41% death rates. Increased disease severity among ventilated patients, associated co- morbidities, prolonged stay and our relative inexperience may be contributory to the higher mortality rates.

Micheal et al[91] (2001) reviewed studies from 1968 to 2001 and found mortality of 21 to 82 percent among Patients COPD requiring mechanical ventilation for acute respiratory failure. However, the duration of stay can be reduced by appropriate therapy and the use of NIV in patients with respiratory failure. In our study out of 50 patients 5 patients died in the hospital and remaining were discharged. A total of 20 variables were compared with the patients who died and those who were discharged from the hospital. Out of the 20 variables 11 variables listed below had statistically significant association with increased mortality. Jeffrey et al[79] (1992) studied 95 patients and observed that hypotension and acidosis as the predictors of mortality which co- relate with our findings. However they also found that elevated blood urea concentration was the predictor of mortality, which is not significant in our study. Portier et al[80] (1992) and Burk et al[95] (1973) studied 322 patients and 74 patients respectively and observed that the need for mechanical ventilation was the predictor of mortality which co-relates with our study. Robert et al[76] studied 1342 patients of AECOPD and observed that acidosis, presence of pedal edema and poor performance status were the predictors of mortality, in our study also we had similar findings with pedal edema (P =0.02) being significant determinant of mortality. JJ Soler et al[88] – Cataluna et al (2005) studied 304 patients with AECOPD and observed that Hypercapnia as the predictor of mortality, which is similar to our study. They also found that old age and previous acute exacerbation episode also contributed to mortality which do not co-relate with our study. H Gunen et al[89] (2005) prospectively studied 205 patients with AECOPD and observed that Hypoxia, Hypercapnia and longer hospital stay were the predictors of mortality. Except hypoxia other two findings co-relate with our study.

In a study by Ramakrishna et al[83] (2006) showed in their study of 48 patients that Overall mortality was 10.46%. Altered Sensorium, Cyanosis, hypotension, Hypoalbuminemia, severe acidosis, hypercapnia and hypoxia atthe time of admission predict adverse outcome. Those who need IMV had high mortality. Survivors had less hospital stay. In our study also altered sensorium, hypotension, cyanosis, acidosis, Hypercapnia and the need for invasiveventilation had significant results and are the major contributors of mortality in patients. In a study done in Tirupathi, South India by Alladi Mohan et al[82]: Stepwise multivariate logistic regression analysis revealed need for invasive ventilation ($p < 0.001$); presence of co-morbid illness ($p < 0.01$) and hypercapnia ($p < 0.05$) were predictors of death. Which co relates with our study. Ian G steel et al[98] (2014) in their study of 354 patients had the following results. In which patients with cyanosis, Hypercapnia, elevated blood urea, Acidemia, presence of co- morbidities were the factors affecting the poor outcome in these patients. In our study also cyanosis, hypercapnia, acidemia, presence of Cor pulmonale were the predictors. Various studies identified that elderly age group,[9,78,80,86,87] associated co morbidities[87], Hyponatremia[84], Hypoalbuminemia[79], Raised blood urea[79] were the predictors of mortality, and however in our study this was not significant.

Patients at the time of discharge were offered vaccinations and were asked to come for follow up for pulmonary function tests after 1 to 2 weeks, however few came for regular follow up. Limitation of our study was small sample size, spirometry, limitation in microbial isolation of the patients could not be assessed, follow up of the discharged patients and repeat admissions due to exacerbation were not studied.

Conclusion

66 % of the patients studied were more than 60 years of age suggesting that COPD is a

disease of the aged. 84% of the patients were males, and all had history of smoking. This male preponderance was due to greater prevalence of smoking in the male population. All the females were non-smokers; however, they had history of exposure to domestic fuel, which may be the cause of the disease in them. All the patients who presented to the Hospital had worsening breathlessness, cough, increased sputum volume or purulence as their main complaint, more than 30% of the patients had signs of cardiac failure. More than 50% of the cases had history of fever and leukocytosis, indicating that infective etiology being the most common cause COPD exacerbation in our setup, the other half of the cases may be due to non infective causes like discontinuation of medication, atypical organisms, poor compliance with inhaled medication, dehydration especially in summers and worsening of co-morbid illnesses could have precipitated the exacerbation. Only 24% of the cases the causative organism was found. Pre-hospital antibiotic, limitations in the availability of the serological tests, non availability virological isolation tests contributed to the low diagnostic yield in the present study.

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