



Original Research Article

Predictors of morbidity and mortality in acute exacerbation in chronic obstructive pulmonary disease: A study in a tertiary care unit

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ABSTRACT

Introduction: Chronic obstructive pulmonary disease is one of the leading causes of morbidity and mortality worldwide. Many people with COPD suffer from Acute exacerbations of COPD which affects their health and poor prognosis, leading to increased costs of hospitalization and quality of life.

Materials and Methods: 69 patients were initially screened by Gold criteria to establish COPD Exacerbations were measured as per Anthonisen's criteria and the patient was admitted into the ICU. Hematological and biochemical investigations were done and exacerbation were graded.

Results: The mean age of the patients was 67.2 ± 9.8 years. Out of the 69 patients, 6 of them died during their stay at the hospital. 58% of them were smokers having more than 2 pack of cigarettes per day. The most common comorbidity present among these patients was Diabetes in 44.9% of them followed by tuberculosis in 34.8% patients.

Conclusion: Some of the risk factors for acute exacerbations in COPD are age, diabetes, FEV1 volume, PaCO2 levels, smoking. Therefore, to reduce the morbidity and mortality of the patient's an early detection is essential so that treatment can be started. Moreover, since future exacerbations normally occur in such patients, they need to be monitored before their symptoms become more prominent.

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1. Introduction

Chronic obstructive pulmonary disease is one of the leading causes of morbidity and mortality worldwide.¹ It is said to be the 5th most common cause of death worldwide and expected to become the 4th most common cause by 2030 by World Health organization.² It is observed that 90% of all cases of COPD occur in middle and low income countries.³ The main cause is tobacco and smoking – both active and passive. Other risk factors associated with COPD is pollution, fumes and dust.³ Patients who have Chronic Obstructive Pulmonary Disease may have acute worsening of their condition. This is called Acute Exacerbation of COPD.⁴ These acute exacerbations may vary from patient to patient. The various symptoms include increased dyspnea, cough with sputum with difference in

colour.⁵ The frequency of the exacerbations also may lead to failing pulmonary function.⁶

Many people with COPD suffer from AECOPD which affects their health and poor prognosis, leading to increased costs of hospitalization and quality of life.⁷ 50% of the exacerbations are difficult to assess and are not reported by the patients.⁸ It is reported by WHO that the global burden of COPD in 2016 was 251 million cases worldwide and 3.17 million death in 2015 were due to COPD3. In England, 2.4% of the patients requiring hospitalization is due to AECOPD.⁹ 59% of the patients with AECOPD, after their discharge from hospitalization have been reported to be readmitted within a year.¹⁰ 10% mortality is suspected among the patients who have been hospitalized. In case of ventilated patients, this rate may go up higher to 40%.^{11–13} In India, a mortality rate of 12% has been reported among the persons who were hospitalized.¹⁴

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During COPD, there is an increased decline in the forced expiratory volume in 1 second by the patient with age leading to airway inflammation.¹⁵ It is difficult for the patients to identify the exacerbations as a worsening feature of their clinical condition, thus not reporting it to the hospital at an early stage.¹⁶

The recovery of pulmonary function takes many weeks after the exacerbation, thereby reducing the quality of life of the individual.¹⁷ The key to this remains in the early detection of the exacerbation and its risk factors, so that the treatment can start at the earliest. The patient required constant monitoring during the course of the disease to reduce the morbidity of the patients. This would prevent a lot of anxiety to the patient, his relatives as well as the treating clinician. There are not many studies identifying the AECOPD patients and its risk factors in India. This study was thus done to identify the outcome of COPD and its exacerbations.

2. Materials and Methods

This clinically based prospective study was done by the Department of Pulmonology, NRI Medical college and hospital from April 2019 to 2020 April. 69 patients who came to the emergency room of our hospital with exacerbations were included into the study. After acquiring the Ethical Committee clearance from our institution, the nature of the study was explained to all the patients and informed consent was taken. Those who refused to give the informed consent were excluded from the study. All these patients were initially screened by Gold criteria to establish COPD3. Exacerbations were measured as per Anthonisen's criteria and the patient was admitted into the ICU. Patients with malignancy, sputum positive for Tuberculosis, other lung disease other than COPD and patients on immunosuppressive therapy were excluded from the study.

Information such as demographic details, previous medical history, history of hospitalization, status of pneumococcal and influenza vaccination, antibiotic history was taken in the form of a questionnaire. During clinical examination, blood pressure, temperature, heart rate, pulse rate, mentation and breathing is noted. Venous blood was taken for complete blood picture, random blood sugar, liver function test, renal function test was done. Arterial blood gas examination was done by radiometer machine. Chest X ray, ECG, Echocardiography was also done for all the patients. Partial oxygen levels (PaO₂) and carbondioxide levels (PaCO₂) were also measured

Dyspnea is graded using MRC dyspnea scale, which is a set of 5 questions.¹⁸

All the patients were followed up though out the duration of their stay in the hospital till their discharge or death.

Statistical analysis was done using SPSS software and Microsoft excel. Chi square test was done for comparison.

Table 1: MRC Dyspnea scale

| Grade | Identification |
|---------|--|
| Grade 1 | Not troubled by breathlessness except on strenuous exercise |
| Grade 2 | Short breath when hurrying on the level or walking up a slight hill |
| Grade 3 | Walks slower than most people on the level, stops after a mile or so, or stops after 15 minutes of walking |
| Grade 4 | Stops for breath after walking about 100 yards or after few minutes on ground level |
| Grade 5 | Too breathless to leave the house, or breathless when undressing |

3. Results

Out of the 69 patients enrolled in the study, 53 were males and 16 were females (Figure 1).

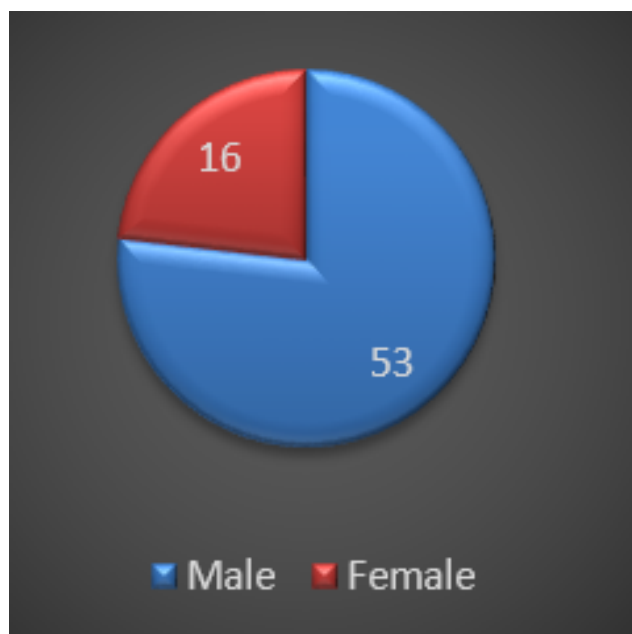


Fig. 1: Genderwise distribution of the patients

Most of the patients were between 61-70 years. 29 (54.7%) of the males and 8 (50%) of the females belonged to this age group. This was followed by 12 (22.6%) of the males and 5 (31.3%) of the females belonging to 51-60 years age group. 8 (15.1% of the males and 2 (12.5%) of the females were between 71-80 years (Table 2). The mean age of the patients was 67.2 ± 9.8 years

Out of the 69 patients, 6 of them died during their stay at the hospital. 40 (58%) of them were smokers having more than 2 pack of cigarettes per day. 7 of the regular smokers were women. Most of the women were either passive smokers, within close quarters with a smoker. Most of the time, the smoker was a spouse or son in the house. Most of the patients were either overweight or obese. The mean

Table 2: Age wise distribution of patients

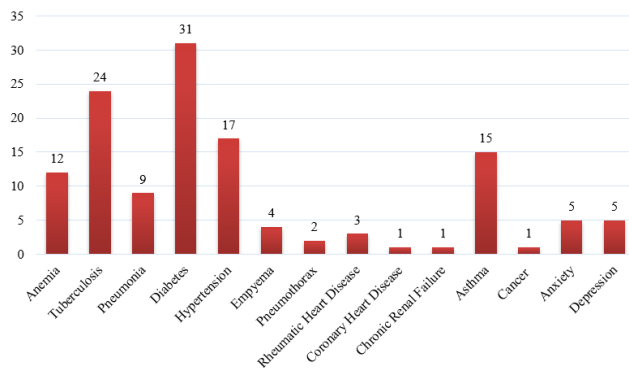
| Age (in years) | Males | Females |
|----------------|------------|-----------|
| 40-50 | 3 (5.7%) | 1 (6.3%) |
| 51-60 | 12 (22.6%) | 5 (31.3%) |
| 61-70 | 29(54.7%) | 8 (50%) |
| 71-80 | 8 (15.1%) | 2 (12.5%) |
| >80 | 1 (1.5%) | 0 (0) |
| Total | 53 | 16 |

Body mass index in the study was 28.6 ± 6.2 . 51 (73.9%) of the patients had a prior history of hospitalizations for COPD and its complications (Table 3).

Table 3: Demographic details of the patients

| Demographic details | Number |
|------------------------------|---------------------------|
| Total patients | 69 |
| Survived | 63 (91.3%) |
| Expired | 6 (8.7%) |
| Mean age (in years) | 67.2 ± 9.8 |
| Smoking status | |
| Current smokers Past smokers | 40 (58%) 17 (24.6%) |
| Passive smokers | 5 (7.2%) |
| Non smokers | 7 (10.1%) |
| Body mass Index | 28.6 ± 6.2 |
| Mean Blood Pressure | 128/88 (115/70 – 225/136) |
| Prior hospitalization | 51 (73.9%) |

The most common comorbidity present among these patients was Diabetes in 31 (44.9%) of them. Second was tuberculosis affecting 24 (34.8%), followed by hypertension in 17 (24.6%). Others were asthma in 15 (21.7%) anemia in 12 (17.4%) and pneumonia in 9 (13 %) (Figure 2)

**Fig. 2:** Comorbidities

The hemoglobin was in the normal range in most of the patients with a mean level of 12.76 ± 2.1 gms%. The mean total leucocyte count was 14304 ± 4099 . The random blood sugar was quite high among all the patients with a mean of 171.8 ± 27.1 . The lowest was 127 mg/dL and the highest was 359 mg/dL. The mean total and direct bilirubin levels

were slightly more than the normal range, with 1.25 ± 0.82 mg/dL and 0.59 ± 0.11 mg/dL respectively. The SGPT and SGOT levels were also marginally higher. The urea levels for the patients were significantly higher with 43.49 ± 19.15 mg/dL (Table 4).

Table 4: Hematological and biochemical Investigations

| Investigations | Mean \pm SD |
|------------------------------------|--------------------|
| Hemoglobin (gm%) | 12.76 ± 2.1 |
| Total Leucocyte count (cells/cumm) | 14304 ± 4099 |
| Random Blood sugar (mg/dL) | 171.8 ± 27.1 |
| Direct bilirubin (mg/dL) | 0.59 ± 0.11 |
| Total bilirubin (mg/dL) | 1.25 ± 0.82 |
| SGPT (IU/L) | 58.2 ± 13.5 |
| SGOT (IU/L) | 63.9 ± 27.1 |
| Total protein (mg/dL) | 6.97 ± 0.41 |
| Albumin (mg/dL) | 4.21 ± 0.97 |
| Urea (mg/dL) | 43.49 ± 19.15 |
| Creatinine (mg/dL) | 1.55 ± 0.37 |
| Potassium (mmol/L) | 4.33 ± 1.18 |
| Sodium (mmol/L) | 128.91 ± 14.58 |
| C Reactive Protein | 33.56 ± 10.38 |

Most of the people had shortness of breath with the breath per minute being 32/min. The MRC score grade among the patients was predominantly Grade 2, with 38 (55.1%). 17 (24.6%) patients belonged to Grade 3. The mean pH present in the patients alive was 7.35 ± 0.09 and the PaO₂ was 58.37 ± 19.33 , while among the patients who died, PaO₂ was more than 63 mmHg. PaCO₂ was around 44 in the living, while among the persons who died, their PaCO₂ was more than 47 mmHg. The mean length of hospital days among the patients was 8 days. 536 patients (52.2%) required ventilator support. (Table 5).

Table 5: Respiratory variables in patients

| Variables | Value |
|--|----------------------|
| Breaths / min | 32 (range : 13 – 56) |
| MRC Score | |
| Grade 1 | 10 (14.5%) |
| Grade 2 | 38 (55.1%) |
| Grade 3 | 17 (24.6%) |
| Grade 4 | 3 (4.3%) |
| Grade 5 | 1 (1.4%) |
| pH | 7.35 ± 0.09 |
| PaO ₂ (mmHg) | 58.37 ± 19.33 |
| PaCO ₂ (mmHg) | 45.33 ± 12.29 |
| HCO ₃ ⁻ (mmol/L) | 32.92 ± 6.33 |
| SO ₂ (%) | 86.12 ± 31.11 |
| Alveolar arterial difference | 41.38 |
| FVC (L) | 2.27 ± 0.28 |
| FEV ₁ (L) | 1.05 ± 0.51 |
| LTOT | 41 |
| LOS (mean days) | 8 |
| Need for ventilator support | 36 (52.2%) |

4. Discussion

COPD as a one of the leading cause of mortality is increasing worldwide. In the present study, there were predominantly more number of males than females. More number of patients belonged to the 61-70 years age group (53.6%), followed by 51-60 years (24.6%) The mean age was 67.2 ± 9.8 years. A study by Chandra et al reported the mean age to be 61.3 years which was in accordance to our study.¹⁹ A higher age group was also considered to be a risk factor for exacerbations which was observed in our study and supported by Kumar et al and Hansen et al in their respective studies^{13,20}. Mehta, in a study found the mean age to be around 71 years and also found that as the age increases, the risk for mortality also increases.²⁰

8.7% of the patients died during their hospital stay. 10-15% of mortality rate was reported in other studies.^{19,21,22} In a study by Kumar et al, 17% of mortality rate was observed, which was considerably higher than our study. In another study by Connors et al, 8% of inhouse mortality was observed.¹³

58% of the patients were smokers, and 7.2% were passive smokers with the active smoker being a spouse or a son. 24.6% were ex smokers. Only about 10% of them were non smokers. Tobacco smoke is reported to be one of the leading causes of exacerbations.^{23,24} However, the number of exacerbation and its severity was not significant in the smokers and non smokers, showing that the damage was already done the stoppage of smoking was late.²⁵

Most of the patients were either overweight or obese with the mean BMI being 28.6 ± 6.2 . Among the patients who died, the BMI was significantly higher, showing that a higher BMI may be associated with higher mortality. The MRC score was predominantly grade 2 in our study. Patients with higher MRC score had a longer length of hospital stay. This was confirmed in a study by Tsimogianni et al, who reported that BMI and MRC scores are the independent predictors of the length of hospital stay for patients with AECOPD.²⁶ The duration of the exacerbation was also directly associated with the severity, which was in concurrence with other studies²⁷⁻²⁹ A history of previous exacerbations also predicts future hospitalizations.³⁰⁻³²

PaCO₂ levels in our study was slightly elevated in our study in the patients who died compared to those who survived. It has been observed that there is an elevation of PaCO₂ in COPD patients with and without exacerbations. This is due to the mismatch of alveolar hypoventilation and ventilation perfusion. Elevated PaCO₂ is a sign of acidosis, which in chronic patients is compensated by increased bicarbonate levels, keeping the pH in the normal range.¹¹

Another predictor of severe morbidity and mortality was FEV₁ volume which was 1.05 ± 0.51 L in our study. The average FEV₁/FVC ratio was 46.3%. FEV₁ was considered to be an independent predictor of mortality, but now, there are studies which have reported that FEV₁, although a

useful predictor, cannot be considered as an independent predictor.²⁶

The most common comorbidity seen among the patients was diabetes in 44.9%, followed by tuberculosis in 34.8%, hypertension in 24.6%, asthma in 21.7%. Depression was seen in 7.2% of the patients. In some other studies, an association was observed between the psychiatric illnesses and exacerbations. In a study by Fitzgerald et al, 20% of the patients with exacerbations had depression.³³ Higher glucose levels were observed in other similar studies. Kumar et al also found hyperglycemia in the patients with AECOPD. Diabetes is one of the etiological factors to cause exacerbations as these patients are more prone to secondary infections, thereby causing further complications. There was a significant imbalance in the electrolytes in our study. Similar was found in a study by Kumar et al as this imbalance may lead to hyponitremia.¹¹

5. Conclusion

Some of the risk factors for acute exacerbations in COPD maybe age, diabetes, FEV₁ volume, PaCO₂ levels, smoking. MRC score predicts the length of stay in the hospital. Other predictors may be sodium levels, SGPT levels. Therefore, to reduce the morbidity and mortality of the patients, an early detection is essential so that treatment can be started. Moreover, since future exacerbations normally occur in such patients, they need to be monitored before their symptoms become more prominent.

6. Conflict of Interest

None.

7. Source of Funding

None.

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