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RESEARCH ARTICLE

The Management and Outcomes of Acute Exacerbations of Chronic Obstructive Pulmonary Disease (AECOPD) at Dr. George Mukhari Academic Hospital

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Abstract

Introduction: Chronic obstructive pulmonary disease is a significant cause of ill-health and mortality among sufferers throughout the world.

Objective: The purpose of the study was to describe the management and outcomes of patients admitted to the medical wards of DGMAH with an acute exacerbation of COPD.

Methods: A review of the medical records of a cohort of medical patients admitted with an acute exacerbation of COPD over a 12-month period (August 2022-August 2023).

Results: A total of ninety-seven patients were studied. The mean age was 64.6 years. A quarter of the cases had more than 40 pack-year smoking history. Seventy-seven percent of the patients had one or more comorbidity. Thirty-eight patients (39.1%) had had at least one previous exacerbation requiring hospitalization in the past 12-months. More than 75% (79.4%) of the flare-ups were deemed infective in origin. Seven patients required high care admission. Eighteen patients (18.5%) succumbed in association with the exacerbations. There was no association between the presence of comorbid disease, a previous episode of an exacerbation or gender and poor outcome. There were also no significant differences noted between survivors and non-survivors with regards to mean age, mean pack year history or admission biochemical abnormalities.

Conclusion: COPD exacerbations can be associated with loss of life. This means any flare-up should be treated with the seriousness it deserves as it carries a potential for poor outcome. Most of the flare-ups were infective in origin; suggesting empiric antimicrobial coverage may be appropriate in our setting.

1. Introduction

Globally, the burden of COPD is expected to increase over the coming years because of continued exposure to COPD risk factors and aging of the population. It is preventable but not curable once established; effective therapies exist.(1). COPD is characterised by exacerbations, described as acute worsening of respiratory symptoms in a patient with the disease that results in the need for additional therapy .(2). Exacerbations are important because the majority of patients die during these episodes.(3-4). Exacerbations are burdensome on healthcare facilities. In a study aimed at assessing the burden of AECOPD on the ED in the US over a 9-year study period, an estimated 7,508,000 visits were observed .(5). A pattern of decline in lung function and deterioration in quality of life has been observed following AECOPD. (6).

Exacerbations can be precipitated by a variety of factors, the most common being respiratory tract infections. (7). Clinically important differentials for

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AECOPD include pneumothoraxes, acute pulmonary embolism and cardiogenic pulmonary oedema. (8).

The standard of care for moderate to severe exacerbations is inpatient care and may include the use of more sophisticated respiratory support systems such as non-invasive and invasive ventilatory support. (9,10).

2. Aim and Objectives

2.1 Aim of Study

To audit the management and outcomes of patients admitted to the medical wards with an acute exacerbation of COPD.

2.2 Objectives of Study

- To describe the therapies offered to the patients.
- To determine the length of hospital stay of the cohort.
- To determine the mortality rate of the cohort.

3. Materials and Methods

The study was retrospective and took place during a 12-month period (August 2022- August 2023). It was a review of the records of adult (≥18 years) patients admitted to the medical wards of DGMAH with an exacerbation of COPD during the study period. The ward admission record was used to identify potential subjects and the researchers tracked down the records with the assistance of the ward clerk. A diagnosis of COPD was deemed likely if the consultant subsequently confirmed it during the ward round. In addition, both the patients' chest radiology and spirometry, when available, were reviewed by the researchers with the help of respiratory physicians for confirmation.

An exacerbation was deemed infective in origin by the researchers if any two of the following were recorded: elevated temperature >37.5 ^{0}C, purulent secretions, elevated white cell count, c-reactive protein and procalcitonin.

3.1 Ethical Considerations

Permission to conduct the study was requested from the Sefako Makgatho Health Sciences University's research ethics committee [SMUREC/M/241/2022] before the study began. Permission to conduct the study was also sought from the Hospital Management of Dr George Mukhari Academic Hospital. The data collection tool used unique codes to avoid patient identification and all information was kept confidential. The completed data sheets were stored password protected on the researcher's computer. The study was a review of patient charts; obtaining of informed consent was waived by the committee.

3.2 Data Collection

The data collection sheet was compiled by the researcher and piloted on the first five cases to ensure its reliability. No changes needed to be effected after the pilot study and the cases were included in the in the final tally.

3.3 Data Analysis

Categorical data are presented as frequencies and percentages. Continuous variables are indicated using means and standard deviation. The rate of admission to the high care or intensive care unit, and the mortality rate is presented as percentages with 95% confidence intervals. All the data was captured into a Microsoft "Excel" sheet and analyzed using the Statistical Package for Social Sciences (SPSS, version 21.0 IBM, USA). -

4. Results

A total of 97 patient files were studied. Twelve files could not be traced. The mean age of the study population was 64.6 ± 11.8 years. The majority (81.4%; *n* = 79) were male.

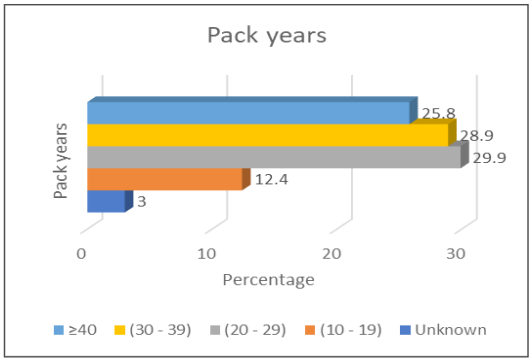

Figure 1. *Pack years*

More than 70% of the patients (73.2%; *n=71*) were current tobacco users and approximately 26% had a pack-year history in excess of 40 years. Figure 1 is a summary of the smoking status of the patients. The mean pack years of females and males didn't differ significantly (32.1 v/s 30.5; *p=0.634*).

The median (IQR) length of stay of the study population was 7(4-11) days. Figure 2 depicts the hospital length of stay of the cohort

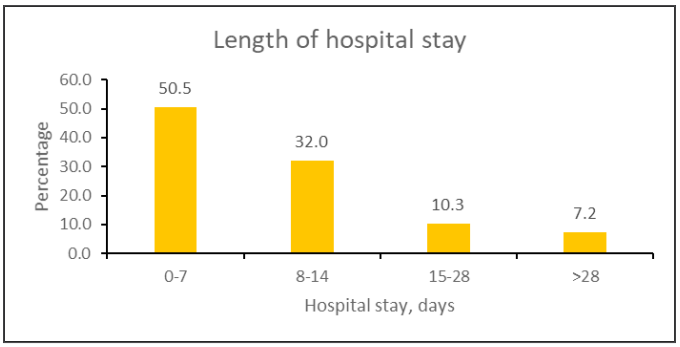

Figure 2. *Length of hospital stay*

Comorbidities were present in 77% of the cases with concomitant hypertension being the most frequent (50.6% of the cases). The frequency of other accompanying illnesses is summed up in Figure 3.

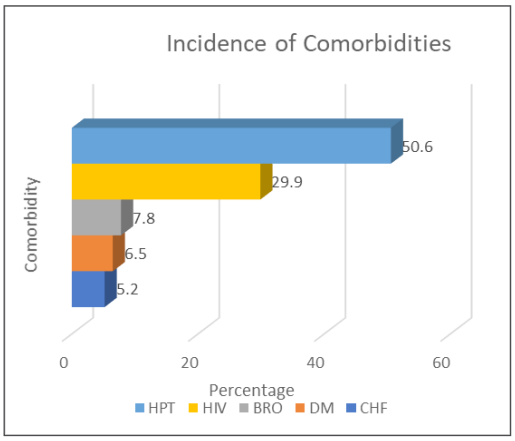

Figure 3. *Co-morbidities*

HPT: Hypertension; *HIV*: Human immunodeficiency virus; *BRO*: bronchiectasis; *DM:* Diabetes mellitus; *CHF:* congestive cardiac failure.

Thirty-eight patients (39.1%) had had one COPD exacerbation in the preceding 12 months; with two of the patients having suffered 3 flare-ups in the year preceding the current admission.

The precipitant for the acute flare-ups in this study was thought infectious in origin in 79.4% (n=77) of the patients. Out of the 18 patients with non-infective COPD exacerbations, only 1 had a CTPA confirming a pulmonary embolism.

5. Management

All the patients received nebulization with a short acting B2 agonist and short acting anticholinergic agent. Sixty-seven (69.1%) and eighty-eight (90.7%) were treated additionally with steroids and antibiotics respectively. Seven patients (7.2%) were admitted to the high care unit; all survived. Two (2.1%) received NIV(CPAP), three (3.1%) were treated with high flow nasal cannulae (HFNC) and two (2.1%) received invasive mechanical ventilation. Intravenous aminophylline or magnesium sulphate were not used in any of the patients.

Eighteen (18.5%) patients demised in association with the exacerbation. The number of female patients who demised did not differ significantly from males (22.2% v/s 16.5%; *p = 0.513)*. A history of a previous hospitalization for an exacerbation of COPD in this study was not associated with an increased risk of death. Thirteen (22.8%) of the 57 patients who had no previous admissions demised versus 2 (5.3%) of the 38 patients who had previous admissions. The two percentages differ significantly (*p=0.024*). The mean age of the patients was not statistically significantly different between survivors and non-survivors (67,3

v/s 64.0; *p*=0.267). The mean number of pack-year smoking history was no different between the patients who demised compared to those who survived (29.2 v/s 31.1; *p*=0.570*)*.

The presence of comorbidities, differences in admission PA02, PAC02, and pH did not adversely affect patient outcomes from the acute flare of their disease. (see Table 1)

Table 1. *Impact of comorbidities and admission blood gas parameters on outcomes of AECOPD patients.*

Risk factor for poor outcome	survivors	non-survivors	P= value
Presence of comorbidities	10(16.7%)	8(18.9%)	P= 0.513
Mean Admission PA02	72.99	65.95	P= 0.467
Mean admission PAC02	42.66	36.36	P= 0.052
Mean Admission PH	7.387	7.385	P=0.928

The mean duration of hospital length of stay of the patients that demised compared to survivors differed significantly (p<0.001); with patients who survived staying significantly longer in hospital (see table 4).

6. Discussion

Exacerbations are known to be prevalent in COPD and are associated with poor clinical outcomes including death, a faster decline in lung function and a reduction in quality of life. (6). The mortality associated with an exacerbation in this study was elevated at 18.5%. A recent national survey found an in-hospital mortality of 3% among patients admitted to Internal Medicine departments with AECOPD in Israel. (11). In a study of AECOPD requiring ICU admission in Egypt an in-hospital mortality of 34.9% was observed. (12).

Thirty-eight patients (39,1%) patients had suffered at least one exacerbation in the previous 12 months. Patients with COPD are prone to exacerbations, with 30%-50% experiencing at least one per year. (13). The entity of frequent exacerbation phenotype has been described and is defined when an individual has two or more episodes per year. (14). Three (0.03%) of the study participants in this study cohort met the criteria for frequent exacerbators. In the prevention of exacerbations with tiotropium in COPD trial, frequent exacerbators had a three-fold increase in mortality. (15). Despite the sizable number of cases with previous flares of the disease, the study was not able to establish previous exacerbations as a risk factor for death. It is possible patients became more aware of the seriousness of their disease and were encourage into better adherence.

Approximately 70 to 80 percent of exacerbations of COPD are thought due to respiratory infections, with viral and bacterial infections causing most exacerbations. (16). A South Korea study estimated that up to 83% of their cases with acute exacerbations of chronic obstructive pulmonary disease cases had a precipitating respiratory tract infection, based on compatible infective symptoms and computed tomography findings. (17). A prospective study from Australia estimated that 56% of the acute exacerbation of COPD was due to respiratory infection based on positive microbiological results, irrespective of radiological findings. (18).

The literature recommends consideration of pulmonary thrombo-embolic disease in the differential diagnosis of COPD exacerbations. (19,20). This study only picked up one case (0.01%) with a pulmonary embolus. There is a possibility some were missed as CTPAs are not done routinely in cases of AECOPD but only in those cases where the index of suspicion is high. In a recent systematic review published in Chest, the pooled prevalence of PE in unexplained AECOPD was 16.1%. (19) . In a study from South Korea, pulmonary embolism comprised 5% of the causes of COPD exacerbation. (17).

COPD is a predominately older patient population disease. The mean age of the cohort was 64.6 years; very similar to that of a study from a number of hospitals in Cape Town looking at a similar group of study participants. (21). The mean age was 63 years. The mean age of the group found during the national survey of AECOPD carried out in Israel was higher at 74 years. (11). In a retrospective study conducted in Geneva University Hospitals, the average age was 72 years. (22).

Males were in the majority (81.4%) in this cohort. The study by Pienaar et al also found a male predominance of approximately 66%. (21). It has to be appreciated that whilst the disease was once thought to primarily affect older male smokers, recent evidence suggests that the prevalence and mortality of COPD have increased more rapidly in women than in men. (23).

Unlike the Cape Town study in which only 34% were smoking at the time of enrolment, more than 70% of

the subjects in this study were current smokers. (21). An analysis of risk factors for AECOPD identified amongst others current tobacco use as an important risk factor with an odds ratio = 1,84. (24).

More than seventy percent of the participants had at least one comorbidity. COPD is predominantly a disease of the elderly and the presence of concomitant illnesses is to be expected. Pienaar and colleagues found the presence of at least one comorbidity in 78% of their patients. (21). Comorbidities are not only frequent among COPD patients but are also reported to significantly impact their quality of life, exacerbation frequency and survival. (25). report]. Although this study was not able to establish a deleterious effect of the presence of comorbid disease on exacerbation-associated mortality; other studies found the presence of certain comorbid diseases to be associated with poor outcomes. (26,27). In the Flattet et al study, comorbidities, and notably diabetes and cancer, were closely associated with poor outcome. (22). Prior recorded congestive heart failure was associated with poor outcome in the study by Slenter and colleagues. (27).

In this study, admission biochemical abnormalities did not influence outcome. These findings are not consistent with previous studies. An audit of COPD exacerbation admissions from 13 European countries found among others, the presence of acidotic respiratory failure to be associated with increased risk of in-hospital and post-discharge mortality. (29). A PaCO2 >6 kPa at hospital admission seemed to be independent predictor of increased mortality. (27).

In this study there were no gender differences in mortality from exacerbations. The effect of gender on mortality in patients with COPD remains unclear. A review by Italian authors suggested increased death rates among women.(30). In a retrospective study on gender differences among Swedish COPD patients, women exacerbated more frequently than men, however, the mortality rate was found significantly higher in men compared to women. (31). In van Hirtum's study, male gender was found to be a negative prognostic factor for survival after an exacerbation of COPD. (32). In a retrospective analysis of the database of the Hungarian National Health Insurance Fund on severe exacerbations and mortality in COPD patients, female patients had a markedly lower risk of death. (33).

7. Conclusion

This study provides an overview of the management and outcomes of patients with COPD admitted to the medical wards of DGMAH with an acute exacerbation of the disease. It demonstrates that exacerbations represent an important event in the natural history of COPD patients and are associated with significant morbidity and mortality. Infections are recognized as provoking factors of the great majority of acute exacerbations of COPD; for this reason it is important to effectively control viral and bacterial infections by putting in place prophylactic and therapeutic measures to prevent or treat these flares.

Tobacco consumption remains an important risk factor for COPD in the community served by the institution. Survivors stay much longer in hospital presumably utilising lots of health care resources.

The surprise finding in this study was that the usual determinants of increased mortality in COPD exacerbation such as comorbidities, previous exacerbations and biochemical abnormalities did not influence the outcome, and these are in contrast with existing theories and previous research. This might be due to differences in severity of comorbidities or other factors such as differences in inpatient care.

The limitation of this study is the lack of information on the severity of COPD as assessed by spirometry. It is known the more severe the disease the poorer the outcomes during an exacerbation.

Recommendations

Future studies are still needed clarify the prognostic implications of comorbid disease and biochemical abnormalities for exacerbations. Follow up studies on quality of life of the survivors of AECOPD in the community we serve seem indicated.

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