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Assessment of Prescribing Patterns of Drugs in COPD Patients with Cor Pulmonale and Pulmonary Hypertension in A Teaching Hospital

	
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ABSTRACT

Introduction: Chronic Obstructive Pulmonary Disease (COPD), a progressive ailment induced by pulmonary irritants, exhibits irreversible airway obstruction and inflammation. COPD poses an independent risk for cardiovascular morbidity, including right ventricular (RV) dysfunction and Cor Pulmonale (CP) due to Pulmonary Hypertension (PH). This study aimed to scrutinize drug usage patterns in treating COPD patients with exacerbations, CP, and PH, emphasizing echocardiographic findings to refine diagnostic approaches. **Objectives:** The primary objective was to assess drug prescription patterns for COPD patients, focusing on alternative medications. Additionally, the study aimed to explore echocardiographic findings among COPD patients. **Methodology:** An observational study involved 40 in-patients diagnosed with COPD, CP, and/or PH. Patient data, collected from admission to discharge, underwent statistical analysis, utilizing descriptive statistics and chi-square tests. **Results:** Analysis revealed a prevalence of COPD among non-smoking women over 50 years. PH was present in 35%, and CP prevalence increased during exacerbations. Dyspnea was a predominant symptom. Drug prescriptions favored bronchodilators, corticosteroids, and antibiotics. Aspirin was a frequently prescribed cardiovascular drug. Echocardiographic findings aided in identifying RV dysfunction and PH. **Conclusion:** The study underscores COPD's predominance in non-smoking women over 50, emphasizing the influence of age on disease progression. Echocardiography facilitates the early detection of PH and CP in COPD patients. Prescription patterns mainly targeted symptom relief and exacerbation prevention, with a preference for bronchodilators, corticosteroids, and antibiotics. Recognition of RV dysfunction and PH in CP patients may enhance treatment outcomes and life expectancy. The findings contribute valuable insights for optimizing COPD management strategies.

INTRODUCTION

Global Initiative for Chronic Obstructive Lung Disease (GOLD 2022) guidelines define Chronic Obstructive Pulmonary Disease (COPD) as a disease distinguished by irreversible expiratory airflow limitation that is typically progressive and accompanied by an aberrant inflammatory response of the lungs to noxious particles or gases. ^[1,2] COPD is a commonly progressing disorder usually brought on by pernicious lung irritants and is defined by a completely irreversible airway obstruction and an inflammatory component. In men over the age of 35 in India, the prevalence of chronic obstructive pulmonary disease is 5%, whereas in women it is around 3.2 % ^[3] COPD is in the limelight around the world as its high prevalence, morbidity and mortality pose significant problems to the healthcare system. According to the World Health Organization (WHO), the total number of deaths in the world due to COPD is estimated to increase by more than 30% in the next 10 years and by 2030, COPD will become the fourth leading cause of death worldwide. ^[3,4] COPD causes disability and degrades the quality of life, as well as loss of productivity, increased hospital admissions, increased healthcare costs, and early death. ^[5]

The key to managing COPD patients is pharmacotherapy which entails systemic, oral, and inhalational therapy for the maintenance and relief of drugs. Long-acting bronchodilators (long-acting β_2 agonists) or LABA and (long-acting antimuscarinics) or LAMA, either alone or in combination, are the cornerstone of pharmacological therapy for stable COPD patients to ease symptoms, boosting exercise capacity, and enhancing the quality of life and prognosis.

Acute exacerbations of COPD (AECOPD) are characterized by an increase in cough, sputum output, purulence, and dyspnoea, as well as the worsening of COPD symptoms. ^[6] The primary goal of AECOPD management is to reduce the severity of the current exacerbation while also preventing future exacerbations. ^[7] Formerly published systematic reviews and clinical guidelines on the case of AECOPD patients hospitalized have predominantly focused on medical management, with hardly any consideration paid to physical therapy-specific interactions. ^[8] Archiving current practice designs is a significant stage in the advancement of best practice rules. ^[9]

COPD related Pulmonary Hypertension

Pulmonary hypertension (PH) associated with lung disease can be defined as a resting mean pulmonary artery pressure greater than 20mmHg. The development of PH is a notable inconvenience of COPD. PH often arises when there is substantial airway obstruction and is accompanied by prolonged hypoxemia, with chronic alveolar hypoxia being the most prevalent pathophysiologic cause, however, other pathways have recently emerged. ^[10] PH in COPD is classified as Group 3 by the World Health Organization (WHO). ^[4,11]

Pulmonary Hypertension and Cor Pulmonale in COPD

COPD is a significant and independent risk factor for cardiovascular morbidity, including right ventricular (RV) dysfunction and cor pulmonale due to pulmonary arterial hypertension.

Cor Pulmonale (CP) is described by WHO as "hypertrophy of the right ventricle caused by disorders affecting the function and/or structure of the lungs, except when these pulmonary abnormalities are caused by diseases principally affecting the left side of the heart, as in congenital heart disease." In Cor pulmonale, PH is always the underlying pathogenic cause causing right ventricular hypertrophy.

The reported prevalence ranges from 20% to 91% depending on the definition of pulmonary hypertension, the severity of lung illness in the study group, and the technique of assessing PASP. ^[12,13]

The prevalence of PH increases as COPD worsens, and the development of PH and Cor pulmonale appears to have an impact on COPD patients' survival. ^[14]

Comorbidities have a substantial impact on the prognosis of chronic obstructive pulmonary disease (COPD). Additionally, cardiovascular comorbidities are regarded as a leading cause of hospitalization and mortality in COPD patients.

Drug usage or drug use measures are well-structured and valid quality assurance approaches. These studies are designed to investigate drug usage and uncover pharmacological trends based on current recommendations or guidelines for treating a certain ailment.

Aim and objective of the study: This study aimed to analyze the prescribing pattern of drugs in COPD patients with Cor Pulmonale and Pulmonary hypertension and to determine

the echocardiographic findings and the presence of symptoms associated with the diagnosis of COPD patients admitted in the department of General Medicine of a teaching hospital.

PATIENTS AND METHODS:

Study Design: This was a prospective observational study.

Study Duration: 6 months of study, including planning, data collection, interpretation, and thesis writing.

Study Centre: The study was conducted in the Department of General Medicine at ESI PGIMSR, Rajajinagar, Bengaluru.

Study Population: The study was conducted in subjects drawn from the population admitted in the General Medicine ward at ESI-MC & PGIMSR, Bengaluru, who had given informed consent and assent forms.

Sample Size: The sample size was calculated using a prevalence of 12% in the Department of General Medicine and was estimated to be 40.

$$n = \frac{Z_{1-\alpha/2}^2 * p * (1 - p)}{d^2}$$

Inclusion criteria:

- a. Patients diagnosed with COPD with Cor pulmonale and/or Pulmonary hypertension admitted as in-patient in the department of General Medicine.
- b. Patients above 18 years of age.

Exclusion criteria:

- a. Patients who tested COVID-19+VE at the time of admission.
- b. Pregnant and lactating women.

Ethical approval: this study was approved by epic-medical college & primer (No.532/L/11/12/Ethics/ESICMC&PGIMSR/Estt. Vol.-IV).

Source of data:

Patient demographics and treatment details were collected from patients' case sheets admitted in the in-patient department of General Medicine.

Study tool:

Self-designed data collection form: Data was collected by using a self-designed data collection form, which consists of details like age, sex, lab data, disease condition, echocardiography report, ECG report, symptoms, co-morbidities, drug therapy, and other relevant information.

Study procedure:

Subjects for the study were identified by the investigators during the ward visits based on the inclusion and exclusion criteria. The patients were explained the purpose of the study and informed consent was obtained. Relevant data such as demographic details, medication charts, etc., was recorded. The data thus obtained was entered in a Microsoft Excel sheet and appropriate analysis was performed.

Statistical analysis:

All recorded data were entered using MS Excel software and analyzed using MS Excel. Descriptive statistics such as mean and standard deviation were computed for quantitative variables and frequencies and percentages were calculated for categorical variables. Histograms and pie charts were applied to find the nature of data distribution.

Parameters Analysed:

The prescription pattern for patients with COPD diagnosed with Cor pulmonale and/or Pulmonary hypertension was analyzed and it was correlated to the treatment provided for symptomatic relief and to prevent exacerbations. The Doppler echocardiography and ECG report of individual patients were obtained and the presence of right ventricular hypertrophy was confirmed. The PASP values were correlated with the presence of comorbidities. The symptoms were correlated with the presence of COPD, COPD patients with exacerbations and cardiovascular complications.

RESULTS

The study was conducted in subjects drawn from the population admitted to the General Medicine ward at ESI-MC & PGIMSR, Bengaluru based on the inclusion criteria. A total of 40 study subjects were included in the study.

Gender Distribution

Out of 40 study subjects enrolled in the study, 19 (47.5%) were male and 21 (52.5%) were female as enlisted in Table 1.

Age Distribution:

The maximum number of male patients were found to belong to the age group of 60-69 years, 9 (22.5%), and the maximum number of female patients were found to belong to the age group of 50-59 years, 8 (20%) as enlisted in Table 1.

Table 1: Distribution of patients based on age group and gender

Age Group (Years)	Male		Female		Total No of Patients	
	n	(%)	n	(%)	n	%
30-39	0	0%	0 (0%)		0 (0%)	
40-49	2	5%	1 (2.5%)		3 (7.5%)	
50-59	5	12.5%	8 (20%)		13 (32.5%)	
60-69	9	22.5%	5 (12.5%)		14 (35%)	
70-79	3	7.5%	6 (15%)		9 (22.5%)	
80-89	0	0%	1 (2.5%)		1 (2.5%)	
Total	19		21		40	

Smoking Status:

Out of 40 COPD patients included in the study, 17 (42.5%) male patients were found to be smokers and 3 (7.5%) patients were non-smokers and out of 20 (50%) female patients all were non-smokers as enumerated in Figure 1.

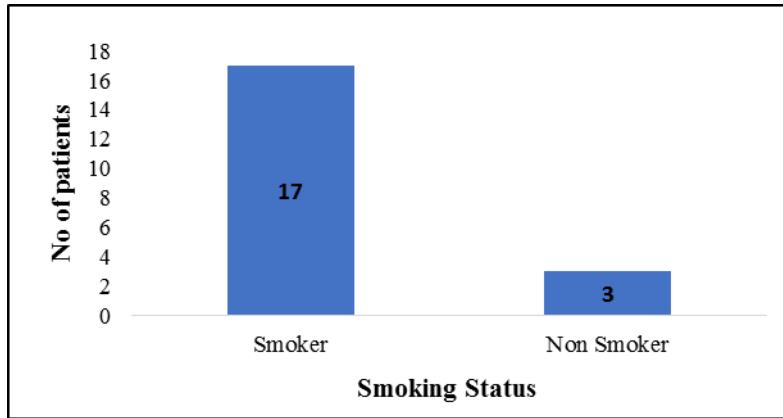


Figure 1: Distribution of smoking status

Distribution of COPD Subjects Based on Ejection Fraction:

Ejection fraction was measured for 11 (27.5%) male patients, out of which 10 (25%) patients were found to be in the normal range (52-72%) and 1 (2.5%) patient in the mildly abnormal range (41-51%). Ejection fraction was measured for 14 (35%) female patients among which 11 (27.5%) patients were found to be in the normal range of 52-72%, 1 (2.5%) patient in the mildly abnormal range (30-40%) and 2 (5%) patients in the moderately abnormal range (30-40%) as enlisted in Figure 2.

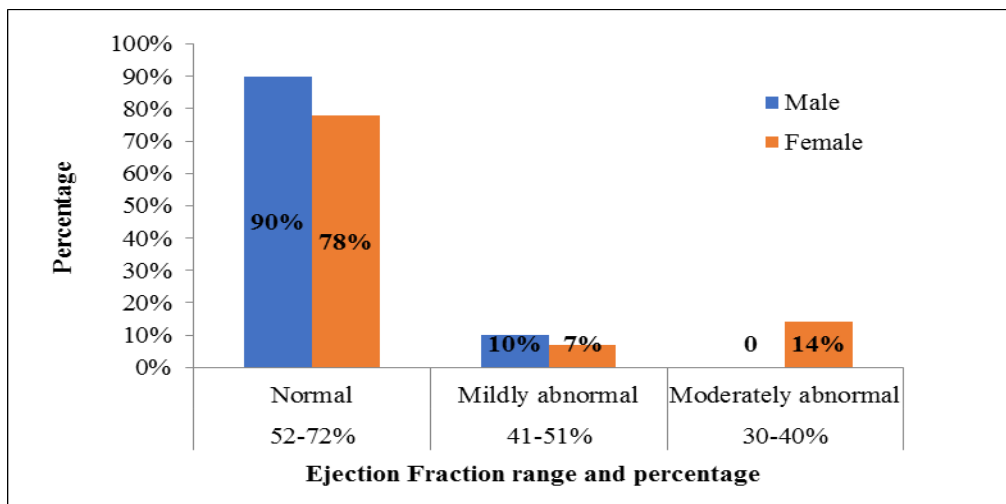
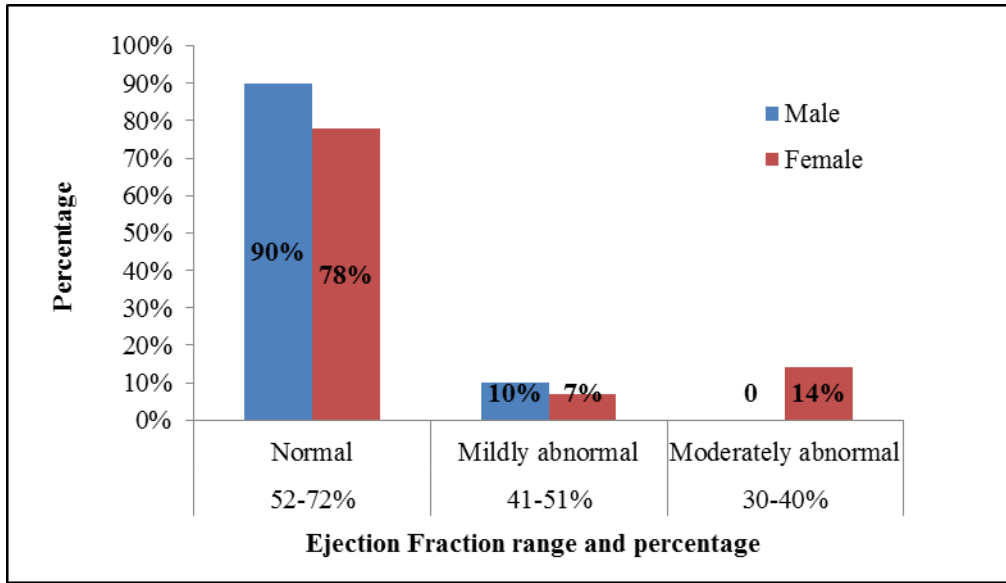


Figure 2: Distribution of COPD patients based on ejection fraction

Distribution of COPD Patients based on RVH as Found in ECG:



Out of the total COPD patients screened for ECG, 21 patients (52.5%) had the presence of rightventricular hypertrophy as shown in Figure 3.

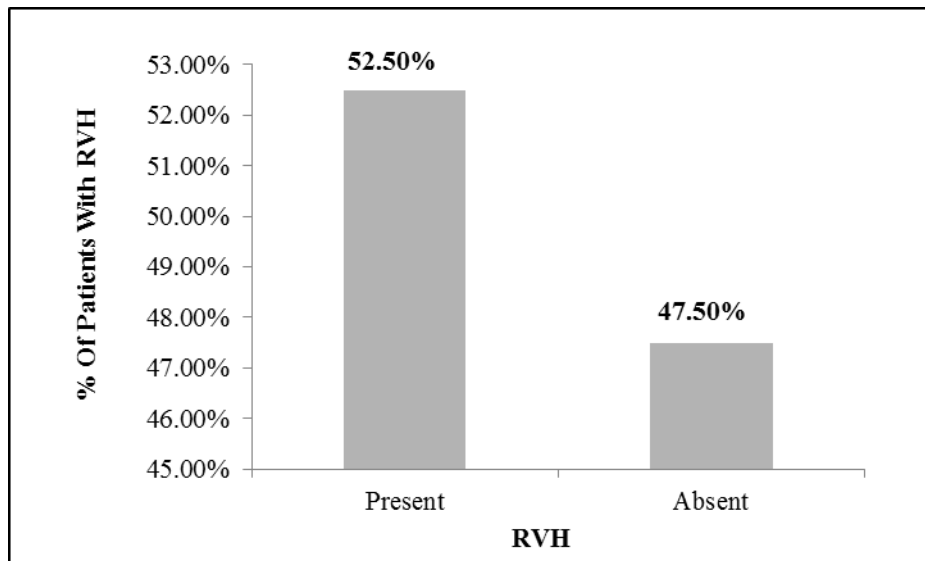


Figure 3: Distribution of COPD patients based on RVH as found in ECG

Distribution of COPD Patients Based on the Presence of Complications:

Out of 40 COPD patients, 14 (22%) patients were diagnosed with COPD with Cor pulmonale, 14 patients (22%) with COPD with pulmonary hypertension, and 6 patients (10%) as COPD with Cor pulmonale and pulmonary hypertension as seen in Figure 4.

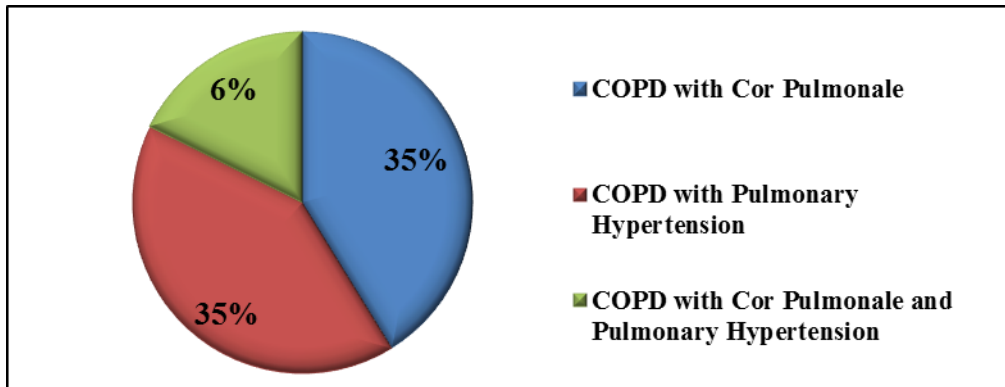


Figure 4: Distribution of COPD patients based on the presence of complications

Distribution Of COPD Patients with Acute Exacerbation and Complications:

Out of 40 patients who had a history of COPD, 15 (37.5%) patients were diagnosed as AECOPD with Cor pulmonale, 9 (22.5%) patients with AECOPD with Pulmonary hypertension, and 5 (12.5%) patients as AECOPD with Cor pulmonale and Pulmonary hypertension as shown in Figure 5.

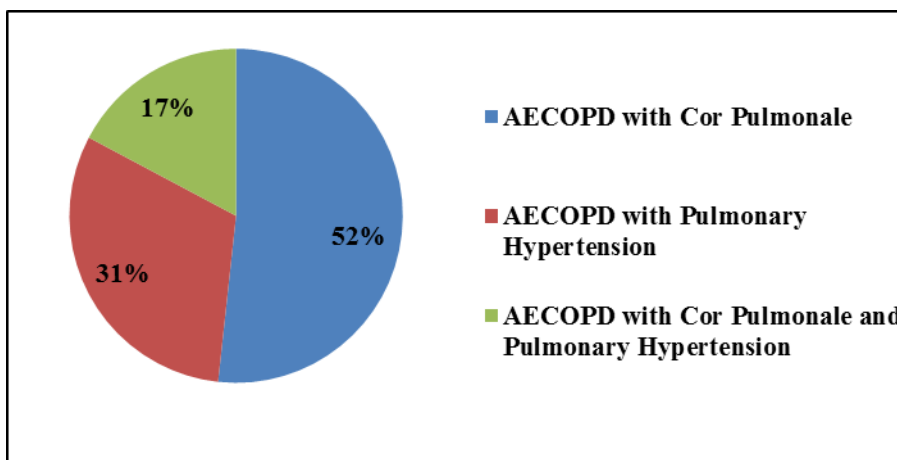


Figure 5: Distribution of COPD patients with acute exacerbation and complications

Distribution Of Comorbidities in COPD Patients:

Out of 40 COPD patients with Pulmonary hypertension and/or Cor pulmonale, Hypertension (n=16,40%) was found to be the most common comorbidity followed by common distribution between Type 2 DM (n= 12, 30%) Type I Respiratory failure (n= 12, 30%), atrial flutter (n= 4, 10%), left midzone consolidation (n= 4, 10%) and hypertensive heart disease (n= 1,2.5%) being the most least comorbidity found in patients as shown in Figure 6.

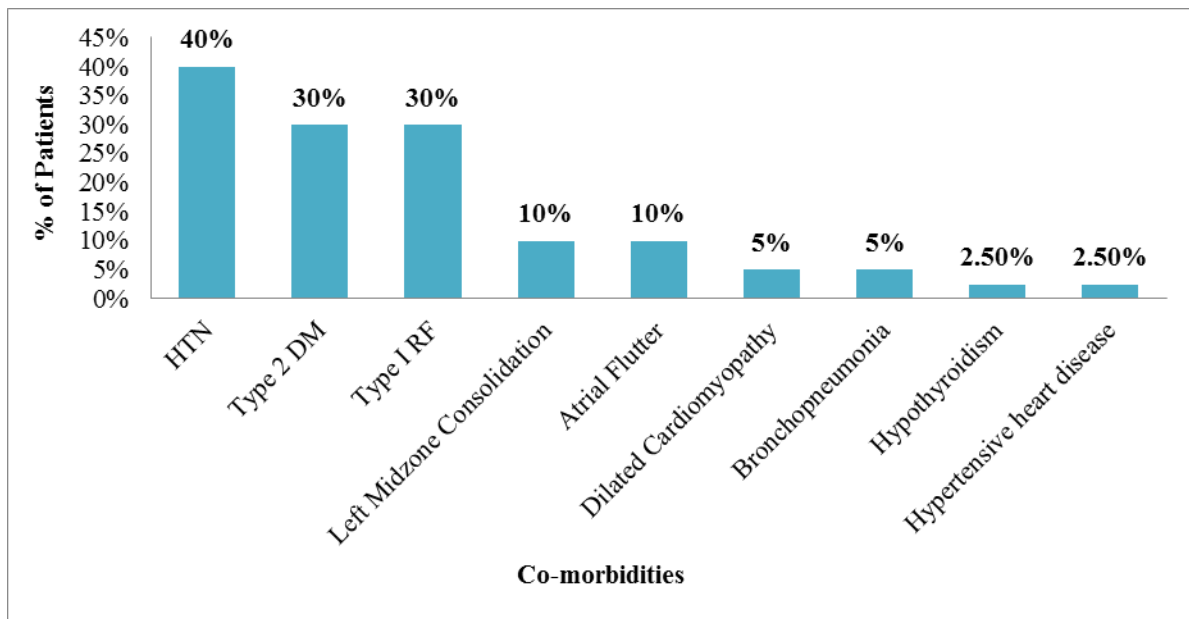


Figure 6: Distribution of comorbidities in COPD patients

Distribution of Symptoms Among COPD Patients:

Out of 40 COPD patients, dyspnea (n=39, 98%) was found to be the most prevalent symptom followed by cough (n=31, 78%), pedal edema (n=17, 42.5%), fever (n=16, 40%), chest pain (n=9, 22.5%), wheezing (n=8, 20%), fatigue (n=6, 15%) and the least common symptom was found to be puffiness and giddiness sharing common distribution in 1 patients (2.5%) respectively as enlisted in table 2.

<i>Table 2: Distribution of symptoms among COPD patients</i>		
Symptoms	No Of Patients	Percentage (%)
Dyspnea	39	98%
Cough	31	78%
Pedal edema	17	42.50%
Fever	16	40.00%
Chest pain	9	22.50%
Wheezing	8	20%
Fatigue	6	15%
Puffiness	1	2.50%
Giddiness	1	2.50%

Distribution of Patients on Basis Of Dyspnea Grading:

Out of a total of 40 COPD patients, 39 were found to have dyspnea, with 18 patients (45%) having Grade I Dyspnea, 3 patients (7.5%) having Grade II Dyspnea, 9 patients (22.5%) having Grade III Dyspnea, and 8 patients (20%) having Grade IV Dyspnea, according to mMRC Scale as enlisted in Table 3.

Dyspnea Grading (mMRC Scale)	No Of Patients	Percentages
Grade I	18	45%
Grade II	4	10%
Grade III	9	22.50%
Grade IV	8	20%

Distribution of Medications Prescribed for COPD Patients:

This study observed that bronchodilators (n=37, 92.5%) were the most frequent class of drug, tied for first place with corticosteroids followed by antibiotics given to 28 patients (70%), cardiovascular drugs (n=23, 57.5%), anti-inflammatory and diuretics shares a common distribution of 17 patients (42.5%). Antitussives were given to 16 patients (40%), calcium channel blockers (n=7, 17.5%), PDE-5 Inhibitors (n=6, 15%), antihypertensives (n=5, 12.5%) and antidysrhythmic was given to least number of patients (n=2, 5%) as enlisted in Table 4.

Class of drug	No. Of patients received	Percentage (%)
Bronchodilators	37	92.50%
Corticosteroids	37	92.50%
Antibiotics	28	70%
Cardiovascular drugs	23	57.50%
Anti Inflammatory	17	42.50%
Diuretics	17	42.50%
Antitussives	16	40%
Calcium channel blockers	7	17.50%
PDE-5 Inhibitors	6	15%
Antihypertensives	5	12.50%
Antidysrhythmic	2	5%

Distribution Of COPD Patients Receiving Bronchodilators And Corticosteroids:

The most commonly prescribed class of drug was a combination of short-acting beta 2 agonists and anticholinergics (SABA+SAMA), with 37 patients (92.5%) receiving levosalbutamol + Ipratropium bromide, followed by long-acting anticholinergics (LAMA) and short-acting anticholinergics (SAMA) sharing an equal distribution, with tiotropium bromide and ipratropium bromide. The combination of long-acting beta 2 agonist and corticosteroid (LABA+ICS) is also equally distributed with methyl xanthines comprising formoterol fumarate+budesonide (5%), and deriphyllin (5%) and Budesonide (92.5%) were found to be the most commonly prescribed drug among corticosteroids followed by methylprednisolone and hydrocortisone sharing an equal distribution of 32.5% as enlisted in Table 5.

Table 5: Distribution of COPD patients receiving bronchodilators and corticosteroids:

Group Of Drug	Drug Class	Drugs	No Of Patients	Percentages
Bronchodilators	SABA	Salbutamol	1	2.50%
	(SABA+SAMA)	Levosalbutamol + Ipratropium bromide	37	92.50%
	(LAMA)	Tiotropium bromide	2	5%
	(LABA+ICS)	Salmeterol + Fluticasone propionate	1	2.50%
		Formoterol fumarate + Budesonide	2	5%
	(SAMA)	Ipratropium bromide	2	5%
	Methyl Xanthines	Theophylline	1	2.50%
	Deriphyllin	2	5%	
Corticosteroids	-	Budesonide	37	92.50%
		Methyl Prednisolone	13	32.50%
		Hydrocortisone	13	32.50%

Distribution Of COPD Patients Receiving Antibiotics :

The most frequently prescribed medicine class was cephalosporin antibiotics, of which ceftriaxone was prescribed to 28 patients (70%) and cefixime to 5 patients (5%). Macrolide antibiotics were the second most frequently given class of drugs, with 55% of patients receiving azithromycin. This was followed by penicillin antibiotics, beta-lactam antibiotics,

and levofloxacin, which were provided to 30%, 7.5%, and 2.5% of patients, respectively as enlisted in Table 6.

Table 6: Distribution of COPD patients receiving antibiotics

Class Of Drugs	Drugs	No Of Patients	Percentages
Cephalosporin antibiotics	Ceftriaxone	28	70%
Macrolide antibiotics	Cefixime	2	5%
	Azithromycin	22	55%
Penicillin antibiotics	Piperacillin and Tazobactam	12	30%
Beta-Lactam antibiotics	Meropenem	3	7.50%
Fluoroquinolones	Levofloxacin	1	2.50%

Distribution of Combination Drugs Used in COPD Patients:

Out of 40 prescriptions, levosalbutamol+Ipratropium bromide was found to be the most commonly prescribed combination of drugs followed by monteleukast+levocetizine given to 42.5% of patients, piperacillin + tazobactam to 30% of patients while acebrophylline + monteleukast, ambroxol + acetylcysteine, and salmeterol + fluticasone propionate shares a common distribution of 2.5% as enlisted in Table 7.

Table 7: Distribution of combination drugs used in COPD patients

Combination Of Drugs Used In Patients	No Of Patients (n=40)	Percentages
Piperacillin and Tazobactam	12	30%
Levosalbutamol + Ipratropium bromide	37	92.50%
Salmeterol + Fluticasone propionate	1	2.50%
Monteleukast sodium + levocetizine	17	42.50%
Acebrophylline + Monteleukast	1	2.50%
Ambroxol + Acetylcysteine	1	2.50%

Distribution of Patients Based on Route of Administration:

Inhalation was determined to be the most generally favored route of administration (n=39, 97.5%) followed by injection (n=31, 77.5%) and oral (n=23, 57.5%) as shown in Figure 7.

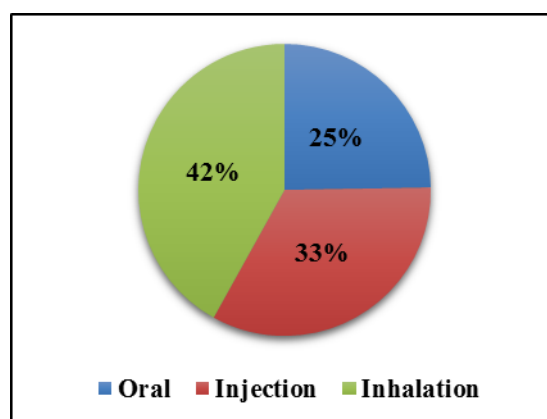


Figure 7: Distribution of patients based on the route of administration

DISCUSSION

The study included 40 patients, 19 (47.5% of the subjects) were male and 21 (52.5% of the subjects) were female. Our research revealed that female patients suffer from COPD at a higher rate than male patients, which may be attributable to occupational exposure and epidemiological factors. The average length of stay (LOS) for COPD patients in the hospital was 10.22 (± 4.6) days, with 4 days being the shortest stay and 22 days being the longest. The mean length of hospital stay was 4.5 days, which is similar to the study conducted by *Hoskins et al. (2000)*^[15].

The 40 COPD participants were categorized by smoking status, revealing that 42.5% of males and 7.5% of females were smokers. Contrary to *Avinash Teli et al.*'s study (87% smokers), our findings indicated a majority of non-smokers (57.5%).^[16]

On obtaining the ECG report of all COPD patients from their case sheets, it was discovered that right ventricular hypertrophy (RVH) was present in 21 (52.5%) of the patients. Our findings correlate with the findings of *D Radha Krishnan et al.*, where COPD subjects diagnosed with Cor pulmonale had the presence of RVH in 30/100 cases (30%).^[17]

The combination of levosalbutamol and ipratropium bromide (42.5%) was the most recommended for individuals with RVH, followed by budesonide (42.5%).

Our study found a higher prevalence of Cor pulmonale in COPD patients with acute exacerbations (37.5%) compared to those with COPD alone (35%). These results align with *Hang Fang et al.*, who reported a more frequent detection of Cor pulmonale in subjects with

exacerbation (27.2%) compared to those without exacerbation (18.8%) [18]. Additionally, Pulmonary hypertension was more prevalent in COPD subjects (35%) than in AECOPD subjects (22.5%), supporting *Buklioska-llievaska et al.*'s findings, indicating a significantly higher frequency of PH among COPD patients (33.3% vs. 0%) than those without COPD. [19]

In our study, COPD was most commonly associated with hypertension (40%), followed by type 2 diabetes (30%) and type I respiratory failure (30%). *Aiswarya et al.*, reported similar findings, with hypertension being the most prevalent comorbidity (38.33%), followed by diabetes mellitus (30%) [20]. Conversely, *Avinash Teli et al.*, found that Cor pulmonale (15%) was the most prevalent comorbid condition, followed by hypertension (10%) and diabetes mellitus (3%). [16]

Dyspnea (98%) was the predominant symptom in our study, followed by cough (78%), pedal edema (42.5%), and other less prevalent symptoms. Our results align with *D. Radha Krishnan et al.*, who reported dyspnea (100%) as the most prevalent symptom, followed by cough (96%) [21].

Bronchodilators (n=37, 92.5%) were the most commonly prescribed class of drugs followed by corticosteroids (n=37, 92.5%). Antibiotics (n=28, 70%) were the second most commonly prescribed class of drugs.

In our study, commonly prescribed drug combinations included levo-salbutamol and ipratropium bromide (92.5%), monteleukast and levocetizine (42.5%), piperacillin and tazobactam (30%), and salmeterol and fluticasone propionate (2.5%). These findings are consistent with *Amit Kumar et al.*, who reported a high prevalence of salbutamol and ipratropium bromide combination (20.9%) and other common pairings [22].

Inhalation (97.5%) was the preferred route, followed by injection (77.5%) and oral administration (57.5%), consistent with findings by *DB Jyothi et al.*, [23].

After analyzing the prescriptions of 40 COPD subjects it was found that a total of 49 drugs were prescribed to the patient population among which 31 (63.2%) drugs were prescribed from the National List of Essential Medicines (NLEM) 2022.

CONCLUSION

In this study on Chronic Obstructive Pulmonary Disease (COPD), our findings emphasize

notable gender disparities, with females exhibiting a higher COPD incidence possibly linked to occupational exposures. Non-smokers constituted the majority of subjects, suggesting cardiovascular comorbidities beyond age 50, potentially independent of smoking. Evaluation of pulmonary function impairment and pulmonary hypertension revealed a spectrum of severity, emphasizing the need for long-term prognosis assessment.

Right ventricular hypertrophy (RVH) was prevalent among patients diagnosed with Cor pulmonale, highlighting its association with pulmonary hypertension. Dyspnea emerged as the predominant symptom, indicating the significant impact of COPD on patients. Bronchodilators and corticosteroids, particularly levosalbutamol plus ipratropium bromide and budesonide, were the most frequently prescribed drugs, administered primarily through inhalation.

Antibiotic prescriptions, notably cephalosporins and macrolides, lacked culture sensitivity tests, suggesting potential irrational antibiotic use. Amlodipine, among calcium channel blockers, was commonly recommended, aligning with previous research indicating its positive effects on pulmonary hemodynamics in COPD.

Combinations like levosalbutamol and ipratropium bromide, montelukast and levocetirizine, and piperacillin and tazobactam were frequently recommended, showcasing diverse treatment approaches.

Prescriptions primarily focused on symptomatic relief, highlighting the symptomatic nature of COPD management in our study. Left ventricular function remained unaffected in COPD patients, as evidenced by normal LVEF values. Echocardiographic techniques efficiently detected pulmonary hypertension and cor pulmonale, underscoring their utility in early identification and subsequent treatment for improved life expectancy in affected individuals.

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