



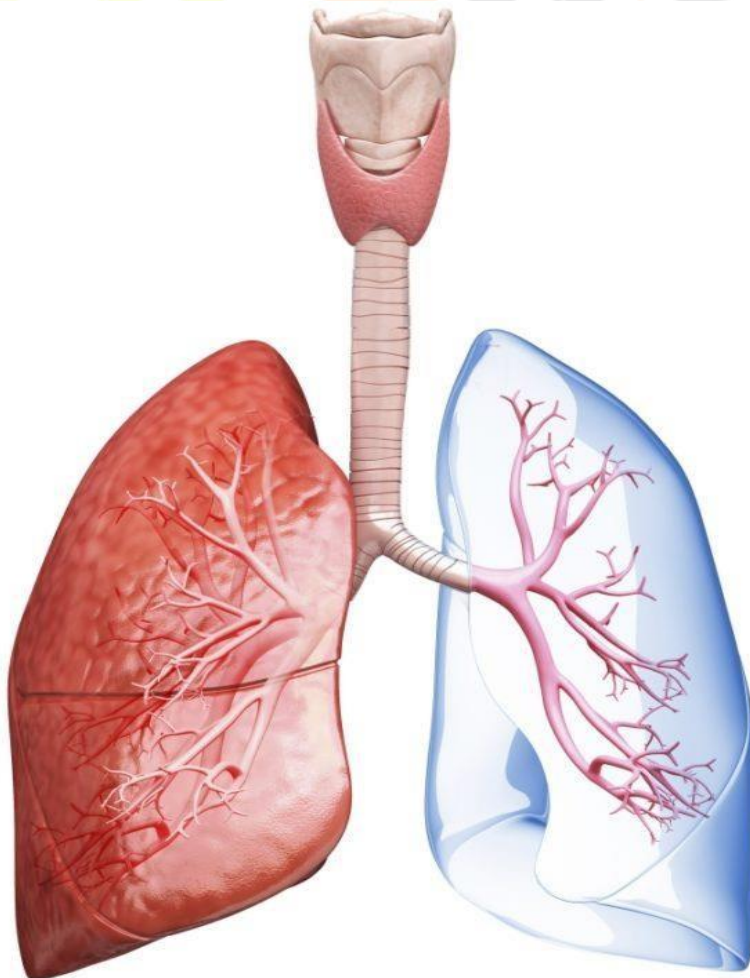
A study on drug utilization pattern and possible drug - drug interactions among patients with chronic obstructive pulmonary disease in a tertiary care hospital

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INTRODUCTION



1. INTRODUCTION

1.1 DEFINITION:

According to WHO, Chronic Obstructive Pulmonary Disease (COPD) is a common, preventable, and treatable chronic lung disease which affects men and women. Abnormalities in the lungs lead to limitation of airflow in and out of the lungs. A number of processes cause the airway to become narrow. There may be destruction of parts of the lung, mucus blocking the airways, and inflammation and swelling of the airway lining [1]

Chronic bronchitis and emphysema are the two phenotypes of COPD.

Chronic bronchitis is an inflammation of the bronchial tubes' lining, which transports air to and from the lungs' air sacs (alveoli). Coughing and sputum production are present on a daily basis.

Emphysema is a disease in which the air sacs (alveoli) at the extremities of the lungs' tiniest air channels (bronchioles) are destroyed by harmful exposure.

Exacerbation in COPD is defined as an acute event characterized by a worsening of the patient's respiratory symptoms that is beyond normal day-to-day variations and leads to a change in medication.[2]

1.2 EPIDEMIOLOGY:

Its prevalence has risen globally, with the Global Burden of Disease Study estimating that it now affects one billion people. According to national surveys, the true prevalence of people with chronic airflow obstruction as measured by spirometry may exceed 28 million, although more than half are not diagnosed. By 2030, COPD will be the fourth biggest cause of death.[9]

COPD is the leading cause of death in the world, with millions of people dying each year. Low and middle-income countries account for 90% of all deaths. COPD is a preventable disease that accounts for 8.7% of all deaths in India, with a morbidity of 55.3 million individuals. Between 1990 and 2016, the overall prevalence of COPD has increased by 29%.[10]

Male mortality is six times higher than female mortality. Nevertheless, over the last 25 years, female mortality has increased, and female fatalities have outnumbered male deaths every year since 2000. Compared to blacks, whites have a greater death rate.

1.3 ETIOLOGY

- Tobacco and cigarette smoking are two of the most common causes of COPD worldwide. Because it contains a variety of carcinogenic chemicals and toxins that cause inflammation on the mucosal surface of the lungs and the bronchial track.
- The only hereditary cause of COPD in non-smokers is alpha-1 antitrypsin deficiency, which causes early emphysema and disease development.
- The lungs can also be harmed by passive smoke.
- Long-term exposure to chemical vapors, pollution, or dust.[11]

Table 1: RISK FACTORS FOR DEVELOPING COPD

Exposure	Host factors
Environment tobacco smoke	Genetic predisposition (AAT Deficiency)
Occupational dust and chemicals	Airway hyperresponsiveness
Air pollution	Impaired lung growth

1.4 PATHOPHYSIOLOGY:

COPD pathophysiology is characterized by chronic inflammatory alterations that contribute to damaging modifications and chronic airflow limitation. Neutrophils, macrophages, and lymphocytes are the main players in COPD inflammation. Inflammatory mediators such as cytokines, chemokines, and chemo attractants are released by these inflammatory cells, perpetuating the inflammation and leading to an uncontrolled cascade. Neutrophils recruit neutrophils to the location by producing chemo attractants such as interleukin-8 (IL-8) and leukotriene B4 (LTB4). Proteolytic enzymes generated by

neutrophils, such as elastase, proteinase-3, cathepsin G, cathepsin B, and matrix metalloproteinases (MMP), degrade elastic lung tissue. Examples of oxidative stress include antiprotease and surfactant oxidative inactivation, mucus hypersecretion, membrane lipid peroxidation, alveolar epithelial damage, extracellular matrix remodeling, and apoptosis. [12]

Cigarette smoke contains a variety of dangerous chemicals, including oxygen-derived metabolites, often known as reactive oxygen species (ROS). An excessive amount of ROS causes detrimental changes in lipids, proteins, and DNA. Oxidative stress markers such as lipid peroxidase, hydrogen peroxidase, nitric oxide, nitro tyrosine, and nitrogen oxides are all raised in COPD patients' respiratory tracts, lungs, and blood. [13]

Fig 1: PATHOGENESIS OF COPD

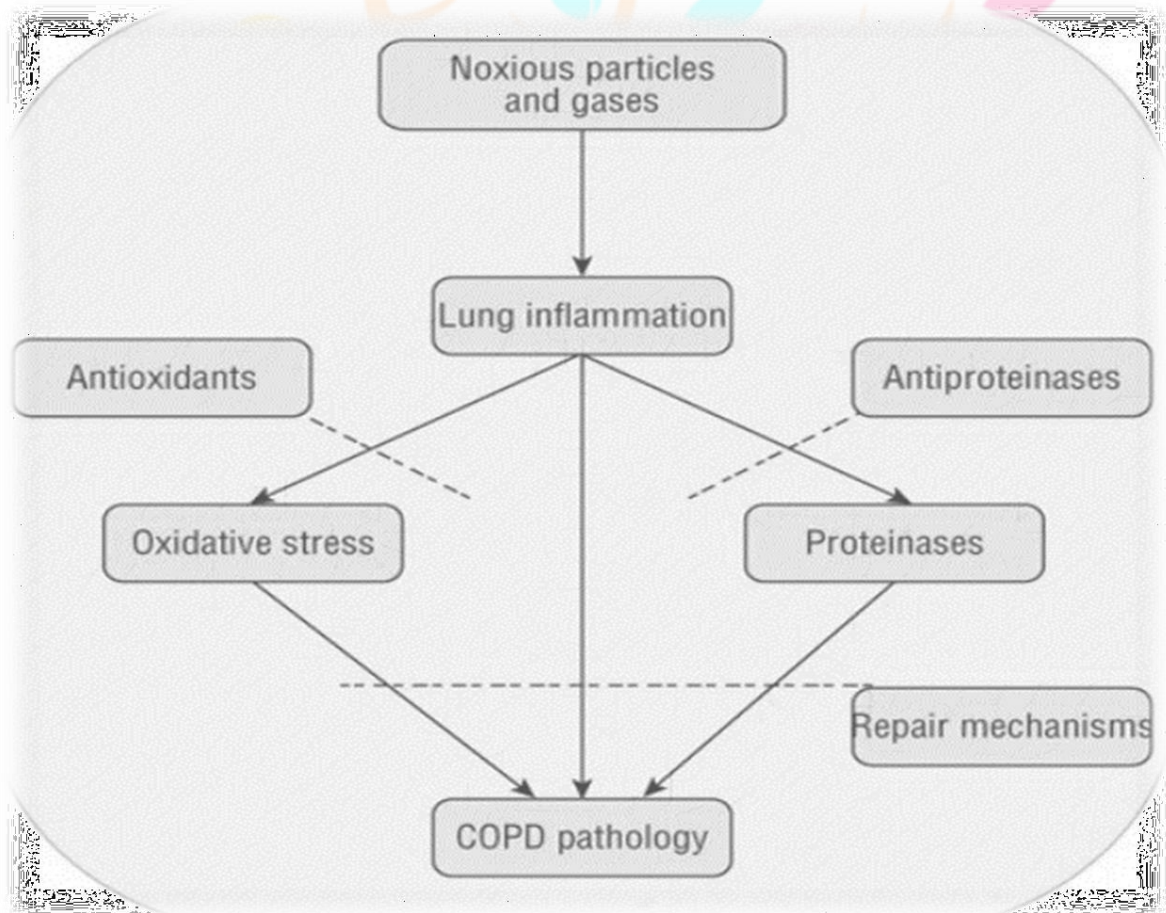
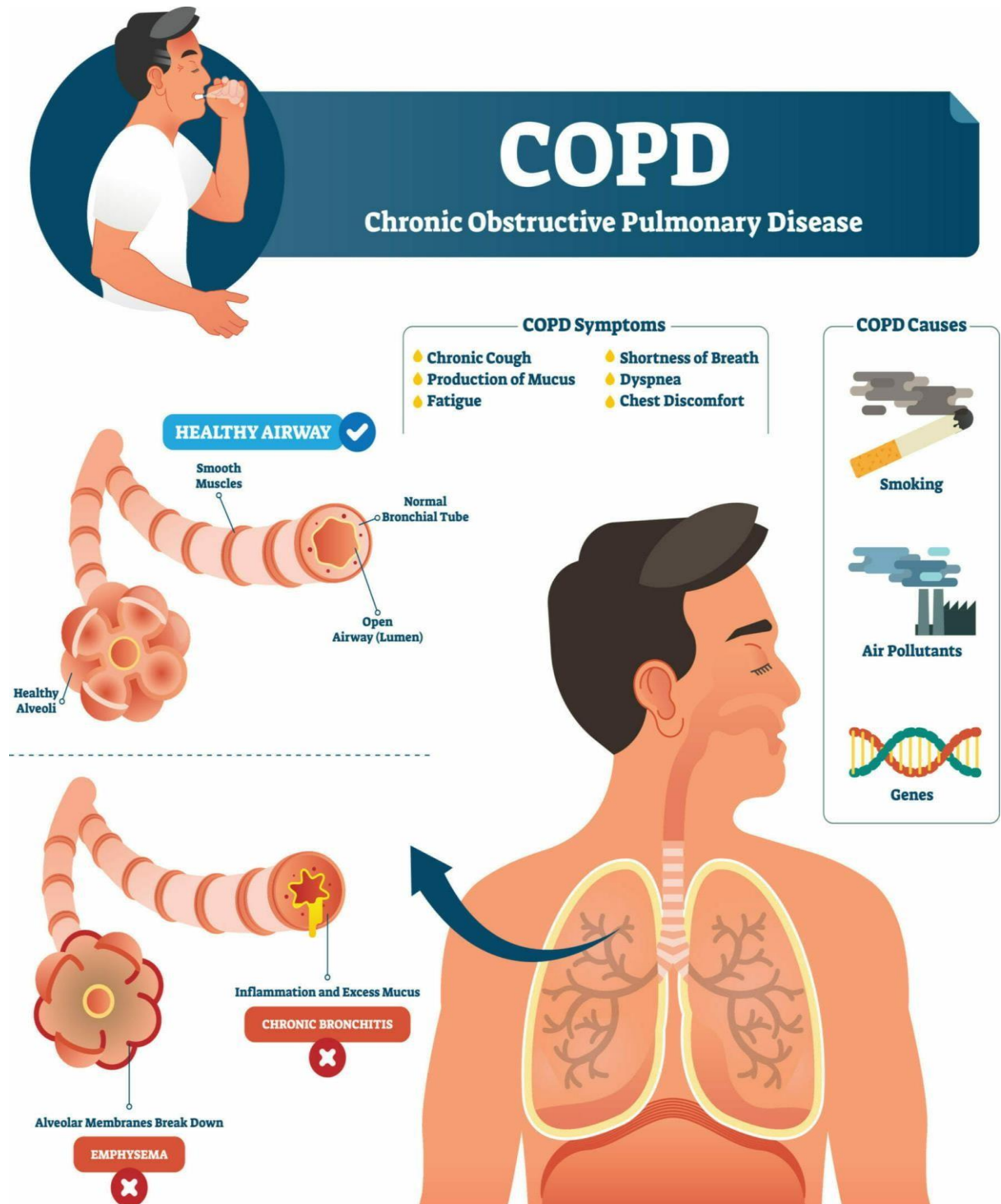


Fig 2: CLINICAL PRESENTATION



1.5 CLINICAL PRESENTATION

1.5.1 Symptoms

- Cough
- Dyspnea
- Increased sputum production

1.5.2 Physical Examination

- Cyanosis of mucosal membranes
- Barrel chest
- Increased resting respiratory rate
- Shallow breathing
- Pursed lips during expiration
- Use of accessory respiratory muscles

1.6 DIAGNOSTIC TEST:

- Spirometry
- Radiography of chest
- Arterial blood gas levels

Table 2: Classification of airflow limitation severity in COPD (based on post-bronchodilator fev1)

In patients with FEV ₁ /FVC < 0.70		
GOLD 1	Mild	FEV ₁ ≥ 80% predicted
GOLD 2	Moderate	50% ≤ FEV ₁ < 80% predicted
GOLD 3	Severe	30% ≤ FEV ₁ < 50% predicted
GOLD 4	Very Severe	FEV ₁ < 30% predicted

1.7 TREATMENT:

1.7.1 MANAGEMENT OF STABLE COPD

Non Pharmacologic Therapy: Smoking cessation, pulmonary rehabilitation, Immunization, Long term oxygen therapy, adjunctive therapies- psychoeducational care and nutritional support, Policies to limit airborne exposures in the workplace and outdoors[14].

Pharmacologic Therapy: Pharmacologic therapy is used to prevent and control symptoms, reduce the frequency and severity of exacerbations, improve health status, and improve exercise tolerance [12].

Table 3: Recommended Pharmacologic Therapy for Stable COPD

Patient Category	First Choice	Second Choice	Alternate Therapy
A (less symptoms, less risk)	SABA prn or SAMA prn	LAMA or LABA or SAMA and SABA	Theophylline
B (more symptoms, less risk)	LAMA or LABA	LAMA and LABA	SABA and/or SAMA theophylline
C(less symptoms, more risk)	ICS and LABA or LAMA	LAMA and LABA or LAMA and PDE4I or LABA and PDE4I	SABA and/or SAMA theophylline
D(more symptoms, more risk)	ICS and LABA and/or LAMA	ICS and LABA and LAMA or ICS and LABA and PDE4I or LAMA and LABA or LAMA and PDE4I	SABA and/or SAMA theophylline

ICS, inhaled corticosteroids; LABA, long-acting beta agonist; LAMA, long-acting muscarinic antagonists; PDE4I, phosphodiesterase type 4 inhibitor (roflumilast); SABA, short acting beta agonist; SAMA, short-acting muscarinic antagonists [14].

a) Bronchodilators

Bronchodilator medications are central to the symptomatic management of COPD. Bronchodilator drugs commonly used in treating COPD include β_2 -agonists, anticholinergics, and methylxanthines. All categories of bronchodilators have been shown

to increase exercise capacity in COPD, without necessarily producing significant changes in Forced Expiratory Volume (FEV1) [12].

1) Short-Acting Sympathomimetics ($\beta 2$ agonists): - $\beta 2$ -agonists cause bronchodilation by stimulating the enzyme adenyl cyclase to increase the formation of cyclic adenosine monophosphate (cAMP). cAMP is responsible for mediating relaxation of bronchial smooth muscle, leading to bronchodilation. In addition, $\beta 2$ -agonists may improve mucociliary clearance. The choices for short-acting, selective $\beta 2$ -agonists are albuterol and levalbuterol [15]. Short-acting inhaled $\beta 2$ -agonists cause only a small improvement in FEV1 acutely but may improve respiratory symptoms and exercise tolerance despite the small improvement in spirometric measurements. Inhaled $\beta 2$ -agonists are generally well tolerated [16].

2) Short Acting Anticholinergics: - Anticholinergics produce bronchodilation by competitively inhibiting cholinergic receptors in bronchial smooth muscle. Ipratropium is the primary short-acting anticholinergic agent used for COPD [17]. Ipratropium is also available as a Metered dose inhaler and Soft mist inhaler in combination with albuterol and as a solution for nebulization at 200 mcg/mL [14]. Both a short-acting $\beta 2$ -agonist and ipratropium represent reasonable choices for initial therapy. When a patient does not achieve adequate control of symptoms with one agent, the combination of a short acting $\beta 2$ -agonist and ipratropium is a reasonable alternative [18].

3) Long-Acting Inhaled $\beta 2$ -Agonists (LABAs): - They provide prolonged activation of beta 2-adrenoreceptors, leading to long-lasting bronchodilation. The clinical benefits of LABAs compared with short-acting therapies include similar or superior improvements in lung function and symptoms, as well as reduced exacerbation rates and need for hospitalization. The use of the long-acting agents should be considered for patients with frequent and persistent symptoms and those at higher risk for exacerbation. e.g. salmeterol, formoterol, and arformoterol [19]

4) Long - Acting Anticholinergics: - They block the effects of acetylcholine by binding to muscarinic receptors in airway smooth muscle and mucus gland, inhibiting cholinergic effects of bronchoconstriction and mucus secretion [14]. Long-acting anticholinergic agents, such as tiotropium, are more selective than ipratropium at blocking important

muscarinic receptors. Aclidinium has a faster onset of action (30 minutes) compared to tiotropium (80 minutes). Aclidinium and umeclidinium are available as dry-powder inhalers. Compared to placebo and ipratropium, treatment with tiotropium results in significantly greater improvements in lung function, quality of life and reduces the frequency of exacerbation and need for hospitalization [20].

5) Combination Anticholinergics and β -Agonists: - Combinations of both short- and long-acting β 2-agonists with ipratropium provide added symptomatic relief and improvements in pulmonary function [18]. A combination of albuterol and ipratropium (Combivent Respimat) is available as a soft-mist inhaler for chronic maintenance therapy of COPD [22]. Combination therapy of long acting β 2 agonist and tiotropium resulted in significant improvement in FEV1 and quality-of-life measures compared with tiotropium alone [21].

6) Methylxanthines: - The methylxanthines may produce bronchodilation through numerous mechanisms, including (a) inhibition of phosphodiesterase, thereby increasing cyclic adenosine monophosphate(cAMP) levels, (b) inhibition of calcium ion influx into smooth muscle, (c) prostaglandin antagonism, (d) stimulation of endogenous catecholamines, (e) adenosine receptor antagonism, and (f) inhibition of release of mediators from mast cells and leukocytes [14]. It includes theophylline and aminophylline. Theophylline therapy generally is considered for patients who are intolerant or unable to use an inhaled bronchodilator [23]. Chronic theophylline use for patients with COPD may offer improvements in lung function, including vital capacity, FEV1, minute ventilation, and gas exchange. Subjectively, theophylline has been shown to reduce dyspnea, increase exercise tolerance, and improve respiratory drive in COPD patients [24].

b) Corticosteroids

The anti-inflammatory mechanisms whereby corticosteroids exert their beneficial effect in COPD include (a) reduction in capillary permeability to decrease mucus, (b) inhibition of release of proteolytic enzymes from leukocytes, and (c) inhibition of prostaglandins [14]. The appropriate situations to consider corticosteroids in COPD include (a) short-term systemic use for acute exacerbations and (b) inhalation therapy for chronic stable COPD in selected patients. The recommended role of Inhaled corticosteroid therapy is for patients

with severe or very severe COPD and at high risk of exacerbation who are not controlled with inhaled bronchodilators.eg, fluticasone, budesonide [25].

c) Combination Therapy: Bronchodilators and Inhaled Corticosteroids

The availability of combination inhalers (eg, salmeterol plus fluticasone, budesonide plus formoterol, and mometasone plus formoterol) makes administration of both inhaled corticosteroids and long-acting bronchodilators more convenient for patients and decreases the total number of inhalations needed daily [26].

d) Phosphodiesterase Inhibitors

Inhibition of phosphodiesterase 4 results in relaxation of airway smooth muscle cells and decreased activity of inflammatory cells and mediators such as TNF- α and IL-8 [14]. When either used as monotherapy or added to a maintenance regimen with other inhaled bronchodilators, roflumilast was associated with a modest increase in FEV1 and reduction in rate of exacerbation by approximately 15% [27].

e) Alpha 1-Antitrypsin Replacement Therapy

For patients with inherited Alpha 1-antitrypsin (AAT) deficiency-associated emphysema, treatment focuses on reduction of risk factors such as smoking, symptomatic treatment with bronchodilators, and augmentation therapy with replacement AAT. The enzyme (AAT) is responsible for inhibiting several protease enzymes, including neutrophil elastase. In the presence of unopposed activity, elastase attacks elastin, a major component of alveolar walls. The recommended dosing regimen for replacement AAT is 60 mg/kg administered IV once a week at a rate of 0.08 mL/kg/min, adjusted to patient tolerance [14].

1.7.2 MANAGEMENT OF COPD EXACERBATION

The goals of therapy for patients experiencing exacerbations of COPD are (a) prevention of hospitalization or reduction in hospital stay, (b) prevention of acute respiratory failure and death, and (c) resolution of exacerbation symptoms and a return to baseline clinical status and quality of life [28].

Non-Pharmacologic Therapy:

Controlled oxygen therapy, Noninvasive Mechanical Ventilation [14].

Pharmacologic Therapy:

a) **Antibiotic:** It is thought that most acute exacerbations of COPD are caused by viral or bacterial infections. Recommended if two or more of the following are present: Increased dyspnea, Increased sputum production, Increased sputum purulence.

Example-Azithromycin, clarithromycin, doxycycline, etc. [29]

b) **Corticosteroids:** Oral or IV therapy may be used. If IV is used, it should be changed to oral after improvement in pulmonary status. If continued longer than 14 days, then the dose should be tapered to avoid Hypothalamic-pituitary-adrenal (HPA) Axis suppression. It appears that a regimen of prednisone 40 mg orally daily (or equivalent) for 10 to 14 days can be effective for most patients [30].

c) **Bronchodilators:** Metered dose inhalers and Dry powder inhalers equal in efficacy to nebulization. Short acting β 2-Agonists are preferred owing to rapid onset of action. Anticholinergic agents may be added if symptoms persist despite increased doses of Long-acting β -agonists or long-acting antimuscarinics should not be used for quick relief of symptoms or on an as-needed basis [31].

1.7.3 MANAGEMENT OF COPD WITH COMORBIDITIES

According to the Global initiative for chronic obstructive lung disease (GOLD), below is a brief guide to the management of some common comorbidities occurring in patients with COPD with stable disease [4].

a) **Heart Failure:** Treatment with b1 blocker improves survival in heart failure and is recommended in patients with heart failure who also have COPD. Selective b1 blocker should be used, and only used, to treat patients with COPD for approved cardiovascular condition; not solely for purpose of preventing exacerbation of COPD [32].

- b) **Ischemic Heart Disease:** The treatment of ischemic heart disease should be according to guidelines irrespective of the presence of COPD and vice versa [33].
- c) **Arrhythmia:** There is an overall acceptable safety profile for long acting b2 agonist, anticholinergic drugs. Nevertheless, caution is advised when using short acting b2 agonists and theophylline, which may precipitate atrial fibrillation and make control of the ventricular response rate difficult [4].
- d) **Peripheral Vascular Disease (PAD):** Clinician should consider PAD in patients with COPD to those at risk for vascular events and to fully understand their functional impairment [34].
- e) **Hypertension:** The role of treatment with selective b blocker is less prominent in recent hypertension guidelines and there is no evidence that in patients with COPD and increased cardiovascular risk beta blockers either reduce the benefits of treatment with Long acting b2 agonist or increase cardiovascular risk. COPD should be treated as usual as there is no direct evidence that COPD should be treated differently in the presence of hypertension [4].
- f) **Lung Cancer:** The preventive measure for lung cancer is smoking prevention and in smokers, smoking cessation. Use of low dose chest computed tomography screening have shown improved survival in older subjects, current smokers or those who quit within the previous 15 years [35].
- g) **Osteoporosis:** It should be treated according to usual guidelines. Systemic corticosteroids significantly increase the risk of osteoporosis and repeated courses for COPD exacerbation should be avoided if possible [36].
- h) **Anxiety and Depression:** COPD should be treated as usual. The potential impact of pulmonary rehabilitation should be stressed [37].
- i) **Metabolic Syndrome and Diabetes:** COPD and diabetes should be treated according to the usual guidelines [38].

- j) **Gastroesophageal Reflux Disease (GERD):** Proton pump inhibitors are often used for treatment of GERD. These agents decrease the risk of exacerbation, but their value in preventing these events remains controversial most effective treatment for this condition in COPD has yet to be established [39].
- k) **Bronchiectasis:** Bronchiectasis should be treated according to the usual guidelines. Regarding COPD treatment, some patients may need more aggressive and prolonged antibiotic therapy. Inhaled corticosteroids may not be indicated in patients with bacterial colonization or recurrent lower respiratory tract infections [40].
- l) **Obstructive Sleep Apnea (OSA):** The apneic events with combined OSA and COPD have more profound hypoxemia and more cardiac arrhythmias and are more likely to develop daytime pulmonary hypertension. The treatment of choice for overlap syndrome in stable patients is Continuous Positive Airway Pressure (CPAP) with supplemental oxygen for correction of upper airway obstructive episodes and hypoxemia during sleep [41].
- m) **Cognitive Impairment (CI):** The impact of CI on self-management skills in COPD patients remain unclear, although inhaler incompetency has been linked to CI [4].
- n) **COPD as part of Multimorbidity:** COPD is treated as usual. Treatment should be kept simple in the light of the unbearable polypharmacy that these patients are often exposed to [4].

1.8 DRUG UTILIZATION PATTERN

According to the World Health Organization, Drug utilization is defined as the marketing, distribution, prescription, and use of drugs in a society with a special emphasis on the resulting medical, social, and economic consequences.[44]

Drug utilization studies can help to reform and update clinical medicine and pharmacotherapy procedures by providing important insights into existing prescribing practices.[42]

Drug utilization studies are useful tools for determining the function of drugs in society. These studies provide a solid sociomedical and health-economic foundation for making healthcare decisions. COPD is underdiagnosed and frequently misdiagnosed, which may explain the disease's continuing rise in frequency, illness, and death.[43]

Drug utilization studies can reveal patterns, quality, factors, and effects of drug use. Drug usage research is an important tool for achieving cost-effective healthcare since it may be used to suggest changes to drug guidelines and rational drug use. Despite the fact that COPD is one of the leading causes of death in India, there are few drug utilization studies on the illness.[44]

Prescription errors include overuse or underuse of oxygen therapy; fear of administering oral steroids; and

overuse of antibiotics to treat COPD exacerbations, to name a few. Because theophylline has a small margin of safety, life-threatening consequences are common. A guideline-based strategy holds a lot of promise for reducing errors and improving evidence-based management. So the objective of this study is to assess the present prescribing pattern was compared to WHO prescribing indicators to evaluate if the hospital's prescription pattern followed WHO guidelines.[45]

1.9 DRUG - DRUG INTERACTIONS

The pharmacological or clinical response to the administration or co-exposure of a drug with another drug that affects the patient's response to the drug index is referred to as a drug-drug interaction.[4]

A drug-drug interaction can cause a drug's therapeutic impact to deteriorate, as well as an increase in adverse drug reactions (ADRs) and poor treatment results. The presence of several prescribers, advanced age, and polypharmacy have all been identified as risk factors for the occurrence of possible medication interactions.[5]

A pharmacokinetic interaction occurs when the drug's pharmacological impact is altered throughout the absorption, distribution, metabolism, or elimination process.[6] Pharmacodynamic interactions are the effects of synergism and antagonism among medications at the site of action.[6]

DDI is common in COPD patients who are hospitalized, but only a small percentage of them pose a clinically significant risk. The majority of type X interactions were between a non-selective beta-blocker and a beta 2-adrenoreceptor agonist, which was most likely indicated and could be used safely in COPD patients.[7]

In general, potassium-sparing diuretics, angiotensin-converting enzyme (ACE) inhibitors or angiotensin receptor blockers (ARB), and aspirin with non-selective beta-blockers in patients concomitantly treated with beta 2-adrenoreceptor agonists, antibiotics, and COPD drugs were the most common combinations of medications in which potential DDI occurred during hospitalization.[8]

Clarithromycin and itraconazole are some of the examples of cytochrome P4503A4 inhibitors that significantly enhance systemic exposure to inhaled budesonide, most likely by blocking budesonide metabolism mediated by cytochrome P4503A4 during both the first-pass and elimination phases. As seen by cortisol suppression, Budesonide's systemic effects were amplified as a result of this interaction. Long-term coadministration of budesonide with a strong CYP3A4 inhibitor may increase the risk of budesonide side effects.[46]

Monitor patients for signs and symptoms of corticosteroid excess if nasal budesonide is used in a patient taking a strong CYP3A4 inhibitor. [46]

Beta2-agonist prescribing literature states that hypokalemia caused by non-potassium- sparing diuretics (such as loop or thiazide diuretics) can be rapidly aggravated by beta- agonists, especially when the beta-agonist

recommended dose is exceeded.

In patients taking beta2-agonists and loop diuretics at the same time, keep an eye out for hypokalemia and its side effects (such as cardiac conduction issues). Patients with low baseline serum potassium levels or who take high doses of beta2-agonists are more prone to experiencing negative side effects.

NEED FOR THE STUDY



2. NEED FOR THE STUDY

COPD is the third leading cause of death worldwide, which caused 3.23 million deaths in 2019. It is also one of the leading causes of death among Indian.

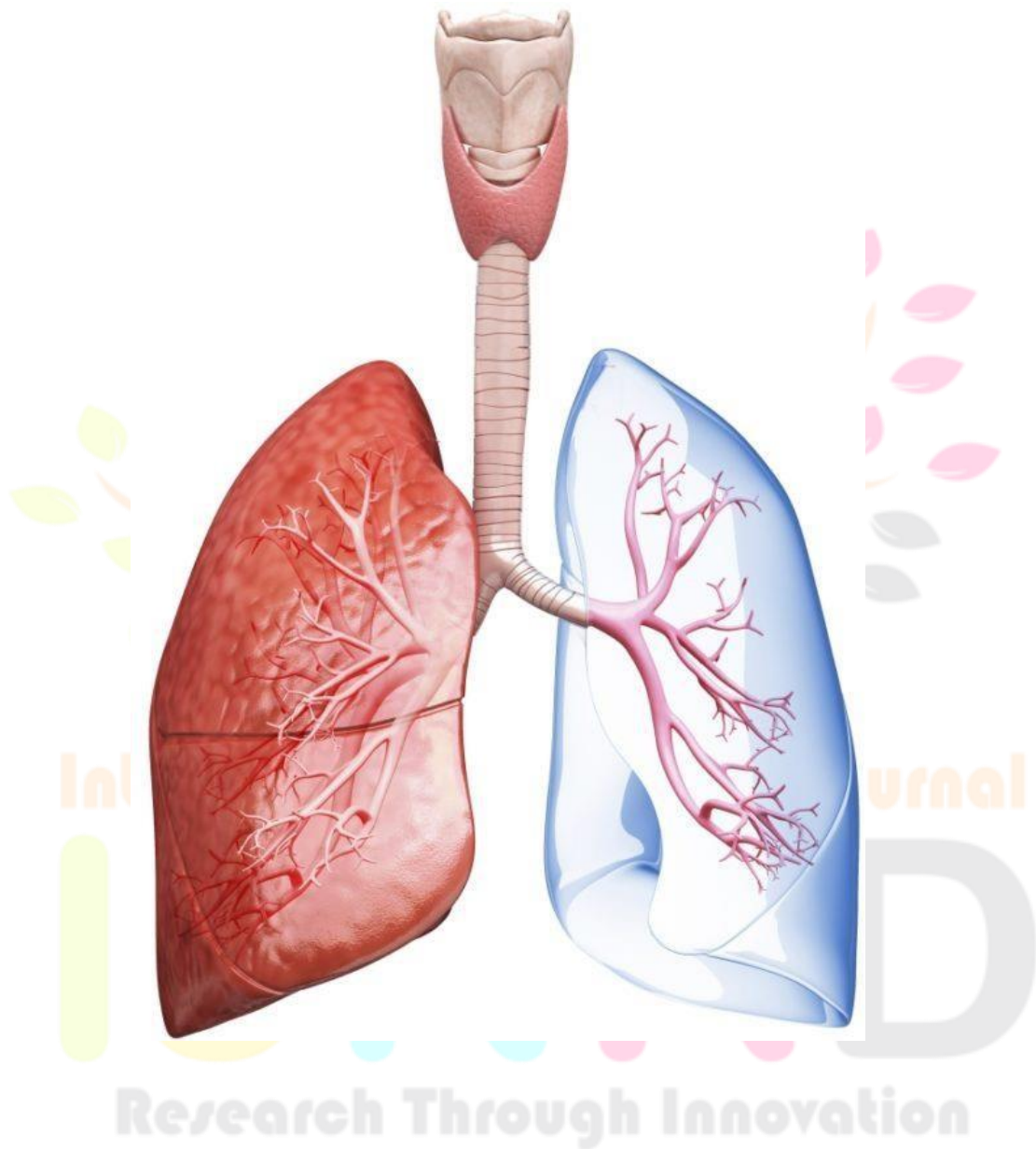
Drug utilization studies provide useful insights into the current prescribing pattern and it is important in understanding the prescription pattern of drug to find the quality of prescription in terms of rationality and drug interactions. There is a lack of drug utilization studies in this field, even though COPD is a major concern for the health care sector.

The WHO has developed various indicators to evaluate about the condition of the services offered to the population concerning medication, among which the core prescribing indicators are aimed at measuring the degree of polypharmacy, tendency to prescribe drugs by generic name, overall level of use of antibiotics and injections, and the degree to which drugs are prescribed from the essential drug list. However, the periodic assessment of the prescribing practices in a health-care facility is necessary to identify specific drug use problems, to sensitize practitioners on rational drug prescription.

Drug-drug interactions (DDIs) are major concern among patients receiving multidrug therapy. DDIs contributes to 3%-4% of adverse drug reaction and it is the fourth leading cause of mortality. The probability of DDIs increases with number of drugs prescribed to patients. The incidence ranges from 13% for two drugs prescribed, to 82% for seven or more drugs. Comorbidity leads to prescribing more drugs on regular basis if individual guidelines are implemented as appropriate. The complexity of treatment regimen increases the probability of potential DDIs and prolongs hospitalization. COPD often coexists with other disease (comorbidities) that may complicate COPD management and may have significant impact on prognosis. DDIs are common in patients with COPD.

There is a lack of studies on DDIs incidence in patients with COPD, therefore it is important to determine the frequency and severity of potential DDIs during hospitalization of COPD patients to enable healthcare professionals to implement strategies that ensure patient safety.

OBJECTIVES



3.

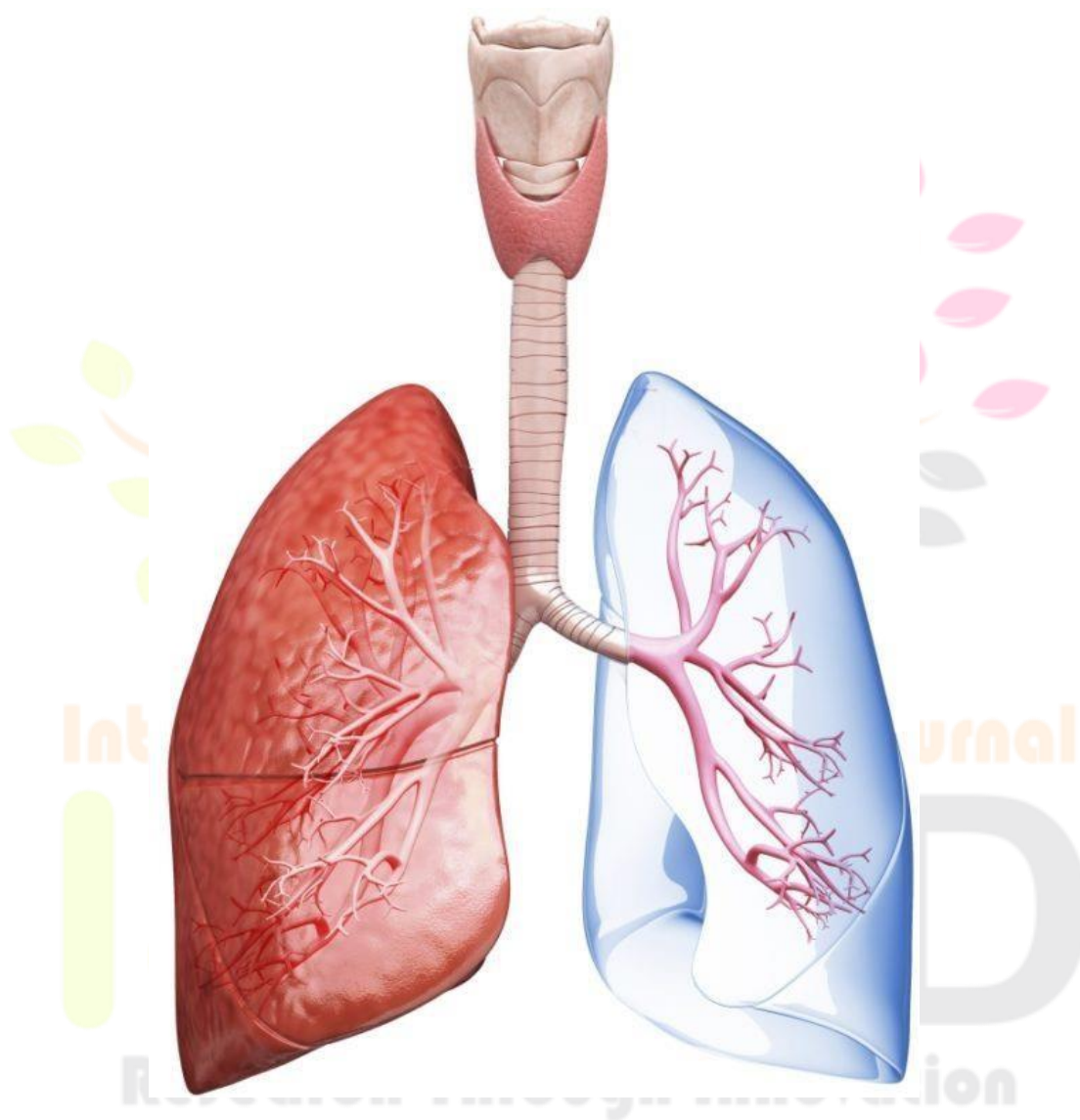
OBJECTIVES

✦

To analyze drug utilization pattern among COPD patients.

- ✦ To evaluate potential drug-drug interactions in COPD patients.
- ✦ To assess prescribing pattern using World Health Organization (WHO)prescribing indicators.

LITERATURE REVIEW



4. LITERATURE REVIEW

Soherwardi S et al., (2012) conducted a study on Surveillance of the Potential Drug-Drug Interactions in the Medicine Department of a Tertiary Care Hospital. Drug-Drug Interactions (DDIs) account for 6-30% of all adverse drug events, pose a considerable danger to the patient's health, and cost the health system. Polypharmacy has a crucial role in these interactions. The goal of this study was to evaluate the drug-drug interaction encounters at a medicine department with in- patients tertiary care facility.

Materials and Procedures: The medical records of 250 patients admitted to the medical ward were evaluated in terms of the patient's demographics, the prescription, and the interaction facts such as the substance in question, its severity, therapy, and outcome

The patients were given medications that varied from DDIs were found in 5 to 18 percent of the patients, with the majority being female, moderate in intensity and affecting people who have received cardiovascular medications. Age and gender had no bearing on the results. Drug-drug interactions are affected.

Conclusion: The majority of DDIs can be avoided. The most common DDIs between fluoroquinolones and oral antimicrobials are common. Iron and pantoprazole, aspirin and clopidogrel for diabetics.[47]

Kulkarni V et al., (2013) conducted a study on drug–drug interactions through prescription analysis in a South Indian teaching hospital. The goal of this study was to investigate drug– drug interactions (DDIs) among inpatients at a South Indian teaching hospital using prescription analysis. The study was a 6-month prospective observational prescription analysis that took place between October 2010 and March 2011. The physician in charge of the ward chose the prescriptions that contained two or more medicines and where a DDI was suspected. The medications in the prescription were then entered into software that checked for drug interactions. The DDIs were categorised based on the mechanism of interactions, intensity of interactions, and relationship to the number of prescriptions prescribed, as well as medical conditions. A total of 204 prescriptions were examined, with 186 of them containing 856 DDIs. The most common DDIs (42%) were pharmacokinetic drug interactions, followed by unknown mechanisms (34%), and pharmacodynamic mechanisms (3%). (24 percent). According to the study's findings, medications for cardiovascular and respiratory illness problems had the most drug interactions on average. The majority of the DDIs were moderate (70 percent), followed by minor (ten percent) (28 percent). According to the findings, the number of DDIs increases as the number of medications in a prescription grows. In most of the DDIs, dosage adjustment (12%) was to be followed, according to the interventions determined. This research contributes to a better knowledge of the factors linked to DDIs, which will aid in the safe and effective use of medications in the future.[48]

A Study of Drug Utilization Pattern for Acute Exacerbation of Chronic Obstructive Pulmonary Disease in Patients Attending a Government Hospital in Kerala, India was conducted by **Veetil SK et al., (2014)**. This study was undertaken in one of the government hospitals in Kerala, India, to determine the drug consumption pattern and prevalent adverse drug responses for the treatment of acute exacerbation of chronic obstructive pulmonary disease (COPD). This was a nonexperimental prospective observational study aiming at identifying

the drug consumption pattern for the treatment of acute COPD exacerbation for 7 days. With the help of a physician, all relevant material for the study was gathered via case records and talks with inpatients and bystanders during ward visits. Furthermore, daily follow-ups were undertaken to collect data on therapeutic changes, add-on therapy, and clinical improvement until the patient was discharged from the hospital or until a 7-day upper limit was reached, whichever came first. In this trial, all of the patients were given a combination of treatments. Salbutamol was the most commonly used inhalational agonist, accounting for 74% of the total. In 78 percent of the patients, parenteral steroids were utilised, and all of them were given hydrocortisone. Only 25% of the patients were prescribed steroid inhalers. In 77.5 percent of cases, anticholinergics were utilised. In 86.7 percent of cases antibiotics were used. Dry mouth (15%) and unpleasant taste (10%) were the most common side effects, and these side effects were highly linked with the usage of anticholinergics (P 0.05). Despite the use of medications based on availability and physician preference, the majority of patients followed the Global Initiative for Chronic Obstructive Lung Disease criteria recommendations, according to the report.[49]

Roblek T et al., (2014) conducted a study on potential drug-drug interactions in hospitalized patients with chronic heart failure and chronic obstructive pulmonary disease. Patients with chronic heart failure (HF) and/or chronic obstructive pulmonary disease (COPD) have a high rate of polypharmacy, but little is known regarding the prevalence and



importance of drug-drug interactions (DDIs). The purpose of this study is to assess DDIs in hospitalized patients. Over a 6-month period, we evaluated medical records for the diagnosis of chronic HF and/or COPD. Lexi-Interact software was used to assess potential DDIs. This study included 778 patients (mean age 75 years, 61% male). The mean number of drugs at admission and discharge was 6 (interquartile range (IQR) 4–9) and 7 (IQR 5–), respectively ($p = 0.10$). We recorded a potential DDI of 6.5 ± 5.7 per patient at admission and 7.2 ± 5.6 at discharge ($p = 0.2$). There was an increase in the potential DDI of types C and X from admission to discharge ($p < 0.05$ for both). Type X interactions were rare ($<1\%$), and combinations of β -blockers and β_2 -agonists were most common (64%). Potential type C and D DDI was significantly higher in patients with chronic heart failure compared to patients with COPD ($p < 0.001$). Patients with chronic heart failure and COPD were more likely to develop type C and type X DDI than patients with a single disease ($p < 0.005$). Aldosterone antagonists and ACE inhibitors/ARBs have glomerular filtration rates $< 30\text{ml}/(\text{min} \times 1.73\text{m}^2)$. Patients with chronic HF and/or COPD have a lot of DDIs, but only a few of them appear to be clinically significant. Instead of bad clinical practice, the increase in possible DDIs from admission to discharge could be due to better guideline implementation.[50]

Unni A et al., (2015) Drug utilization pattern in chronic obstructive pulmonary disease inpatients at a tertiary care hospital. Drug use studies might help you understand how doctors are currently providing medications. As a result, the goal of this study was to determine the medication consumption pattern in hospitalized COPD patients. Methods: All patient data pertinent to the investigation was gathered through a review of the patient's medical records and the hospital information system in this retrospective analysis. A total of 237 individuals who had experienced an acute exacerbation were assessed. Males made up 92.4 percent of the population, and the majority of the patients were between the ages of 61 and 70 years old (39.7 percent). Coughing, sputum production, and dyspnea were seen in 88.2%, 80.6 percent, and 37.6% of patients, respectively. The most prevalent co- morbidity (49.4%) was hypertension. The most prevalent bacteria identified from sputum samples were *Candida albicans* (16 percent) and *Pseudomonas aeruginosa* (4.6 percent). During their hospital stay (98.7%) and upon release, the majority of the patients were on multidrug medication (99.6 percent). Antibiotics and systemic corticosteroids were given to 96.2 percent and 83.1 percent of patients, respectively, during their hospital stay. Antibiotics, inhaled corticosteroids, methyl xanthines, long-acting beta-2 agonist, and tiotropium were administered to 94.1 percent, 93.7 percent, 92.4 percent, 86.1 percent, and

56.5 percent of patients, respectively, at discharge. Our hospital's prescribing pattern appears to be in accordance with current COPD treatment standards.[51]

Barrecheguren M et al., (2016) conducted a study on treatment patterns in COPD patients newly diagnosed in primary care. A population-based study. COPD treatment is personalized to the patient's clinical characteristics and severity. Prescription patterns among COPD patients newly diagnosed in primary care, on the other hand, may diverge from guidelines. We conducted an epidemiological analysis using data from the Information System for Development in Primary Care Research (SIDIA), a population database with information on 5.8 million people (80 percent of the population of Catalonia). From 2007 to 2012, patients who were newly diagnosed with COPD were identified and information regarding their initial treatment patterns was gathered. Phenotype and severity were also used to define the initial treatment. During the study period, 41,492 patients were first diagnosed with COPD. Patients were classified as non-exacerbated patients (28,552 patients, 69%), asthma with COPD overlap syndrome (ACOS) (2152 patients, 5.2%), and frequent exacerbations (10,888 patients, 27.6%). Of the patients with FEV1, 13.9% had GOLD stage 1, 55.2% had stage 2, 26% had stage 3, and 4.8% had stage 4.), long-acting b2 agonists (LABA) plus inhaled corticosteroids (ICS) (17.3%) and triple therapy (12.2%). During the study period, the proportion of patients receiving TABD increased from 15.9% to 19.5%, and the number of patients not receiving treatment decreased from 24.4% to 15.1%. Up to 45.2% of patients were initially treated with ICS, which were frequently prescribed in the ACOS (69.2%) and in the exacerbator phenotype patients (52.4%) while ICS use has decreased from 43.8% in 2007 to 35.8% in 2012 in non-exacerbator patients. Up to 13.6% and 14.8% of GOLD 4 patients received no treatment or only SABD after diagnosis. In newly diagnosed COPD patients, initial therapy patterns frequently do not follow guidelines. The overuse of ICS has decreased, primarily in non-exacerbator patients. Many COPD patients are still mistreated after diagnosis, despite the fact that this is decreasing. After diagnosis, some GOLD 4 patients are still receiving SABD or notreatment at all.[52]

Kyriakos Souliotis et al., (2016) conducted a study using Big Data to Assess Prescribing Patterns in Greece: The Case of Chronic Obstructive Pulmonary Disease. COPD is one of the main causes of death and disability, and treatment focuses on minimising risk factors, alleviating symptoms, and preventing exacerbations. The goal of the study was to use current health administrative data for outpatients to describe COPD prescribing practises in

Greece. This is a retrospective cross-sectional study based on prescriptions collected during the first and last trimesters of 2012 by the largest social insurance fund. Prescriptions for specific active drugs and a diagnosis of COPD were used as selection criteria. Active ingredient, strength, pharmaceutical form, and quantity of packages dispensed, diagnosis, time of dispensing, and insures' age, gender, percentage of co-payment, and social security unique number were among the data extracted. Descriptive statistics and logistic regression were used in the statistical analysis. During the study period, 174,357 individuals received COPD medications. Male and female patients were virtually evenly distributed, and age over 55 was substantially associated with COPD. The majority of patients were given a combination of a long-acting beta agonist and an inhaled corticosteroid (LABA +ICS), followed by a long-acting muscarinic agonist (LAMA). LABA+ICS was given to 63 percent of individuals aged 35 to 54. Males were prescribed LAMA more frequently, and it was closely linked to COPD. The study examines Greek COPD prescribing habits using big data. It emphasises the importance of proper COPD classification in primary care, as well as the importance of electronic prescribing in assuring proper prescribing. It also shows the impact of required co-payments on prescribing, as well as possible gender variations in treatment response or disease severity.[53]

Kothai DR et al., (2017) conducted a study on analysis of prescribing pattern of COPD patients in a tertiary care hospital Salem. COPD is a preventable and curable illness that is one of the primary causes of morbidity and death in both developed and developing nations. Inappropriate and illogical medication usage exacerbates the difficulties. In a tertiary care hospital in Salem, an attempt was undertaken to evaluate the present prescribing pattern using WHO prescribing indicators to see if it met WHO criteria. The medication usage pattern was analyzed using WHO prescribing indicators and drug-drug interactions in the prescriptions of 150 patients hospitalized to the General Medicine department of VMKVMCH, Salem, Tamil Nadu, spanning a six-month period from November 2015 to April 2016. The prescriptions were evaluated using descriptive statistics, and the percentages were calculated. A total of 1015 medications were prescribed, with an average of 7.692.24 pills per prescription. The majority of the medications were administered under a brand name (63.34 percent). According to EDL-WHO 2015, 22.36 percent of medications were prescribed. Deriphylline [123(20.5 percent)] was the most usually given COPD medication. 168 drug-drug interactions were discovered using Medscape's free Drug Interaction Checker. Prescription patterns did not follow WHO standards, thus doctors must be educated about drug usage, the necessity of prescription pharmaceuticals with generic

names, and the safety of prescribing drugs from both an EDL and a patient's perspective.[54]

Sawant PM et al., (2017) conducted a study of drug prescription pattern among COPD patients admitted to medicine in-patient department of tertiary care hospital. Drug usage studies can reveal information on the pattern, quality, factors, and effects of drug use. COPD is one of the primary causes of mortality in the Indian population, and medication consumption studies in this sector are few. A prospective, observational research was done among patients admitted to a Tertiary care hospital's inpatient department of medicine ward. The information was gathered from the admission records of COPD patients. Prescriptions were analyzed for demographic profile, frequent related illnesses, WHO core drug indicators, and commonly prescribed pharmaceuticals. A total of 284 records from inpatients were examined. Males made up 66.19 percent of the 284 cases, while females made up 33.80 percent. Each prescription had an average of seven medicines. 66.9% of the population was above the age of 65. Antibiotics (88.7%), followed by inhaled bronchodilators, were the most usually recommended medications (84.5%). The average number of prescriptions given was greater than WHO guidelines, antibiotics were regularly utilized, and pharmaceuticals prescribed with brand names were more prevalent than drugs prescribed with generic names, according to the study's findings.[55]

Prospective study on drug-drug interactions of narrow therapeutic Index drugs was conducted by **S. Priya Rajam Vivean et al., (2017)**. A drug interaction is defined as a change in a patient's predicted pharmacological reaction as a result of the patient being exposed to another drug or substance. Unintentional drug interactions can cause negative side effects in patients, whereas intended drug interactions might improve therapeutic response or reduce harmful drug effects. Pharmaceutical, pharmacokinetic, and pharmacodynamic interactions are separated into three types based on the underlying mechanism of interaction.[56]

Amin AN et al.,(2018) conducted a study on treatment patterns for patients hospitalized with chronic obstructive pulmonary disease. The features of patients treated with long- acting bronchodilators (LABDs) during hospitalization as well as medication treatment patterns for chronic obstructive pulmonary disease (COPD) in inpatient settings were studied. Inpatient administrative data from hospitals and medical facilities across the United States was used in this retrospective analysis. Patients with a primary discharge diagnosis

of COPD or a secondary diagnosis of COPD with a primary diagnosis of a respiratory illness and therapy with a bronchodilator were included in the study. Short-acting -agonists (SABAs), long-acting -agonists (LABAs), short-acting muscarinic antagonists (SAMAs), and long-acting muscarinic antagonists (LAMAs) were all used in inpatient settings. The characteristics of LABD patients were predicted using logistic regression. Only 5.5 percent of patients did not receive a SABA during their stay: 71.7 percent received a single-product SABA and 46.4 percent received a SABA–SAMA combination product, with some patients rotating between or utilizing SABA and SABA–SAMA combinations at the same time. The majority of patients (80.9%) were given systemic corticosteroids, and almost everyone (91.6%) was given antibiotics. LABDs were given to 52.2 percent of patients (39.3 percent LABAs). LABD patients were more likely to have a primary COPD diagnosis, previous hospitalizations, spirometry use, and less comorbidities. According to an analysis of COPD hospital admissions, the majority of patients received the primary recommended therapies for acute COPD exacerbations (SABAs, systemic corticosteroids, and antibiotics). Only nearly half of the patients received maintenance therapy before being discharged.[57]

A Study of Prescribing Pattern of Drugs in Chronic Obstructive Pulmonary Disease in Tertiary Care Teaching Hospital by **Kumar S et al., (2019)**. COPD is a preventable and treatable disease, has been a major public health issue in this century, and is one of the leading causes of morbidity and mortality in both developed and developing countries. In modern clinical practice, irrational drug usage is a big concern; about half of all medicines are prescribed and given incorrectly. The goal of this prospective study was to examine the drug prescribing patterns in individuals with chronic obstructive lung disease. Between September 2017 and February 2018, 163 patients of either sex were admitted to the general and pulmonary medicine departments at NMCH and RC in Raichur, Karnataka, for a six- month study. Male patients made up 82 percent of the 163 patients in the study, and the bulk of the patients were between the ages of 58 and 68. (45.73 percent). Smoking was shown to be more prevalent in the study population (39.63 percent). Bronchodilators were the most commonly given class of medicines in the therapy of COPD (31.94 percent), followed by antibiotics (25.58 percent). The majority of prescriptions included salbutamol and budesonide as a combination treatment. The most prevalent co-morbidity was hypertension (19.63 percent). Prescriptions for generic medications were discovered to be in short supply (1.42 percent drugs). Our hospital provided symptomatic treatment for COPD patients, according to the findings of the study. Monotherapy was chosen over combination therapy. Bronchodilators were the most commonly prescribed COPD

medication class. All of the patients were given antibiotics. All prescriptions contained polypharmacy. Spirometry was not used in the diagnosis of COPD.[58]

Avinash teli et al., (2020) conducted a study of drug utilization and prescribing patterns of drugs in chronic obstructive pulmonary disease patients (IPD and OPD) in tertiary care hospital. Chronic obstructive pulmonary disease (COPD) is a disease with many different clinical manifestations. It's a multifaceted illness with extrapulmonary manifestations. The goal of the study was to see how different medical practitioners used drugs and prescribed them to COPD patients with and without co-morbidities. The research was carried out at MMIMSR. In this retrospective study a total of 80 COPD patients were randomly chosen. Twenty patients were eliminated from the research due to the exclusion criteria. The remaining 60 patients who met the inclusion criteria were enrolled in the study. Among the total patients, Bi-therapy was prescribed to the majority of patients (55 percent), followed by tritherapy (37 percent), and monotherapy was prescribed to the least number of patients (8 percent). Various medical practitioners prescribed drugs to the COPD patients in the research (A, B, C). A administered drugs to 28 percent of the patients, 33 percent by B, and 39 percent by C. Finally, the greatest improvement was seen with Bi-therapy. Bi-therapy (combination of anticholinergics and xanthene) appears to increase quality of life (SF36 Questionnaire score). Bi-therapy (a combination of anticholinergics and beta-blockers) was also proven to ameliorate the severity of disease (Dyspnea score). And Bi-therapy was prescribed majorly by medical practitioners in COPD patients.[59]

A Prospective Study on Prescription Pattern in Chronic Obstructive Pulmonary Disease was conducted by *Jyothi DB et al., (2020)*. Irrational prescribing has a negative influence on both individual and societal health and economics, resulting in resource waste and broad health risks. Outpatients with mild, moderate, or severe COPD were enrolled in the study. Patient's age and gender, outpatient (OPD) ID number, date of admission, occupation, h/o smoking, alcohol use, etc., disease condition specifics (duration, grading as mild, moderate, and severe, and co-existing conditions), and prescribed medication details were all taken into account (dose, frequency, route of administration, and duration). The severity of the disease was also classified using GOLD criteria, and drug efficacy was measured using the modified MRC dyspnea scale. In this study, the inhalation method was selected by 36.95 percent of participants, followed by the parenteral route (34.34 percent), and the enteral route (34.34 percent) (28.71 percent). GOLD 2015 adherence: Based on the severity of COPD, all patients (n=400) were assigned to one of four Gold phases. There were 11

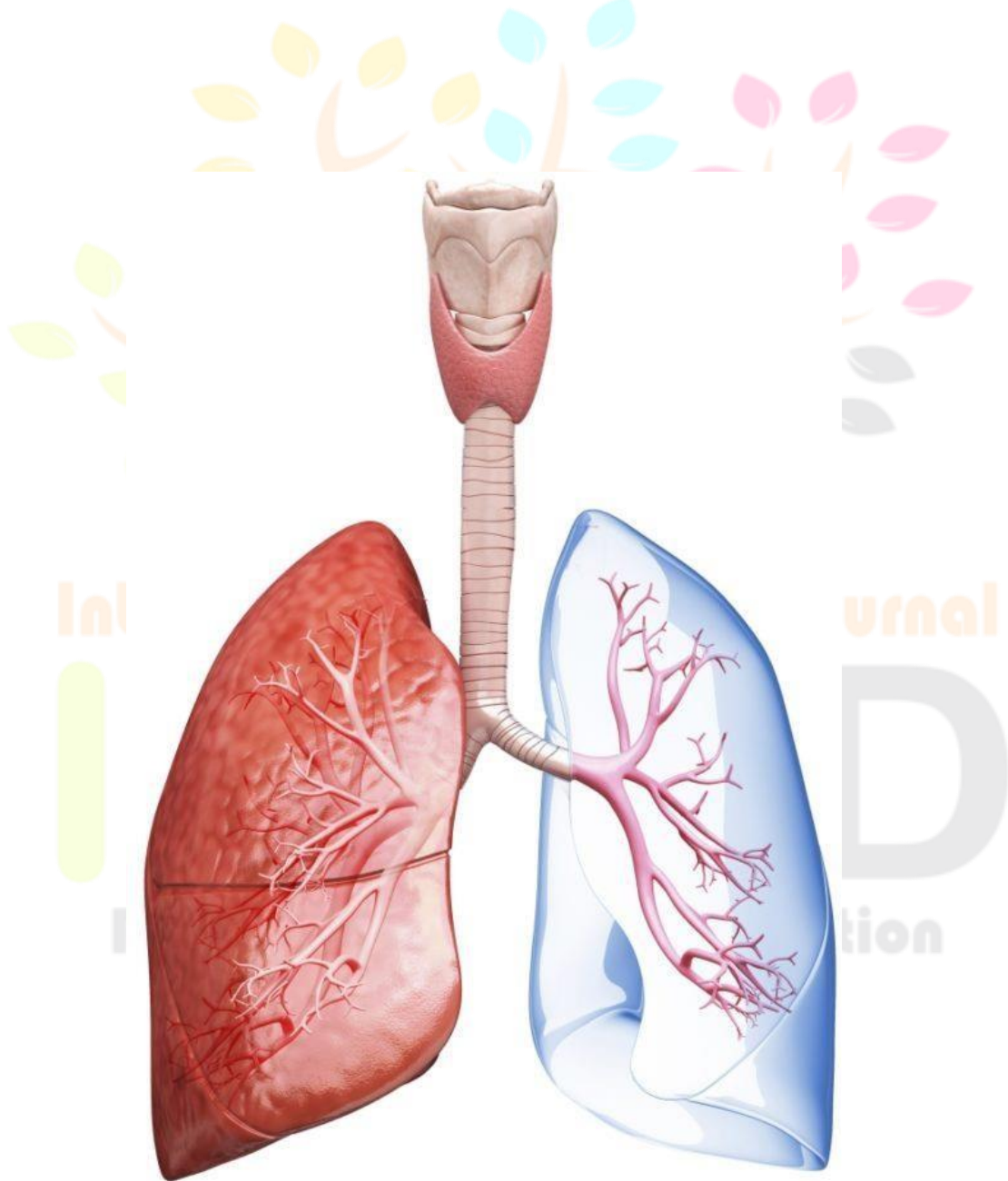
patients in stage I, 146 patients in stage II, 184 patients in stage III, and 59 patients in stage IV among these patients. The majority of the participants were given fixed-dose combination medication, with the most commonly used being levocetirizine + montelukast (77%) and the least commonly used being bromhexine + guaiphenesin + terbutaline + menthol (3%). (18 percent). According to the modified MRC dyspnea scale, dyspnea status was graded from 0 to 4. 18 patients had a rating of zero, 44 had a grade of one, 156 had a grade of two, 133 had a grade of three, and 49 had a grade of four. Overall, the findings of this study imply that following the GOLD guidelines had no discernible effect on symptom prevalence, exacerbation rate, or lung function. Male sex, asthma, and significant co- morbidities as a cerebrovascular insult may all be linked to an increased incidence of exacerbations.[60]

Poonam Salwan¹ et al., (2020) conducted an observational study on prescription pattern in the management of chronic obstructive pulmonary disease patients in a tertiary hospital. Drug utilization studies encourage sensible drug use and aid in the reduction of adverse drug responses. Such studies are effective instruments for assessing the impact of medications on society. The goal of this study is to examine and analyze drug prescribing trends and patterns among individuals with chronic obstructive pulmonary disease (COPD).SGT Medical College, Hospital and Research Institute, SGT University, Gurugram, conducted a prospective observational study on 112 COPD patients hospitalized to the general and pulmonary medicine departments during a one-year period. Patients who met the study's inclusion criteria were included after giving their informed consent. The data was collected and tabulated using a specially built data entry form. The percentages were used to represent the results. For each patient, the following data was gathered: social demographics, smoking history, and prescribed COPD therapies. Validated questionnaires were used to collect health-related quality of life variables. Male patients outnumbered female patients in the 112-study population (76.36 percent). The bulk of the patients (47.2 percent) were between the ages of 61 and 70, with 56.36 percent having a severe quality of life rating (low score) on the COPD assessment test. In the study population, smoking was shown to be more prevalent (71.42 percent). Inhaled corticosteroids (67.85 percent) were the most commonly recommended medication class for COPD treatment, followed by systemic bronchodilators (64.28 percent). Systemic methylxanthine (deriphylline 64.28 percent) was the most usually recommended bronchodilator, followed by systemic 2 agonist (Terbutaline-62.5 percent). Inhaled corticosteroids were used by 67.85% of people. Inhaled corticosteroids were given more frequently than systemic corticosteroids (67.85 percent).

Amoxicillin-clavulanic acid combination (35.71 percent) and ceftriaxone were the most commonly prescribed antimicrobials (35.71 percent). Proton pump inhibitors (73.21 percent) were the most commonly given medications for comorbid illnesses, followed by antihistaminics (37.5 percent) for allergic conditions. According to the study's findings, COPD patients at the hospital were offered symptomatic therapy. The prescribing pattern was discovered to be consistent with the current global Initiative for chronic obstructive pulmonary disease (GOLD) guidelines for COPD patient care.[61]



METHODOLOGY





5. METHODOLOGY

5.1 STUDY PROTOCOL:

The study protocol was prepared by conducting an extensive literature search. It included information on the need for the study, objectives, review of literature and methodology. The protocol was submitted to Dayananda Sagar University for approval.

5.2 STUDY DESIGN:

Retrospective case record analysis.

5.3 ETHICS COMMITTEE APPROVAL:

The study protocol was prepared and submitted to the 'Dayananda Sagar University Ethics Committee' for ethical clearance. The study was approved by the above said institutional ethics committee and issued an ethical clearance certificate for the same.

5.4 SAMPLE SIZE:

- 300 patients.

5.5 PLACE OF STUDY:

- The study will be conducted at Sagar Hospital, Kumaraswamy layout, Bengaluru.

5.6 SOURCE OF DATA:

All the relevant and necessary data will be collected from

- Patients case notes
- Treatment charts
- Relevant laboratory investigations

5.7 DURATION OF STUDY:

- The study will be conducted for a period of 6 months.

5.8 SUBJECTS:

- Patients admitted to Sagar hospital for the treatment of COPD between January 2016 to September 2020, and those who met the inclusion criteria.
-



5.8.1 Inclusion Criteria:

- All in-patients diagnosed with COPD and admitted at least for 24hours, January 2016 to September 2020.
- Patients prescribed with minimum 2 drugs.

5.8.2 Exclusion Criteria:

- Illegible case records.
- Incomplete data.
- Patients below 18 years.
- Out-patients.

5.9 STUDY MATERIAL

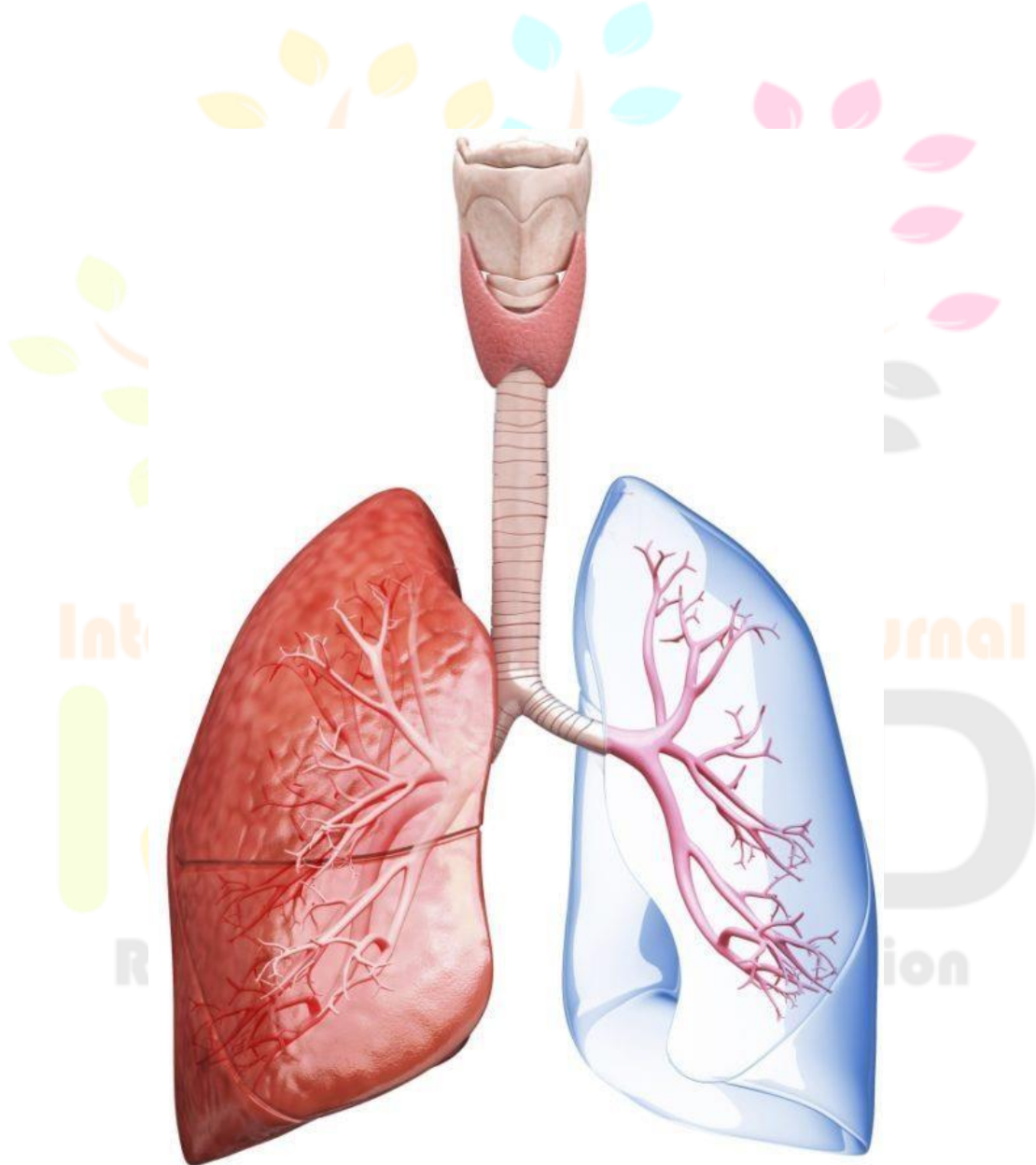
Patient data collection form: A suitably designed data collection form was prepared. This form contains all preliminary information about the subject, their name, age, gender, IP number, past medical history, current medical problem, current diagnosis and their treatment.

5.10 STUDY PROCEDURE

After obtaining approval and clearance from Institutional Ethics Committee (IEC) this study was carried out for a period of 6 months in Medical Records Department of Sagar Hospitals, Bengaluru. 300 prescriptions were selected from among those prescribed from January 2016 to September 2021 based on inclusion and exclusion criteria. Patients details including age, sex, past medical history, present diagnosis, present medication details were collected from patients records and documented in the patient profile form (Annexure II). The data was analyzed using Microsoft Excel. The drug interactions were assessed using Lexicomp software



RESULTS





6.

RESULTS

A retrospective observational study was carried out by reviewing prescription of 300 COPD patients in tertiary care hospital. The patients were categorized on the basis of gender, age, smoking history, comorbid conditions. This study was conducted to analyze the drug utilization pattern among COPD patients. Total number of COPD drugs prescribed was found to be 1554.

Table 4: Age distribution of patients studied

Age in years	No. of patients	%
<40	7	2.3
41-50	11	3.7
51-60	44	14.7
61-70	111	37.0
>70	127	42.3
Total	300	100.0

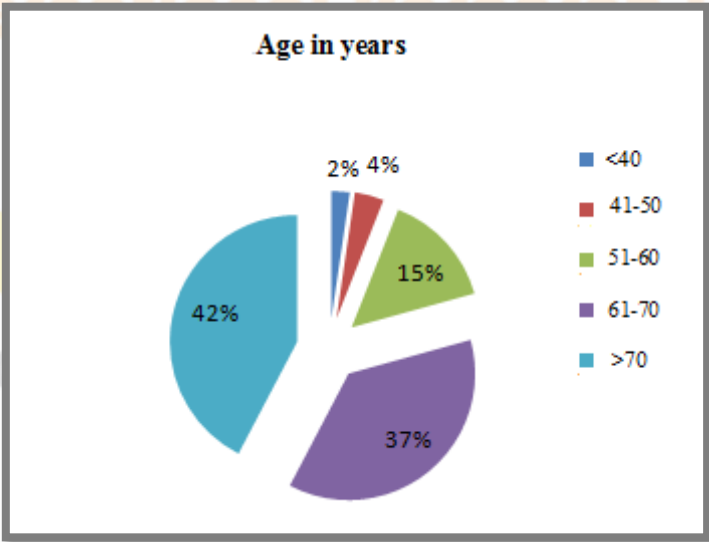


Fig 3: Age distribution of patients

Among the study population, majority of patients (42.3%) were above the age of 70 and the least (2.3 %) was found to be below the age of 40.



Table 5: Gender distribution of patients studied

Gender	No. of patients	%
Female	102	34.0
Male	198	66.0
Total	300	100.0

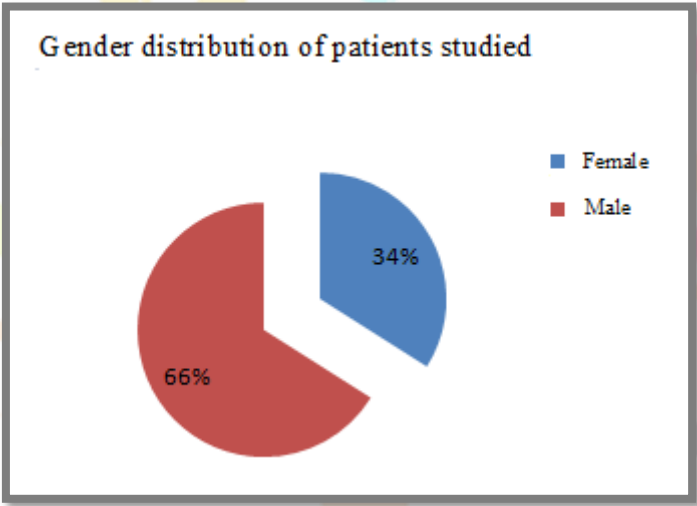


Fig 4: Gender distribution of patients

Out of 300 patients, 102 (34 %) were female and 198 (66%) were found to be male. Hence our analysis showed that occurrence of COPD was greater in male than in female.

Table 6: LOHS (length of hospital stay)-frequency distribution of patients studied

LOHS	No. of patients	%
10	277	92.3
0-20	17	5.7
20	6	2.0

total	300	100.0
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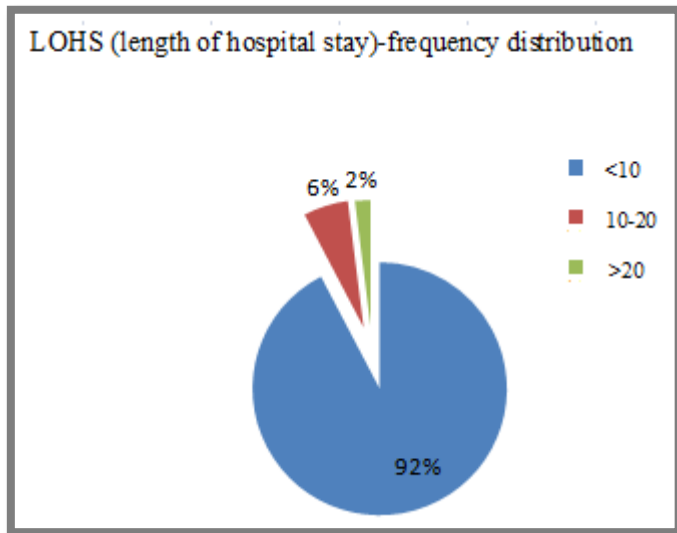


Fig 5: Length of hospital stay frequency distribution

Length of hospitalization was less than 10 days for maximum patients (92.3%) and only 6 patients (2%) were found to be admitted for more than 20 days.

Table 7: Smoking-frequency distribution of patients studied

	o. of patients (n=300)	%
Smoker	37	12.3
Ex-Smoker	27	9.0
Non-Smoker	236	78.6

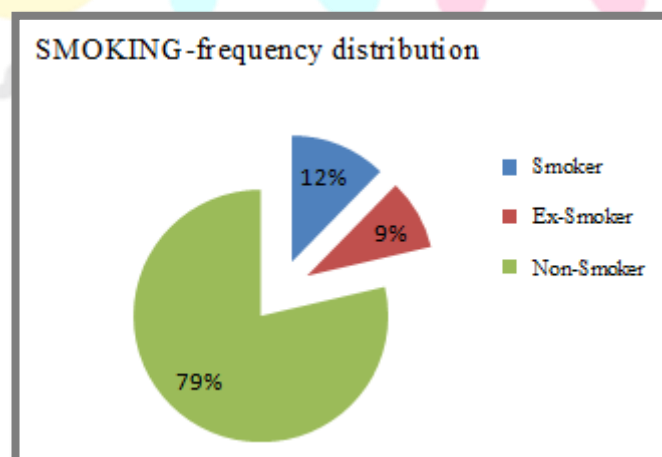


Fig 6: Smoking frequency distribution



Among 300 patients, 37(12.3%) were smokers, 27(9%) were Ex-smoker, 236(78.6%) were Non-smokers.

Table 8: No. of comorbidities-frequency distribution of patients studied

No. of comorbidities	No. of patients	%
	69	23.0
	93	31
	81	27.0
	41	13.7
	15	5.0
	1	0.3
Total	300	100.0

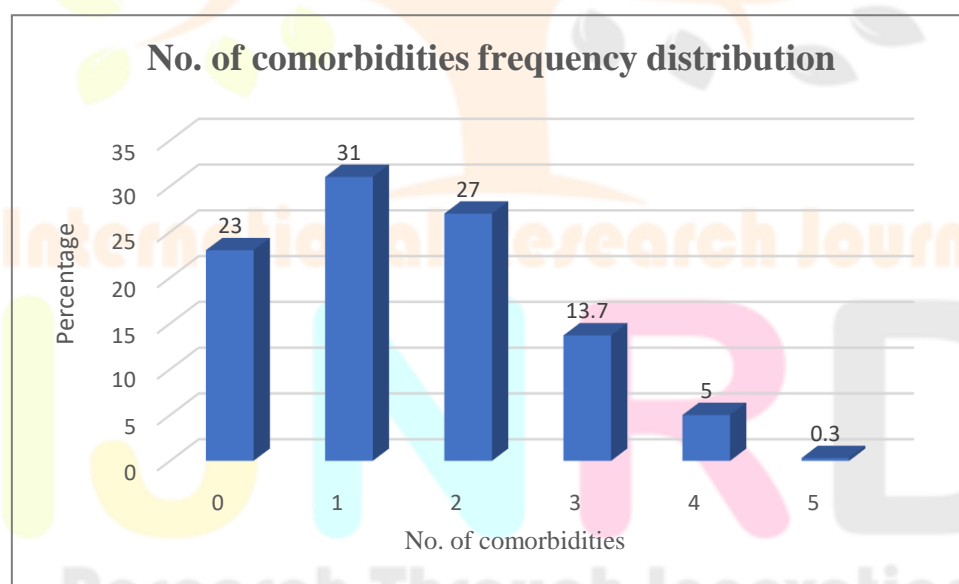


Fig 7: COMORBIDITIES-frequency distribution of patients studied

Among study population, 69(23%) patients were not having any other comorbid conditions. The majority of patients (31%) had only one comorbid condition. Out of 300 patients, only one patient was suffering from 5 comorbidities.



Table 9: Frequency distribution of Comorbidities

COMORBIDITIES	No. patients (n=300)	Percentage
Hypertension	170	56.7
Diabetes Mellitus	123	41
Ischemic Heart Disease	51	17
Bronchial asthma	27	9
Hypothyroidism	20	6.7
Chronic Kidney Disease	13	4.3
Cerebrovascular Accident	7	2.7
Atrial Fibrillation	7	1.7
Reactive Airway Disease	3	1.3
Bronchitis		
PH (Benign prostatic hyperplasia)		
Epilepsy		
Cor pulmonale		
Parkinsonism		1.7
Osteoarthritis		1.7

The most commonly found comorbid condition among the 300 COPD patients was Hypertension (56.7%) followed by diabetes (41%), Ischemic heart disease (17%), bronchial asthma (9%), hypothyroidism (6.7%), chronic kidney disease (4.3%), Cerebrovascular accident (2.7%), atrial fibrillation (1.7%), reactive airway disease (1.3%) and the least observed conditions were cor-pulmonale, gouty arthritis, acute kidney injury, dyslipidemia etc.



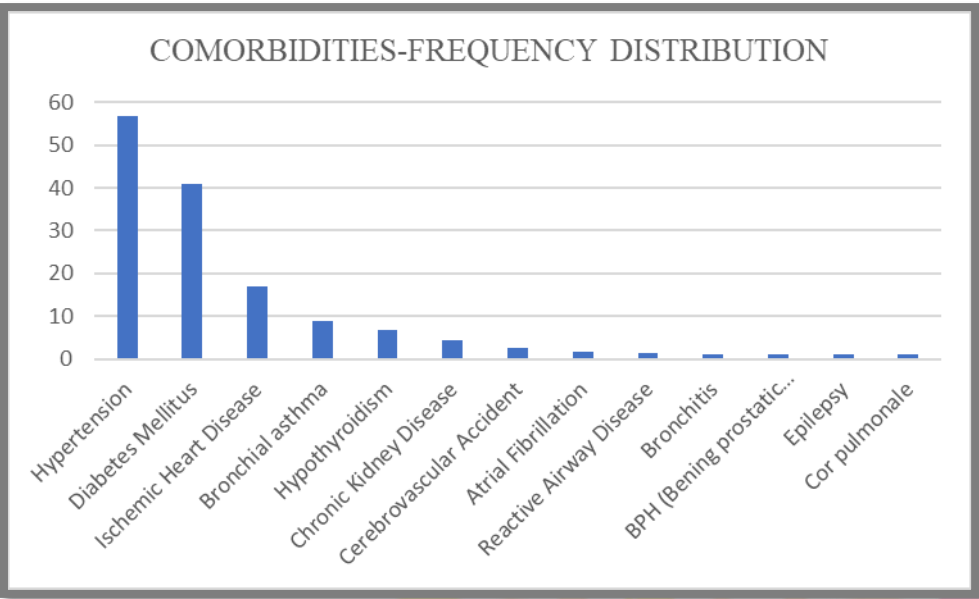


Fig 8: Comorbidities Frequency distribution

Table 10: COPD Drugs-frequency distribution of patients studied

COPD DRUGS	o of patients (n=300)	%
udesonide	50	3.3
pratropium+Levosalbutamol	28	6
Montelukast + Levocetirizine	6	2
cefoperazone + Sulbactam	9	5.3
ydrocortisone	6	5.3
ethyl prednisolone	3	4.3
larithromycin	0	3.3
eriphylline	5	1.7
cebrophylline + Acetyl cysteine	2	0.7
cetylcysteine	5	3.3
iperacillin + Tazobactam	5	3.3
evosalbutamol	9	5.3
evofloxacin	7	5.7
ormoterol + Budesonide	5	5

eftriaxone	3	4.3
moxicillin + Clavulanic acid	1	0.3
cebrophylline	0	0
efuroxime	5	3



doxophylline	3	7
fluticasone	5	
montelukast	4	7
ticarcillin + Clavulanate	4	7
loxifloxacin	4	7
formoterol	3	3
ambroxol	2	

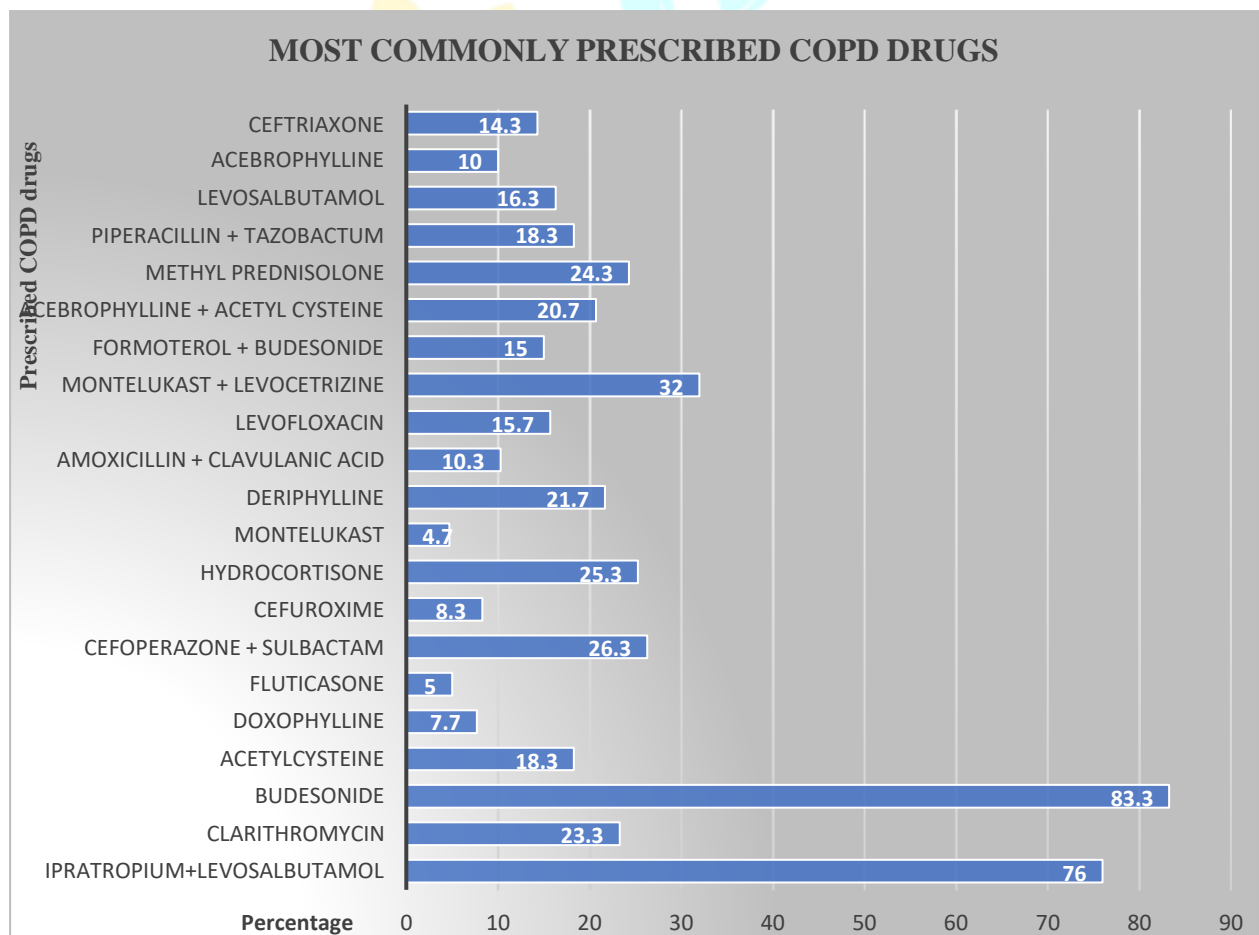


Fig 9: Most commonly prescribed COPD drugs

A total of 1554 COPD drugs were prescribed for 300 patients for the management of COPD. The most commonly prescribed COPD drugs were found to be budesonide (83.3%), followed by ipratropium+levosalbutamol(76%), Montelukast+levocetirizine(32%), cefoperazone+ sulbactam(26.3%), hydrocortisone (25.3%),methylprednisolone(24.3%), clarithromycin(23.35%), deriphylline(21.7%)etc. The oral inhalation of

route of administration was mostly used with prescribed drugs in COPD patients.



Table 11: Different class of drugs prescribed for the management of COPD

CLASS OF THE DRUG	O. OF PATIENTS	PERCENTAGE (%)
Short acting b2 agonist	271	90.3
Long acting b2 agonist	68	22.6
Short acting muscarinic antagonist	224	74.6
Long acting muscarinic antagonist	11	3.6
Systemic corticosteroid	134	44.6
Inhaled corticosteroid	261	87
Antibiotics	257	85.6
Anthine derivatives	165	55
Antihistamines	96	32
Leukotriene Receptor Antagonist	109	36.3
Mucolytic Agent	129	43
Antitussive	3	1
Expectorant	10	3.3

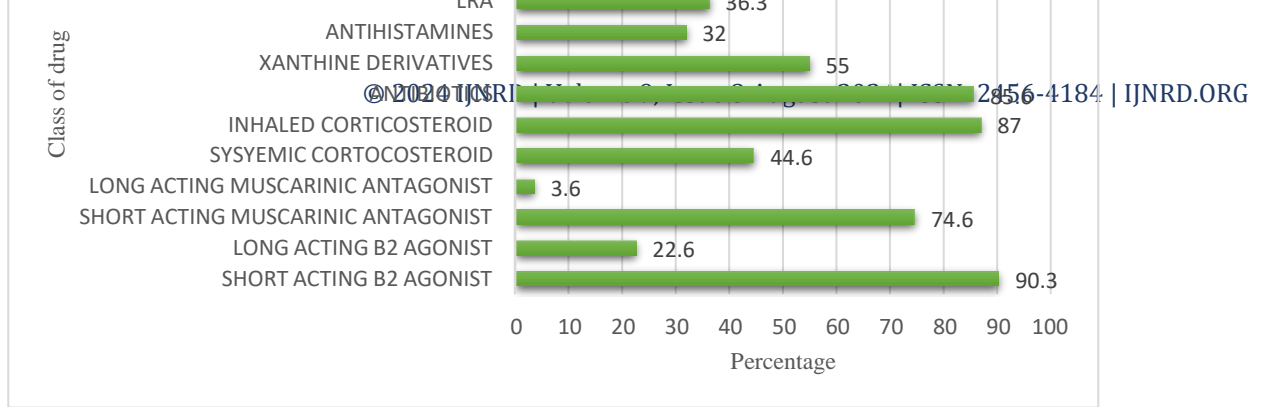


Fig 10: Different class of drugs prescribed for the management of COPD



Under evaluation of different classes of drugs used in therapy, we found that the most frequently used class of drug was short acting beta 2 agonist (90.3%), followed by inhaled corticosteroids (87%), antibiotics (85.6%), short acting muscarinic antagonist (74.6%) etc.

Table 12: Drug Utilization Pattern Of Antibiotics

ANTIBIOTICS	NO. OF PATIENTS	PERCENTAGE (%)
fluoroquinolones	62	24.1
Macrolides	68	26.4
Penicillin	95	36.9
Cephalosporin	163	63.4

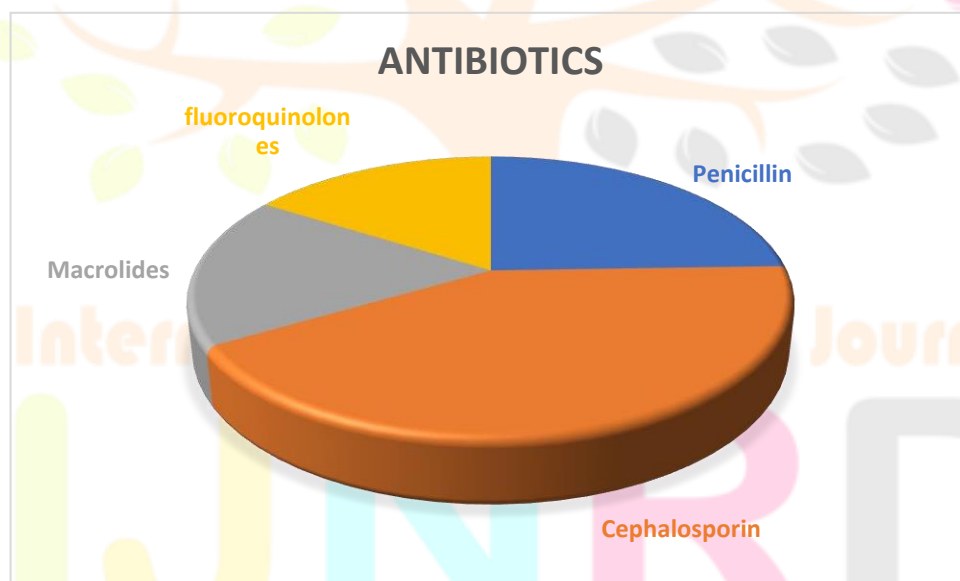


Fig 11: Percentage of Drug Utilization Pattern of Antibiotic

Among antibiotics classes of drug, Cephalosporins was the most prescribed drug, and the least was Fluoroquinolones.



Table 13: Categories of drugs used

DRUG CATEGORY	No. of patients	Percentage
Short acting beta 2 agonist		
Nil	29	9.7
Levosalbutamol	258	86.0
Levosalbutamol, Levosalbutamol (syrup)	6	2.0
Levosalbutamol, Terbutaline	3	1.0
Levosalbutamol (syrup)	2	0.7
Salbutamol	2	0.7
Long acting beta 2 agonist		
Nil	232	77.3
Formoterol	55	18.3
Salmeterol	7	2.3
Indacaterol	4	1.3
Formoterol,Salmeterol	1	0.3
Salmeterol, Indacaterol	1	0.3
Short acting muscarinic antagonist		
Nil	76	25.3
Ipratropium	224	74.7
Long acting muscarinic antagonist		
Nil	289	96.3
Tiotropium	7	2.3
Glycopyrrolate	3	1.0
Glycopyrrolate,Tiotropium	1	0.3
Systemic corticosteroids		
Nil	166	55.3
Hydrocortisone	61	20.3
Methyl prednisolone	56	18.7

Methyl prednisolone, hydrocortisone	16	5.3
Prednisolone	1	0.3



Inhaled corticosteroids		
Nil	39	13.0
Budesonide	237	79.0
Budesonide, Fluticasone	19	6.3
Fluticasone	4	1.3
Mometasone	1	0.3
Penicillins		
Nil	205	68.3
• Piperacillin + Tazobactam	49	16.3
• Amoxicillin + Clavulanate	27	9.0
Ticarcillin + Clavulanate	13	4.3
• Amoxicillin + Clavulanate, Piperacillin + Tazobactam	5	1.7
• Ticarcillin + Clavulanate, Piperacillin + Tazobactam	1	0.3
Cephalosporins		
Nil	137	45.7
• Cefoperazone + Sulbactam	77	25.7
Ceftriaxone	38	12.7
Cefuroxime	23	7.7
Ceftazidime	6	2.0
Cefotaxime	5	1.7
Cefoperazone	4	1.3
Cefixime	4	1.3
Ceftriaxone, Cefixime	3	1.0
Cefixime, Cefotaxime	1	0.3
Cefoperazone + Sulbactam, ceftriaxone	1	0.3
• Cefuroxime, Cefpodoxime	1	0.3
Macrolides		

Nil	232	77.3
Clarithromycin	64	21.3
Azithromycin	2	0.7
Clindamycin	1	0.3



Quinolones		
Nil	238	79.3
Levofloxacin	47	15.7
Moxifloxacin	14	4.7
Ofloxacin	1	0.3
xanthine derivatives		
Nil	135	45.0
Acebrophylline	77	25.7
Deriphylline	34	11.3
Doxophylline	17	5.7
Theophylline	16	5.3
Deriphylline, Acebrophylline	10	3.3
Acebrophylline, Theophylline	3	1
Doxophylline, Acebrophylline	2	0.7
Deriphylline, Doxophylline	3	1
Aminophylline, Deriphylline	2	0.6
Theophylline, Doxophylline	1	0.3
Anti-histamines		
Nil	204	68.0
Levocetirizine	96	32.0
Leukotriene receptor antagonists		
Nil	191	63.7
Montelukast	109	36.3
Mucolytic agent		
Nil	171	57.0
Acetyl cysteine	107	35.7
Ambroxol	18	6.0
Acetyl cysteine, Ambroxol	4	1.3

ntitussive		
Nil	297	99.0
Dextromethorphan	3	1.0



Expectorant		
Nil	290	96.7
Guaifenesin	10	3.3

Our data showed that under SABA category of drugs, Levosalbutamol was prescribed for 258 patients (86%) and oral inhalations was the most preferred route of administration than oral route. Under LABA, Formoterol was mostly prescribed than salmeterol and indacaterol. Ipratropium was prescribed for 224 patients and this was the only prescribed SAMA. Tiotropium which belongs to LAMA was the preferred drug over glycopyrrolate. Inhaled steroids such as Budesonide was prescribed to 79% of patients, while systemic steroids like Hydrocortisone was prescribed to 20.3%. Under antibiotics, Piperacillin+Tazobactam (16.3%), Cefoperazone+Sulbactam (25.7%), Clarithromycin(21.3%), Levofloxacin (15.7%) were the most preferred drugs under each category by the prescriber. Acebrophylline was given to 77 patients and was the most frequently prescribed Xanthine derivative. Mucolytics such as Acetyl

cysteine was prescribed to 107 patients followed by Ambroxol. Leukotriene receptor antagonists, Montelukast was prescribed to 36.3% of study group patients. Levocetirizine was the only prescribed antihistaminic drug. Dextromethorphan and Guaifenesin were the only prescribed antitussives and expectorant respectively.

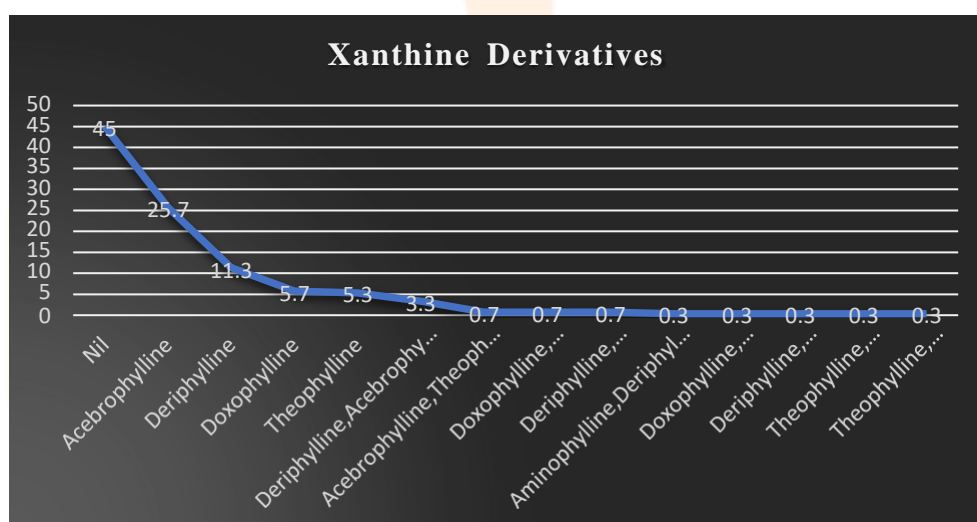


Fig 12: Xanthine Derivatives



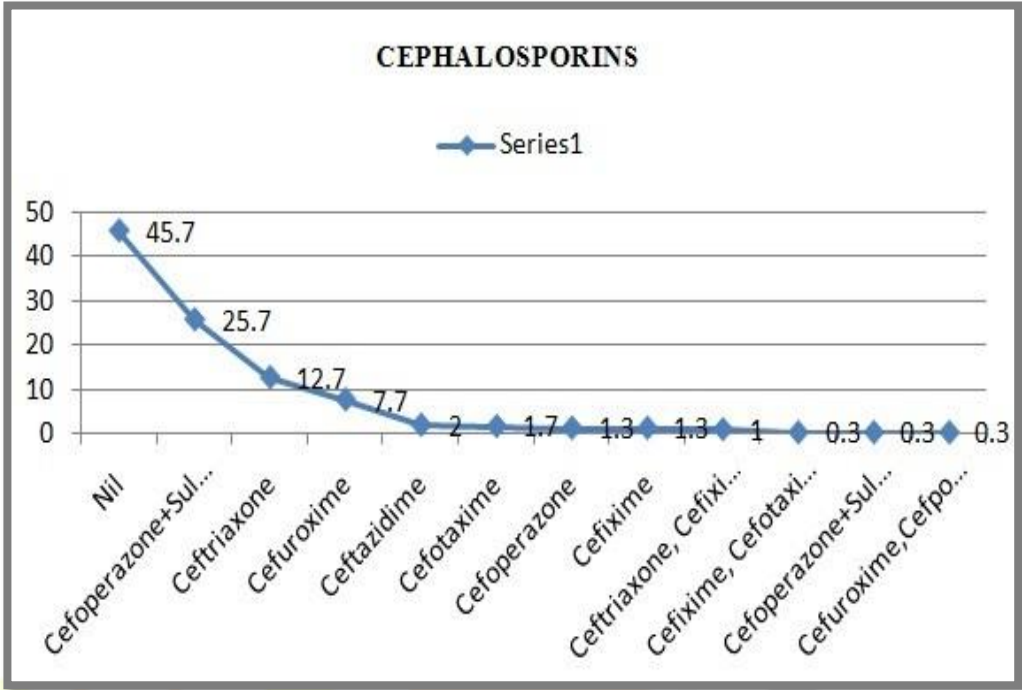


Fig 13: Class of Cephalosporins

Table 14: Distribution of patients based on combination therapy

Combination drugs	o. of patients (n=300)	%
Nil	9	3
Yes	81	3.6

Table 15: Combination therapy in study population

COMBINATION DRUGS	O. OF PATIENTS	PERCENTAGE (%)
-------------------	----------------	----------------

Ipratropium+levosalbutamol	227	80.7
Montelukast +levocetirizine	96	34.1



Cefaperazone+sulbactam	79	28.1
Acebrophylline+acetylcysteine	62	22
Pipercillin+tazobactam	55	19.5
Formoterol+budesonide	45	16
Amoxicillin+clavulaunate	31	11
Ticarcillin+clavulaunate	14	4.9
Salmeterol+fluticasone	8	2.8
Formoterol+ mometasone	1	0.3

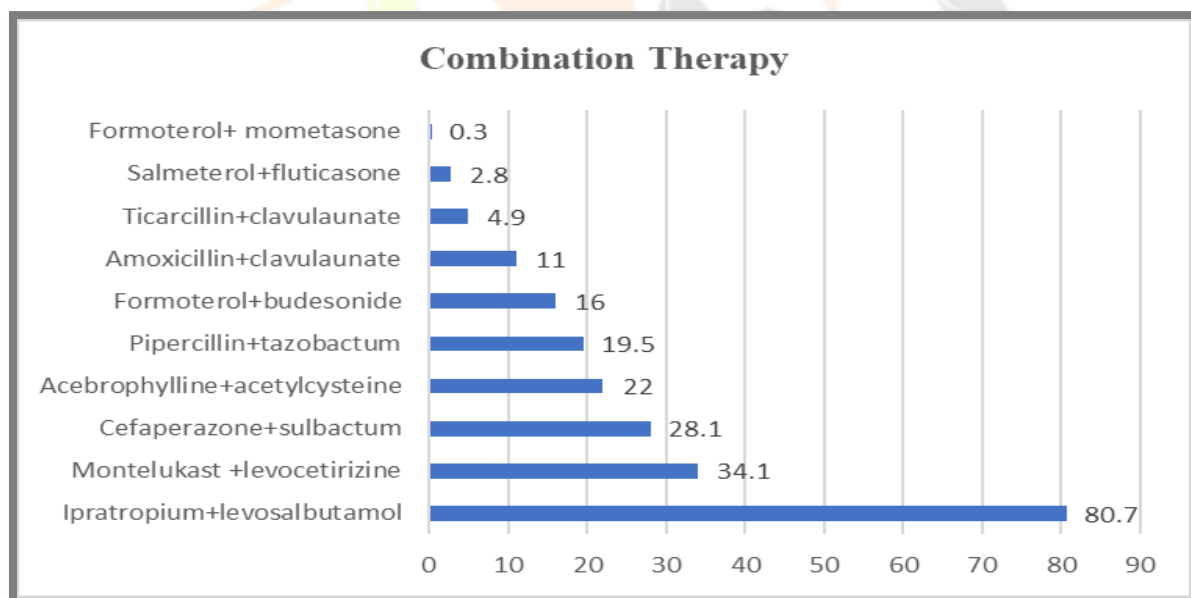


Fig 14: Percentage of Drug Combination

Among study population, combination therapy was given to 281 patients. Ipratropium + Levosalbutamol (80.7%) was preferred combination therapy for COPD patients followed by

Montelukast+Levocetirizine(34.1%),Cefoperazone+Sulbactam(28.1%),Acebrophylline+acetylcysteine(22%),Pipercillin+tazobactam(19.5%),Formoterol+budesonide(16%),Amoxicillin+clavulaunate(11%),Ticarcillin+clavulaunate(4.9%),Salmeterol+fluticasone (2.8%), Formoterol+mometasone(0.3%).



Table 16: WHO Drug Indicators

WHO DRUG INDICATORS		
	Standard value	Test value
Average number of drugs per prescription	1.6 – 1.8	5.18
Percentage of prescription with an antibiotic prescribed	20.0 – 26.8 %	85.6 %
Percentage of prescription with an injection prescribed	13.4 – 24.10 %	87.6 %
Percentage of drugs prescribed by generic name	100 %	5.4 %
Percentage of drugs prescribed from Essential Drug List	100 %	49.4 %

Data analysis showed that with 1554 total number of drugs being prescribed, the average number of drugs per prescription was 5.18 which deviates from the standard value of WHO indicators, which concludes the presence of polypharmacy practice in the hospital. Percentage of prescription with an antibiotic prescribed is 85.6%. The most commonly prescribed drugs among antibiotics are Cefoperazone + Sulbactam followed by Clarithromycin, Piperacillin + Tazobactam, Levofloxacin etc. Percentage of prescription with an injection prescribed is 87.6%. Most of the drugs were prescribed by brand name and only 5.4% were prescribed by generic name. The percentage of drugs prescribed from WHO EDL was 49.4%.

Table 17: Drugs numbers to facilitate treatment of no. of 300 patients in different modalities with % analysis.

	no. of patients (n=300)	%
no. of COPD drugs		
<5	112	37.3
5-10	183	61.0

>10	5	1.6
o. of ANTIBIOTIC		



0	43	14.3
1	127	42.3
2	113	37.7
3	14	4.7
4	3	1.0
o. of IV drugs		
0	37	12.3
1	89	29.7
2	95	31.6
3	51	17.0
4	19	6.3
5	5	1.7
6	4	1.3
o. of drugs prescribed in generic name		
0	229	76.3
1	56	18.7
2	15	5.0
o.of drugs prescribed from DL(essential drug list)		
0	25	8.3
1	6	2.0
2	49	16.3
3	215	71.7
4	5	1.7

Table 18: Drugs Details According to Gender of Patients Studied

DRUGS	Gender		total (n=300)
	female(n=102)	male (n=198)	

o. of COPD drugs			
<5	0(29.4%)	82(41.4%)	112(37.3%)
5-10	1(69.6%)	112(56.6%)	183(61%)
>10	(1.96%)	(1.5%)	5(1.6%)



o. of ANTIBIOTIC			
0	10(9.8%)	33(16.7%)	43(14.3%)
1	45(44.1%)	82(41.4%)	127(42.3%)
2	39(38.2%)	74(37.4%)	113(37.7%)
3	7(6.9%)	3(3.5%)	14(4.7%)
4	1(1%)	1(1%)	3(1%)
o. of IV drugs			
0	7(6.9%)	30(15.2%)	37(12.3%)
1	30(29.4%)	59(29.8%)	89(29.7%)
2	36(35.2%)	59(29.8%)	95(31.6%)
3	21(20.6%)	30(15.2%)	51(17%)
4	5(4.9%)	4(7.1%)	19(6.3%)
5	2(2%)	1(1.5%)	5(1.7%)
6	2(2%)	1(1%)	4(1.3%)
o. of drugs prescribed in generic name			
0	78(76.5%)	151(76.3%)	229(76.3%)
1	19(18.6%)	37(18.7%)	56(18.7%)
2	5(4.9%)	10(5.1%)	15(5%)
o. of drugs prescribed from DL			
0	5(4.9%)	20(10.1%)	25(8.3%)
1	1(1%)	2(2.5%)	6(2%)
2	19(18.6%)	30(15.2%)	49(16.3%)
3	75(73.5%)	140(70.7%)	215(71.7%)
4	2(2%)	1(1.5%)	5(1.7%)

As per the Table-10, the drug utilization or prescribed to different patient owing to gender's here. The below histogram shows a different % of plots variations.

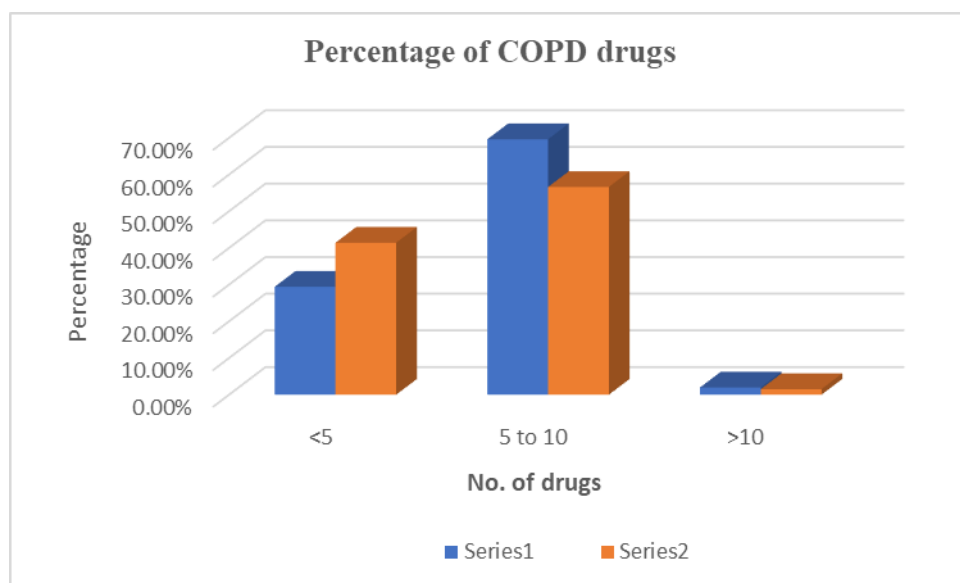


Fig 15: Percentage of COPD drugs

Table 19: Incidence of Polypharmacy

No.of drugs	No.of prescription	Percentage (%)
5	58	19.3
6	51	17
7	37	12.3
8	19	6.3
9	10	3.3
10	7	2.3
11	4	1.3

Number of drugs per prescription is shown in the above table, the average number of drugs per prescription was 5.18. 19.3% of prescriptions contain 5 drugs, and 42.5% of prescriptions had more than 5 drugs which is considered as polypharmacy.

Table 20: Percentage of Types of Drug Drug Interaction

YPES	o.of drug druginteraction	ercentage
harmacokineticinteraction	6	1.4 %
harmacodynamicinteraction	9	8.95 %

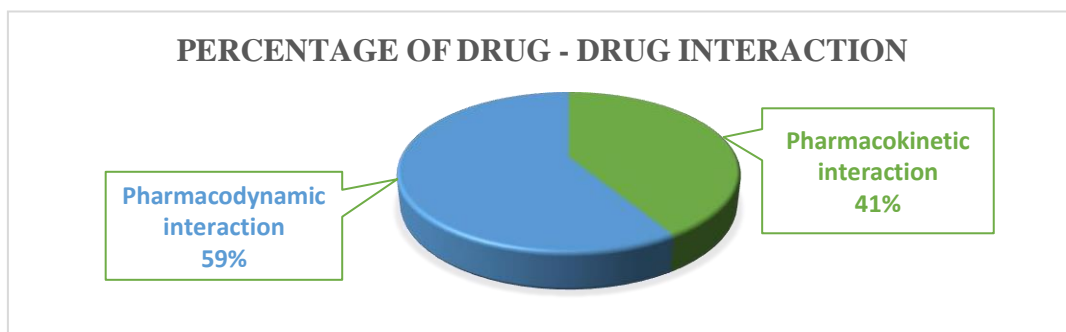


Fig 16: Percentage of Drug Drug Interaction

Among 135 drug-drug interactions, 59% was found to be Pharmacodynamic interactions and 41 % to be Pharmacokinetic interactions.

Table 21: Severity of Drug Drug Interaction

Severity	No.of drug interaction	Percentage (%)
MAJOR	15	11.2
MODERATE	117	86.6
MINOR	3	2.2

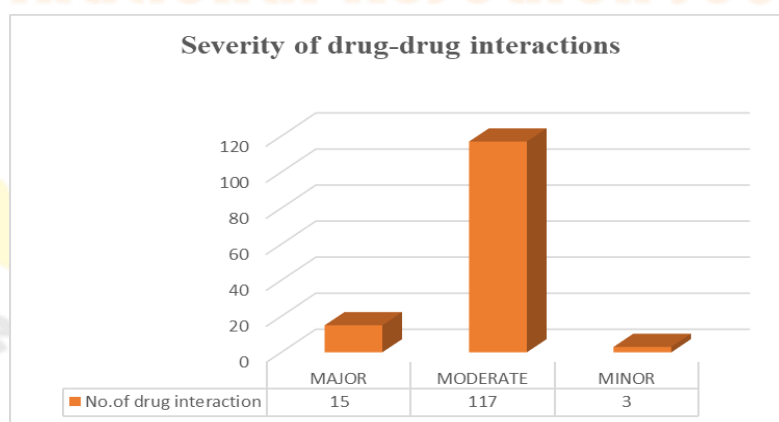


Fig 17: Severity of Drug Drug Interaction

Drug -drug interactions were categorized based on severity as major, moderate and minor. The severity assessment of DDIs in our study showed that most of interactions were moderate 117(86.6%) followed by major

15(11.2%) and minor 3(2.2%) interactions.



Table 22: Commonly found possible drug drug interactions among COPD patients.

Severity level	Interacting drugs	No. of patients
MAJOR	pratropium + levosalpiride	
	larithromycin + Salmeterol	
	cebrophylline + Theophylline	
MODERATE	evosalbutamol + furosemide	2
	udesonide + clarithromycin	2
	cebrophylline + levosalbutamol	
	evofloxacin + methylprednisolone	
	heophylline+levosalbutamol	
	heophylline+clarithromycin	
	pratropium+glycopyrrolate	
	esoprolol + Levosalbutamol	
MINOR	heophylline + clarithromycin	
	urosemide+ hydrocortisone	
	orsemide+Levosalbutamol	

The interaction between budesonide+ clarithromycin and Levosalbutamol+furosemide were found in maximum that augments corticosteroid toxicity and hypokalemia respectively.

Table 23: Frequency of Drug Drug Interactions

Frequency of DDIs	No. of patients	Percentage
1	59	9.3
2	6	9
3		6

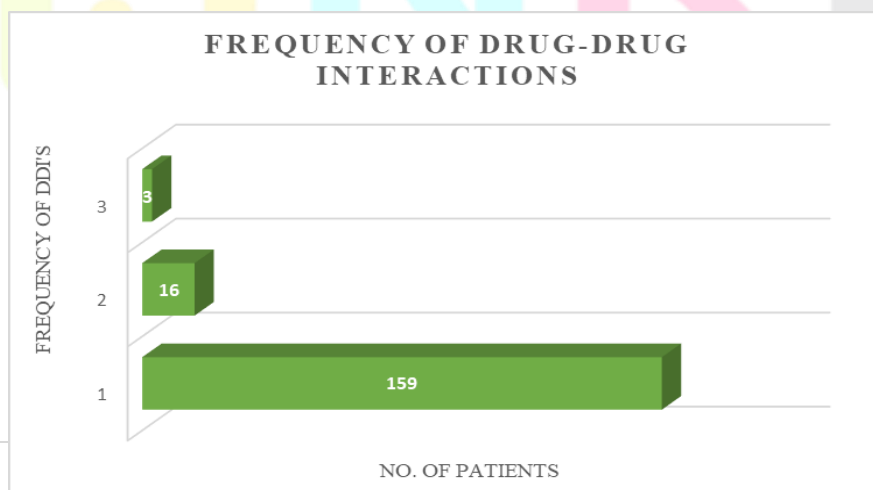


Fig 18: Frequency of Drug Drug Interaction



Among 300 patients, 159 patients had 1 drug-drug interaction and 19 patients had 2 or more drug-drug interactions.

Table 24: Severity of Drug Drug Interaction According to Gender

Minor	Gender		Total
	Female	Male	
One	101(99%)	196(99%)	297(99%)
Two or more	1(1%)	3(1%)	3(1%)
Total	102(100%)	198(100%)	300(100%)
Moderate			
One	63(61.8%)	136(68.7%)	199(66.3%)
Two or more	39(38.2%)	62(31.3%)	101(33.7%)
Total	102(100%)	198(100%)	300(100%)
Major			
One	97(95.1%)	190(96%)	287(95.7%)
Two or more	5(4.9%)	13(4%)	13(4.3%)
Total	102(100%)	198(100%)	300(100%)

A total of 300 prescriptions were analyzed during the study period, of which 114 prescriptions showed 135 drug-drug interactions. On comparing the drug interaction in two sexes, 13 prescriptions were found with major interactions out of which 4% found in male and 4.9% found in female. 101 prescriptions found moderate interactions, out of which 31.3 % were male and 38.2% were females. 3 prescriptions found with minor interaction, out of which 1% were female and 1% were male.

Table 25: Number of drugs prescribed and % of interactions in patients

No. of drugs prescribed	% INTERACTION		
	MINOR	MODERATE	MAJOR
5	0	9.3	0
6	3.92	5.09	3.92

7	0	1.35	3.40
8	10.53.68		5.26



9	0	70	20
10	0	42.85	28.57
11	0	75	0

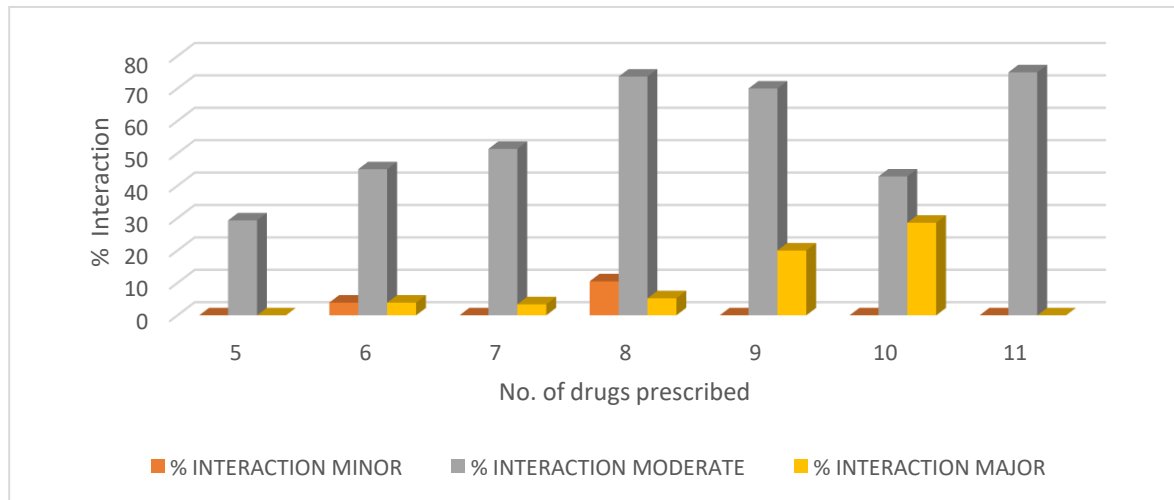


Fig 19: Percentage of Interaction in prescribed drugs

Maximum number of minor interactions were found in prescriptions containing 8 drugs. The prescriptions containing 11 drugs had majority of moderate interactions. Major interactions were seen higher in prescriptions containing 10 drugs.

Table 26: Percentage of major Interaction based on Age group

AGE GROUP	MAJOR INTERACTION (%)
18 - 25	0
26 - 33	0
34 - 41	0
42 - 49	0
50 - 57	20
58 - 65	20
66 - 73	33.3
74 - 81	13.3
82 - 89	13.3

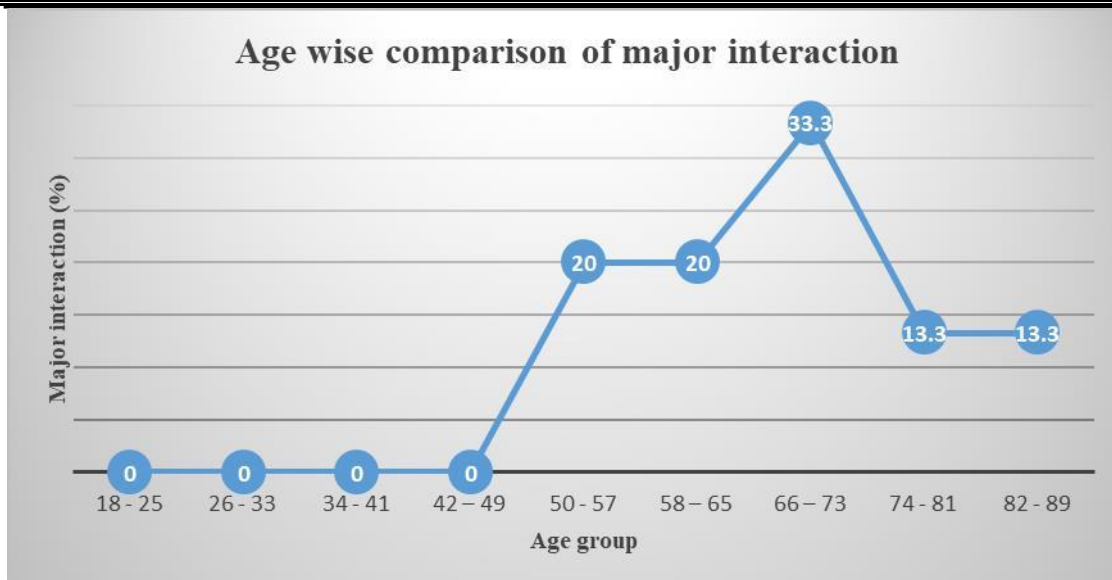
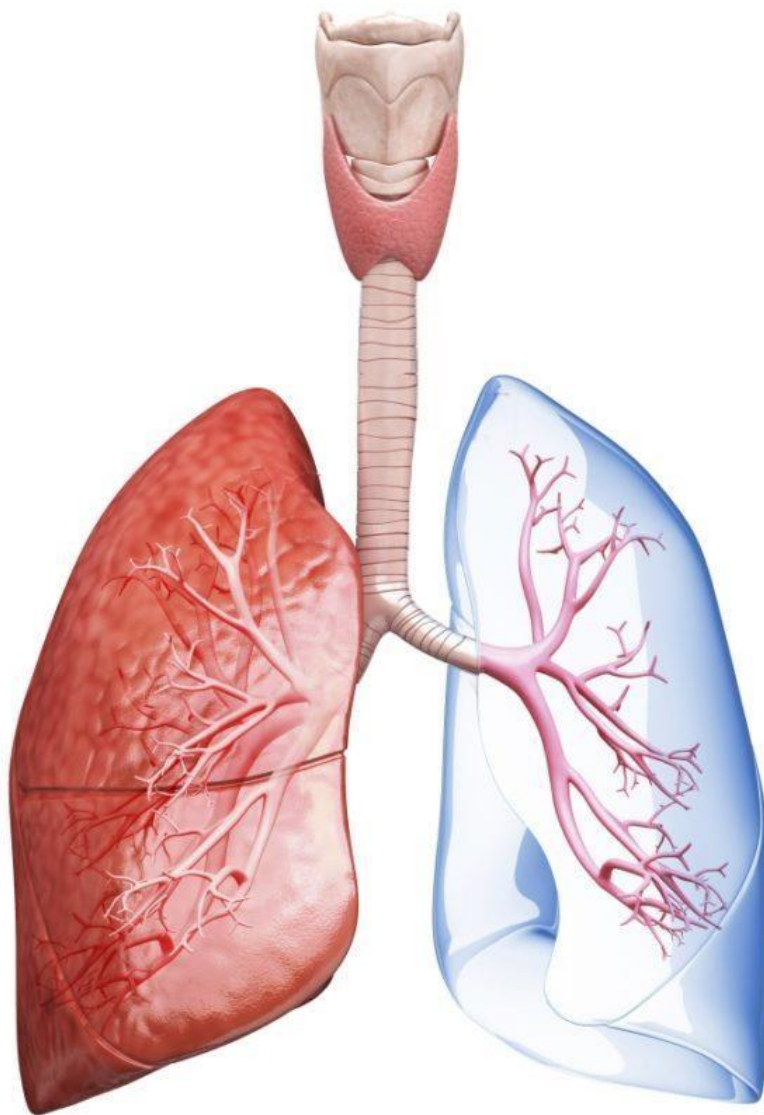


Fig 20: Age wise comparison of major interaction

On dividing the patients into different age groups, it was found that the maximum number of patients were above the age of 70. The maximum number of major interaction (33.3%) was found between the age group of 66-73. This shows that elderly patients were at high risk of having major drug-drug interactions.

DISCUSSION



7.

DISCUSSION

A retrospective case record study was performed on 300 COPD patients' prescriptions. There were 102 females and 198 males among the 300 patients. COPD was found to be more common in males than females, which is consistent with findings from prior studies by Unni Aswathy et al., Sawant PM et al., and Shiv Kumar et al. This could be caused by cigarette smoking, as well as environmental and occupational exposure. A large percentage of COPD patients were beyond the age of 70. Patients under the age of 40 were discovered in the smallest number. COPD is a slowly progressing disease. Occupational factors and age-related changes in the structure and function of the lungs may enhance pathogenic vulnerability to COPD, hence COPD may be more commonly found in elderly individuals. There were 37 smokers, 27 ex-smokers, and 236 non-smokers among the 300 patients. One of the most important risk factors for COPD is a history of smoking. Because cigarette smoking contains toxic substances that alter lung function, such as stiffness of air sacs, degradation of air sac walls, thickening and inflammation of airway walls, and an increase in mucus production in the airways, resulting in airway obstruction.

Out of 300 patients, 69 were not having any other comorbid conditions. The most common comorbid condition in our study population was hypertension, which was similar to Sawant MP et al., Unni A et al., and Shiv Kumar et al. Because of the loss of alveolar remodelling of the pulmonary arteries caused by chronic hypoxia and inflammation, decreases in the levels of endothelial vasodilators such as nitric oxide, and vasospasm produced by factors such as Endothelin 1, hypertension is common in COPD patients. Stress, age, and lifestyle changes may all play a role in hypertension. Diabetes was the most common concomitant condition, followed by IHD, bronchial asthma, and so on.

Budesonide and a marketed combination of Ipratropium bromide and Levosalbutamol were the most commonly prescribed COPD treatments, this is as per the study of Avinash Teli et al., Unni A et al., Veetil S et al. Inhaled corticosteroids improve lung function and decrease exacerbation frequency. Montelukast + Levocetirizine, Cefoperazone + Sulbactam, Hydrocortisone, and other medications were prescribed. Inhaled corticosteroids (87%) are preferable over systemic corticosteroids (44.6%), this is in accordance with the findings of previous studies by Vikneswari et al. and Shiv kumar et al., because systemic side effects

can be reduced when using inhaled corticosteroids. Systemic steroids and antibiotics, as indicated by GOLD recommendations, can speed up recovery, improve lung function and arterial hypoxemia, and lower the chance of relapse, treatment failure and length of hospital stay.. Among bronchodilators beta 2 agonist such as Levosalbutamol and anticholinergic drugs like Ipratropium bromide was commonly used this was similar to the study of Sawant MP *et al.* As per GOLD guidelines, inhalation route is preferred and drugs such as beta 2 agonist and anticholinergics can be used. Among antibiotics Cefoperazone + Sulbactam was most commonly prescribed drug.

Antibiotics and bronchodilators were commonly prescribed in the form of combination therapy this is in accordance with study of Sawant MP *et al.* Combination therapy has the potential to increase patient compliance. The majority of patients in our study were given multi-drug therapy, which could be justified because it is required to control acute exacerbation symptoms, avoid recurrence, enhance patient lung function, and expedite recovery.

As per our study data an average number of drugs prescribed were 5.18 per patient, but it is higher than the WHO norms and previous similar study Shinde et al., which states that average drugs per prescription should be 2-3 drugs. This is an important index for identifying polypharmacy practice in healthcare sector. Polypharmacy has negative implications such as increased health-care costs, adverse drug events, drug interactions, and prescription non-adherence, and it should be limited to the bare minimum. Our study showed that most of the drugs were prescribed by brand name and less was prescribed by generic name (5.4%) which deviates from the WHO standard value, this result is similar to the study of Kothai *et al.*, prescribing drugs with brand names increases cost of therapy. Prescribing drugs with generic name reduces confusion relating to drug names, cost and stock items.

The majority of the patients were admitted for treatment of a COPD exacerbation. The majority of exacerbations are caused by infections of the respiratory tract.. Antibiotics were most commonly prescribed drugs, about 85.6 % of study group patients were prescribed with antibiotics and it is similar to the results of previous studies in India by Unni A et al., and Veetil S et al., A high percentage of antibiotic prescriptions would contribute to a rise in the prevalence of pathogenic organism resistance strains. Most commonly used antibiotics ere Cefoperazone + Sulbatcam.

These findings are in accordance with GOLD guidelines according to which Antibiotics may be necessary in the management of infective exacerbation COPD patients who have an elevated incidence of increasing dyspnea, sputum volume, and sputum purulence.

Dosage prescribed in injection form were 87.6. The usage of a large volume of injectables could be due to patient and physician views and attitudes about injections' superior efficacy as compared to oral therapy. The disadvantage is that injections are quite expensive and must be administered by trained individuals.

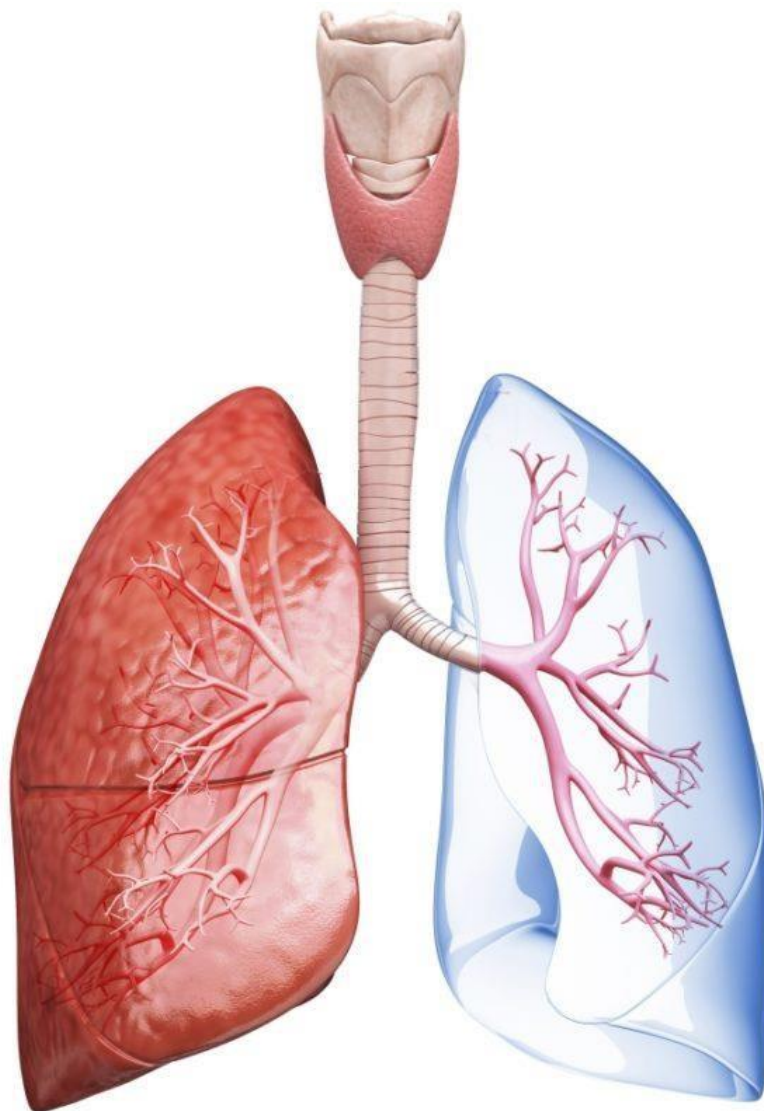
The percentage of medications prescribed from the WHO EDL was 49.4%. Physicians should be encouraged to prescribe more EDL pharmaceuticals because these medicines are chosen with consideration for public relevance, efficacy and safety evidence, and comparative cost effectiveness.

Drug- drug interactions can lead to alteration of therapeutic response or increase untoward effects of many drugs. Special attention and thorough monitoring is definitely required for the patients who are at the most risk of developing potential drug-drug interactions. Among 135 drug-drug interactions, PD interactions were dominant over PK which is different from the study conducted by S Priya Rajam Vivean et al. The severity assessment of DDIs showed that most of the interactions were moderate (86.6%) this is similar to the study of Dambro and Kallgren ,1988.

The drug-drug interactions are classified as mild, moderate and severe according to their severity and undesirable effects. Mild drug-drug interactions limit the clinical effects. The manifestations include an increase in the frequency or the severity of the adverse effects, but these usually do not require a change in the therapy. Moderate drug-drug interactions may result in exacerbation of the disease of the patient and/or a change in the therapy. The severe drug-drug interactions are life threatening and/or they require medical treatment or an intervention to minimize or to prevent the severe adverse effects. Drug-Drug interactions cause 4.8% of the hospitalizations in the elderly [5]. They are attributed to polypharmacy, non-compliance of the patients, and deterioration because of illnesses or secondary infections. An increased number of drugs enhances the risk of the potential drug- drug interaction. An awareness on the most prevalent potential DDIs can help the practitioners in preventing the concomitant use of these dangerous medication combinations. The average number of drugs which were prescribed in this study was 5.18 per patient, which was similar

to the study which was conducted in Mexico, in family medicine clinics in ambulatory patients, which was 5.9 per patient. Our results showed that maximum percentage of major interaction found between age group of 66-73 which not in accordance with the study of Shahabuddin soherwadi et al. This may probably be due to polypharmacy, but in our study, all the patients were inpatients and they were thereby on polypharmacy. So, in our study, it was not the age but the number of the drugs which were prescribed, that determined the incidence of the drug interactions. No influence of gender on the incidence of the drug interactions was observed. Our study found that average number of DDIs per patient increased as the number of drugs in prescription increased this in accordance with the study of Vijay Kulkarni et al. The most common moderate interaction in our study was between budesonide and clarithromycin, levosalbutamol and furosemide. As per the study of D M Newnham et al, the interaction between levosalbutamol and furosemide may cause hypokalemic effect which should be monitored during concomitant use. As per the study of Raaska k et al, the concomitant use of budesonide and clarithromycin may lead to increased corticosteroid effects, so consider alternative to this combination whenever possible. The drug drug interaction between theophylline and levosalbutamol was found in less number of patients which is not in accordance with the study of Dr. R Kothai et al. The most common major interaction was found between ipratropium and levosulpiride. This concomitant use should be avoided to prevent the decreased therapeutic effect of levosulpiride. The best way to identify and treat drug interactions is the use of computer programs like Lexicomp software. Detection and reporting of Drug-drug interactions should be done by all health professionals to ensure patient's safety.

LIMITATION

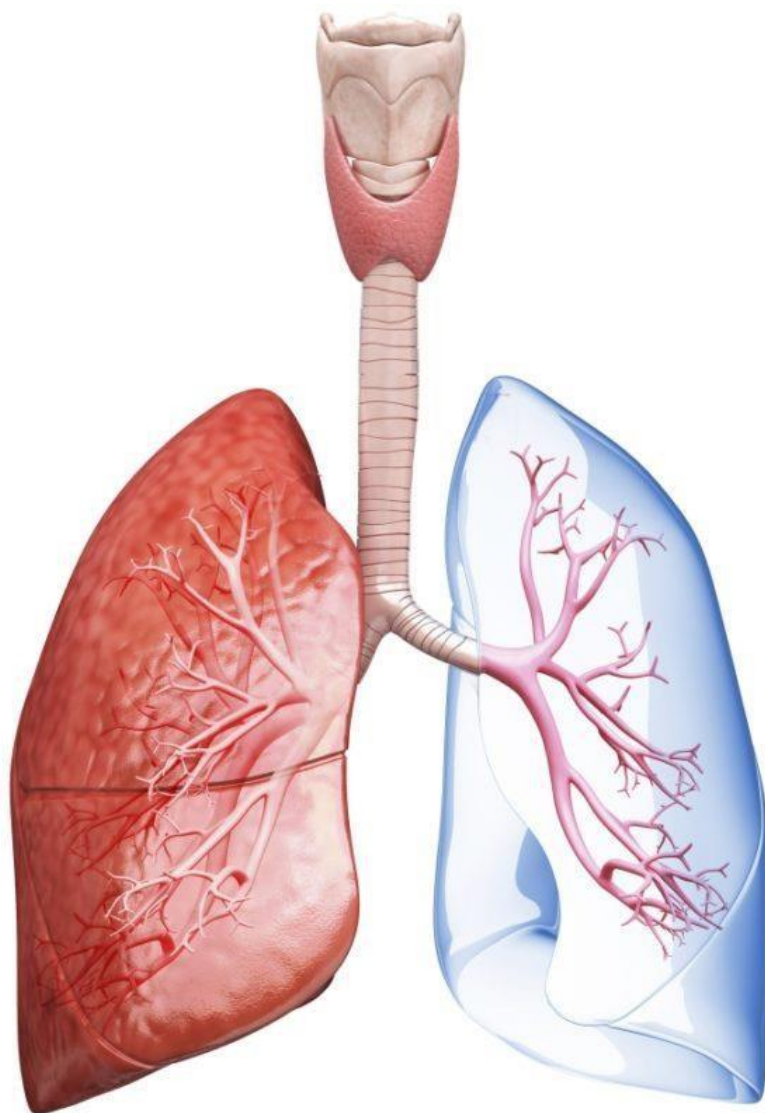


8. LIMITATIONS

The main limitation of the study was that, thejhio0 data was collected retrospectively. However, the present study provides a representative data of drug utilization likely to be encountered in hospitalized COPD patients.

Another limitation was the incomplete information on the medication prescribed and the evaluation of potential DDIs with software, which provides only a general estimate of clinical significance. Based on previous research, this is the most frequently used software and provides information with the highest sensitivity, although it detects potential DDIs that may not be of high clinical significance. All DDIs should therefore be interpreted individually; from available data. The DDIs are also influenced by daily doses and patient characteristics (e.g. renal function, blood pressure, heart rate, etc), and we controlled for this only partially.

CONCLUSION

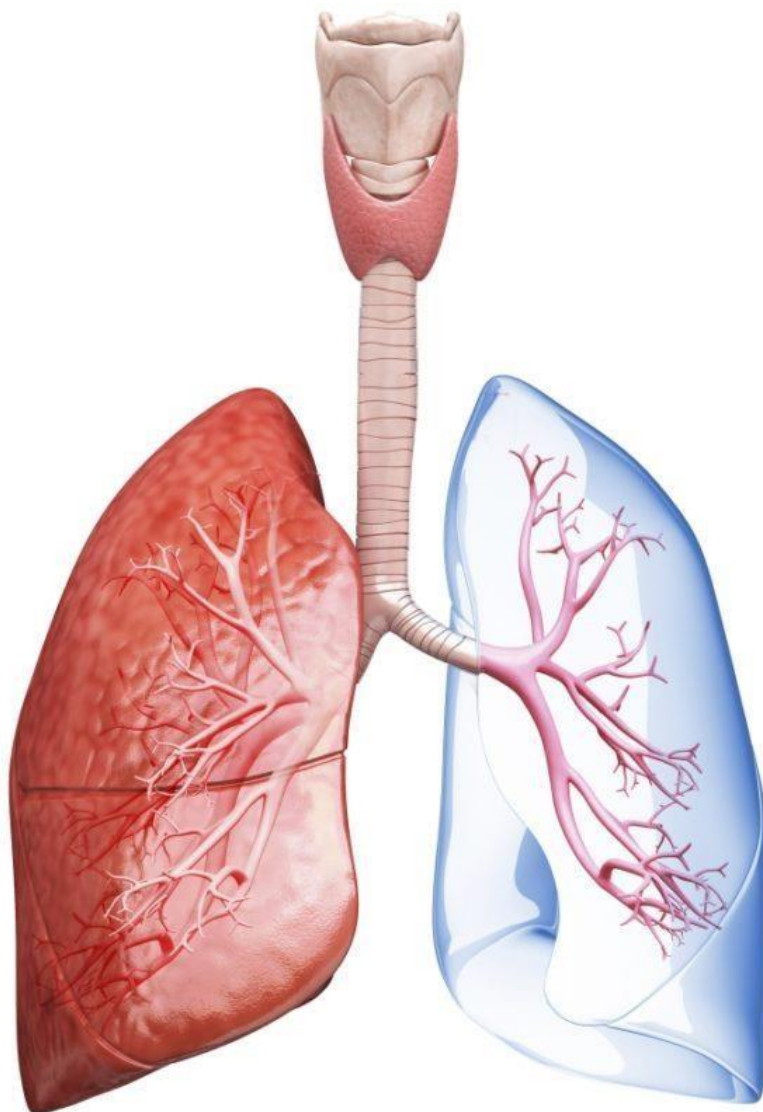


9. CONCLUSION

This study put forth the common interactions which we come across in tertiary care hospital. A thorough knowledge of these can decrease incidence of DDIs, particularly during A review of COPD related inpatient admissions found that the majority of patients received the primary recommended treatment for acute exacerbation of COPD. According to the findings of our study, we can conclude that prescribing patterns did not follow WHO core prescribing indicators with polypharmacy being common, the concept of generic name prescribing was negligible and reduced prescription from WHO-EDL, the prescription of antibiotic and injection was not under normal limits. It is therefore crucial to understand about the drug use, the importance of prescribing drugs with generic names, and the safety of prescribing drugs from both an EDL and a patient perspective.

prescription of multiple medications. The majority of possible medication interactions were PD in nature, according to the current analysis. Our study helped in understanding about most prone age groups that can cause DDIs in inpatient prescription. Hence, periodic prescription auditing is essential for promoting rational drug usage, improving therapeutic efficacy, cost effectiveness, and decreasing drug interactions. Before prescribing medicines, using computer-assisted drug interaction software can help us discover these potential drug- drug interactions, which can assist us to detect and prevent DI. As a result, pharmacist involvement can improve the management of hospitalised patients while also promoting drug safety.

BIBLIOGRAPHY



10. BIBLIOGRAPHY

1. World Health Organisation. - Chronic obstructive pulmonary disease (COPD) (who.int)
 2. Aswathy U, Akshaya Kj, Yadukrishnan M, Uma Devi P. Drug Utilization Pattern In Chronic Obstructive Pulmonary Disease Inpatients At A Tertiary Care Hospital.
 3. Lee D, Bergman U. Studies of drug utilization. In: Strom BL. editor. Pharmacoeconomics. 4th ed. John Wiley and Sons; 2005. p. 401.
 4. Vivekan S, Rajam P, Kumar MA, Shanmugasundaram P. Prospective Study On Drug- Drug Interactions Of Narrow Therapeutic Index Drugs. International Journal Of Pharmaceutical Sciences And Research. 2017 Dec 1;8(12):5303-7.
 5. Bjerrum L, Lopez-Valcárcel BG and Petersen G: Risk factors for potential drug interactions in General practice. Eur J Gen Pract 2008; 14: 23-9
 6. Tatro DS. Drug Interaction Facts: The Authority on Drug Interactions, Facts and Comparisons. St. Louis. 2006.
 7. Roblek T, Trobec K, Lainč M. Drug-drug interactions in hospitalized patients with chronic obstructive pulmonary disease. 2012 40: P2159
 8. Moura CS, Prado NM, Belo NO, Acurcio FA. Evaluation of drug–drug interaction screening software combined with pharmacist intervention. International journal of clinical pharmacy. 2012 Aug 1;34(4):547-52
 9. Lee J, Jung HM, Kim SK, Yoo KH, Jung KS, Lee SH, Rhee CK. Factors associated with chronic obstructive pulmonary disease exacerbation, based on big data analysis. Scientific reports. 2019 Apr 30;9(1):1-8
 10. Roy MP. Socio-demographic factors of COPD mortality in India. Clinical Epidemiology and Global Health. 2020 Sep 1;8(3):939-42.
 11. Teli A. A Study of Drug Utilization and Prescribing Patterns of Drugs in Chronic Obstructive Pulmonary Diseased Patients (IPD and OPD) in Tertiary Care Hospital. Acta Scientific Pharmacology. 2020;1:01-9.
 12. Brashier BB, Kodgule R. Risk factors and pathophysiology of chronic obstructive pulmonary disease (COPD). J Assoc Physicians India. 2012 Feb 1;60(Suppl):17-21
 13. McGuinness AJ, Sapey E. Oxidative stress in COPD: sources, markers, and potential mechanisms. Journal of clinical medicine. 2017 Feb;6(2):21.
 14. DiPiro JT, Talbert RL, Yee GC, Matzke GR, Wells BG, Posey L. eds. Pharmacotherapy: A Pathophysiologic Approach. 10e. United States: McGraw Hill; 2017. Chapter 27, Chronic obstructive pulmonary disease; p.1252-1309
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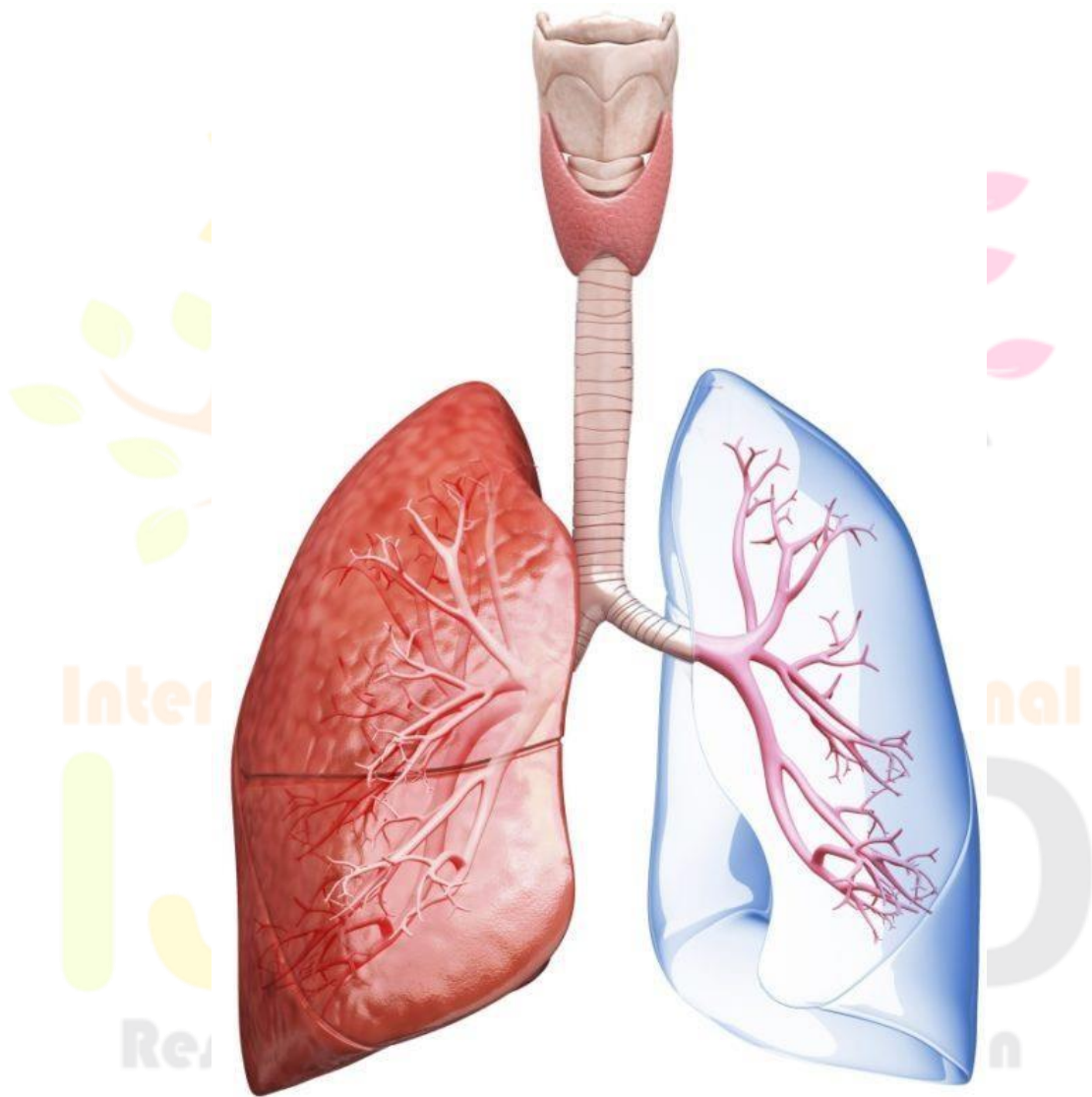
15. Roblek T, Trobec K, LainÅ M. Drug-drug interactions in hospitalized patients with chronic obstructive pulmonary disease. 2012 40: P2159
16. Truitt T, Witko J, Halpern M. Levalbuterol compared to racemic albuterol: efficacy and outcomes in patients hospitalized with COPD or asthma. Chest. 2003 Jan 1;123(1):128-35
17. Sestini P, Renzoni E, Robinson S, Poole P, Ram FS. Short-acting beta2-agonists for stable chronic obstructive pulmonary disease. Cochrane Database of Systematic Reviews. 2002(3)
18. Gross NJ. Anticholinergic agents in asthma and COPD. European journal of pharmacology. 2006 Mar 8;533(1-3):36-9
19. COMBIVENT Inhalation Aerosol Study Group. In chronic obstructive pulmonary disease, a combination of ipratropium and albuterol is more effective than either agent alone: an 85-day multicenter trial. Chest. 1994 May 1;105(5):1411-9
20. Ejiofor S, Turner AM. Pharmacotherapies for COPD. Clinical Medicine Insights: Circulatory, Respiratory and Pulmonary Medicine. 2013 Jan;7:CCRPM-S7211.
21. Cheyne L, Irvin-Sellers MJ, White J. Tiotropium versus ipratropium bromide for chronic obstructive pulmonary disease. Cochrane Database of Systematic Reviews. 2015(9).
22. Jung KS, Park HY, Park SY, Kim SK, Kim YK, Shim JJ, Moon HS, Lee KH, Yoo JH, Do Lee S. Comparison of tiotropium plus fluticasone propionate/salmeterol with tiotropium in COPD: a randomized controlled study. Respiratory medicine. 2012 Mar 1;106(3):382-9
23. ZuWallack R, De Salvo MC, Kaelin T, Bateman ED, Park CS, Abrahams R, Fakhri F, Sachs P, Pudi K, Zhao Y, Wood CC. Efficacy and safety of ipratropium bromide/albuterol delivered via Respimat® inhaler versus MDI. Respiratory medicine. 2010 Aug 1;104(8):1179-88.
24. Veetil SK, Kingston Rajiah SK. Study of drug utilization pattern for acute exacerbation of chronic obstructive pulmonary disease in patients attending a government hospital in Kerala, India. Journal of family medicine and primary care. 2014 Jul;3(3):250
25. Mahler DA. The role of theophylline in the treatment of dyspnea in COPD. Chest. 1987 Jul 1;92(1):2S-6S.
26. Barnes PJ. Inhaled corticosteroids in COPD: a controversy. Respiration. 2010;80(2):89-95.
27. Calverley PM, Rabe KF, Goehring UM, Kristiansen S, Fabbri LM, Martinez FJ. Roflumilast in symptomatic chronic obstructive pulmonary disease: two randomised clinical trials. The Lancet. 2009 Aug 29;374(9691):685-94.

- 28.** Crisafulli E, Barbeta E, Ielpo A, Torres A. Management of severe acute exacerbations of COPD: an updated narrative review. *Multidisciplinary respiratory medicine*. 2018Dec;13(1):1-5.
- 29.** Ram FS, Rodriguez-Roisin R, Granados-Navarrete A, Garcia-Aymerich J, Barnes NC. Antibiotics for exacerbations of chronic obstructive pulmonary disease. *Cochrane Database of Systematic Reviews*. 2006(2).
- 30.** Walters JA, Tan DJ, White CJ, Gibson PG, Wood-Baker R, Walters EH. Systemic corticosteroids for acute exacerbations of chronic obstructive pulmonary disease. *Cochrane Database of Systematic Reviews*. 2014(9). 16.
- 31.** Salpeter SR. Bronchodilators in COPD: impact of β -agonists and anticholinergics on severe exacerbations and mortality. *International journal of chronic obstructive pulmonary disease*. 2007 Mar;2(1):11.
- 32.** Lim KP, Loughrey S, Musk M, Lavender M, Wrobel JP. Beta-blocker under-use in COPD patients. *International journal of chronic obstructive pulmonary disease*. 2017;12:3041.
- 33.** Campo G, Pavasini R, Malagu M, Mascetti S, Biscaglia S, Ceconi C, Papi A, Contoli M. Chronic obstructive pulmonary disease and ischemic heart disease comorbidity: overview of mechanisms and clinical management. *Cardiovascular drugs and therapy*. 2015Apr 1;29(2):147- 57.
- 34.** de Lucas-Ramos P, Izquierdo-Alonso JL, Moro JM, Frances JF, Lozano PV, Bellón- Cano JM, CONSISTE Study Group. Chronic obstructive pulmonary disease as a cardiovascular risk factor. Results of a case-control study (CONSISTE study). *International journal of chronic obstructive pulmonary disease*. 2012;7:679.
- 35.** de-Torres JP, Wilson DO, Sanchez-Salcedo P, Weissfeld JL, Berto J, Campo A, Alcaide AB, García-Granero M, Celli BR, Zulueta JJ. Lung cancer in patients with chronic obstructive pulmonary disease. Development and validation of the COPD Lung Cancer Screening Score. *American journal of respiratory and critical care medicine*. 2015 Feb 1;191(3):285-91.
- 36.** Biskobing DM. COPD and osteoporosis. *Chest*. 2002 Feb 1;121(2):609-20.
- 37.** Janssen DJ, Spruit MA, Leue C, Gijzen C, Hameleers H, Schols JM, Wouters EF, Ciro network. Symptoms of anxiety and depression in COPD patients entering pulmonary rehabilitation. *Chronic respiratory disease*. 2010 Aug;7(3):147-57.
- 38.** Rogliani P, Calzetta L, Segreti A, Barrile A, Cazzola M. Diabetes mellitus among outpatients with COPD attending a university hospital. *Acta Diabetologica*. 2014 Dec 1;51(6):933-40.

39. Su VY, Liao HF, Perng DW, Chou YC, Hsu CC, Chou CL, Chang YL, Yen JC, Chen TJ, Chou TC. Proton pump inhibitors use is associated with a lower risk of acute exacerbation and mortality in patients with coexistent COPD and GERD. *International Journal of Chronic Obstructive Pulmonary Disease*. 2018;13:2907.
40. Martinez-Garcia MA, Miravittles M. Bronchiectasis in COPD patients: more than a comorbidity?. *International journal of chronic obstructive pulmonary disease*. 2017;12:1401.
41. Zamarrón C, Paz VG, Morete E, del Campo Matías F. Association of chronic obstructive pulmonary disease and obstructive sleep apnea consequences. *International journal of chronic obstructive pulmonary disease*. 2008 Dec;3(4):671.
42. Aswathy U, Akshaya KJ, Yadukrishnan M, Uma Devi P. Drug Utilization Pattern In Chronic Obstructive Pulmonary Disease Inpatients At A Tertiary Care Hospital.
43. Veettil SK, Kingston Rajiah SK. Study of drug utilization pattern for acute exacerbation of chronic obstructive pulmonary disease in patients attending a government hospital in Kerala, India. *Journal of Family Medicine and Primary Care*. 2014 Jul;3(3):250.
44. Sawant PM, Padwal LS, Kale SA, Pise NH, Shinde MR. Study of drug prescription pattern among COPD patients admitted to medicine in-patient department of tertiary care hospital. *IJBCP*. 2017 Sep;6(9):2228-32.
45. Kothai DR, Rangabashayan D, Arul DB, Sunny PM, Nair RR, Mathew RE. Analysis of prescribing pattern of COPD patients in a tertiary care hospital Salem. *World Journal Of Pharmacy And Pharmaceutical Sciences*. 2017(6):10.
46. Raaska K, Niemi M, Neuvonen M, Neuvonen PJ, Kivistö KT. Plasma concentrations of inhaled budesonide and its effects on plasma cortisol are increased by the cytochrome P4503A4 inhibitor itraconazole. *Clinical Pharmacology & Therapeutics*. 2002 Oct;72(4):362-9
47. Soherwardi S, Chogtu B, Faizal P. Surveillance of the Potential Drug-Drug Interactions in the Medicine Department of a Tertiary Care Hospital. *Journal of Clinical & Diagnostic Research*. 2012 Sep 1;6(7).
48. Kulkarni V, Bora SS, Sirisha S, Saji M, Sundaran S. A study on drug-drug interactions through prescription analysis in a South Indian teaching hospital. *Therapeutic advances in drug safety*. 2013 Aug;4(4):141-6.
49. Veettil SK, Kingston Rajiah SK. Study of drug utilization pattern for acute exacerbation of chronic obstructive pulmonary disease in patients attending a government hospital in Kerala, India. *Journal of Family Medicine and Primary Care*. 2014 Jul;3(3):250.





- 50.** Roblek T, Trobec K, Mrhar A, Lainscak M. Potential drug-drug interactions in hospitalized patients with chronic heart failure and chronic obstructive pulmonary disease. Archives of Medical Science: AMS. 2014 Oct 27;10(5):920.
- 51.** Unni A, Jayaprakash AK, Mc Y. Drug utilization pattern in chronic obstructive pulmonary disease inpatients at a tertiary care hospital. International Journal of Pharmacy and Pharmaceutical Sciences. 2015 Nov 1:389-91.
- 52.** Barrecheguren M, Monteagudo M, Ferrer J, Borrell E, Llor C, Esquinas C, Miravittles M. Treatment patterns in COPD patients newly diagnosed in primary care. A population- based study. Respiratory Medicine. 2016 Feb 1;111:47-53.
- 53.** Kyriakos Souliotis, Chara Kani, Manto Papageorgiou, Dimitrios Lionis, Konstantinos Gourgoulialis. Using Big Data to Assess Prescribing Patterns in Greece: The Case of Chronic Obstructive Pulmonary Disease. Plos one.2016 May 8; 11(5);1-10
- 54.** Kothai DR, Rangabashayan D, Arul DB, Sunny PM, Nair RR, Mathew RE. Analysis of prescribing pattern of COPD patients in a tertiary care hospital Salem. World Journal Of Pharmacy And Pharmaceutical Sciences. 2017(6):10.
- 55.** Sawant PM, Padwal LS, Kale SA, Pise NH, Shinde MR. Study of drug prescription pattern among COPD patients admitted to medicine in-patient department of tertiary care hospital. IJBCP. 2017 Sep;6(9):2228-32.
- 56.** S. Priya Rajam Vivean, M. Ashok Kumar And P. Shanmugasundaram.Prospective Study On Drug-Drug Interactions Of Narrow Therapeutic Index Drugs.International Journal Of Pharmaceutical Sciences And Research. 2017 Dec 01;8(12):5303-5307.
- 57.** Amin AN, Bollu V, Stensland MD, Netzer L, Ganapathy V. Treatment patterns for patients hospitalized with chronic obstructive pulmonary disease. The Bulletin of the American Society of Hospital Pharmacists. 2018 Mar 15;75(6):359-66.
- 58.** Kumar S, Madhuri G, Wilson A, George TS, Saini K, Singh R, Agrawal D, Johnson P, Lavanya S, Abraham J, Kishore G. Study of prescribing pattern of drugs in chronic obstructive pulmonary disease in tertiary care teaching hospital. Indian Journal of Pharmacy Practice. 2019 Jul;12(3):161.
- 59.** Avinash Teli, Arvind Kumar, Akshi Denod, Azaz Ahmad and Parminder Nain. A Study of Drug Utilization and Prescribing Patterns of Drugs in Chronic Obstructive Pulmonary Diseased Patients (IPD and OPD) in Tertiary Care Hospital. Acta Scientific Pharmacology. 2020 March 3;1(3):04-12
- 60.** Jyothi DB, Prasad SV, Vangoori Y, Bharatha A. A prospective study on prescription pattern in chronic obstructive pulmonary disease. Maedica. 2020 Mar;15(1):37.
- 61.** Poonam Salwan1*, Juhi Singla2 , Shalini Salwan .Prescription pattern in the management of chronic obstructive pulmonary disease patients in a tertiary hospital: an observational study International.Journal of Basic & Clinical Pharmacology 2020 Oct;9(10):1578-1582

ANNEXURES



ANNEXURES

ANNEXURE 1: ETHICAL COMMITTEE APPROVAL LETTER

	Dayananda Sagar University <small>Established in 1984</small>	Shuviga Malleshwara Hills, Kumaraswamy Layout, Bangalore - 560 078, Karnataka, India. Tel : +91-80-26662226 42201997, 42113666. Fax : 080-42201997, 080 26660709 www.dsu.edu.in
COLLEGE OF PHARMACEUTICAL SCIENCES		
Ref.: DSUP-D/IEHC/2021-22/0019		Date: 12.11.2021
INSTITUTIONAL HUMAN ETHICAL CLEARANCE FOR DISSERTATION STUDY		
<p>Institutional Human Ethical meeting was held on 12/11/2021 at Conference Hall, Sagar Hospitals, Banashankari, Bengaluru.</p> <p>Members of the committee discussed on all the ethical issues concerned with the opinion of the members and ethical clearance was granted for the project titled "A Study on Drug Utilization Pattern and Possible Drug-Drug Interactions Among Patients with COPD in a Tertiary Care Hospital " submitted by Ms. Archa S Kumar (USN No.HSC17PD0002), Mr. Kabilan R. (USN No.HSC17PD0010), Ms. Prithvika Wagle (USN No.HSC17PD0022) and Mr. Dheeraj Kumar Bhakat (USN No. HSC 17PD0004) for the academic year 2021 – 2022 under the guidance of Mr. Ramakrishna Prudhivi, Assistant Professor, Department of Pharmacy Practice, College of Pharmaceutical Sciences, Dayananda Sagar University, Bengaluru. and co- guidance of Dr Vishwajith S.M., Consultant Pulmonologist, Sagar Hospitals, Banashankari, Bangalore.</p>		
 Dr. Venkatesh Vikram H. C. Chairman	 Dr. Madhumita Das Clinician	 Dr. V. Murugan Principal

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ANNEXURE II: DATA COLLECTION FORM



PATIENT DATA COLLECTION FORM

PATIENT DEMOGRAPHIC DETAILS:

Name:			DOA:
			DOD:
Age:	Sex: M/F	UHID:	Unit/Ward:
Occupation:		IP/OP no:	Department:
			Consultant:
			Health Insurance:
Phone No:			
Height(cm):	Weight(kg)	BMI:	
History of Allergies: Y/N if yes please specify:			

SOCIAL HABITS:

Alcoholic: Yes/No

Smoker: Yes/No

Substance use: Yes/No

Duration:

Duration:

Duration:

PAST MEDICAL HISTORY:

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PAST MEDICATION HISTORY

S.No	Generic name	Dose	Freq:	Duration of use

PROVISIONAL DIAGNOSIS:

.....

LABORATORY PARAMETERS (IFANY)

Test								Reference range

CONFIRMATORY DIAGNOSIS:

.....



DRUG TREATMENT CHART:

S.No	Brand name	Generic name	Dose	Freq:	Route	Duration



DRUG INTERACTIONS

S.No	Drug interactions		Type of interaction	Mechanism involved	Management	Severity
	Drug A	Drug B				



ANNEXURE III – WHO INDICATORS

S. No	INDICATORS	STANDARD VALUE
	Average number of drugs per prescription.	1.6-1.8
	Percentage of encounters with an antibiotic prescribed.	0.0-26.8
	Percentage of encounters with injection prescribed.	3.4-24.1
	Percentage of drugs prescribed by generic name.	100.0
	Percentage of drugs prescribed from the essential drug list/formulary.	100.0

