

Profile of Potential Drug Interactions in Chronic Obstructive Pulmonary Disease Patients in One of the Jember District Hospitals

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Background: Chronic Obstructive Pulmonary Disease or often abbreviated as COPD is a term used for a number of non-communicable diseases that affect the lungs for the long term. COPD is the third leading cause of death in the world. The use of drugs in COPD patients with or without comorbidities is included in the category of drug use with more than two drug items, resulting in one of the DRPs, one of which is drug interaction. The prevalence of patients with potential drug interactions in Ethiopian hospitals was found to be 72.2%. The number of COPD cases is projected to increase by 112 million to a total of 592 million by 2050 (9.5% of the total eligible population), a relative increase of 23.3% from 2020 to 2050. **Purpose:** The purpose of this study was to determine the study of drug interactions in patients with Chronic Obstructive Pulmonary Disease at the Jember Pulmonary Hospital. **Methods:** This type of research is qualitative research using the observation method, retrospective data collection taken from medical record data of COPD patients. The number of samples in this study was 96 patients calculated using the Slovin formula. The sampling technique used was random sampling technique. Data were processed using Microsoft Excel and displayed in the form of frequencies and percentages. **Conclusion:** Potential drug interactions in COPD patients that occurred in one of the Jember Regency hospitals amounted to 97.92% using drug interaction checker with details of minor interaction categories 26,48%, moderate 68,80% and major 4,72%. Monitoring the occurrence of potential drug interactions is carried out in order to minimize the risk of drug side effects. Complaints of potential interactions in patients do not occur which can be seen from clinical manifestations in patients. The limitation of this study is that it does not know the patient's complaints directly because it only uses medical record data.

Keywords: Chronic obstructive pulmonary disease; Drug interactions; Hospitals; Drug interaction checker.

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1. Introduction

Chronic Obstructive Pulmonary Disease (COPD) is a type of non-communicable disease related to the respiratory tract. This disease causes the respiratory tract to narrow, leading to shortness of breath and a decrease in the amount of oxygen in the body. By 2030, the World Health Organization (WHO) estimates that COPD will be the third leading cause of death worldwide. COPD has a greater impact in Asia than in Western countries (1)

Globally, the prevalence of COPD recorded in 2020, in both men and women, is estimated to reach 10.6%, which translates to 480 million cases. The number of COPD cases is projected to increase by 112 million, reaching a total of 592 million by 2050 (9.5% of the total eligible population), a relative increase of 23.3% from 2020 to 2050 (2).

Preliminary studies conducted at the pulmonary clinic of a hospital in Jember Regency found that COPD ranked second as the most common case in the 2024 period, with 2,223 cases at a hospital in Jember Regency. The researchers chose to conduct the study at a hospital in Jember Regency because research on

the potential for drug interactions in patients with chronic obstructive pulmonary disease had not been conducted previously. In addition, the hospital in Jember Regency specializes in pulmonary rehabilitation.

The symptoms and signs of COPD range from mild to severe. On physical examination, no abnormalities were found, although clear abnormalities and signs of inflammation were detected. Symptoms and signs of COPD include progressive shortness of breath that worsens over time, chronic cough that comes and goes and may not produce phlegm, and chronic cough with phlegm (3)

The impact of COPD if left uncontrolled is that it can trigger or worsen various diseases and other serious complications, both related to the respiratory system and other organs. Some of the diseases and conditions that can develop or worsen due to poorly managed COPD include pneumonia, heart failure, emphysema, chronic bronchitis, respiratory failure, asthma, metabolic disorders/diabetes, depression (anxiety disorders), lung cancer, and lower circulatory diseases

COPD can be treated with non-invasive therapies such as education and self-management, pulmonary rehabilitation, breathing exercises, psychosocial support, discontinuation of oxygen therapy, nutritional therapy, influenza vaccination, pneumococcal vaccination, mechanical respiratory support, non-invasive mechanical ventilation, and invasive mechanical ventilation with intubation. In addition, COPD can be treated with pharmacological therapies such as the use of bronchodilators, beta-2 agonists, anticholinergics, bronchodilator combinations, anti-inflammatory drugs, LABA and inhaled corticosteroid combinations, systemic corticosteroids, phosphodiesterase-4 inhibitors, mucolytics, and antioxidants (4).

Pharmacists play an important role in patient treatment. Research conducted by Li et al (2021) has shown that the involvement of a pharmacist (5) in COPD management not only helps patients gain better knowledge about the disease, overcome medication-related problems, improve disease control and treatment effectiveness, and reduce treatment costs, but also demonstrates the benefits of pharmaceutical care for COPD patients (6).

According to Saftarina's research, chronic diseases cannot be cured and require ongoing cooperation between patients, families, and health workers to prevent worsening and complications. Explain to patients that COPD cannot be cured but only controlled/prevented to prevent it from occurring and that treatment is lifelong. This research is expected to serve as a source of information for the public so that they can prevent COPD or control it before the worst happens. (7).

Based on research conducted by Ayenew from the included studies, approximately 8717 potential drug interactions were found in 3259 people out of 5761 COPD patients. The prevalence of patients with potential drug interactions in Ethiopian hospitals was found to be 72.2%. Based on severity, the prevalence of major, moderate, and minor potential drug interactions was 25.1%, 52.8%, and 16.9%, respectively (8).

Based on the background description above, the researcher was interested in conducting research related to drug interactions in COPD patients at a hospital in Jember Regency. This study was conducted to determine the potential for drug interactions at a hospital in Jember Regency in COPD patients in 2024.

2. Method

This study was conducted in January 2025 in the Medical Records department of a hospital in Jember Regency. This type of research is descriptive, which means that it describes events, symptoms, and incidents to reach conclusions. This study was conducted retrospectively by collecting data from the medical records of patients at a hospital in Jember Regency. The population in this study were COPD patients at a hospital in Jember Regency in 2024 who met the inclusion and exclusion criteria. The research

sample was the medical records of COPD patients. Sampling was done using random sampling with the Slovin formula. The sample size in this study was 96 patients.

Data were collected retrospectively and analyzed using univariate analysis or descriptive analysis that took into account patient characteristics consisting of age and gender. The data were then processed by describing the potential for drug interactions in patients with chronic obstructive pulmonary disease in terms of frequency and presented as a percentage.

The research instrument used in data collection was a data recapitulation sheet. The procedure for collecting patient medical records was 2223 in accordance with the population and medical records that met the inclusion criteria of 96 medical record data samples. The medical records were observed/examined in terms of patient identity (age, gender, and diagnosis), then the drugs used by the patients were studied. Next, the drugs used by these patients were entered into a drug interaction checker in the form of the drugs.com application to see if there were any drug interactions if there were interactions drugs, these interactions are grouped according to their clinical significance into minor, moderate, or major categories. The analysis in this study used univariate analysis, with data presented in the form of frequencies and percentages. Data processing was performed using Microsoft Excel. The use of Microsoft Excel as an analysis tool facilitates rapid and efficient data visualization and interpretation (9).

3. Results and Discussion

The study entitled “Assessment of Drug Interaction Potential in Patients with Chronic Obstructive Pulmonary Disease at a Hospital in Jember Regency” aims to identify drug interactions that occur in patients with COPD. This study was conducted in January 2025 at a hospital in Jember Regency. The sample in this study consisted of medical records of patients with Chronic Obstructive Pulmonary Disease at a hospital in Jember Regency during the 2024 period. This study obtained ethical approval with No. 592/KEPK/UDS/XII/2024. The number of COPD patients based on gender and age can be seen in Table 1.

Table 1. Number of COPD Patients by Gender and Age

No.	Characteristics	Amount	Percentage
1	Gender		
	Male	81	84,38
	Female	15	15,63
2	Age		
	17-29	0	0,00
	30-39	3	3,13
	40-49	8	8,33
	>50	85	88,54
	Total	96	100,00

The results of the study show that patients diagnosed with COPD at a hospital in Jember Regency in 2024 consisted of 81 male patients (84.38%) and 15 female patients (15.63%). Smoking habits are a major cause because there are more male smokers than female smokers. This is in line with the 2010 Riskesdas results, which stated that the prevalence of smokers was 16 times higher in men than in women. The 2007 Riskesdas results also stated that the prevalence of smoking in men was higher than in women. Research conducted in five developing countries where tobacco is consumed shows that the main predictor of current tobacco consumption is the male population. This occurs because there are factors that cause this behavior in individuals, namely the social stigma in Indonesian, Malaysian, and Nigerian societies that smoking is considered normal in social life (10). Burning cigarette smoke can irritate the bronchioles and

trigger permanent changes in the glands that produce mucus, which can cause excessive mucus secretion. Smoking can also cause inflammation of the respiratory organs and damage to the alveolar walls, which worsens emphysema (11).

The results of the group distribution study show that the age group with the highest percentage is the >50 age group, with a percentage of 88.54%. Age is closely related to an increase in COPD, which occurs after the age of 30, indicating that age is related to the aging process, whereby the older a person is, the greater the likelihood of a decline in lung capacity. The respiratory system reaches maturity around the age of 20-25 years, after which its function begins to decline from the age of 30 (12).

Table 2. Diagnosis of Comorbidities in COPD Patients

Diagnosis of concomitant diseases	Amount	Percentage
Copd	22	22,91
Copd + anemia	1	1,04
Copd + anemia + dipsnoe	1	1,04
Copd + bradycardia	1	1,04
Copd + bronkhopneumonia	3	4,02
Copd + dipsnoe	18	18,72
Copd + dipsnoe + chronic bronchitis	1	1,04
Copd + dipsnoe + acute respiratory failure	3	4,02
Copd + dipsnoe + hearth failure	3	4,02
Copd + dipsnoe + hypertension	3	4,02
Copd + dipsnoe + hypertension + pneumonia	2	2,08
Copd + dipsnoe + coronary hearth	1	1,04
Copd + dipsnoe + pneumonia	1	1,04
Copd + dipsnoe + pneumonia + tb	1	1,04
Copd + dipsnoe + tb	1	1,04
Copd + dyspepsia	1	1,04
Copd + hearth failure	4	5,06
Copd + hearth failure + hearth hypertension	2	2,08
Copd + acute respiratory failure + hearth hypertension + pneumonia	1	1,04
Copd + acute respiratory failure + pneumonia + tb	1	1,04
Copd + kidney disorders	1	1,04
Copd + lung disorders + coronary heartg + pnemothorax	1	1,04
Copd + hemoptitis	1	1,04
Copd + hypertension	2	2,08
Copd + hearth hypertension + pneumonia + tb	1	1,04
Copd + hypoglycemia + diabetes	1	1,04
Copd + pneumonia	11	12,35
Copd + pneumonia + tb	2	2,08
Copd + pneumonia + pleuritis	2	2,08
Copd + tb	2	2,08
Copd + lung disorders	1	1,04
Total	96	100,00

Comorbidity is another disorder or disease that accompanies a specific disease. Comorbidity can occur at all stages of COPD, which can increase mortality in those suffering from COPD. Based on the results of the above study, COPD is a disease accompanied by other diseases, one of which is COPD with dyspnea and

COPD with pneumonia. COPD with dyspnea was present in 18 patients (18.72%), with dyspnea being the most common symptom experienced by COPD patients. To avoid dyspnea due to activity, many patients lead a sedentary lifestyle, which can be predicted to cause widespread skeletal muscle deconditioning, social isolation, and negative psychological effects. This “dyspnea spiral” is well documented, and it is not surprising that reducing these bothersome symptoms has become a primary goal highlighted throughout COPD guidelines (12). Shortness of breath/dyspnea is the primary symptom of COPD. This shortness of breath typically occurs during physical activity and worsens with exercise, so it arises when the patient is engaging in physical exertion. The severity of COPD can be measured based on the patient's complaints of shortness of breath (13).

Next, COPD with pneumonia in 11 patients (12.35). Patients with advanced COPD are at risk of developing pneumonia. Compared to patients without COPD, patients with COPD tend to experience more severe pneumonia, an increase in the number of hospitalizations, and poorer outcomes. In the first year after COPD diagnosis, individuals have a 16 times greater risk of pneumonia compared to those without COPD. In a recent study, the incidence rate of community-acquired pneumonia was 22.4 cases per 1,000 person-years in the 10 years after COPD diagnosis, and more than 50% higher in those categorized as having severe COPD. Furthermore, the economic impact of pneumonia is greater for those with COPD, illustrated by double the direct medical costs after hospitalization for pneumonia compared to those without COPD in a study of older individuals. More recent studies evaluate the risk of pneumonia in COPD patients who also have other comorbid conditions such as cardiovascular disease (CVD)(14).

Table 3. COPD Medication Regimen

Type of therapy	Drug class	Drug name	Amount	Percentage
Single therapy	Mucolytic and antioxidant	Acetylcystein	28	6,35
		Bromheksin Hcl	9	2,04
		Bromhexine + Guaifenesin +	3	0,68
		Salbutamol		
		Erdostein		
		Megestrol Acetate	10	2,27
		Ubidecarenone	3	0,68
	corticosteroids	Budesonide	50	11,34
		Dexamethasone	5	1,13
		Methyl prednisolone	57	12,93
	anticholinergic	Atropine	1	0,23
		Tiotropium Bromide Monohydrate	1	0,23
	Methylxanthine	Aminophylline	33	7,48
		Theophylline)	39	8,84
Beta-2 agonist	Salbutamol	5	1,13	
Penicilin antibiotics	Ampicillin + Sulbactam	8	1,81	
Macrolide antibiotics	Azitromycin	4	0,91	
Chepalosporin antibiotics	Cefoperazone Sulbactam	12	2,72	
	Ceftazidim 1 Gram Injeksi	24	5,44	
Combination therapy	Combination of saba	Budesonide + Formoterol Fumarate Dihydrate)	11	2,49

Ipratropium Bromide + Albuterol Sulfate	34	7,71
Ipratropium Bromida + Salbutamol Sulfat	63	14,29
TOTAL	441	100,00

Based on the research conducted, as shown in Appendix Table 3, the most commonly used COPD medications are SABA combinations, namely ipratropium bromide and salbutamol sulfate, accounting for 63 (14.29%) cases. Although many COPD patients do not experience reversible airflow obstruction, many have reported improvement in symptoms with the use of SABA. All COPD patients are advised to obtain a prescription for short-acting inhaled bronchodilators (SABA/SAMA) with the aim of relieving acute exacerbation symptoms (15). SABA is used in both acute and chronic COPD management, with salbutamol being the most commonly used. After administration, the onset of action occurs within 3 minutes with peak activity after 2.5 hours. The duration of action is between 4 and 6 hours. Salbutamol is primarily metabolized into sulfate conjugates. Approximately 50% is excreted in this form, with a smaller proportion as unchanged drug. A recent Cochrane review showed that the use of bronchodilators for at least seven days improves lung function in patients with severe COPD. Patients also experience less dyspnea and are more likely to adhere to treatment (16). SABA can be administered via inhalation, intramuscular, or parenteral routes. However, because this drug works relatively quickly and has few side effects, administration via inhalation is more recommended. The mechanism of action of SABA is the same as other β 2 agonists, helping the airways, increasing mucociliary clearance, decreasing vascular clearance, and modulating the release of mast cell mediators from eosinophils (17).

The second group of drugs is corticosteroids, namely methylprednisolone, which accounts for 57 (12.93%). Corticosteroids are thought to reduce chronic inflammation in the bronchial tree, thereby improving obstructed airflow. Inhaled corticosteroids (ICS) in COPD are known to improve symptoms, lung function, quality of life, and reduce exacerbations. Methylprednisolone acts as an anti-inflammatory agent by stimulating the biosynthesis of lipomodulin, which inhibits the activity of the enzyme phospholipase A2, thereby preventing the release of inflammatory mediators, arachidonic acid and its metabolites, such as prostaglandins, leukotrienes, thromboxanes, and prostacyclins. Methylprednisolone is recommended in patients with acute COPD to shorten recovery time and improve lung function (18).

The third class of drugs is the mucolytic class, which contains erdostein and is used in 41 (9.30%) cases. Drugs in this class, which are generally defined as “mucolytics,” are agents that have long been used in Europe for chronic bronchitis (CB) and COPD. The mechanisms of action of mucolytics that may be beneficial in COPD include thinning or regulating mucus production, enhancing mucociliary clearance and expectoration, and antioxidant or antibacterial activity (19). Data on the treatment outcomes and efficacy of xanthine-class drugs have demonstrated significant effects when combined with inhaled corticosteroids and long-acting bronchodilators. In addition to having bronchodilator effects, it also relaxes smooth muscles, particularly bronchial muscles. Compared to placebo, the xanthine group was found to be more effective in reducing the frequency and duration of COPD exacerbations over 12 months (20).

Table 4. Drug Interactions Based on Clinical Significance Level

Category	Amount	
Minor	172	26,48%
Moderate	451	68,80%
Mayor	34	4,72%
Total	657	100.00%

Based on the results of the study shown in Table 6, which was conducted at a hospital in Jember Regency, the most common interaction was moderate interaction at 68.80%. Moderate interactions often require dose modification and increased monitoring. Despite this interaction, both drugs continue to be used together with periodic monitoring of liver enzymes (21). The most common moderate interaction is between albuterol and aminophylline, with a percentage of 3.81%. The use of aminophylline with albuterol can increase side effects such as palpitations, increased heart rate and pulse, and increased blood pressure. This combination of drugs may also increase the risk of hypokalemia, or low blood potassium levels. The inhaled Short Acting β -2 Agonist class is the first choice in the treatment of asthma exacerbations, and salbutamol is the most commonly used SABA in asthma exacerbations to treat airway obstruction. Salbutamol is the first-line treatment for asthma because it is a selective β 2 stimulant that causes relaxation of bronchial smooth muscle, which increases intracellular cyclic adenosine monophosphate (22). According to the Global Initiative for Asthma guidelines, methylxanthines are used as adjunctive therapy in the management of asthma exacerbations, with theophylline being the most commonly used. Aminophylline is widely used in Indonesia for the treatment of asthma symptoms, as it is easily available and even produced in over-the-counter form, which means its use must be under the supervision of a healthcare professional (22).

Furthermore, the interaction with the second highest percentage is minor interaction. The highest percentage of minor interactions is between methylprednisolone and budesonide, reaching 7.15%. Minor interactions are drug interactions that have clinically significant effects and should therefore be avoided in drug combinations. Furthermore, if drug combinations must still be used to achieve a therapeutic effect, close monitoring is required in case of side effects so that immediate action can be taken (23). The simultaneous use of LABAs with xanthine derivatives (aminophylline, theophylline) or steroids (prednisone, methylprednisolone) can increase the hypokalemic effects of adrenergic agonists (24).

Furthermore, major interactions accounted for the lowest percentage of interactions at 4.72%. Drug interactions that need to be considered are those at a high severity level that can cause significant clinical risks, resulting in harmful effects and requiring medical intervention. These major interactions should be a priority for prevention because they carry more risks than benefits. Therefore, major interactions can be managed by avoiding the simultaneous use of drugs (24).

Table 5. Potential Drug Interactions Based on Number of Patients

Category	Number of patient	
Potential for drug interaction	94	97,92%
No potential for drug interaction	2	2,08%
Total	96	100.00%

The results of the study showed that 97.92% of the 96 samples experienced drug interactions, while 2.08% did not. The potential for drug interactions at a hospital in Jember Regency was based on the simultaneous use of drugs. However, this study was limited to identifying the possibility of potential interactions in patients. There were no complaints of potential drug interactions in patients, as seen from the clinical manifestations in patients.

In the medical records, patient sample Mr. Xxx2, aged 84 years, who had a diagnosis of COPD, used the drugs budesma, combivent, meprovent inh, methylprednisolone inj, ondansetron inj, pantoprazole inj, pulmicort resp, and santagesik inj. The medications used by patient Mr. Xxx2 have 3 potential drug interactions, namely albuterol – ondansetron, which has a moderate interaction. Using albuterol together with ondansetron may increase the risk of irregular heart rhythms that may be serious and potentially life-threatening, although this is a rare side effect. Patients are more vulnerable if they have a heart condition

called congenital long QT syndrome, other heart diseases, conduction abnormalities, or electrolyte disturbances (e.g., magnesium or potassium loss due to severe or prolonged diarrhea or vomiting). If using albuterol (inhaler/nebulizer), administer it before ondansetron to avoid respiratory distress caused by nausea from the medication. If combining the two, allow at least 1-2 hours between doses. The second interaction is between methylprednisolone and albuterol, which is a minor interaction. When methylprednisolone is used together with albuterol, there is a risk of hypokalemia, heart palpitations, and increased blood sugar. The solution is to take methylprednisolone in the morning to minimize the side effects of insomnia and to take albuterol when experiencing shortness of breath or before activities. The third interaction is between albuterol and budesonide, which is a minor interaction. Concomitant use of beta-2 agonists and corticosteroids can cause additive hypokalemic effects. Because beta-2 agonists can cause QT interval prolongation, the development of hypokalemia can potentially increase the risk of ventricular arrhythmias, including torsade de pointes. However, clinical data are limited, and the potential significance is unknown. Patients receiving systemic formulations or nebulized beta-2 agonists, high doses of inhaled beta-2 agonists, or systemic corticosteroid therapy may be at greater risk of hypokalemia. The appropriate solution is to wait 5–10 minutes after using albuterol before using budesonide. However, drug interactions in Mr. Xxx2's case are not necessarily occurring, as they are only potential and may or may not occur. To determine whether interactions are occurring, it is more important to observe clinical manifestations and ask the patient directly about their condition.

The use of more than three types of drugs simultaneously, known as polypharmacy, is common, especially in patients with chronic diseases or comorbidities. However, this condition also carries risks that cannot be ignored, namely the potential for drug interactions, which can affect the effectiveness of therapy and increase the likelihood of side effects. In the context of healthcare, it is important for healthcare professionals to conduct regular medication reviews, especially for patients undergoing long-term therapy with multiple medications. With the right approach and collaboration among healthcare professionals, the risk of drug interactions can be minimized, ensuring that the therapy is conducted optimally and safely (25).

This study only looks at the potential; its limitation is that it does not look at complaints or the impact of interactions on patients. The researchers suggest that future researchers conduct prospective preliminary studies that directly observe the impact of drug interactions on patients. This will enable monitoring of the use of drugs that have an impact on drug interactions.

4. Conclusion

Based on the results of research on the study of potential drug interactions in patients with chronic obstructive pulmonary disease at a hospital in Jember Regency for the 2024 period, it can be concluded that the majority reached 97.92% and the highest percentage of interactions was moderate interactions at 68.80%.

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