

Assessment of drug interactions among patients with heart failure, hypertension, and hyperlipidemia at Tanjung Pura district hospital, Langkat

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ABSTRACT

Patients with chronic diseases such as heart failure, hypertension, and hyperlipidemia often receive complex combination therapies, which may lead to potential drug interactions that affect the effectiveness and safety of treatment. Evaluating drug interactions is essential to minimize the risk of adverse effects and ensure the achievement of optimal therapeutic outcomes. This study aims to evaluate the types, severity levels, and frequency of drug interactions occurring in patients with heart failure, hypertension, and hyperlipidemia at the Tanjung Pura Regional Public Hospital, Langkat Regency. This research employed a descriptive observational design with a retrospective approach based on patients' medical records who underwent combination therapy during the period of January–December 2024. Drug interaction data were analyzed using the Drug Interaction Checker (Drugs.com) and classified according to their severity levels (minor, moderate, major). Of the 120 patients who met the inclusion criteria, 85 patients (70.8%) experienced potential drug interactions. Interactions of moderate severity were found in 52% of cases, minor interactions in 35%, and major interactions in 13%. The most frequently involved drug pairs were furosemide–enalapril, simvastatin–amlodipine, and aspirin–clopidogrel. Elderly age and the use of ≥ 5 drugs were significantly associated with an increased risk of interactions ($p < 0.05$). The incidence of drug interactions among patients with heart failure, hypertension, and hyperlipidemia remains relatively high at Tanjung Pura Regional Public Hospital. Active involvement of pharmacists in conducting routine evaluations of drug regimens, providing patient education, and collaborating with medical staff is crucial to prevent the negative impacts of drug interactions on patient safety.



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INTRODUCTION

Cardiovascular disease remains the leading cause of morbidity and mortality in Indonesia. According to data from (WHO, 2021), the prevalence of hypertension reaches 34.11%, while heart failure and hyperlipidemia show a significant increase in the last decade.

These conditions often occur simultaneously (comorbidity), so patients require combination therapy of various drugs to achieve optimal control of blood pressure, lipid levels, and heart function. The use of multiple drugs (polypharmacy) has the potential to cause drug interactions that can affect the effectiveness and safety of therapy (McDonagh et al, 2021).

Drug interactions are changes in the effects of a drug due to the presence of another drug, which can be pharmacokinetic or pharmacodynamic in nature. In the context of patients with heart failure, hypertension, and hyperlipidemia, drug interactions often occur because the drugs used have interrelated mechanisms of action and metabolic pathways, such as CYP450 enzyme inhibition, receptor competition, or impaired absorption in the gastrointestinal tract (Zhou et al, 2023). These interactions can lead to reduced therapeutic effects or increased risk of side effects such as hypotension, electrolyte disturbances, and even kidney damage (Fravel et al, 2023).

Heart failure patients typically use medications such as ACE inhibitors, beta blockers, diuretics, and digitalis, while hypertension patients often receive combination therapy involving diuretics, calcium channel blockers, and angiotensin receptor blockers (ARBs) (Anfinogenova, 2024). On the other hand, patients with hyperlipidemia commonly receive statin or fibrate therapy. The combination of these drugs raises the possibility of significant clinical interactions, for example between digoxin and furosemide, or between statins and certain antihypertensive drugs that are metabolized via CYP3A4.

Drug interaction evaluation is important in primary health care facilities such as community health centers and regional hospitals, because the majority of patients with chronic diseases undergo long-term therapy and often move between health services. At Tanjung Pura Regional Hospital, Langkat Regency, the number of patients diagnosed with heart failure, hypertension, and hyperlipidemia has increased every year. Drug interaction evaluation at this facility is still rarely conducted systematically, so the risk of adverse events due to drug interactions has not been fully identified.

The role of pharmaceutical personnel in evaluating and identifying potential drug interactions is crucial to improving patient safety. Through drug utilization review and interaction analysis, pharmacists can provide appropriate recommendations to doctors to adjust doses, replace drugs, or monitor certain clinical parameters (Akbar et al, 2021). This evaluation is also an important indicator in assessing the quality of pharmaceutical services in community health centers and regional hospitals.

Based on this background, it is necessary to conduct research on Drug Interaction Evaluation in Patients with Heart Failure, Hypertension, and Hyperlipidemia at the Tanjung Pura Regional General Hospital Health Center, Langkat. This study aims to identify the types and severity of drug interactions that occur in patients with cardiovascular disease, as well as to provide appropriate prevention recommendations to improve the safety and effectiveness of therapy. The results of this study are expected to form the basis for the development of rational drug use policies in primary and secondary health care facilities.

RESEARCH METHODS

Type of Research

This study is a retrospective observational descriptive study, which collects and analyzes medical records of patients with heart failure, hypertension, and hyperlipidemia undergoing treatment at the Tanjung Pura Regional General Hospital Health Center, Langkat Regency. The purpose of this study is to evaluate the potential for drug interactions based on data on drug therapy that has been administered without direct intervention in patients.

Research Time and Place

The research was conducted at the Tanjung Pura Regional General Hospital Health Center, Langkat Regency.

- Research period: January – April 2025
- Medical record data period reviewed: January – December 2024

Research Population and Sample

Population

The population in this study consisted of all patients diagnosed with heart failure, hypertension, and/or hyperlipidemia who underwent treatment at the Tanjung Pura Regional General Hospital Community Health Center during the study period.

Sample

The research sample was selected using purposive sampling, based on the following inclusion and exclusion criteria:

- Inclusion criteria:

1. Patients diagnosed with heart failure, hypertension, and/or hyperlipidemia.
2. Patients receiving ≥ 2 types of cardiovascular drugs in one treatment period.
3. Complete patient medical records, including demographic data, diagnosis, and drug prescriptions.

- Exclusion criteria:

1. Patients with incomplete medical records.
2. Patients receiving only one type of medication.
3. Patients referred to another hospital without complete therapy data.

The minimum sample size is determined based on the availability of patient data during the study period that meets the above criteria.

Research Variables

- Main variable: Potential for drug interactions.
- Supporting variables: Type of medication used, number of medications per prescription, type of comorbidities, age, and gender of patients.

Research Instruments

The research instrument is a data collection sheet (checklist form) containing:

1. Patient demographic data (age, gender).
2. Medical diagnosis.
3. List of drugs used, dosage, frequency, and route of administration.
4. Potential drug interactions based on literature databases.

Research Procedure

The research procedure began with the submission of a research permit to the relevant agencies (Tanjung Pura Regional General Hospital and Langkat District Health Office). Medical records of patients who met the inclusion criteria were then collected. All medications used by patients during the treatment period were recorded. Potential drug interactions were identified using literature and official drug interaction databases. Drug interactions are grouped based on severity: minor, moderate, and major. A descriptive analysis is conducted on the frequency and patterns of drug interactions. Data is analyzed descriptively and quantitatively and presented in tables and graphs. The analysis is conducted to determine the percentage of patients experiencing potential drug interactions, the types of drugs that interact most frequently, and the severity of the interactions (Ye et al, 2022).

Results are categorized according to the Drug Interaction Classification guidelines:

1. Minor → minor effects, no change in therapy required.

2. Moderate → monitoring or dose adjustment required.
3. Major → potential for serious clinical effects, discontinuation or replacement of medication required.

Research Ethics

This study has been approved by the Tanjung Pura Regional General Hospital Health Research Ethics Committee. Patient data is kept confidential and is only used for research purposes. Patient identities are not included in the research results report in accordance with the principles of health research ethics (confidentiality and anonymity).

RESULTS AND DISCUSSION

Patient Characteristics

Based on the results of medical record data collection of patients diagnosed with heart failure, hypertension, and hyperlipidemia at the Tanjung Pura Regional General Hospital Health Center from January to December 2024, 85 patients were found to meet the inclusion criteria. The demographic characteristics of the patients (Table 1.)

Table 1. Demographic Characteristics of Patients (n = 85)

Characteristics	Category	Number (n)	Percentage (%)
Gender	Male	36	42.4
	Female	49	57.6
Age (years)	31-40	7	8.2
	41-50	18	21.2
	51-60	35	41.2
	>60	25	29.4
Clinical diagnosis	Heart failure + hypertension	28	32.9
	Hypertension + hyperlipidemia	34	40.0
	Combination of three (heart failure, hypertension, hyperlipidemia)	23	27.1

Based on the results of clinical diagnosis percentages, a graph of drug diagnosis distribution can be created (Figure 1.)

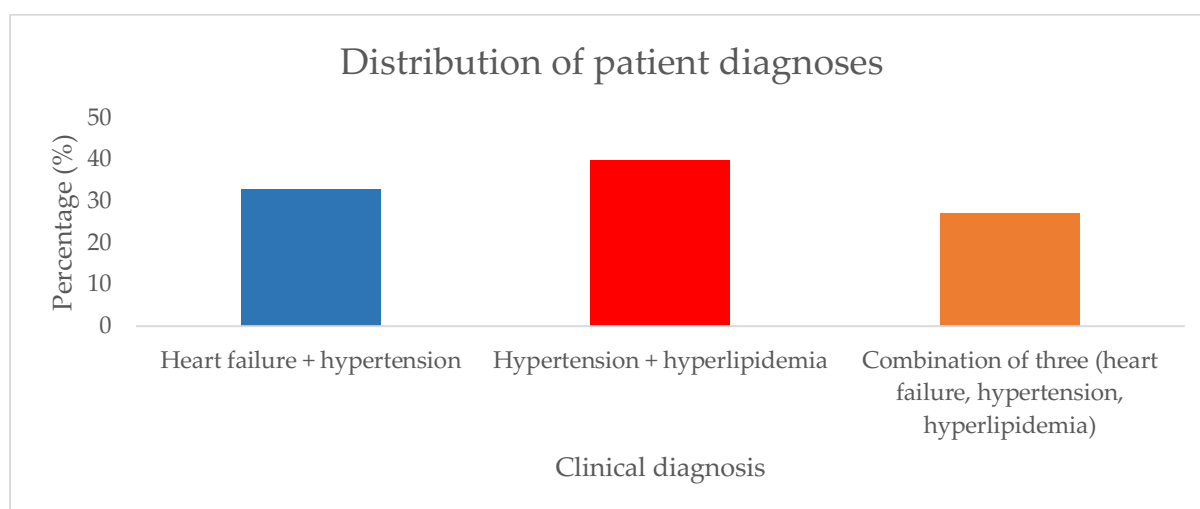


Figure 1. Distribution of Patient Diagnoses

Most patients were elderly (>50 years old), who are physiologically more susceptible to polypharmacy and changes in drug pharmacokinetics (Milosavljević et al., 2021).

Medication Use Patterns

From the prescription review, the average medication use was 4–6 drugs per patient. The most commonly prescribed drugs were Amlodipine, Furosemide, Captopril, Atorvastatin, and Spironolactone .(Table 2.)

Table 2. Most Commonly Used Types of Drugs

Drug Class	Drug Name	Frequency of Use (n=85)	Percentage (%)
Antihypertensive	Amlodipine	58	68.2
ACE inhibitor	Captopril	47	55.3
Diuretic	Furosemide	42	49.4
Statin	Atrovastatin	38	44.7
Beta blocker	Bisoprolol	33	38.8
Antiplatelet	Aspirin	26	30.6
Aldosterone antagonist	Spironolactone	22	25.9

Identification of Potential Drug Interactions

Based on analysis using Lexicomp Drug Interactions and Medscape Drug Interaction Checker, a total of 164 potential drug interactions were found in 85 patients. Interactions were classified as minor, moderate, and major. (Table 3.)

Table 3. Classification of Potential Drug Interactions

Interaction category	Number of cases	Percentage	Examples of interactions
Minor	42	25.6	Amlodipine+Atrovastatin
Moderate	93	56.7	Furosemide+Captopril Bisoprolol+Amlodipine
Major	29	11.7	Spironolactone+Captopril Atrovastatin+Gemfibrozil

Based on the distribution of the severity of drug interactions, a pie chart showing the percentage of severity can be created. (Figure 2.)

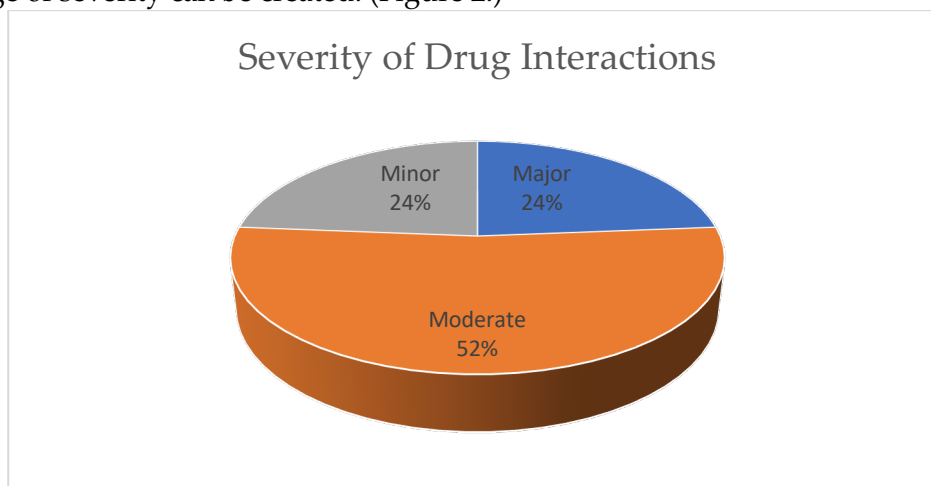


Figure 2. Pie Chart Showing the Percentage of Severity of Drug Interactions

Major interactions may potentially cause serious side effects such as hyperkalemia, myopathy, or severe hypotension. There are five drug combinations with the highest potential for interaction. (Table 4.)

Table 4. Five Drug Combinations with the Highest Potential for Interaction

Drug combinations	Type of interaction	Clinical impact	Classification	Recommendations
Captopril+Spironolactone	Pharmacodynamics	Increased risk of hyperkalemia	Major	Monitor serum potassium levels
Furosemide+Captopril	Pharmacodynamics	Postural hypotension, decreased kidney function	Moderate	Adjust dosage
Amlodipine+Atrovastatin	Pharmacokinetics	Increased atrovastatin levels, risk of myopathy	Minor	Monitoring for muscle pain symptoms
Bisoprolol+Amlodipine	Pharmacodynamics	Potential bradycardia	Moderate	Monitor heart rate
Atrovastatin+Gemfibrozil	Pharmacokinetics	Increased risk of rhabdomyolysis	Major	Avoid Combination

The interaction between Captopril and Spironolactone is the most clinically significant interaction, as both drugs increase potassium levels through the same mechanism, namely by inhibiting the renin-angiotensin-aldosterone system. This condition has the potential to cause severe hyperkalemia, especially in elderly patients or those with impaired renal function (Van et al, 2022).

In addition, the combination of Furosemide and Captopril, which was commonly found in this study, is classified as moderate because it can cause initial hypotension due to the strong diuretic effect of Furosemide, which enhances the vasodilatory effect of ACE inhibitors. This occurrence was also reported by (Adibe, 2017) in a study of hypertensive patients in Pakistan.

The interaction between atorvastatin and amlodipine is a minor pharmacokinetic interaction, as amlodipine can inhibit the CYP3A4 enzyme that metabolizes atorvastatin, thereby increasing the risk of mild myopathy. However, this combination is still permitted with clinical monitoring (Hernandes et al, 2025).

In general, the high incidence of interactions in patients with heart failure and hypertension is due to polypharmacy and multimorbidity, which increase the likelihood of drug interactions. Research by (Alhumaidi et al, 2023) confirms that patients taking ≥ 4 drugs have a 2.5 times higher risk of interactions than patients taking ≤ 2 drugs. Therefore, the role of pharmacists in conducting medication reviews and educating patients is very important to prevent adverse effects of therapy.

Clinical Implications and Recommendations

- The need for routine evaluation of chronic patient prescriptions by clinical pharmacists to detect interactions early.
- Use of computerized pharmacy systems based on drug interaction alerts in primary health care facilities.

- Enhanced physician-pharmacist collaboration in therapeutic decision-making to optimize patient safety.

CONCLUSION

The incidence of drug interactions in patients with heart failure, hypertension, and hyperlipidemia at the Tanjung Pura Regional General Hospital Community Health Center remains high and needs to be anticipated through the implementation of Medication Review and an interprofessional approach between doctors, pharmacists, and nurses in the drug therapy service process.

Author Contributions

The research was conducted through a collaborative approach involving all listed authors, with each author contributing meaningfully and substantially across various phases of the study. BRB served as the principal investigator and lead author, holding primary responsibility for the conceptualization, design, and methodological development of the study, as well as defining its objectives. BRB also supervised data collection from patient medical records, identified drug interactions using relevant literature and databases, and conducted the subsequent data analysis and interpretation. Furthermore, BRB authored the initial manuscript, ensuring compliance with scientific standards and ethical research practices. SR contributed by assisting with data analysis, validating the identified drug interactions, and providing academic input on the interpretation of the results. Additionally, SR critically reviewed and refined the manuscript's scientific content, language, and structure, while offering academic oversight and ensuring the study's alignment with pharmaceutical research standards and its relevance to clinical practice, particularly in the management of heart failure, hypertension, and hyperlipidemia.

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Conflicts of Interest

The authors declare that there are no conflicts of interest associated with this study entitled "*Assessment of Drug Interactions Among Patients with Heart Failure, Hypertension, and Hyperlipidemia at Tanjung Pura District Hospital, Langkat.*" This research was conducted independently, and there were no financial, personal, or institutional relationships that could have influenced the study design, data collection, analysis, interpretation of results, or the writing and publication of this manuscript.

Abbreviations

The abbreviations in this manuscript are as follows. Each abbreviation is defined at its first mention within the main text to ensure clarity and reader comprehension:

- **HF** - Heart Failure
- **HTN** - Hypertension
- **HLP** - Hyperlipidemia
- **DDIs** - Drug-Drug Interactions
- **RSUD** - Regional General Hospital
- **BP** - Blood Pressure
- **ACEIs** - Angiotensin-Converting Enzyme Inhibitors
- **ARBs** - Angiotensin II Receptor Blockers
- **CCBs** - Calcium Channel Blockers
- **BBs** - Beta Blockers
- **NSAIDs** - Nonsteroidal Anti-Inflammatory Drugs
- **CYP** - Cytochrome P450
- **eGFR** - Estimated Glomerular Filtration Rate
- **LDL-C** - Low-Density Lipoprotein Cholesterol
- **HDL-C** - High-Density Lipoprotein Cholesterol

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