ISSN 2985-5667 (Online) | 2985-6353 (Print) | Vol. 4, No. 3, August (2026), pp. 155-162

Published by: IARN Institute

International Journal on Health and Medical Sciences

Journal homepage: https://journals.iarn.or.id/index.php/HealMed/index

Analysis of potential drug interactions and their management in hypertensive patients receiving coronary heart disease medications at x hospital, Jambi city, Indonesia

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Article Info

Article history:

Received Jul 16, 2026
Revised Jul 24, 2026
Accepted Aug 4, 2026

Keywords:

Coronary Heart Disease;
Drug Interactions;
Hypertension;
Interaction Management.

ABSTRACT

Hypertension is a chronic condition that may lead to various complications, including coronary heart disease (CHD). Patients with hypertension complicated by CHD commonly receive multiple medications, thereby increasing the risk of potential drug interactions that may compromise therapeutic efficacy or increase the incidence of adverse drug reactions. This study aimed to analyze the potential drug interactions based on their mechanisms and severity levels, as well as to describe the strategies used to manage these interactions among hypertensive patients receiving CHD medications at X Hospital, Jambi City. A descriptive retrospective study was conducted using outpatient medical records collected between January and December 2025. A total of 93 patients who fulfilled the inclusion and exclusion criteria were enrolled. Potential drug interactions were identified using the Drugs.com Drug Interaction Checker. The findings revealed that most patients were male and aged over 65 years. Prescriptions containing six to seven medications accounted for the highest proportion (56.99%). Based on severity, moderate interactions predominated, accounting for 507 cases (69.26%), followed by minor interactions with 167 cases (22.81%) and major interactions with 58 cases (7.92%). Regarding the underlying mechanism, pharmacodynamic interactions were considerably more frequent than pharmacokinetic interactions, representing 687 cases (93.85%) and 45 cases (6.15%), respectively. The combination of aspirin and bisoprolol was identified as the most frequently encountered drug interaction, occurring in 61 cases. Management of potential drug interactions primarily involved therapeutic monitoring and regular clinical evaluation to optimize treatment safety and effectiveness.

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1. INTRODUCTION

Hypertension remains one of the leading non-communicable diseases and continues to pose a major public health challenge in Indonesia. According to the 2023 Indonesian Health Survey, the national prevalence of hypertension reached 30.8%, while the prevalence in Jambi Province was reported at 23.6% (Kementerian Kesehatan Republik Indonesia, 2023). Inadequately controlled hypertension

may result in various cardiovascular complications, particularly coronary heart disease (CHD) (Sri Wahyuni, Kiki Rawitri, Syilvi Rinda Sari, 2025).

Hypertension is also recognized as one of the most important modifiable risk factors for cardiovascular morbidity and mortality worldwide. Appropriate blood pressure control is therefore essential to prevent major cardiovascular events and improve patient outcomes (Tamargo et al., 2022).

Coronary heart disease is the leading cause of mortality among cardiovascular disorders worldwide. Persistent elevation of blood pressure accelerates the development of atherosclerosis, thereby increasing the likelihood of coronary artery obstruction and subsequent CHD (Nurhidayah et al., 2022). Consequently, patients diagnosed with both hypertension and CHD commonly require multiple medications to control blood pressure, relieve cardiac symptoms, and prevent disease progression. Patients with concomitant hypertension and coronary heart disease frequently receive antiplatelet agents, antihypertensive drugs, statins, and other cardiovascular medications simultaneously. Such therapeutic complexity substantially increases the occurrence of polypharmacy and drug-related problems (Shreya Patel, Manish Kumar, Craig J Beavers, Saad Karamat, 2022).

The simultaneous administration of several medications, commonly referred to as polypharmacy, substantially increases the likelihood of drug interactions. These interactions may alter the pharmacokinetic or pharmacodynamic properties of medications, potentially reducing therapeutic efficacy or increasing the occurrence of adverse drug reactions. As a result, identifying potential drug interactions has become an essential component of pharmaceutical care to ensure safe and effective pharmacotherapy (Saragih et al., 2022). Several studies have demonstrated that increasing numbers of prescribed medications are strongly associated with a higher incidence of clinically significant drug interactions among cardiovascular patients. Therefore, medication review is recommended as an integral component of pharmaceutical care (Michelle A Fravel, 2021).

However, evaluating potential drug interactions solely based on their occurrence is insufficient to support clinical decision-making. Simultaneous assessment of the interaction mechanism and severity provides complementary information that is essential for optimizing patient care. Classification according to the mechanism explains how an interaction occurs, whether through pharmacokinetic alterations affecting drug absorption, distribution, metabolism, or elimination, or through pharmacodynamic interactions resulting from additive, synergistic, or antagonistic pharmacological effects. Meanwhile, severity classification indicates the potential clinical consequences of these interactions and helps determine the level of intervention required, ranging from routine monitoring to therapy modification or avoidance of specific drug combinations. Therefore, integrating both dimensions allows healthcare professionals to prioritize clinically significant interactions and implement appropriate management strategies to improve medication safety and therapeutic outcomes.

Understanding the mechanisms and clinical significance of drug interactions is essential for optimizing treatment outcomes in patients with cardiovascular diseases. Early identification of potentially harmful drug combinations enables healthcare professionals to implement appropriate management strategies, including dose adjustment, therapeutic monitoring, laboratory evaluation, and patient education, thereby minimizing medication-related risks. Early identification of potential drug interactions enables healthcare professionals to optimize medication therapy, prevent avoidable adverse drug events, and improve treatment effectiveness, particularly among older adults with multimorbidity (Tamargo et al., 2022).

The implementation of drug interaction management is particularly urgent in patients receiving polypharmacy because these patients are at substantially greater risk of clinically significant drug interactions, adverse drug events, therapeutic failure, and hospital readmission. Identifying potential interactions alone is insufficient unless followed by appropriate management strategies, including medication review, therapeutic monitoring, laboratory evaluation, dose adjustment, and patient education. Such interventions enable healthcare professionals to detect

clinically relevant interactions at an early stage, minimize medication-related harm, and optimize the safety and effectiveness of pharmacotherapy. Therefore, effective drug interaction management has become an essential component of pharmaceutical care to improve patient safety, especially among older adults with multiple comorbidities.

Although previous studies have reported the prevalence and severity of potential drug interactions in cardiovascular patients, most have focused primarily on identifying the occurrence of interactions rather than integrating interaction mechanisms, severity, and their management strategies within a single analysis. Furthermore, evidence regarding these aspects among hypertensive patients with concomitant coronary heart disease in Indonesian healthcare settings remains limited. Addressing this gap is important to provide clinically relevant evidence that can support medication review and pharmaceutical care in routine clinical practice.

Although previous studies have reported the prevalence of potential drug–drug interactions among patients with cardiovascular diseases, most investigations have primarily focused on the frequency or severity of these interactions. Limited evidence has comprehensively evaluated both the mechanisms (pharmacokinetic and pharmacodynamic) and the severity of potential drug interactions while simultaneously describing practical management strategies in hypertensive patients with concomitant coronary heart disease. Furthermore, evidence from Indonesian healthcare settings, particularly secondary hospitals, remains limited. Therefore, a more comprehensive evaluation is needed to provide clinically relevant information that can support medication review, optimize pharmaceutical care, and improve patient safety in this high-risk population.

Therefore, this study aimed to analyze the potential drug interactions based on their mechanisms and severity levels, as well as to describe the management strategies implemented for hypertensive patients receiving coronary heart disease medications at X Hospital, Jambi City.

2. RESEARCH METHOD

This study employed a descriptive retrospective design using outpatient medical records of hypertensive patients diagnosed with coronary heart disease at X Hospital, Jambi City, Indonesia. The medical records were collected from the period of January to December 2025.

A total of 93 patients who fulfilled the predetermined inclusion and exclusion criteria were included in the study. The inclusion and exclusion criteria were established to ensure that only medical records containing complete demographic information, confirmed diagnoses of hypertension with concomitant coronary heart disease, and complete medication data were analyzed. Records with incomplete clinical or prescription information were excluded to minimize information bias and improve the accuracy and consistency of drug interaction assessment.

Potential drug interactions were identified using the Drugs.com Drug Interaction Checker and subsequently classified according to their mechanism, namely pharmacokinetic and pharmacodynamic interactions, as well as their severity level, which included minor, moderate, and major interactions.

The classification of drug interactions followed the criteria provided by the Drugs.com Drug Interaction Checker. Interaction mechanisms were categorized as pharmacokinetic interactions when one drug altered the absorption, distribution, metabolism, or excretion of another drug, and as pharmacodynamic interactions when two or more drugs produced additive, synergistic, or antagonistic pharmacological effects without altering drug concentrations. Severity was classified into three categories: minor interactions, which generally have limited clinical significance and rarely require therapy modification; moderate interactions, which may require closer monitoring, dose adjustment, or clinical intervention; and major interactions, which have the potential to cause serious adverse outcomes and generally require avoidance of the drug combination or immediate clinical management.

The collected data were analyzed descriptively using Microsoft Excel. The results are presented as frequencies and percentages to describe patient characteristics, medication utilization,

and the distribution of potential drug interactions based on their severity and underlying mechanisms.

3. RESULTS AND DISCUSSIONS

In this section, it is explained the results of research and at the same time is given the comprehensive discussion. Results can be presented in figures, graphs, tables and others that make the reader understand easily (Bayraksan & Love, 2015)(Jiang & Guan, 2016). The discussion can be made in several sub-chapters.

Patient Characteristics

Table 1. Distribution of patients by age group and sex

Age Group (Years)	Male, n (%)	Female, n (%)
36–45	3 (5.88)	1 (2.38)
46–55	4 (7.84)	8 (19.05)
56–65	21 (41.18)	18 (42.86)
>65	23 (45.10)	15 (35.71)
Total	51 (100)	42 (100)

Table 1 shows that patients aged over 65 years constituted the largest proportion of the study population, with male patients slightly outnumbering females. The predominance of older adults is consistent with the increasing prevalence of hypertension associated with age-related physiological changes in the cardiovascular system (Susanti et al., 2023). Aging contributes to arterial stiffness, reduced vascular elasticity, and endothelial dysfunction, all of which facilitate sustained elevations in blood pressure. Long-standing hypertension also accelerates the progression of atherosclerosis, thereby increasing the risk of coronary heart (Nasution et al., 2025). Previous studies have also reported that advancing age is associated with increased arterial stiffness, multimorbidity, and polypharmacy, all of which contribute to a greater risk of cardiovascular complications and drug interactions (Shreya Patel, Manish Kumar, Craig J Beavers, Saad Karamat, 2022).

Number of Medications Prescribed

Table 2. Distribution of the number of medications per prescription

Number of Medications	n	Percentage (%)
3–5	19	20.43
6–7	53	56.99
8–10	21	22.58
Total	93	100

As presented in Table 2, prescriptions containing six to seven medications accounted for the highest proportion (56.99%), indicating a high prevalence of polypharmacy among hypertensive patients with coronary heart disease.

Polypharmacy is frequently required in patients with multiple chronic conditions because several therapeutic agents are necessary to control blood pressure, alleviate cardiac symptoms, and prevent disease progression. However, an increasing number of medications is associated with a greater likelihood of clinically significant drug interactions, which may compromise therapeutic outcomes or increase the incidence of adverse drug reactions (Susanti et al., 2023; Bahana et al., 2021). A systematic review by Beezer et al. (2022) also demonstrated that polypharmacy is highly prevalent among cardiovascular patients and is associated with an increased risk of adverse drug reactions, hospital admission, and medication-related problems. Similar findings were reported by Patel et al. (2022).

The high prevalence of polypharmacy observed in this study has important clinical implications because the likelihood of drug interactions increases as the number of prescribed

medications rises. Polypharmacy may contribute to adverse drug reactions, medication errors, reduced treatment adherence, prolonged hospitalization, and increased healthcare costs. Consequently, comprehensive medication review, multidisciplinary collaboration, and continuous monitoring should be integrated into routine clinical practice to improve patient safety and optimize therapeutic outcomes in patients with multiple cardiovascular comorbidities.

Potential Drug Interactions Based on Severity and Mechanism

Table 3. Distribution of potential drug interactions according to severity and mechanism

Variable	Number of Cases	Percentage (%)
Severity		
Moderate	507	69.26
Minor	167	22.81
Major	58	7.92
Mechanism		
Pharmacodynamic	687	93.85
Pharmacokinetic	45	6.15

Table 3 demonstrates that moderate drug interactions predominated, accounting for 69.26% of all identified interactions. In contrast, major interactions represented only 7.92% of the total cases.

Based on the interaction mechanism, pharmacodynamic interactions were substantially more frequent than pharmacokinetic interactions. This finding is consistent with previous reports indicating that pharmacodynamic interactions are more frequently encountered than pharmacokinetic interactions in cardiovascular pharmacotherapy because multiple drugs often produce additive effects on blood pressure, heart rate, and electrolyte balance (Asiimwe & Pirmohamed, 2022; Michelle A Fravel, 2021).

The predominance of moderate interactions suggests that most potential drug combinations were not absolutely contraindicated but required careful clinical monitoring and appropriate management to prevent progression to clinically significant adverse events. This finding indicates that routine medication review and therapeutic monitoring may be more beneficial than simply avoiding drug combinations, as many moderate interactions involve medications that remain essential for achieving optimal cardiovascular outcomes.

Most Frequently Identified Potential Drug Interactions

Table 4. Ten most frequently identified potential drug interactions

No.	Drug Combination	Severity	Mechanism	Frequency
1	Aspirin – Bisoprolol	Minor	Pharmacodynamic	61
2	Amlodipine – Bisoprolol	Moderate	Pharmacodynamic	59
3	Furosemide – Bisoprolol	Moderate	Pharmacodynamic	54
4	Spironolactone – Bisoprolol	Moderate	Pharmacodynamic	53
5	Aspirin – Amlodipine	Moderate	Pharmacodynamic	51
6	Aspirin – Candesartan	Moderate	Pharmacodynamic	45
7	Furosemide – Aspirin	Moderate	Pharmacodynamic	43
8	Nitroglycerin – Amlodipine	Moderate	Pharmacodynamic	43
9	Aspirin – Spironolactone	Minor	Pharmacokinetic	41
10	Spironolactone – Candesartan	Major	Pharmacodynamic	40

Table 4 summarizes the ten most frequently identified potential drug interactions. The combination of spironolactone and candesartan was categorized as a major interaction because both drugs increase serum potassium levels through complementary mechanisms acting on the renin–angiotensin–aldosterone system. Candesartan suppresses aldosterone secretion, thereby reducing potassium excretion, whereas spironolactone directly antagonizes aldosterone receptors and further inhibits renal potassium elimination. The combined effect substantially increases the risk of clinically significant hyperkalemia, particularly in older adults, patients with impaired renal function, or those receiving multiple cardiovascular medications. Because severe hyperkalemia may lead to life-

threatening cardiac arrhythmias and sudden cardiac death, this drug combination requires close laboratory monitoring, careful dose adjustment, and individualized clinical assessment before and during therapy. Concomitant administration of these agents may markedly increase serum potassium levels, thereby predisposing patients to hyperkalemia, cardiac arrhythmias, muscle weakness, and potentially life-threatening complications. Therefore, periodic monitoring of serum potassium concentrations and patient education regarding the symptoms of hyperkalemia are strongly recommended (Ferry Effendi, 2021; Zulfa et al., 2022). Current cardiovascular pharmacotherapy guidelines also recommend close laboratory monitoring when mineralocorticoid receptor antagonists are administered together with angiotensin receptor blockers because of the increased risk of hyperkalemia (Tamargo et al., 2022).

This recommendation is consistent with recent evidence emphasizing that patients with hypertension receiving multiple medications require continuous monitoring to identify clinically relevant drug interactions and optimize treatment safety (Özokcu et al., 2024).

Among the moderate interactions, the combination of furosemide and bisoprolol was frequently observed. Furosemide promotes sodium and water excretion, whereas bisoprolol selectively blocks β_1-adrenergic receptors, thereby reducing heart rate and myocardial contractility (Muresan et al., 2022; Wola et al., 2022). Their concurrent administration may increase the risk of metabolic disturbances, including hyperglycemia and hypertriglyceridemia. Consequently, routine monitoring of blood pressure, serum potassium, and blood glucose levels is recommended throughout treatment (Saragih et al., 2022). Medication review by clinical pharmacists is recommended to detect clinically significant interactions and optimize therapeutic outcomes in patients receiving multiple cardiovascular medications (Asiimwe & Pirmohamed, 2022).

Another commonly reported moderate interaction involved amlodipine and bisoprolol. Similar findings were reported by Aliyah et al. (2022), who identified this combination as one of the most prevalent moderate interactions. Because both agents exert antihypertensive effects, their concomitant use may produce additive reductions in blood pressure and heart rate. Therefore, dose adjustment and close clinical monitoring are recommended to minimize the risk of excessive hypotension or bradycardia (Ayu Fajariyani et al., 2024). Patients receiving multiple antihypertensive agents require individualized monitoring because excessive blood pressure reduction may increase the risk of falls, dizziness, and reduced treatment adherence (Shreya Patel, Manish Kumar, Craig J Beavers, Saad Karamat, 2022).

The combination of aspirin and amlodipine was also classified as a moderate interaction. Kurniawati et al. (2024) reported that this drug combination was among the most frequently identified moderate potential drug interactions in hypertensive patients with comorbidities. Therefore, careful clinical monitoring is recommended to ensure therapeutic effectiveness and patient safety.

The most frequently observed minor interaction involved aspirin and bisoprolol, accounting for 61 cases. This finding is consistent with the report by Gadis et al. (2022). Aspirin may inhibit prostaglandin synthesis, thereby reducing the antihypertensive effect of bisoprolol. Although this interaction is generally considered clinically mild, routine therapeutic monitoring remains necessary to maintain optimal blood pressure control. Routine medication reconciliation and continuous monitoring remain important because repeated minor interactions may contribute to suboptimal therapeutic outcomes in patients receiving long-term cardiovascular treatment (Michelle A Fravel, 2021). Although the aspirin–bisoprolol interaction was classified as minor, its high frequency suggests that it deserves particular attention in routine clinical practice. Repeated exposure to this drug combination may reduce the antihypertensive effectiveness of bisoprolol, especially in older patients receiving long-term cardiovascular therapy. Therefore, regular blood pressure monitoring, periodic medication review, and individualized risk assessment are recommended to ensure sustained therapeutic effectiveness while minimizing the risk of avoidable cardiovascular complications.

Another minor interaction was identified between aspirin and spironolactone. Aspirin may reduce the diuretic effect of spironolactone by interfering with renal sodium excretion. Consequently, regular blood pressure monitoring and continuous assessment of the patient's clinical response are recommended throughout therapy (Aliya Rahmah Adriani et al., 2022). These findings further emphasize the importance of pharmaceutical care, medication review, and regular monitoring to prevent adverse drug events associated with polypharmacy in cardiovascular patients ((Beezer et al., 2022).

4. CONCLUSION

The majority of hypertensive patients with concomitant coronary heart disease were male and aged over 65 years. Moderate drug interactions and pharmacodynamic mechanisms were the most frequently identified potential interactions. The combination of aspirin and bisoprolol was the most commonly observed drug interaction among the prescribed medications. Appropriate management, including therapeutic monitoring, regular clinical evaluation, and laboratory assessment, is essential to minimize the risk of adverse drug interactions while enhancing the safety and effectiveness of pharmacotherapy. These findings contribute to pharmaceutical care practice by providing evidence on the predominant mechanisms, severity levels, and frequently encountered drug combinations among hypertensive patients with concomitant coronary heart disease. This information may assist pharmacists and other healthcare professionals in prioritizing medication review, identifying high-risk drug combinations, and implementing targeted monitoring strategies to improve medication safety and optimize cardiovascular pharmacotherapy. Hospitals are encouraged to strengthen routine medication review programs involving clinical pharmacists, implement standardized drug interaction screening using electronic interaction-checking systems, establish regular laboratory and clinical monitoring protocols for high-risk drug combinations, and provide continuous education for healthcare professionals and patients regarding the prevention and management of drug interactions. These measures may reduce medication-related problems and improve patient safety among individuals receiving polypharmacy. Future studies should evaluate the actual clinical outcomes associated with potential drug interactions, including adverse drug reactions, hospitalization, treatment effectiveness, and mortality, through prospective multicenter studies with larger sample sizes. Such investigations would provide stronger evidence regarding the clinical significance of potential drug interactions and the effectiveness of various drug interaction management strategies in improving patient outcomes.

ACKNOWLEDGEMENTS

The authors would like to express their sincere gratitude to STIKES Harapan Ibu Jambi for providing academic support throughout this study. The authors also extend their appreciation to the management and healthcare staff of X Hospital, Jambi City, for granting permission to conduct this research and facilitating access to the required medical record data. Finally, the authors sincerely thank all individuals who contributed, directly or indirectly, to the successful completion of this study.

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