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Potential Drug–Drug Interactions and Associated Factors among Outpatients with Coronary Heart Disease at Cempaka Putih Islamic Hospital, Jakarta

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ABSTRACT

Coronary heart disease (CHD) is a major cause of morbidity and mortality worldwide, and its pharmacological management often involves multiple medications that may increase the risk of potential drug–drug interactions (pDDIs). This study aimed to describe the profile of pDDIs and evaluate their associations with age, gender, number of medications, and comorbidities among outpatients with CHD at Jakarta Cempaka Putih Islamic Hospital. An analytical observational study with a retrospective cross-sectional design was conducted using medical records of 200 outpatients treated between January and March 2026. Total sampling was applied to eligible patients with complete medical records and concurrent use of at least two medications. Potential drug interactions were identified using Drugs.com and Medscape, while descriptive and bivariate analyses were performed using SPSS. Of the 200 patients, 190 (95.0%) had at least one potential drug interaction, with 848 drug-pair occurrences identified. Pharmacodynamic interactions predominated, accounting for 713 occurrences (84.1%), while pharmacokinetic interactions accounted for 135 (15.9%). Most interactions were classified as moderate in severity (782; 92.2%), followed by major (38; 4.5%) and minor interactions (28; 3.3%). Bisoprolol and candesartan constituted the most frequently identified interacting drug pair, with 68 occurrences (8.02%). Bivariate analysis revealed no statistically significant associations between pDDIs and age ($p = 0.499$), gender ($p = 1.000$), or number of medications ($p = 0.603$). However, cardiovascular disorders ($p < 0.001$) and other comorbidities ($p = 0.017$) were significantly associated with pDDIs, whereas hypertension, diabetes mellitus, dyslipidemia, and renal disorders were not. These findings demonstrate the high prevalence of potential drug interactions among CHD outpatients and emphasize the importance of routine medication review, systematic interaction screening, and appropriate clinical monitoring. Collaborative pharmaceutical care is essential to support rational prescribing and improve medication safety.

Keyword: *coronary heart disease; potential drug–drug interactions; pharmacodynamic interactions; interaction severity; outpatient care*

Introduction

Coronary Heart Disease (CHD) persists as a primary contributor to global illness and death, continuing to represent a significant public health burden. Patients with CHD typically need extended pharmacological regimens to manage the disease, avert complications, and address coexisting conditions. Therapy often includes various drug categories, such as antiplatelet agents, beta-blockers, angiotensin-converting enzyme inhibitors or angiotensin receptor blockers, calcium channel blockers, statins, and drugs for comorbid issues like

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hypertension, diabetes mellitus, and dyslipidemia. Taking multiple drugs at once raises the likelihood of potential drug–drug interactions (pDDIs), which may alter therapeutic outcomes and elevate the risk of adverse drug events (Dolzhenko et al., 2025; Ferri et al., 2022). Thus, in everyday clinical work, spotting pDDIs is a crucial element of medication safety and pharmaceutical care.

Previous studies have reported a high prevalence of pDDIs among patients with cardiovascular diseases. Khan and Hussain (2024) reported that 93% of hospitalized cardiovascular patients experienced pDDIs, while Septiani and Rahmawati (2025) reported pDDIs in 97% of cardiac patients. Elderly patients with cardiovascular diseases may be particularly vulnerable because of polypharmacy and physiological changes associated with aging, with Sheikh-Taha and Asmar (2021) reporting that approximately 77.5% of older adults with cardiovascular diseases experienced at least one severe pDDI. In addition, studies of cardiovascular and coronary heart disease patients have identified interactions involving antiplatelet, anticoagulant, and lipid-lowering agents, with pharmacodynamic interactions frequently identified among the potential interactions (Febriyenti et al., 2025). These findings demonstrate the importance of systematically identifying pDDIs in patients receiving cardiovascular pharmacotherapy.

Despite the evidence from previous studies, there remains limited evidence regarding pDDIs specifically among outpatients with CHD in Indonesia. Previous Indonesian studies have largely focused on hospitalized patients, elderly populations, or specific cardiovascular conditions, while some studies have primarily described the prevalence and characteristics of drug interactions without simultaneously evaluating the association of patient characteristics with pDDIs. Furthermore, evidence from individual hospital settings may vary according to patient characteristics, prescribing patterns, comorbidities, and medication regimens. Therefore, local data are needed to provide a more specific description of the pattern of pDDIs among CHD outpatients and to assess whether patient characteristics are statistically associated with their occurrence.

The present study addresses this gap by examining the profile of pDDIs and their association with age, gender, number of medications, and comorbidities among outpatients with CHD at Jakarta Cempaka Putih Islamic Hospital. The study identifies pDDIs using established drug interaction-checking databases and describes their mechanisms and severity, while the association between selected patient characteristics and the occurrence of pDDIs is evaluated statistically. This approach provides both descriptive information on the characteristics of pDDIs and analytical evidence regarding factors potentially associated with their occurrence in an outpatient CHD population.

Therefore, this study aimed to describe the profile of potential drug–drug interactions (pDDIs) and evaluate their associations with age, gender, number of

medications, and comorbidities among outpatients with CHD at Jakarta Cempaka Putih Islamic Hospital. The findings are expected to provide local evidence to support medication review and pharmaceutical care, particularly in identifying patients who may require closer evaluation of their medication regimens to promote medication safety.

Methods

This research adopted a quantitative analytical observational design with a retrospective approach, drawing on secondary data from the medical records of outpatients with *coronary heart disease* (*CHD*) at Jakarta Cempaka Putih Islamic Hospital. The medical records of *CHD* outpatients treated between January and March 2026 formed the basis of the analysis. The target population encompassed all *CHD* patients receiving outpatient care at the facility during that timeframe. A total sampling method was applied, meaning every patient satisfying the predefined inclusion criteria was incorporated into the study. The final sample comprised 200 patients. The inclusion criteria required a *CHD* diagnosis, outpatient status during the study period, complete medical records, and the use of at least two concurrent medications. Patients were excluded if their records were incomplete or if medication data were missing.

Patient data extracted from medical records comprised age, sex, medication count, comorbidities, CHD diagnoses, and prescribed drugs. The medication data then underwent evaluation for potential drug–drug interactions (pDDIs) using the Drugs.com Drug Interaction Checker and the Medscape Drug Interaction Checker. Drugs.com served as the primary reference for identifying and categorizing pDDIs, whereas Medscape acted as a supplementary tool to confirm the detected interactions. Whenever the two databases produced conflicting classifications, the Drugs.com classification was maintained to ensure uniformity. The identified pDDIs were grouped according to their mechanism—either pharmacokinetic or pharmacodynamic—and by severity, falling into minor, moderate, or major categories. For every drug pair detected, the interaction details from the databases were documented. A pDDI signified a potential interaction identified through the databases, not a clinically manifested interaction or adverse drug event. Each occurrence of a drug pair was tallied individually per patient; thus, identical drug pairs appearing in different patients were counted as separate events. The final total of 848 pDDIs represented the cumulative count of drug pair occurrences across the 200 patients, not the number of unique drug combinations.

The function of the *SPSS* software in this study was to perform all statistical analyses. Descriptive analysis served to outline patient demographics and the *pDDI* landscape, presenting categorical data (age, sex, medication count, comorbidities, *pDDI* occurrence, interaction mechanisms, and severity) as

frequencies and percentages. Bivariate analysis then assessed whether age, sex, medication number, and comorbidities correlated with *pDDI* occurrence. The *Chi-square* test was used when appropriate; however, when the test's requirements were violated more than 20% of cells having expected counts under 5 *Fisher's Exact Test* was applied for 2 × 2 tables, and the *Fisher–Freeman–Halton Exact Test* for larger ones. Statistical significance was defined at a 95% confidence level ($\alpha = 0.05$), with $p \leq 0.05$ indicating a significant result.

The function of the ethical approval process in this study was to ensure compliance with research standards. Approval came from the *Health Research Ethics Committee of Universitas 17 Agustus 1945 Jakarta* (*Komite Etik Penelitian Kesehatan Universitas 17 Agustus 1945 Jakarta*), documented as Ethical Clearance No. 214/KEPK-UTA45JKT/EC/EXP/6/2026. This clearance confirmed that the study adhered to the seven ethical principles of the *WHO* 2011 framework. The approval period spanned from 11 June 2026 to 11 June 2027. Furthermore, before any data were collected, institutional authorization to access and use patient records was obtained from Jakarta Cempaka Putih Islamic Hospital.

Result and Discussion

This investigation took place at the Cardiology Outpatient Clinic of Jakarta Cempaka Putih Islamic Hospital, drawing on medical records of coronary heart disease (CHD) outpatients seen from January to March 2026. The sample comprised 200 patients selected via total sampling, all of whom satisfied the inclusion criteria. From the records, the team gathered patient characteristics such as age, sex, number of medications, and comorbidities. Two interaction checkers—Drugs.com and Medscape served to identify potential drug–drug interactions (pDDIs), which were later categorized by mechanism and severity. Data analysis, encompassing descriptive and bivariate methods, was carried out with SPSS.

1.1 Patient Characteristics

The study enrolled 200 outpatients with *Coronary Heart Disease* (*CHD*) who satisfied the inclusion criteria. Every medical record was complete and suitable for analysis, with no missing information. Table 1 displays the demographic and clinical profile of the participants.

Table 1 .Patient Characteristics (n=200)

Characteristics		Frequency (n)	Percentage (%)
Age	36-45 years	12	6.0
	46-55 years	29	14.5
	56-65 years	65	32.5
	> 65 years	94	47.0
Gender	Male	109	54.5
	Female	91	45.5
Number of Medications	<5 drugs	19	9.5
	≥5 drugs	181	90.5
Comorbidities	Cardiovascular disorders	111	51.4
	Hypertension	8	3.7
	Diabetes mellitus	18	8.3
	Dyslipidemia	4	1.9
	Renal disorders	7	3.2
	Others	68	31.5
Potential Drug Interactions	Yes	190	95.0
	No	10	5.0

*Comorbidity frequencies represent the total number of recorded comorbidity occurrences (n = 216), rather than the number of patients. Patients could have more than one comorbidity; therefore, the total number of comorbidity occurrences exceeds the number of patients. Percentages were calculated based on the total number of recorded comorbidity occurrences.

Patients aged >65 years constituted the largest age group (47.0%), followed by those aged 56–65 years (32.5%). Male patients accounted for 54.5% of the study population. The predominance of older patients and males is consistent with previous studies reporting similar demographic characteristics among patients with CHD (Humaira et al., 2023; Saputri & Dewi, 2023).

Regarding medication use, 181 patients (90.5%) received ≥5 medications, while 19 patients (9.5%) received <5 medications. The high proportion of patients receiving multiple medications reflects the complexity of pharmacotherapy commonly encountered in patients with cardiovascular disease and comorbid conditions (Oktaviani et al., 2024; Fajariyani et al., 2024).

A total of 216 comorbidity occurrences were recorded among the 200 patients. Cardiovascular disorders were the most frequently recorded comorbidity (51.4%), followed by other comorbidities (31.5%) and diabetes mellitus (8.3%). The presence of multiple comorbidities may contribute to greater therapeutic complexity and the need for concomitant medication use (Resmiati et al., 2023;

Ayuningsih, 2023). Because patients could have more than one comorbidity, these frequencies represent comorbidity occurrences rather than individual patients.

Potential drug–drug interactions (pDDIs) were identified in 190 patients (95.0%), whereas 10 patients (5.0%) had no identified pDDIs. The high prevalence of pDDIs is consistent with previous studies reporting frequent potential interactions among patients with cardiovascular disease receiving multiple medications (Buldan et al., 2023; Rahmi & Marbun, 2025). However, the identified pDDIs were based on drug interaction-checking databases and therefore represent potential interactions rather than confirmed clinical drug interactions or adverse drug events.

1.2 Profile of Potential Drug–Drug Interactions

A total of 848 pDDI pair occurrences were identified among the 200 patients. This number represents the cumulative occurrence of identified interacting drug pairs across patients. Therefore, the same drug pair was counted again when it occurred in another patient and the value of 848 does not represent the number of unique drug pairs.

Table 2. Distribution of Potential Drug Interactions Based on Mechanism and Severity (n = 848)

Characteristics		Frequency (n)	Percentage (%)
Mechanism	Pharmackinetic	135	15.9
	Pharmacodynamic	713	84.1
Severity	Minor	28	3.3
	Moderate	782	92.2
	Major	38	4.5

A total of 848 potential drug–drug interaction (pDDI) pair occurrences were identified among 200 patients. Pharmacodynamic interactions predominated, accounting for 713 occurrences (84.1%), while pharmacokinetic interactions accounted for 135 occurrences (15.9%). Regarding severity, most pDDIs were classified as moderate (782; 92.2%), followed by major (38; 4.5%) and minor interactions (28; 3.3%).

The predominance of pharmacodynamic interactions may be related to the concurrent use of cardiovascular medications with similar or complementary pharmacological effects. Combinations of antiplatelets, antihypertensives, beta-blockers, diuretics, and other cardiovascular agents may produce additive or synergistic effects on blood pressure, heart rate, platelet aggregation, or fluid balance (Oktaviani et al., 2024; Tamarah et al., 2023). This finding is consistent with Saputri and Dewi (2023), who reported that pharmacodynamic interactions were predominant among patients with CHD. Similar findings were reported by Aprillia

et al. (2025), who found that pDDIs in CHD patients were predominantly pharmacodynamic and moderate in severity. Kaltimurti (2023) also reported a predominance of pharmacodynamic interactions among outpatients with CHD, particularly involving cardiovascular medications.

The predominance of moderate interactions indicates that most identified pDDIs require clinical attention and monitoring rather than necessarily representing contraindications to concurrent therapy. Appropriate monitoring may include assessment of blood pressure, heart rate, coagulation parameters, renal function, and other relevant clinical or laboratory parameters according to the medications involved (Sari et al., 2024). Similar predominance of moderate interactions has been reported in patients with acute coronary syndrome and CHD (Oktovina et al., 2024; Saputri & Dewi, 2024).

Overall, the findings indicate that pDDIs in this CHD outpatient population were predominantly pharmacodynamic and moderate in severity. These findings support the importance of routine medication review, interaction screening, and appropriate clinical monitoring. However, the reported interactions were identified using interaction-checking databases and therefore represent potential interactions rather than confirmed clinical adverse events.

1.3 Most Frequently Occurring Potential Drug–Drug Interaction Pairs

A total of 848 potential drug–drug interaction (pDDI) pair occurrences were identified among the 200 patients. The frequency of each interaction pair was calculated based on the number of occurrences across the study population; therefore, the same drug pair identified in different patients was counted as a separate occurrence. The 25 most frequently occurring pDDI pairs are presented in Table 3.

Table 3. Most Frequently Occurring Potential Drug–Drug Interaction Pairs

No.	Drug combination	Mechanism	Severity	Frequency (n)	Percentage (%)
1	Bisoprolol + Candesartan	Pharmacodynamic	Moderate	68	8.02
2	Bisoprolol + Furosemide	Pharmacodynamic	Moderate	45	5.31
3	Clopidogrel + Lansoprazole	Pharmacokinetic	Moderate	45	5.31
4	Candesartan + Furosemide	Pharmacodynamic	Moderate	44	5.19
5	Candesartan + Spironolactone	Pharmacodynamic	Moderate	42	4.95
6	Bisoprolol + Spironolactone	Pharmacodynamic	Moderate	40	4.72

7	Furosemide + Spironolactone	Pharmacodynamic	Moderate	39	4.60
8	Aspilet + Bisoprolol	Pharmacodynamic	Moderate	25	2.95
9	Candesartan + V Bloc	Pharmacodynamic	Moderate	22	2.59
10	Adalat Oros + Bisoprolol	Pharmacodynamic	Moderate	19	2.24
11	Aspilet + Furosemide	Pharmacodynamic	Moderate	17	2.00
12	Aspilet + Spironolactone	Pharmacodynamic	Moderate	17	2.00
13	Amlodipine + Nitrokaf	Pharmacodynamic	Moderate	16	1.89
14	Candesartan + Nospirinal	Pharmacodynamic	Moderate	16	1.89
15	Bisoprolol + Nospirinal	Pharmacodynamic	Moderate	15	1.77
16	Lansoprazole + Sucralfate	Pharmacokinetic	Minor	15	1.77
17	Aspilet + Candesartan	Pharmacodynamic	Moderate	14	1.65
18	Aspilet + Clopidogrel	Pharmacodynamic	Moderate	14	1.65
19	Furosemide + V Bloc	Pharmacodynamic	Moderate	14	1.65
20	Amlodipine + Simvastatin	Pharmacokinetic	Moderate	10	1.18
21	Furosemide + Ramipril	Pharmacodynamic	Moderate	10	1.18
22	Spironolactone + V Bloc	Pharmacodynamic	Moderate	10	1.18
23	Adalat Oros + Simvastatin	Pharmacokinetic	Major	9	1.06
24	Amlodipine + Aspilet	Pharmacodynamic	Moderate	8	0.94
25	Aspilet + Ramipril	Pharmacodynamic	Major	8	0.94

Note: Frequencies represent pDDI pair occurrences across patients. The same drug pair identified in different patients was counted as a separate occurrence. Percentages were calculated using 848 total pDDI pair occurrences as the denominator.

The most frequently occurring pDDI was bisoprolol + candesartan, with 68 occurrences (8.02%), followed by bisoprolol + furosemide and clopidogrel + lansoprazole, with 45 occurrences each (5.31%). Other frequently identified pairs included candesartan + furosemide (44; 5.19%), candesartan + spironolactone (42;

4.95%), bisoprolol + spironolactone (40; 4.72%), and furosemide + spironolactone (39; 4.60%).

Most frequently occurring pairs were classified as pharmacodynamic and moderate in severity. The predominance of pharmacodynamic interactions (713/848; 84.1%) was consistent with findings reported by Kaltimurti (2023). Pharmacokinetic interactions included clopidogrel + lansoprazole, lansoprazole + sucralfate, amlodipine + simvastatin, and Adalat Oros + simvastatin, while major interactions included Adalat Oros + simvastatin and Aspilet + ramipril. Moderate interactions accounted for 782 occurrences (92.2%), consistent with Aprillia et al. (2025).

These findings highlight the importance of routine medication review, interaction screening, and appropriate clinical monitoring in patients with CHD. However, the identified pDDIs represent potential interactions from drug-interaction databases and do not necessarily indicate clinically manifested adverse drug events.

1.4 Association Between Patient Characteristics and Potential Drug–Drug Interactions

The associations between patient characteristics and the occurrence of potential drug–drug interactions (pDDIs) were evaluated using bivariate analysis. The Chi-square test was applied when its assumptions were met. When the assumptions were not met, Fisher's Exact Test was used for 2 × 2 contingency tables, and the Fisher–Freeman–Halton Exact Test was used for contingency tables larger than 2 × 2. Statistical significance was set at $p < 0.05$.

1.4.1 Association Between Age and Potential Drug–Drug Interactions

Table 4. Association Between Age and pDDIs

Age	Potential		No Potential		Total	p-value
	n	%	n	%		
36–45 years	12	100	0	0	12	0.499
46–55 years	29	100	0	0	29	
56–65 years	62	95.4	3	4.6	65	
>65 years	87	92.6	7	7.4	94	
Total	**190**		**10**		**200**	

The bivariate analysis demonstrated no statistically significant association between age and the occurrence of potential drug interactions among outpatients with Coronary Heart Disease (CHD) at Jakarta Cempaka Putih Islamic Hospital ($p = 0.499$). These findings indicate that potential drug interactions occurred across almost all age groups, suggesting that increasing age was not statistically associated

with the occurrence of potential drug interactions.

Theoretically, advanced age is considered an important risk factor for drug interactions. Aging is associated with physiological changes that influence pharmacokinetic and pharmacodynamic processes, including reduced renal and hepatic function, alterations in body composition, and decreased drug metabolism and excretion. In addition, older adults generally have multiple comorbidities requiring treatment with several medications (polypharmacy), which further increases the likelihood of potential drug interactions (Maulida & Puspitasari, 2021; Suardi et al., 2021).

However, the present study found no significant association between age and potential drug interactions. This finding may be explained by the fact that almost all patients across every age group received combination therapy based on current CHD treatment guidelines. Consequently, potential drug interactions were observed consistently across all age groups, resulting in no statistically significant differences. Furthermore, the study population was predominantly composed of older adults (>65 years), leading to relatively limited variation between age groups and reducing the statistical influence of age on the occurrence of potential drug interactions.

The findings of the present study are consistent with those reported by Oktovina et al. (2024) at Fatmawati General Hospital, who found that age was not significantly associated with potential drug interactions among patients with acute coronary syndrome ($p > 0.05$). The authors suggested that the widespread use of combination therapy across all age groups resulted in a similarly high prevalence of potential drug interactions, indicating that age alone was not a determining factor.

These findings are further supported by Kaltimurti (2023), who studied outpatients with CHD at Ibu Fatmawati Soekarno Regional General Hospital, Surakarta. The study demonstrated that potential drug interactions were more strongly influenced by the types of drug combinations prescribed and the presence of polypharmacy than by patients' age. As the complexity of the therapeutic regimen increases, the likelihood of potential drug interactions also increases, regardless of the patient's age group.

Overall, the present study found no statistically significant association between age and the occurrence of pDDIs among outpatients with CHD at Jakarta Cempaka Putih Islamic Hospital. Although potential interactions were frequently identified across age groups, the present analysis does not demonstrate that age was associated with the occurrence of pDDIs. The high prevalence of pDDIs across the study population supports the importance of medication review regardless of patient age.

1.4.2 Association Between Gender and Potential Drug–Drug Interactions

Table 5. Association Between Gender and pDDIs

Gender	Potential		No Potential		Total	p-value
	n	%	n	%		
Male	104	95.4	5	4.6	109	1.000
Female	86	94.5	5	5.5	91	
Total	**190**		**10**		**200**	

The bivariate analysis demonstrated no statistically significant association between gender and the occurrence of potential drug interactions among outpatients with Coronary Heart Disease (CHD) at Jakarta Cempaka Putih Islamic Hospital (p = 1.000). These findings indicate that both male and female patients had a relatively similar likelihood of experiencing potential drug interactions.

Theoretically, gender may influence drug response through physiological differences, including body fat composition, drug distribution volume, metabolic enzyme activity, and hormonal effects on pharmacokinetic and pharmacodynamic processes. However, these physiological differences do not directly determine the occurrence of potential drug interactions. Instead, the risk of drug interactions is more strongly influenced by the types of medications prescribed, the number of medications included in the therapeutic regimen, and the pharmacological mechanisms of the drugs than by patients' biological characteristics (Labibah & Rusdiana, 2022; Sumartin & Sukandar, 2024).

The absence of a significant association between gender and potential drug interactions in the present study may be explained by the fact that both male and female patients received relatively similar treatment regimens based on current CHD management guidelines. Most patients in both groups were prescribed combination therapy consisting of antiplatelet agents, antihypertensive drugs, statins, and medications for the management of comorbid conditions. Consequently, the likelihood of potential drug interactions was comparable between male and female patients.

The findings of this study are consistent with those reported by Nugroho et al. (2024), who found no significant association between gender and potential drug interactions (p = 1.000). The authors concluded that the occurrence of drug interactions was more strongly associated with the complexity of therapeutic regimens and the combination of prescribed medications than with patients' demographic characteristics, indicating that gender was not a determining factor for potential drug interactions.

These findings are further supported by Kaltimurti (2023), who reported that potential drug interactions among patients with CHD were more strongly

influenced by combination therapy and polypharmacy than by patient characteristics, including gender. As the complexity of the therapeutic regimen increases, the likelihood of potential drug interactions also increases.

Overall, the present study found no statistically significant association between gender and the occurrence of pDDIs among outpatients with CHD. The prevalence of pDDIs was similar between male and female patients. Therefore, gender was not demonstrated to be statistically associated with pDDI occurrence in this study. These findings support the importance of assessing medication regimens and potential interactions in both male and female patients rather than relying on gender as an indicator of pDDI risk.

1.4.3 Association Between Number of Medications and Potential Drug–Drug Interactions

Table 6. Association Between Number of Medications and pDDIs

Number of Medications	Potential		No Potential		Total	p-value
	n	%	n	%		
<5 drugs	19	100	0	0	19	0.603
≥5 drugs	171	94.5	10	5.5	181	
Total	**190**		**10**		**200**	

The bivariate analysis demonstrated no statistically significant association between the number of medications and the occurrence of potential drug–drug interactions (pDDIs) among outpatients with coronary heart disease (CHD) at Jakarta Cempaka Putih Islamic Hospital ($p = 0.603$). Among patients receiving fewer than five medications, all 19 patients (100.0%) had at least one pDDI, whereas 171 of 181 patients (94.5%) receiving five or more medications had at least one pDDI. The high prevalence of pDDIs in both groups resulted in no statistically significant difference between the groups. These findings indicate that, within this study population, the number of medications was not significantly associated with the occurrence of pDDIs.

Theoretically, an increasing number of medications may increase the opportunity for drug–drug interactions because more concomitantly administered drugs create a greater number of possible drug combinations. Patients with CHD may also require multiple medications to manage the primary cardiovascular condition and accompanying comorbidities (Maulida & Puspitasari, 2021). However, the present analysis did not demonstrate a statistically significant association between the number of medications and pDDIs.

The absence of a statistically significant association may partly be explained by the high prevalence of pDDIs in both medication groups. All patients receiving fewer than five medications had at least one pDDI, while pDDIs were also identified

in most patients receiving five or more medications. In addition, only 10 patients (5.0%) had no identified pDDI, resulting in a highly imbalanced distribution of the outcome variable. This limited variation may have reduced the ability of the statistical analysis to detect a significant association.

The findings differ from those reported by Saputri and Dewi (2023), who described a higher frequency of potential drug interactions among patients receiving polypharmacy at I.A. Moeis Regional General Hospital, Samarinda. However, their study primarily described the frequency of potential drug interactions and did not statistically evaluate the association between the number of medications and pDDI occurrence. Differences in study design, population characteristics, medication patterns, and analytical approaches may therefore contribute to the differing findings.

The present findings should also be interpreted in relation to Kaltimurti (2023), who reported that potential drug interactions were commonly identified among patients with CHD receiving multiple medications. However, the presence of frequently occurring interacting drug combinations does not necessarily demonstrate a statistical association between the number of medications and the occurrence of pDDIs. In the present study, such an association was not statistically demonstrated ($p = 0.603$).

Overall, the present study found that the number of medications was not significantly associated with the occurrence of pDDIs among outpatients with CHD. Although pDDIs were highly prevalent in both medication groups, the findings do not establish that a greater number of medications was associated with a higher occurrence of pDDIs. Therefore, medication review and monitoring remain important for patients with CHD, particularly because of the high prevalence of database-identified pDDIs in this study population.

1.4.4 Association Between Comorbidities and Potential Drug Interactions

Table 7. Association Between Comorbidities and pDDIs

Comorbidity	Potential Interaction n (%)	No Potential Interaction n (%)	Total n	p-value*
Cardiovascular disorders	111 (55.5)	89 (44.5)	200	<0.001
Hypertension	8 (4.0)	192 (96.0)	200	1.000
Diabetes mellitus	18 (9.0	182 (91.2)	200	0.604
Dyslipidemia	4 (2.0)	196 (98.0)	200	1.000
Renal disorders	7 (3.5)	193 (96.5)	200	1.000
Other comorbidities	68 (34.0)	132 (66.0)	200	0.017

Note: *Fisher's Exact Test, two-sided. Statistical significance was set at $p < 0.05$. Patients could have more than one comorbidity; therefore, the frequencies of individual*

comorbidities are not mutually exclusive and may exceed the total number of patients.

The bivariate analysis demonstrated that the association between comorbidities and potential drug–drug interactions (pDDIs) varied across the different comorbidity categories. Cardiovascular disorders were significantly associated with the occurrence of pDDIs ($p < 0.001$), with 111 patients (55.5%) classified as having potential interactions and 89 patients (44.5%) as having no potential interaction. Other comorbidities also showed a statistically significant association with pDDIs ($p = 0.017$), with 68 patients (34.0%) having potential interactions and 132 patients (66.0%) having no potential interaction. In contrast, hypertension ($p = 1.000$), diabetes mellitus ($p = 0.604$), dyslipidemia ($p = 1.000$), and renal disorders ($p = 1.000$) were not significantly associated with the occurrence of pDDIs.

Theoretically, the presence of comorbidities may increase the risk of drug interactions because patients with additional diseases generally require more complex therapeutic regimens and a greater number of medications. As the complexity of pharmacotherapy increases, the likelihood of potential drug interactions also rises (Maulida & Puspitasari, 2021). In the present study, the significant association observed for cardiovascular disorders may be related to the complexity of pharmacotherapy commonly required for patients with cardiovascular conditions. These patients may receive combinations of antiplatelet agents, antihypertensive drugs, statins, and other cardiovascular medications, thereby increasing the opportunity for potential drug interactions. However, the absence of significant associations for hypertension, diabetes mellitus, dyslipidemia, and renal disorders suggests that the presence of an individual comorbidity alone may not be sufficient to determine the occurrence of pDDIs.

The findings of the present study are consistent with those reported by Kaltimurti (2023), who demonstrated that potential drug interactions among patients with coronary heart disease were more strongly influenced by the combination of prescribed medications than by patients' clinical characteristics. The study also reported that patients with various comorbidities remained at high risk of potential drug interactions because most received similar cardiovascular combination therapies, including antiplatelet agents, antihypertensive drugs, statins, and medications for the management of comorbid conditions. This finding supports the interpretation that the occurrence of pDDIs may be influenced more strongly by the overall medication regimen and pharmacotherapy complexity than by the presence of a particular comorbidity.

These findings are further supported by the study conducted by Aprillia et al. (2025), which reported that patients with coronary heart disease commonly receive combination therapy consisting of multiple medication classes to manage both the primary disease and accompanying comorbidities. Their study found that

potential drug interactions were predominantly pharmacodynamic in mechanism and mostly classified as moderate in severity, indicating that concurrent use of multiple medications is an important factor contributing to potential drug interactions. Therefore, the significant association between cardiovascular disorders and pDDIs in the present study may reflect the greater complexity of treatment among patients with cardiovascular conditions, while the lack of significant associations for several other individual comorbidities may indicate that the medication combinations themselves play a more important role in determining interaction potential.

It is important to note that comorbidities in this study were not mutually exclusive. A patient could have more than one comorbid condition and could therefore be included in more than one comorbidity category. Each comorbidity was assessed separately as a binary variable (present or absent) in the bivariate analysis. Consequently, the frequencies of individual comorbidities should not be interpreted as mutually exclusive groups of patients. This approach reflects the clinical reality that patients with coronary heart disease may simultaneously have multiple chronic conditions requiring different pharmacological therapies.

Overall, the present study suggests that cardiovascular disorders and other comorbidities were significantly associated with pDDIs, whereas hypertension, diabetes mellitus, dyslipidemia, and renal disorders were not statistically associated with pDDIs. These findings indicate that medication safety assessment should not be limited to the presence of a specific comorbidity but should also consider the overall complexity of pharmacotherapy. Regular medication review, identification of potential drug interactions, and appropriate clinical monitoring remain important to minimize the potential risks associated with multidrug therapy in patients with coronary heart disease.

1.5 Limitations

This study has several limitations. First, its retrospective single-center design and relatively short study period may limit the generalizability of the findings to other healthcare settings and patient populations. Second, pDDIs were identified using drug interaction-checking databases and therefore represent potential interactions rather than confirmed clinical adverse drug events. Third, the distribution of the pDDI outcome was highly imbalanced, with 190 patients having at least one pDDI and only 10 patients having no identified pDDI, which may have limited the ability of bivariate analyses to detect associations. Fourth, patients could have multiple comorbidities, resulting in non-mutually exclusive comorbidity categories. Finally, the study focused on bivariate associations and did not assess potential confounding effects between patient characteristics, comorbidities, and medication-related factors.

Conclusion

This study demonstrated a high prevalence of potential drug–drug interactions (pDDIs) among outpatients with coronary heart disease at Jakarta Cempaka Putih Islamic Hospital. Of the 200 patients, 190 (95.0%) had at least one pDDI, with a total of 848 pDDI pair occurrences identified. Pharmacodynamic interactions were predominant (84.1%), while most identified interactions were classified as moderate in severity (92.2%).

Bivariate analysis showed that age, gender, and number of medications were not significantly associated with the occurrence of pDDIs ($p = 0.499$, $p = 1.000$, and $p = 0.603$, respectively). The association between comorbidities and pDDIs varied across individual comorbidity categories. Cardiovascular disorders and other comorbidities were significantly associated with pDDIs, whereas hypertension, diabetes mellitus, dyslipidemia, and renal disorders were not statistically significantly associated with pDDIs.

Overall, the findings indicate that pDDIs were highly prevalent among this outpatient CHD population. However, the observed associations do not establish causality, and the absence of a significant association between the number of medications and pDDIs indicates that medication count alone should not be considered a determinant of pDDIs in this study. Given the high prevalence of pDDIs and the predominance of moderate-severity interactions, routine medication review, interaction screening, and appropriate clinical monitoring are recommended to support medication safety among patients with CHD receiving multidrug therapy.

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