International Journal of Health Science (IJHS)

E-ISSN: 2827-9603
P-ISSN: 2827-9603

Research Article

Analysis of Statin Drug Interactions for Dyslipidemia in In-patients at Royal Prima Hospital in 2022 -2024

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Abstract: Dyslipidemia is a metabolic disorder characterized by abnormal lipid profiles, including elevated levels of low-density lipoprotein (LDL) cholesterol and triglycerides, or reduced high-density lipoprotein (HDL), which increase the risk of cardiovascular diseases. Statins are the primary lipid-lowering agents used to manage dyslipidemia; however, their concomitant use with other medications may result in clinically sig-nificant drug interactions that can compromise therapeutic outcomes and patient safety. This study aimed to analyze the types and severity of drug interactions involving statins in hospitalized dyslipidemia patients at Royal Prima Hospital Medan in 2022-2024. A non-experimental, retrospective study design was em-ployed through a review of patient medical records. Data were analyzed descriptively using Stockley's Drug Interactions and Drugs.com to identify potential interactions and classify them by mechanism and severity. A total of 156 drug interaction cases were identified, comprising 131 moderate (83.98%), 24 major (15.38%), and 1 minor (0.64%) interaction. The most frequent interactions were observed between atorvastatin and amlodipine (39.69%), followed by atorvastatin and clopidogrel (27.49%). Most interac-tions were pharmacokinetic in nature, primarily associated with CYP3A4 enzyme inhibition. In conclu-sion, moderate drug interactions were the most prevalent among statin users, emphasizing the critical role of clinical pharmacists in monitoring andmanaging combination therapies to enhance the safety and ef-fectiveness of dyslipidemia treatment.

Keywords: Drug Interactions; Dyslipidemia; Pharmacodynamics; Pharmacokinetics; Statins.

Received: December 23, 2025
Revised: January 31, 2025
Accepted: February 19, 2026
Online Available: February 21, 2026
Curr. Ver.: February 21, 2026

1. Introduction

Dyslipidemia is a condition in which there is an imbalance in lipid levels in the blood, such as total cholesterol, LDL (Low Density Lipoprotein), HDL (High Density Lipoprotein), and triglycerides. This imbalance can be influenced by unhealthy diets, lack of physical activity, smoking habits, genetic factors, and other metabolic diseases, which can ultimately increase the risk of cardiovascular disease with serious complication (Ballena et al., 2025). Several factors play an important role in the development of dyslipidemia, especially an unhealthy lifestyle and metabolic conditions. Consuming foods rich in saturated fats, trans fats, and cholesterol can increase LDL and triglyceride levels, while lack of physical activity contributes to obesity and impaired lipid metabolism. In addition, smoking can worsen the lipid profile by increasing free fatty acids and lowering HDL cholesterol levels. Metabolic disorders such as obesity, insulin resistance, and diabetes mellitus also contribute to lipid abnormalities by increasing triglyceride production and disrupting normal lipid regulation. These factors collectively increase the risk of dyslipidemia and related cardiovascular complications (Patramurti & Virginia, 2025).

According to the 2018 Basic Health Research (Riskesdas) report, the prevalence of dyslipidemia in Indonesia is relatively high, with 72.8% of the population aged 15 years and older having LDL levels above 100 mg/dL and 28.8% having total cholesterol levels above

200 mg/dL (Ministry of Health of the Republic of Indonesia, 2018). Dyslipidemia has a relatively high prevalence and represents a significant health problem, particularly due to elevated LDL-C and total cholesterol levels in a large proportion of the population. Studies have shown that a considerable percentage of individuals have LDL-C levels above recommended limits, with approximately 45.7% of patients presenting elevated LDL-C concentrations. This condition plays an important role in increasing the incidence of cardiovascular diseases, including coronary heart disease and stroke, which remain the leading causes of death globally. Therefore, dyslipidemia is recognized as a major modifiable risk factor that requires appropriate management to prevent serious cardiovascular complica-tions (Ziółkowski et al., 2025).

Statins are the mainstay of dyslipidemia treatment because they have been proven effective in lowering LDL and total cholesterol levels. These drugs work by inhibiting the HMG-CoA reductase enzyme, which plays a crucial role in cholesterol synthesis in the liver. In addition to lowering LDL, statins can also increase HDL levels by 5–15% and reduce triglycerides by up to 30% (Schetz et al., 2025). Types of statins widely used in Indonesia include simvastatin, atorvastatin, and rosuvastatin, with atorvastatin and simvastatin being the most frequently prescribed due to their effectiveness and high availability (Mach et al., 2020).

Statins are widely metabolized by cytochrome P450 enzymes, particularly CYP3A4, and concomitant administration with other drugs that inhibit this enzyme can increase statin plasma concentrations and enhance the risk of adverse effects, including myopathy and rhabdomyolysis. Calcium channel blockers such as amlodipine may inhibit CYP3A4-mediated metabolism, thereby increasing systemic exposure to certain statins and potentially leading to statin-related toxicity. This interaction may compromise the safety of therapy and requires careful monitoring when both drugs are prescribed together (Mach et al., 2020). Therefore, monitoring drug use is an essential component of clinical pharmacy services to ensure patient safety and therapeutic effectiveness (Wirdatus et al., 2024). In line with this, analyzing potential drug interactions in dyslipidemia patients undergoing statin therapy is crucial, particularly in those with comorbidities who require concomitant medi-cations, in order to prevent adverse effects and maintain optimal therapeutic outcomes.

Based on this background, this study was conducted to analyze statin drug interactions in inpatients with dyslipidemia at Royal Prima Hospital Medan in 2022 -2024. This study is expected to provide a comprehensive overview of the types, mechanisms, and severity of drug interactions that occur, thus providing a basis for improving patient safety and therapeutic effectiveness in hospital healthcare.

2. Literature Review

2.1. Dyslipidemia

Dyslipidemia is defined as an abnormality in lipid metabolism characterized by elevated levels of low-density lipoprotein cholesterol (LDL-C) and triglycerides, along with decreased levels of high-density lipoprotein cholesterol (HDL-C) (Grundy et al., 2023). Primary dyslipidemia is mainly associated with inherited genetic disorders that affect lipid metabolism, whereas secondary dyslipidemia develops as a consequence of external factors such as an unhealthy lifestyle, metabolic disorders, or other underlying medical conditions (Ballena et al., 2025). Dyslipidemia is one of the main causes of atherosclerosis. which leads to cardiovascular diseases such as coronary heart disease and stroke, elevated LDL cholesterol contributes to plaque formation in blood vessels, increasing cardiovascular risk (Ziółkowski et al., 2025).

2.2. Statins

Explained that statins are lipid-lowering agents that inhibit HMG-CoA reductase, the key enzyme responsible for cholesterol synthesis in the liver, which leads to increased LDL receptor expression and enhanced clearance of LDL cholesterol from circulation, thereby reducing cardiovascular risk and improving lipid profiles by lowering triglycerides and modestly increasing HDL cholesterol (Mach et al., 2020). Stated that statins are widely used due to their effectiveness in preventing cardiovascular events; however, their use may cause adverse effects, particularly muscle-related toxicity such as myalgia, myopathy, and rhabdomyolysis, especially when administered concomitantly with other interacting drugs (Schetz et al., 2025).

2.3. Drug Interaction

Drug interactions occur when the pharmacological effect of one drug is modified by the concomitant administration of another drug, which may result in increased toxicity or decreased therapeutic effectiveness (Lin et al., 2023). These interactions may involve

pharmacokinetic processes, including absorption, distribution, metabolism, and excretion, which can alter drug concentrations in the body, or pharmacodynamic mechanisms that influence drug action at the receptor level and modify the therapeutic response (Wirdatus et al., 2024). Based on their clinical significance, drug interactions are commonly classified into minor, moderate, and major categories, where major interactions have the potential to cause serious adverse effects and require careful monitoring or therapy modification (Mar'athus et al., 2022). The evaluation of drug interactions involving statins is particularly important because such interactions may increase the risk of toxicity and negatively affect therapeutic outcomes, especially in patients receiving multiple medications(Mach et al., 2020)

3. Proposed Method

3.1. Study Design and Type

This study was a non-experimental study using a retrospective approach. The purpose of this study was to evaluate potential drug interactions involving statin therapy in hospitalized patients diagnosed with dyslipidemia at Royal Prima Hospital Medan in 2022-2024.

3.2. Study Time and Setting

The study was conducted from April to June 2025 at Royal Prima Hospital Medan. The research data were obtained from inpatient medical records of dyslipidemia patients treated in 2022-2024.

3.3. Population and Sample

The population of this study included all hospitalized patients diagnosed with dyslipidemia who received statin therapy at Royal Prima Hospital Medan in 2022-2024. The sample size was determined using the Lemeshow formula, with a minimum required sample of 101 patients.

3.4. Inclusion Criteria

The inclusion criteria were patients aged 18 years or older, diagnosed with dyslipidemia, receiving statin treatment, and having complete medical record data.

3.5. Data Collection Procedure

Data were collected retrospectively from patients' medical records. The collected information included patient demographics, diagnosis, and details of medications adminis-tered during hospitalization.

3.6. Drug Interaction Analysis

Potential drug interactions were evaluated using the Drugs.com and Medscape data-base as a reference source. Drug interactions were categorized based on interaction type, mechanism (pharmacokinetic or pharmacodynamic), and severity level, including minor, moderate, and major interactions.

3.7. Data Analysis

The collected data were analyzed using descriptive quantitative methods to describe the pattern and characteristics of statin drug interactions among hospitalized dyslipidemia patients at Royal Prima Hospital Medan in 2022-2024.

4. Results and Discussion

4.1. Patient Characteristics

Characteristics based on patient gender and age. The distribution of patient characteristics by gender and age is shown in the following table.

Table 1. This is a Table Patient Characteristics by Gender.

Variable	Category	Recipe Total	Precentage (%)
Gender	Male	62	43,97
	Female	79	56,03
Age	40 - 49	16	11,34
	50 - 59	43	30,49
	60 – 69	52	36,87
	70 – 79	27	19,14
	80 - 89	3	2,12
Recipe Total		141	100

The results of Table 1 show that the majority of dyslipidemia patients using statins were female (56.03%), consistent with the 2013 RISKESDAS (National Health Research and Development Agency), which reported a higher prevalence of abnormal cholesterol levels in

women. This condition is related to hormonal factors, central obesity, and body fat distribution, which affect lipid metabolism (Nazar et al., 2024). Furthermore, the highest number of dyslipidemia sufferers was found in the 60–69 age group (39.72%), indicating an increased risk of dyslipidemia with aging due to changes in lipid metabolism and insulin sensitivity (Streja et al., 2020), and (Rosada et al., 2020). Thus, gender and age play significant roles in the high incidence of dyslipidemia in this population.

4.2. Statin Drug Use Profile

According to Table 2, the most commonly prescribed statin drug among inpatients with dyslipidemia at Royal Prima Hospital was atorvastatin, with 104 prescriptions (73.76%), followed by simvastatin (33) (23.41%), and rosuvastatin (4) (2.83).

Table 2. This is a Table. Statin Drug Use Profile.

Drug Class	Recipe Total	Precentasg (%)
Atorvastatin	104	73,76
Simvastatin	33	23,41
Rosuvastatin	4	2,83
Total	141	100

Based on Table 2, atorvastatin is the most commonly used statin in patients with dyslipidemia (73.76%), followed by simvastatin (23.41%) and rosuvastatin (2.83%). This dominance reflects clinicians' preference for atorvastatin due to its high efficacy in lowering LDL, good safety profile, and dosage flexibility. According to previous research (Bhattarai et al., 2020), atorvastatin received the highest preference score from clinicians, at 4.48, compared to rosuvastatin (2.9) and simvastatin (2.1). This confirms that although the effectiveness of statins in lowering total and LDL cholesterol is relatively similar, atorvastatin is preferred due to its favorable pharmacokinetic profile, consistent research results, and widespread availability at a more affordable price. This factor is further strengthened by the fact that atorvastatin can be administered in a variety of doses (10–80 mg), making it easier to adjust therapy to the patient's clinical condition. Thus, strong clinician preference for atorvastatin contributes to its high prevalence in daily practice.

Similarly, a study (Gharaibeh et al., 2023) demonstrated the dominance of atorvastatin in clinical use. Of the 752 patients analyzed, 98.4% used atorvastatin, while only a small proportion used simvastatin (1.1%), rosuvastatin (0.4%), and fluvastatin (0.1%). This high use of atorvastatin is influenced by several factors, including available dosing flexibility, its high LDL-C lowering potential, and international guidelines, such as the AHA/ACC, which recommend the use of high-intensity statins (atorvastatin ≥40 mg/day or rosuvastatin ≥20 mg/day) in patients at high cardiovascular risk. The availability of generic forms of atorvastatin also makes this drug more economical and more widely accessible to patients, strengthening its position as a primary choice in the management of dyslipidemia.

4.3. Profile of Other Medication Use

According to Table 3, 590 cases of other drug interactions were found in patients diagnosed with dyslipidemia. The most common comorbidity was antihypertensives, with Amlodipine being the most frequently used medication, in 75 patients (12.71%). Furthermore, other comorbidities, such as gastrointestinal disorders, were most frequently used in the same class of drugs, such as Ranitidine, in 68 patients (11.52%).

Table 3. This is a Table Profile of Other Medication Use.

Diseases	Drug Name	Total Case	Precentage (%)
Hypertension	Amlodipine (Norvasc)	75	12,71
	Telmisartan (Micardis)	2	0,33
	Captopril	24	4,07
	Nifedipine	4	0,68
	Nicardipine	5	0,84
	Ramipril	3	0,50
	Candesartan	55	9,32
	Bisoprolol (Concor)	23	3,89
	Valsartan	1	0,16
	Lisinopril	4	0,68
	Metformin	5	0,84

Diabetes mellitus	Glimepiride	1	0,16
	Insulin glargine (Lantus)	17	2,89
	Insulin aspart (NovoRapid)	7	1,19
	Clopidogrel	37	6,28
Cardiovascular and heart disease	Aspirin (Aspilet)	8	1,35
	Warfarin	2	0,33
	Isosorbide dinitrate	13	2,30
	Digoxin	1	0,16
	Ketorolac	17	2,89
Gastric and digestive disorders	Omeprazole	18	3,05
	Sucralfate	21	3,55
	Ranitidine	68	11,52
	Bisacodyl (Dulcolax)	2	0,33
	Loperamide	5	0,84
	Domperidone	4	0,68
	Ondansetron	47	7,97
Asthma	Budesonide (Pulmicort)	2	0,33
	Prednisolone	3	0,50
	Dexamethasone	6	1,01
	Spironolactone	14	2,38
	Methylprednisolone	5	0,84
Nervous and neurological disorders	Pregabalin	5	0,84
	Flunarizine	12	2,03
	Citicoline	8	1,35
	Alprazolam	6	1,01
Pain and fever	Betahistine	12	2,03
	Paracetamol	32	5,42
	Ketorolac	17	2,89
Total	Drug Name	590	100

Based on Table 3, there were 590 cases of drug interactions in patients with dyslipidemia. The most common comorbidity was hypertension, with antihypertensive drugs, particularly amlodipine, being the most commonly used therapy (75 cases; 12.71%). This indicates that the majority of patients with dyslipidemia also suffer from hypertension, necessitating combination therapy that increases the risk of drug interactions. These results align with research conducted by (Dalal et al., 2024), which analyzed over 6.7 million patients in India and found that hypertension was the most common comorbidity in patients with dyslipidemia. The study explained that the combination of dyslipidemia, hypertension, and type 2 diabetes mellitus often occurs together due to interrelated pathophysiological mechanisms, such as insulin resistance, oxidative stress, and endothelial dysfunction. This condition increases the risk of cardiovascular complications up to 20-fold compared to patients without comorbidities. Furthermore, the study confirmed that despite antihypertensive therapy such as calcium channel blockers (amlodipine) and lipid-lowering medications, blood pressure and lipid control in patients remained low, necessitating a more comprehensive and integrated management approach.

In addition to hypertension, another comorbidity frequently found in patients with dyslipidemia is gastrointestinal disorders. Based on the study results, H_2 receptor antagonists, such as ranitidine, were the most frequently used drugs in this group, occurring in 68 patients (11.52%). This indicates that some patients with dyslipidemia also experience digestive complaints, possibly related to the presence of gastrointestinal disorders as comorbidities. These findings align with research by (Wu et al., 2024), which demonstrated a strong association between dyslipidemia and digestive disorders, particularly gastroesophageal reflux disease (GERD). This study showed that patients with GERD tended to have elevated LDL and triglyceride levels, as well as decreased HDL levels, which are hallmarks of dyslipidemia. Metabolic and inflammatory disorders in GERD can worsen lipid profiles, while dyslipidemia can affect gastrointestinal mucosal function. Long-term use of ranitidine also has the potential to affect gastric acid secretion and fat absorption, which indirectly impacts lipid metabolism.

4.4. Drug Interactions by Mechanism

Based on the table above, the largest number of drug interactions is pharmacodynamic, with 342 cases (63.46%), followed by pharmacokinetic drug interactions with 197 cases (36.54%). See the table below:

Table 4. Drug Interactions by Mechanism.

Drug Interaction Mechanisms	Number of occurrences	Precentage (%)
Pharmacokinetics	197	36,54
Pharmacodynamics	342	63,46
Total	539	100

In the table above, pharmacokinetic interactions occur when one drug affects the absorption, metabolism, or elimination of another drug, causing changes in plasma drug concentrations and potentially causing toxicity or reducing therapeutic efficacy (Frechen et al., 2021). In this study, the amlodipine–atorvastatin interaction occurred during hepatic metabolism via the CYP3A4 enzyme. Amlodipine acts as a weak inhibitor of CYP3A4, while atorvastatin is a substrate of this enzyme. Therefore, concomitant use can slow atorvastatin metabolism and increase plasma levels. This increase in levels has the potential to increase the risk of statin side effects, such as myalgia and myopathy, although clinically this interaction is considered moderate and can still be used with adequate monitoring (Patel et al., 2022).

Pharmacodynamic interactions occur when a drug combination affects a biological response in the same physiological system without changing plasma drug levels (Frechen et al., 2021). The combination of amlodipine and ketorolac demonstrated a pharmacodynamic interaction at the analgesic level. Amlodipine has antinociceptive effects through calcium channel inhibition, while ketorolac inhibits the COX enzyme, thereby reducing prostaglandin synthesis. The combination of the two produces additive to synergistic analgesic effects without altering pharmacokinetics (Seredynska et al., 2020).

4.5. Drug Interaction Analysis Based on Severity

Analysis of statin drug interactions was performed by categorizing the severity into minor, moderate, and major categories. The distribution of drug interactions based on severity is shown in the table below:

Table 5. Drug Interaction Analysis Based on Severity.

Severity	Total Case	Precentage (%)
Minor	97	18
Moderate	363	67,34
Major	79	14,66
Total	539	100

Based on the table above, the analysis of dyslipidemia medication use in inpatients at Royal Prima Hospital in 2022 covered 141 patients with a total of 539 drug interaction incidents. Of these, the majority of drug interactions fell into the moderate category, with 363 cases (67.34%), followed by minor interactions with 97 cases (18%), and major interactions with 79 cases (14.66%).

4.5.1 Drug Interactions Based on Severity: Minor

Interactions with minor severity generally do not cause significant problems and do not require additional intervention or therapy (Ningrum et al., 2023). A review of drug interactions with minor severity is shown in the following table:

Table 6. Analysis of drug interactions based on minor severity.

Drug interactions	Total Case	Precentage (%)
Atorvastatin + warfarin	1	1,03
Captropil + nifedipine	2	2,07
Captropil + amlodipine	24	24,74
Captropil + nicardipine	5	5,15
ISDN + Omeprazole	1	1,03
Ranitidine + ketorolac	37	38,14
Ranitidine + paracetamol	20	20,61

Ranitidine + nifedipine	3	3,10
Amlodipine + lisinopril	1	1,03
Alprazolam + dexamethasone	1	1,03
Sucralfate + bisoprolol	2	2,07
TOTAL	97	100

Minor drug interactions in this study did not cause significant clinical impact and generally did not require therapeutic intervention. There were 97 cases of minor interactions, with the ranitidine-ketorolac combination being the most common (37 cases; 38.14%). These interactions were categorized as minor because they did not affect drug efficacy or cause serious toxic effects. This is in line with (Park et al., 2024), which stated that the combination of ketorolac and ranitidine is safe both pharmacodynamically and pharmacokinetically. In clinical practice, this combination is used to reduce opioid side effects and provide protection against NSAID-induced gastric irritation.

Furthermore, one case of minor interaction was found with statins, namely atorvastatin and warfarin. This interaction occurs because both are metabolized by CYP liver enzymes, which can increase the INR. (Engell et al., 2021) reported a 0.27-point increase in INR in patients taking this combination. Although not clinically significant, INR monitoring is still necessary to prevent the risk of bleeding.

4.5.2 Drug Interaction Analysis Based on Moderate Severity

Interactions with moderate severity are an important category to consider, as they can cause changes in clinical effects, which can impact patient condition and treatment success (Ningrum et al., 2023). The drug interaction profile for moderate severity is shown in the following table:

Table 7. Drug interaction analysis based on moderate severity.

Drug interactions	Total Case	Precentage (%)
Atorvastatin + Ezetimibe	2	0,55
Atorvastatin + Amlodipine	52	14,32
Atorvastatin + Clopidogrel	36	10,74
Atorvastatin + Nifedipine	8	2,20
Simvastatin + Omeprazole	17	4,68
Atorvastatin + Dexamethasone	9	2,47
Simvastatin + nifedipine	1	0,27
Atorvastatin + Metroridazole	1	0,27
Atorvastatin + Omeprazole	5	1,37
Fenofibrate + Ezetimibe	2	0,55
Captropil + furosemide	13	3,58
Captropil + ISDN	3	0,82
Captropil + dexamethasone	3	0,82
Captropil + ketorolac	19	5,23
Furosemide + ketorolac	17	4,68
Furosemide + omeprazole	8	2,20
Furosemide + dexamethasone	4	1,10
Furosemide + sucralfate	4	1,10
Furosemide + bisoprolol	11	3,03
Furosemide + lanthus	3	0,82
Ketorolac + amlodipine	43	11,84
Ketorolac + candesartan	28	7,71
Ketorolac + spironolactone	4	1,10
Ketorolac + bisoprolol	6	1,65
Nifedipine + ketorolac	3	0,82
Nifedipine + metformin	1	0,27
Nifedipine + bisoprolol	4	1,10
Methylprednisolone + candesartan	3	0,82
Methylprednidolone + amlodipine	2	0,55
Bisoprolol + lantus	3	0,82
Amlodipine + bisoprolol	6	1,65
Alprazolam + amlodipine	4	1,10

Ketorolac + spironolactone	3	0,82
Spironolactone + bisoprolol	4	1,10
Ketorolac + metformin	3	0,82
Sucralfate + metformin	1	0,27
Sucralfate + lantus	3	0,82
Candesartan + lantus	7	1,92
Dexamethasone + nicardipine	2	0,55
Dexamethasone + ketorolac	4	1,10
Dexamethasone + amlodipine	4	1,10
Dexamethasone + spironolactone	2	0,55
Prednisolone + amlodipine	1	0,27
Nicardipine + bisoprolol	2	0,55
Warfarin + omeprazole	1	0,27
Warfarin + sucralfate	1	0,27
TOTAL	363	100

Based on the table above, there were 363 cases of moderate drug interactions, with the combination of atorvastatin and amlodipine being the most common (52 cases; 14.32%), followed by ketorolac and amlodipine (43 cases; 11.84%). The combination of atorvastatin and amlodipine is commonly used in patients with dyslipidemia and hypertension. This interaction is pharmacokinetic, with amlodipine inhibiting CYP3A4, thereby increasing plasma atorvastatin levels and potentially causing myopathy or hepatotoxicity. However, research (Kim et al., 2020), indicated that the toxic effects were not clinically significant during monitoring. Further research (Kim et al., 2024), also demonstrated that the combination remains safe in fixed-dose form without significant pharmacokinetic changes. The interaction between ketorolac and amlodipine is considered moderate because NSAIDs can reduce the antihypertensive effect of amlodipine through inhibition of vasodilatory prostaglandins, thus triggering fluid retention and increased blood pressure (Piszczatoski & Smith, 2022).Therefore, the use of this combination is still permitted with blood pressure monitoring, especially in hypertensive or elderly patients.

4.5.3 Drug Interaction Analysis Based on Major Severity

Drug interactions with major severity are very serious because they can cause major effects, ranging from endangering the patient's life to causing permanent damage to organs. Therefore, they require attention and appropriate management (Ningrum et al., 2023). A review of drug interactions with major severity can be seen in the following table:

Table 8. Drug Interaction Analysis Based on Major Severity.

Drug Interactions	Total Case	Precentage (%)
Simvastatin + Amlodipine	23	29.11
Atorvastatin + Fenofibrate	1	1,27
Captropil + micardis	1	1,27
Captropil + spironolactone	5	6,32
Captropil + valsartan	1	1,27
Ranitidine + loperamide	1	1,27
Amitriptyline + ondansetron	1	1,27
Ramipril + candesartan	1	1,27
Captropil + candesartan	14	17,72
Captropil + spironolactone	1	1,27
Ranitidine + loperamide	4	5,06
Omeprazole + clopidogrel	3	3,79
Ketorolac + clopidogrel	6	7,59
Spironolactone + candesartan	10	12,65
Dexamethasone + candesartan	2	2,53
Dexamethasone + levofloxacin	1	1,27
Spironolactone + candesartan	1	1,27
Levofloxaxin + lantus	1	1,27
Lisinopril + candesartan	1	1,27
Dixocin + spironolactone	1	1,27
TOTAL	**79**	**100**

Minor Based on the table above, there were 79 cases of drug interactions with major severity. The combination of simvastatin with amlodipine was the most common (23 cases; 29.11%), followed by captopril with candesartan (14 cases; 17.72%). This indicates that major interactions commonly occur in combination therapy for cardiovascular disease, particularly in patients with hypertension and dyslipidemia.

Concurrent administration of simvastatin with amlodipine can increase circulating simvastatin levels due to inhibition of its metabolism via the CYP3A4 enzyme. This increase in simvastatin levels is associated with the risk of myopathy and rhabdomyolysis. (Schmelzer et al., 2023) recommend that simvastatin doses not exceed 20 mg per day or consider using other safer statins. A similar finding was also reported (Piszczatoski & Smith, 2022), who stated that amlodipine can significantly increase simvastatin exposure and trigger severe muscle damage. The Drugs.com database confirms that the simvastatin-amlodipine combination is a major interaction, so its use should be approached with caution, with close clinical monitoring and consideration of dose adjustments or alternative therapies if necessary.

Furthermore, the combination of captopril (an ACE inhibitor) and candesartan (an angiotensin receptor blocker/ARB) is also considered a potential interaction (Whitlock et al., 2023). Both drugs act on the renin-angiotensin-aldosterone system (RAAS), so their effects can be mutually reinforcing when used together, leading to the risk of excessive blood pressure reduction, increased blood potassium levels (hyperkalemia), and impaired kidney function. Captopril inhibits the formation of angiotensin II, while candesartan blocks its receptor, completely inhibiting the hormone's activity. Therefore, this combination is not recommended for use together, except in certain circumstances with close monitoring of the patient's kidney function and electrolyte levels.

5. Comparison

The findings of this study were compared with previous studies related to drug interactions involving statins. The present study showed that statins were frequently pre-scribed in hospitalized dyslipidemia patients and had the potential to interact with other medications, particularly cardiovascular drugs such as calcium channel blockers. This finding is consistent with the study conducted by (Mustikaningtias et al., 2020), which re-ported that statins, especially simvastatin and atorvastatin, have a high potential for drug interactions due to their metabolism through the CYP3A4 enzyme pathway.

Furthermore, this study also identified that most drug interactions were categorized as moderate severity. This result is in line with (Mar'athus et al., 2022), who reported that moderate interactions were the most commonly observed in hospitalized patients receiving statin therapy. These interactions may not always require discontinuation of therapy but require monitoring to prevent adverse drug effects. Compared to previous studies, the present study provides additional data specifically from hospitalized dyslipidemia patients at Royal Prima Hospital Medan, thereby contributing to updated and localized evidence re-garding the pattern, mechanism, and severity of statin drug interactions in clinical practice.

6. Conclusion

This study demonstrated that drug interactions involving statin therapy were com-monly found in hospitalized dyslipidemia patients at Royal Prima Hospital Medan. The results showed that statins, particularly simvastatin and atorvastatin, had the potential to interact with other concomitant medications, with most interactions classified as moderate severity. These interactions mainly occurred through pharmacokinetic mechanisms in-volving drug metabolism pathways. The findings of this study support the research ob-jective, which was to analyze potential statin drug interactions in hospitalized dyslipidemia patients. This study provides important information regarding the pattern and severity of drug interactions, which can help healthcare professionals improve patient safety and op-timize therapeutic outcomes. The implication of this study is that healthcare providers, especially pharmacists, should carefully monitor statin therapy in patients receiving multiple medications to prevent adverse drug reactions. This study also contributes to expanding knowledge related to statin drug interactions in clinical settings. However, this study has several limitations, including the use of retrospective data and reliance on medical records, which may not fully reflect the clinical outcomes of drug interactions. Therefore, further prospective studies are recommended to evaluate the clinical impact of statin drug interac-tions more comprehensively.

Author Contributions: Conceptualization: Minaraya Naiborhu and Daimah W.S. Harahap; Methodology: Minaraya Naiborhu; Software: Minaraya Naiborhu; Validation: Minaraya Naiborhu, Daimah W.S. Harahap, and Novitaria br. Sembiring; Formal analysis: Minaraya Naiborhu; Investigation: Minaraya Naiborhu; Resources: Minaraya Naiborhu; Data curation: Minaraya Naiborhu; Writing—original draft preparation: Minaraya Naiborhu; Writing—review and editing: Minaraya Naiborhu, Daimah W.S. Harahap, and Novitaria br. Sembiring; Visualization: Minaraya Naiborhu; Supervision: Daimah W.S. Harahap; Project administration: Minaraya Naiborhu; Funding acquisition: Not applicable.

Funding: This study did not receive financial support from any external funding agencies.

Data Availability Statement: The data supporting the findings of this research were obtained from inpatient medical records at Royal Prima Hospital Medan. Due to ethical considerations and patient confidentiality, these data are not publicly accessible. However, data may be provided by the corresponding author upon reasonable request and with approval from the respective institution.

Acknowledgments: The authors would like to express their appreciation to Royal Prima Hospital Medan for permitting access to the medical records required for this study. The authors are also grateful to the lecturers and academic supervisors from the Faculty of Pharmacy, Universitas Prima Indonesia, for their valuable guidance and support throughout the research process.

Conflicts of Interest: The authors declare that there are no conflicts of interest related to this research. Furthermore, no funding bodies were involved in the study design, data collection, data analysis, interpretation of the results, manuscript writing, or decision to submit the manuscript for publication.

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