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Potential Drug–Drug Interactions in Prescriptions for Outpatients with Type 2 Diabetes Mellitus at A Private Hospital in Bandar Lampung

Harum Puspita Ningrum[1*], Elma Viorentina Sembiring[2], Ageng Hasna Fauziyah[3]
[1,2,3]Pharmacy Department, Health Polytechnic of Tanjung Karang
Corresponding Author: Elma Viorentina Sembiring elmaviorentinas@poltekkes-tjk.ac.id

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A B S T R A C T

Diabetes is a chronic metabolic disease characterized by hyperglycemia, with type 2 diabetes mellitus (T2DM) being the most prevalent worldwide. This descriptive quantitative study aimed to identify potential drug–drug interactions (pDDIs) in T2DM outpatients. A total of 100 medical records from the outpatient department in 2024 were selected using accidental sampling. Most patients were female (57%) and aged 46–65 years (72%). Prescriptions commonly contained fewer than seven drugs (87%), with metformin being the most frequently prescribed antidiabetic (30.9%) and sulfonylureas the most common drug class (34.6%). Drug interactions were identified in 76% of prescriptions, predominantly of moderate severity (63.2%) and pharmacokinetic mechanism (50.6%)

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INTRODUCTION

Cases of Drug-Related Problems (DRPs), particularly drug–drug interactions, are frequently identified in prescriptions written by physicians for patients with diabetes mellitus (Hayati, Ariyani, and Ruslinawati, 2020). Drug–drug interactions are events that may occur when two or more medications are taken concurrently. One type of Drug-Related Problem (DRP) that can affect the body's response to therapy is drug–drug interaction. Patient treatment outcomes may change as a result of increased or decreased drug effects (Mahamudu, Citraningtyas, and Rotinsulu, 2017).

Based on data from the Lampung Province Health Service (2021) the number of patients with diabetes mellitus in Bandar Lampung City in 2022 was ⩾18,600 out of a total of ⩾89,900 diabetes mellitus cases in Lampung Province. Based on these data, there is a possibility that the medications consumed by patients with diabetes mellitus may result in drug–drug interactions. In order to improve therapeutic outcomes and patients' quality of life, it is necessary to evaluate potential drug interactions (pDDIs) among medications used by outpatients with diabetes mellitus. Therefore, research on potential drug–drug interactions in prescriptions for patients with type 2 diabetes mellitus at Advent Hospital, Bandar Lampung City, is essential, as patients with type 2 diabetes mellitus are those who primarily use oral antidiabetic drugs. This is further supported by the fact that the number of diabetes mellitus cases in Bandar Lampung City reached 18,600 in 2022 and is expected to continue increasing annually (Dinas Kesehatan Provinsi Lampung, 2021).

A study in India involving 50 prescriptions of hospitalized patients with diabetes, 35 prescriptions (70%) showed at least one potential drug–drug interaction. Of the interactions identified, 68% were classified as minor, 66% as moderate, and 20% as severe major interactions (Sankar et al., 2015). Another retrospective study reported that 80.9% of patients with diabetes had at least one potential clinically significant interaction (category C), based on assessments using a drug interaction database (Samardzic & Bacic-Vrca, 2015).

A study conducted at Marinir Cilandak Hospital involving 190 medical records found that 36% of patients experienced potential drug–drug interactions. Most of these interactions were pharmacokinetic in nature, with 54.17% classified as minor interactions (Refdanita & Maisarah, 2017). A similar study at AR Bunda Prabumulih Hospital reported that 9 patients (25%) were at risk of experiencing drug–drug interactions. The most common potential interaction involved glimepiride and metformin in combination with the antibiotic levofloxacin, occurring in 8 patients (22.2%) (Niza et al., 2023). At the local level, a study conducted at RS TK. 02.07.04 Bandar Lampung reported that out of 151 patients, 112 patients (74.17%) experienced potential drug–drug interactions. Most interactions were classified as moderate (92.61%) and minor (7.39%), with no major interactions observed (Meiliana et al., 2023). To date, no similar study has been conducted at Advent Hospital in Bandar Lampung, which is the study site of the present research.

The objective of this study was to describe potential drug–drug interactions in prescriptions for patients with type 2 diabetes mellitus at the

outpatient department of Advent Hospital, Bandar Lampung City, in 2024. The specific objectives were to identify sociodemographic characteristics, including sex and age; clinical characteristics, comprising the number of drug items per prescription, types of antidiabetic drugs, classes of antidiabetic drugs, and types of concomitant medications; and to determine the percentage of potential drug–drug interactions based on severity level and mechanism of action.

THEORETICAL REVIEW

Drug–drug interactions are defined as modifications of the effect of a drug caused by another drug when the drugs are administered concurrently, resulting in changes in the effectiveness or toxicity of one or both agents. Changes in drug effects due to interactions may be harmful, leading to increased drug toxicity or reduced therapeutic efficacy. However, interactions between multiple drugs are not always detrimental and, in certain cases, may also produce beneficial effects (Fitri et al., 2022).

There are three levels of severity of drug–drug interactions: minor, moderate, and major. Minor interactions may occur but are generally considered not harmful. Moderate interactions are those that have the potential to worsen adverse drug effects. Major interactions are those that may endanger patients and lead to permanent disability or even death (Agustin & Fitrianingsih, 2020).

Pharmacodynamic and pharmacokinetic mechanisms are two classifications used to categorize drug–drug interactions. Pharmacodynamic interactions result in antagonistic, synergistic, or additive effects when drugs act on the same receptor, site of action, or physiological system. Pharmacokinetic interactions occur when two or more drugs are administered simultaneously and one drug affects the absorption, distribution, metabolism, or excretion of another. This may cause an increase or decrease in plasma drug concentrations, potentially enhancing toxicity or reducing therapeutic effectiveness (Rizqiah dan Damayanti, 2022).

According to Tanty, Meryta, dan Zulfitasari (2023) minor drug-drug interaction occurs between metformin and furosemide, in which metformin reduces the level of furosemide through an undetermined mechanism. An example of a moderate interaction is between glimepiride and ramipril, where the concurrent use of these drugs can increase the risk of hypoglycemia, resulting in lowered blood glucose levels. A major interaction is observed between glimepiride and levofloxacin, in which levofloxacin can enhance the effect of glimepiride through a pharmacodynamic synergistic mechanism. The administration of quinolone antibiotics may lead to hyperglycemia or hypoglycemia (Tanty, Meryta, dan Zulfitasari, 2023).

Based on the study by Nurlaelah, Mukaddas, and Faustine (2015), an example of a pharmacodynamic interaction occurs between glimepiride and captopril, in which captopril enhances the effect of glimepiride via pharmacodynamic synergy, potentially resulting in hypoglycemia. An example of a pharmacokinetic interaction reported by the same study involves metformin and amlodipine, where amlodipine increases the absorption of metformin, which may also lead to hypoglycemia (Nurlaelah, Mukaddas, dan Faustine, 2015).

METHODOLOGY

This is a quantitative descriptive design study, encompassing sociodemographic and clinical characteristics as well as potential drug–drug interactions (pDDIs) to identify possible interactions in patients with type 2 diabetes mellitus. Subject in this study are medical records of patients with type 2 diabetes mellitus. The entire population consisted of medical records of type 2 diabetes mellitus patients from the Outpatient Department of Advent Hospital, Bandar Lampung City, in 2024. Medical records that met the inclusion and exclusion criteria were used as the study sample.

The inclusion criteria were prescriptions for type 2 diabetes mellitus patients using oral antidiabetic drugs or insulin, with or without concomitant medications, and containing more than one type of drug. The exclusion criteria were prescriptions with incomplete data or prescriptions containing topical medications. A total of 100 medical records were included as the sample, determined using Slovin's formula and proportional allocation, and selected using accidental sampling.

The study was conducted at the Medical Records Department of Advent Hospital, Bandar Lampung City, from March to April 2025. Data were collected using a data collection sheet, and potential drug–drug interactions were identified using the Medscape application, Drugs.com website, and DrugBank website (go.drugbank.com). The collected data were then processed and presented as frequency distributions and percentages.

RESEARCH RESULTS

Sociodemographic and Clinical Data

Table 1. Sociodemographic Data

Characteristics	Without pDDIs (%) n = 76	All types of pDDIs (%) n = 24	Total (%) n = 100
Gender			
Male	29 (38,2%)	14 (58,3%)	43 (43%)
Female	47 (61,8%)	10 (41,7%)	57 (57%)
Age (Years)			
21 – 35	3 (3,9%)	1 (4,2%)	4 (4%)
36 – 45	1 (1,3%)	2 (8,3%)	3 (3%)
46 – 65	54 (71,1%)	17 (70,8%)	71 (71%)
66 – 74	17 (22,4%)	4 (16,7%)	21 (21%)
75 – 90	1 (1,3%)	0 (0%)	1 (1%)

The results presented in Table 1 show that type 2 diabetes mellitus was more prevalent among female patients, with 57 patients (57%), compared to male patients, who accounted for 43 patients (43%). Regarding age distribution, the

highest proportion of patients with type 2 diabetes mellitus was observed in the late adulthood age group (46–65 years), comprising 72 patients (72%). In contrast, the lowest proportion was found in the middle adulthood age group (36–45 years), with only 3 patients (3%).

Table 2. Clinical Data

Characteristics	Without pDDIs (%) n = 76	All types of pDDIs (%) n = 24	Total (%) n = 100
Number of Medications			
< 7	63 (82,9%)	24 (100%)	87 (87,0%)
≥ 7	13 (17,1%)	0 (0,0%)	13 (13,0%)
Number of Comorbidities Medication			
Yes	73 (96,1%)	19 (79,2%)	92 (92,0%)
No	3 (3,9%)	5 (20,8%)	8 (8,0%)

The results presented in Table 2 indicate that the highest percentage of prescriptions contained fewer than seven drug items, accounting for 87 prescriptions (87%), whereas prescriptions containing seven or more drugs accounted for 13 prescriptions (13%). Prescriptions that included concomitant medications represented the majority, with 92 prescriptions (92%), compared to only 8 prescriptions (8%) without concomitant medications.

The results presented in Table 3 show that the most frequently prescribed antidiabetic drug was metformin, with 58 prescriptions (30.9%). In contrast, the least frequently prescribed antidiabetic drugs were empagliflozin and acarbose, each prescribed only once (0.5%).

Table 3. Antidiabetic Medication

Medications	Total Amount (%) n = 188
Acarbose	1 (0,5%)
Empagliflozin	1 (0,5%)
Gliclazide	29 (15,4%)
Glimepiride	29 (15,4%)
Gliquidone	7 (3,7%)
Insulin	20 (10,6%)
Linagliptin	5 (2,7%)
Sitagliptin	19 (10,1%)
Vildagliptin	11 (5,9%)
Metformin	58 (30,9%)
Pioglitazone	8 (4,3%)

Potential Drug-Drug Interactions

The results presented in Table 5 indicate that the majority of potential drug–drug interactions were of moderate severity, accounting for 165 interactions (63.2%), with the most frequent case involving the interaction between ramipril and metformin (6.1%). Minor-severity interactions accounted for 79 interactions (30.3%), with the most common interaction occurring between metformin and Cobalamin (15.2%). Meanwhile, major-severity potential drug–drug interactions were the least frequent, totaling 17 interactions (6.5%), with the most prevalent major interaction observed between lansoprazole and gliclazide (23.5%).

Table 4. Potential Drug-Drug Interactions Based on Mechanism of Action

Mechanism of Action	Number of Events N=261	%
Pharmacodynamic	79	30,3
Pharmacokinetic	132	50,6%
Unknown	50	19,2

Table 5. Potential Drug-Drug Interaction Based on Severity

Severity Level	Interacting Pair	Number of Events (%)	Total (%) n = 261
Minor	Amitriptyline + Metformin	1 (1,3%)	79 (30,3%)
	Amitriptyline + Sitagliptin	1 (1,3%)	
	Aspirin + Folic Acid	2 (2,5%)	
	Aspirin + Furosemide	1 (1,3%)	
	Aspirin + Glimepiride	2 (2,5%)	
	Aspirin + Ibuprofen	1 (1,3%)	
	Aspirin + Imidapril	1 (1,3%)	
	Aspirin + Cobalamin	4 (5,1%)	
	Dexketoprofen + Metformin	2 (2,5%)	
	Dexketoprofen + Ofloxacin	1 (1,3%)	
	Diazepam + Paracetamol	1 (1,3%)	
	Furosemide + Calcium Carbonate	1 (1,3%)	
	Furosemide + Metformin	6 (7,6%)	
	Gabapentin + Cobalamin	4 (5,1%)	
	Ibuprofen + Furosemide	1 (1,3%)	
	Diclofenac Potassium + Metformin	1 (1,3%)	
	Lansoprazole + Cobalamin	6 (7,6)	
	Metformin + Alpha Lipoic Acid (ALA)	1 (1,3%)	
	Metformin + Folic Acid	2 (2,5%)	
	Metformin + Cobalamin	12 (15,2%)	
	Methylprednisolone + Aspirin	1 (1,3%)	
	Methylprednisolone + Furosemide	1 (1,3%)	
	Methylprednisolone + Glimepiride	1 (1,3%)	
	Methylprednisolone + Insulin Glargine	1 (1,3%)	
	Methylprednisolone + Metformin	1 (1,3%)	
	Methylprednisolone + Sitagliptin	2 (2,5%)	

Severity Level	Interacting Pair	Number of Events (%)	Total (%) n = 261
	Sodium Bicarbonate + Aspirin	2 (2,5%)	
	Nifedipine + Metformin	4 (5,1%)	
	Ofloxacin + Glimepiride	1 (1,3%)	
	Ofloxacin + Insulin Aspart	1 (1,3%)	
	Ofloxacin + Insulin Glargine	1 (1,3%)	
	Ofloxacin + Vitamin B1	1 (1,3%)	
	Ofloxacin + Vitamin B6	2 (2,5%)	
	Sitagliptin + Glimepiride	3 (3,8%)	
	Spironolactone + Calcium Carbonate	1 (1,3%)	
	Sucralfate + Lansoprazole	5 (6,3%)	
Moderate	Acarbose + Gliclazide	1 (0,6%)	165 (63,2%)
	Amlodipine + Gliclazide	4 (2,4%)	
	Amlodipine + Diclofenac Potassium	1 (0,6%)	
	Amlodipine + Metformin	7 (4,2%)	
	Aspirin + Ciprofloxacin	1 (0,6%)	
	Aspirin + Furosemide	1 (0,6%)	
	Aspirin + Gliclazide	4 (2,4%)	
	Aspirin + Glimepiride	2 (1,2%)	
	Aspirin + Ibuprofen	2 (1,2%)	
	Aspirin + Insulin Aspart	2 (1,2%)	
	Aspirin + Insulin Detemir	1 (0,6%)	
	Aspirin + Insulin Glargine	3 (1,8%)	
	Aspirin + Insulin Glulisine	2 (1,2%)	
	Aspirin + Methylprednisolone	1 (0,6%)	
	Aspirin + Valsartan	3 (1,8%)	
	Atorvastatin + Amitriptyline	1 (0,6%)	
	Atorvastatin + Methylprednisolone	2 (1,2%)	
	Atorvastatin + Valsartan	2 (1,2%)	
	Azithromycin + Simvastatin	1 (0,6%)	
	Bisoprolol + Amlodipine	1 (0,6%)	
	Bisoprolol + Gliclazide	1 (0,6%)	
	Bisoprolol + Valsartan	2 (1,2%)	
	Candesartan + Aspirin	6 (3,6%)	
	Candesartan + Furosemide	1 (0,6%)	
	Candesartan + Insulin Glargine	1 (0,6%)	
	Candesartan + Insulin Glulisine	1 (0,6%)	
	Carvedilol + Amlodipine	1 (0,6%)	
	Cetirizine + Betahistine	1 (0,6%)	
	Ciprofloxacin + Gliclazide	1 (0,6%)	
	Ciprofloxacin + Insulin Aspart	1 (0,6%)	
	Ciprofloxacin + Sitagliptin	1 (0,6%)	
	Dexketoprofen + Gliclazide	2 (1,2%)	
	Dexketoprofen + Pregabalin	1 (0,6%)	
	Diazepam + Gliclazide	1 (0,6%)	
	Empagliflozin + Gliclazide	1 (0,6%)	
	Fenofibrate + Insulin Aspart	1 (0,6%)	
	Fenofibrate + Insulin Glargine	1 (0,6%)	
	Furosemide + Gliclazide	3 (1,8%)	
	Gemfibrozil + Glimepiride	1 (0,6%)	
	Glimepiride + Insulin Glargine	2 (1,2%)	

Severity Level	Interacting Pair	Number of Events (%)	Total (%) n = 261
	Ibuprofen + Furosemide	1 (0,6%)	
	Ibuprofen + Gliclazide	1 (0,6%)	
	Imidapril + Glimepiride	1 (0,6%)	
	Imidapril + Metformin	3 (1,8%)	
	Diclofenac Potassium + Glimepiride	1 (0,6%)	
	Levofloxacin + Insulin Aspart	1 (0,6%)	
	Linagliptin + Gliclazide	3 (1,8%)	
	Lisinopril + Furosemide	1 (0,6%)	
	Lisinopril + Glimepiride	3 (1,8%)	
	Lisinopril + Metformin	2 (1,2%)	
	Lisinopril + Spironolactone	1 (0,6%)	
	Metformin + Insulin Aspart / Degludec	1 (0,6%)	
	Methylprednisolone + Gliclazide	1 (0,6%)	
	Sodium Bicarbonate + Carvedilol	1 (0,6%)	
	Sodium Bicarbonate + Gabapentin	1 (0,6%)	
	Sodium Bicarbonate + Ramipril	1 (0,6%)	
	Sodium Bicarbonate + Ferrous Sulfate	1 (0,6%)	
	Nifedipine + Gliclazide	3 (1,8%)	
	Nifedipine + Metformin	3 (1,8%)	
	Ofloxacin + Glimepiride	1 (0,6%)	
	Ofloxacin + Insulin Aspart	1 (0,6%)	
	Ofloxacin + Insulin Glargine	1 (0,6%)	
	Perindopril + Metformin	1 (0,6%)	
	Pioglitazone + Rosuvastatin	1 (0,6%)	
	Pioglitazone + Simvastatin	1 (0,6%)	
	Pregabalin + Amitriptyline	1 (0,6%)	
	Pregabalin + Diazepam	1 (0,6%)	
	Pregabalin + Gliclazide	7 (4,2%)	
	Pseudoephedrine + Betahistine	1 (0,6%)	
	Ramipril + Aspirin	3 (1,8%)	
	Ramipril + Furosemide	2 (1,2%)	
	Ramipril + Glimepiride	3 (1,8%)	
	Ramipril + Insulin Aspart	1 (0,6%)	
	Ramipril + Insulin Detemir	1 (0,6%)	
	Ramipril + Metformin	10 (6,1%)	
	Ramipril + Spironolactone	1 (0,6%)	
	Simvastatin + Gliclazide	3 (1,8%)	
	Sitagliptin + Gliclazide	8 (4,8%)	
	Sitagliptin + Insulin Glargine	1 (0,6%)	
	Spironolactone + Aspirin	2 (1,2%)	
	Spironolactone + Furosemide	2 (1,2%)	
	Spironolactone + Ibuprofen	1 (0,6%)	
	Triprolidine + Codein	1 (0,6%)	
	Triprolidine + Betahistine	1 (0,6%)	
	Valsartan + Gliclazide	2 (1,2%)	
	Valsartan + Insulin Aspart	1 (0,6%)	
	Valsartan + Insulin Glargine	1 (0,6%)	
	Vildagliptin + Gliclazide	3 (1,8%)	
Mayor	Amlodipine + Simvastatin	1 (5,9%)	17 (6,5%)

Severity Level	Interacting Pair	Number of Events (%)	Total (%) n = 261
	Aspirin + Ramipril	3 (17,6%)	
	Fenofibrate + Atorvastatin	1 (5,9%)	
	Fenofibrate + Simvastatin	1 (5,9%)	
	Ibuprofen + Aspirin	2 (11,8%)	
	Imidapril + Pregabalin	1 (5,9%)	
	Lansoprazole + Gliclazide	4 (23,5%)	
	Sodium Bicarbonate + Ofloxacin	1 (5,9%)	
	Nifedipine + Simvastatin	1 (5,9%)	
	Perindopril + Pregabalin	1 (5,9%)	
	Ramipril + Pregabalin	1 (5,9%)	

DISCUSSION

The results of this study indicate that patients with type 2 diabetes mellitus attending the Outpatient of Advent Hospital, Bandar Lampung, were predominantly female, accounting for 57 patients (57%), while male patients comprised 43 patients (43%). This finding is consistent with previous research by Rosita et al, (2022), which reported that women are more susceptible to weight gain and increased adipose tissue accumulation after menopause due to hormonal alterations compared to men. Consequently, female respondents were found to have a 2.15-fold higher risk of developing type 2 diabetes mellitus. Previous evidence has demonstrated that the hormones progesterone and estrogen play a crucial role in enhancing insulin sensitivity. However, following menopause, the body's ability to respond to insulin declines as circulating levels of estrogen and progesterone decrease (Rohmatulloh et al. 2024).

Patients with type 2 diabetes mellitus attending the Outpatient Department of Advent Hospital, Bandar Lampung, were predominantly in the late adulthood age group (46–65 years), accounting for 72 patients (72%). The youngest patient was 23 years old, while the oldest was 81 years old. The late adulthood age group (46–65 years) constituted the largest proportion of prescriptions both with drug–drug interactions (71.1%) and without drug–drug interactions (70.8%). These findings are consistent with a study by Scarton et al. (2023), which reported that type 2 diabetes mellitus is more prevalent among individuals aged over 45 years compared to those under 45 years. This pattern is primarily attributable to degenerative processes that impair the body's capacity to regulate glucose, which underlie the high prevalence of glucose intolerance in older adults.

Age-related variations in blood glucose levels are associated with a decline in insulin sensitivity, thereby increasing the risk of type 2 diabetes mellitus. The pancreas is affected by rapid and progressive physiological deterioration experienced by most individuals after the age of 40 years (Rohmatulloh et al., 2024). In addition, insulin secretion decreases with advancing age, while changes in body composition and the development of sarcopenia contribute to insulin resistance (Mordarska & Godziejewska-Zawada, 2017). Several physiological disorders are strongly influenced by aging, as the

body gradually loses its functional capacity over time. Aging is defined as a process in which tissues progressively lose their ability to repair, regenerate, and maintain their characteristic structure and function (Sutanto, 2013).

Based on the findings of this study, most patients with type 2 diabetes mellitus attending the Outpatient Department of Advent Hospital, Bandar Lampung, received fewer than seven medications per prescription, accounting for 87 prescriptions (87%), whereas prescriptions containing seven or more medications accounted for 13 prescriptions (13%). This finding is consistent with the study conducted by Febriyanti et al. (2023), which reported that a higher proportion of patients received fewer than five medications per prescription compared to those receiving five or more medications. Polypharmacy may be influenced by various factors, including age. Medication use tends to increase with advancing age and the presence of multiple comorbidities. Furthermore, referrals to multiple healthcare providers may contribute to polypharmacy, as different physicians may prescribe different medications.

The highest proportion of prescriptions with potential drug–drug interactions was observed among prescriptions containing fewer than seven medications (82.9%), compared to those containing seven or more medications (17.1%). Notably, all prescriptions with seven or more medications were identified as having potential drug–drug interactions. These findings contrast with those reported by Susilo, Hidayat, & Dona (2018), who found that prescriptions containing seven or more medications had a higher potential for drug–drug interactions, accounting for 51 prescriptions (60.71%) out of 100, compared to 33 prescriptions (39.29%) containing fewer than seven medications. This discrepancy may be attributed to the higher proportion of prescriptions containing fewer than seven medications in the present study (87%) compared to those containing seven or more medications (13%). Consequently, among the 76 prescriptions with potential drug–drug interactions, prescriptions containing fewer than seven medications accounted for a greater proportion (82.9%) than those containing seven or more medications (17.1%). Drug–drug interactions occur when concomitantly administered medications modify each other's effects, resulting in altered efficacy or increased toxicity of one or more drugs (Sari, Lusia, dan Almasdy, 2023).

Based on the results of this study, metformin was identified as the most commonly prescribed antidiabetic medication for patients with type 2 diabetes mellitus attending the Outpatient Department of Advent Hospital, Bandar Lampung, accounting for 58 prescriptions (30.9%). This finding is consistent with the study conducted by Ardyanto, Sekkti, & Ardianto (2024), which reported that metformin was the most frequently prescribed medication, appearing in 54 out of 59 prescriptions (91%). Metformin does not induce hypoglycemia, making it one of the safest and most effective therapeutic options for older adults.

Metformin exerts its antihyperglycemic effect by inhibiting hepatic glucose production (gluconeogenesis) and enhancing glucose uptake in peripheral tissues. Most patients with type 2 diabetes mellitus initiate pharmacological therapy with metformin (Parman, 2021). Owing to its relatively high efficacy, low risk of hypoglycemia, neutral effect on body weight, favorable

cardiovascular outcomes, and cost-effectiveness, metformin is recommended as the first-line pharmacotherapy for patients with type 2 diabetes mellitus.

This study identified a total of 261 potential drug–drug interactions among 100 prescriptions for patients with type 2 diabetes mellitus at the Outpatient Department of Advent Hospital, Bandar Lampung. These interactions were predominantly classified as pharmacokinetic mechanisms, accounting for 132 cases (50.6%), followed by pharmacodynamic mechanisms with 79 cases (30.3%), and interactions with unknown or unspecified mechanisms comprising 50 cases (19.2%). Pharmacodynamic interactions occur when drugs act on the same receptors, sites of action, or physiological systems, resulting in additive, synergistic, or antagonistic effects. The most frequent pharmacodynamic interactions involved amlodipine–metformin, which may reduce the therapeutic effect of metformin and impair glycemic control, and acetylsalicylic acid–candesartan, which may increase serum potassium levels and reduce the antihypertensive effect of candesartan.

Pharmacokinetic interactions, which involve alterations in drug absorption, distribution, metabolism, or excretion, were the most commonly identified mechanism in this study, consistent with findings reported by (Refdanita & Maisarah, 2017). The most frequent pharmacokinetic interactions included pregabalin–gliclazide and sitagliptin–gliclazide, both of which may increase the risk of hypoglycemia, as well as lansoprazole–vitamin B12, which may reduce vitamin B12 levels by inhibiting gastrointestinal absorption. Interactions with unknown or unspecified mechanisms were most commonly observed between metformin and vitamin B12, potentially leading to vitamin B12 deficiency, and between ramipril and metformin, which may increase metformin toxicity and the risk of hypoglycemia.

Based on the study that was conducted, it was found that among 100 prescriptions of patients with type 2 diabetes mellitus at the Outpatient Department of Advent Hospital, Bandar Lampung City, there were 261 cases of potential drug–drug interactions. These interactions were categorized into minor severity with 79 cases (30.3%), moderate severity with 165 cases (63.2%), and major severity with 17 cases (6.5%).

Minor interactions are defined as drug interactions that occur but cause minimal clinical effects and therefore do not require additional therapeutic intervention. Based on the results of this study, among the 79 potential minor interactions (30.3%), the most frequently identified was the interaction between metformin and vitamin B12, accounting for 12 cases (15.2%), which may reduce vitamin B12 levels. This was followed by the interaction between furosemide and metformin, with 6 cases (7.6%), which may decrease metformin levels, and the interaction between lansoprazole and vitamin B12, also with 6 cases (7.6%), which may reduce vitamin B12 levels by inhibiting gastrointestinal absorption.

Moderate severity drug interactions are those that may result in changes in the patient's clinical status (Hendera & Rahayu, 2018). In this study, moderate interactions constituted the majority of potential interactions, with 165 cases (63.2%). This finding is consistent with the study by Julaiha and Isnenia (2022), which reported that the most common severity level of potential drug

interactions was moderate, accounting for 105 cases (64.8%). Similarly, a study conducted by Susilo et al., (2018) found that moderate drug interactions were the most prevalent, with 290 cases (68.23%).

Among the 165 potential moderate interactions (63.2%) identified in this study, the most frequent was the interaction between ramipril and metformin, with 10 cases (6.1%), which may increase metformin toxicity and subsequently elevate the risk of hypoglycemia. This was followed by the interaction between sitagliptin and gliclazide, with 8 cases (4.8%), which may enhance the hypoglycemic activity of gliclazide, and the interaction between pregabalin and gliclazide, with 7 cases (4.2%), which may increase the risk of hypoglycemia. Therefore, regular monitoring of blood glucose levels is required in patients experiencing these interactions.

Major drug interactions are those with serious clinical consequences that may cause permanent damage or even be life-threatening (Hendera & Rahayu, 2018). In this study, major interactions were the least frequent, with 17 cases (6.5%). This result is in line with the findings of Julaiha & Isnenia (2022), which reported that major drug interactions were the least common, accounting for 11 cases (6.79%).

The most common potential major interaction identified was between lansoprazole and gliclazide, with 4 cases (23.5%), which may reduce the metabolism of gliclazide and thereby increase the risk of hypoglycemia. This was followed by the interaction between acetylsalicylic acid and ramipril, with 3 cases (17.6%), which may impair renal function, and the interaction between acetylsalicylic acid and ibuprofen, with 2 cases (11.8%), which may reduce the antiplatelet effect and consequently increase the risk of blood clot formation.

CONCLUSIONS AND RECOMMENDATION

This study concluded that most patients with type 2 diabetes mellitus at the Outpatient Department of Advent Hospital, Bandar Lampung City were female (57%) and aged 46–65 years (72%), with the majority of prescriptions containing fewer than seven medications (87%). Metformin (30.9%) and sulfonylureas (34.6%) were the most frequently prescribed antidiabetic agents, and concomitant medications were present in 92% of prescriptions, most commonly vitamin B12 (10.2%). Potential drug–drug interactions were identified in 76% of prescriptions, predominantly moderate in severity (63.2%), particularly involving ramipril–metformin (6.1%), followed by minor interactions (30.3%), mainly metformin–vitamin B12 (15.2%), and major interactions (6.5%), most frequently lansoprazole–gliclazide (23.5%). Pharmacokinetic interactions were the most common mechanism (50.6%), followed by pharmacodynamic (30.3%) and undetermined mechanisms (19.2%), highlighting the need for closer monitoring, improved evaluation of actual drug interactions, and enhanced patient education to reduce potential adverse outcomes.

FURTHER STUDY

Future studies are recommended to extend the scope of this research by investigating actual drug–drug interactions and their clinical outcomes, rather than focusing solely on potential interactions identified through databases. Prospective or longitudinal study designs would allow for the assessment of real clinical consequences, such as hypoglycemic events, renal impairment, or other adverse drug reactions. In addition, future research should incorporate more comprehensive clinical variables, including comorbidities, duration of diabetes, laboratory parameters, and patient adherence, to better elucidate the factors contributing to drug–drug interactions in patients with type 2 diabetes mellitus. The involvement of clinical pharmacists in intervention-based studies is also encouraged to evaluate the effectiveness of medication review and counseling in reducing the incidence and severity of drug–drug interactions.

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