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Screening of Drug Interaction Prescreption for Outpatients with Diabetes Mellitus and Hypertension from October to December 2023 at Advent Hospital Medan

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Abstract

Diabetes mellitus and hypertension are two chronic conditions that frequently occur simultaneously and require long-term pharmacological therapy. The combination of treatments in patients with both diseases increases the potential for drug interactions, which can compromise therapeutic effectiveness and elevate the risk of adverse effects. This study aimed to evaluate the severity of drug interactions in outpatients with diabetes mellitus and hypertension at Advent Hospital Medan during the period from October to December 2023. A non-experimental descriptive study with a cross-sectional design was employed, using retrospective data from 191 outpatient prescriptions that met the inclusion criteria. Evaluation was conducted on administrative, pharmaceutical, and clinical aspects of the prescriptions, with a primary focus on identifying drug interactions using the reference database Drugs.com. The results showed that drug interactions were present in 52.4% of the analyzed prescriptions. Most interactions were classified as moderate in severity, predominantly involving pharmacodynamic mechanisms. The most frequent interacting drug combinations included metformin, glimepiride, amlodipine, bisoprolol, and candesartan. The high prevalence of drug interactions among patients with diabetes mellitus and hypertension highlights the importance of systematic prescription screening as a preventive measure. These findings can serve as a basis for developing rational drug use policies and enhancing patient safety in clinical practice.

Keywords: Drug interaction, diabetes mellitus, hypertension, prescription screening, outpatient care

Abstrak

Diabetes mellitus dan hipertensi merupakan dua penyakit kronis yang sering terjadi secara bersamaan dan memerlukan terapi farmakologis jangka panjang. Kombinasi pengobatan pada pasien dengan kedua kondisi ini berpotensi menimbulkan interaksi obat yang dapat memengaruhi efektivitas terapi serta meningkatkan risiko efek samping. Penelitian ini bertujuan untuk mengevaluasi tingkat keparahan interaksi obat pada pasien rawat jalan penderita diabetes mellitus dan hipertensi di RS Advent Medan selama periode Oktober hingga Desember 2023. Penelitian ini menggunakan metode deskriptif non-eksperimental dengan pendekatan potong lintang (cross-sectional), di mana data diperoleh secara retrospektif dari 191 resep rekam medis yang memenuhi kriteria inklusi. Evaluasi dilakukan terhadap aspek administratif, farmasetik, dan klinis pada resep, dengan fokus utama pada identifikasi interaksi obat menggunakan referensi Drugs.com. Hasil penelitian menunjukkan bahwa interaksi obat ditemukan pada 52,4% resep yang dianalisis. Sebagian besar interaksi tergolong keparahan sedang, dengan mekanisme interaksi farmakodinamik yang mendominasi. Kombinasi obat yang paling sering menyebabkan interaksi adalah metformin, glimepirid, amlodipin, bisoprolol, dan candesartan. Tingginya prevalensi interaksi obat pada pasien dengan diabetes mellitus dan hipertensi menunjukkan pentingnya skrining resep secara sistematis sebagai upaya pencegahan. Temuan ini diharapkan dapat menjadi dasar dalam penyusunan kebijakan rasionalisasi penggunaan obat dan peningkatan keselamatan pasien dalam praktik klinis.

Kata kunci: *Interaksi obat, diabetes melitus, hipertensi, skrining resep, rawat jalan.*

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INTRODUCTION

Diabetes mellitus (DM) is a heterogeneous group of chronic metabolic disorders characterized by persistent hyperglycemia due to impaired insulin secretion, insulin resistance, or both. It is classified into four major types: type 1 diabetes, type 2 diabetes, gestational diabetes, and other specific types. Among these, type 2 diabetes mellitus (T2DM) accounts for the vast majority of cases and is closely linked to modifiable risk factors such as sedentary lifestyle, poor dietary habits, obesity, and increasing age[1].

T2DM is pathophysiologically marked by insulin resistance in peripheral

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tissues, particularly muscle and liver, as well as progressive beta-cell dysfunction. These abnormalities disrupt glucose homeostasis and also affect lipid and protein metabolism. If not properly managed, T2DM can lead to long-term complications—both microvascular (e.g., retinopathy, nephropathy, and neuropathy) and macrovascular (e.g., coronary artery disease, stroke, and peripheral arterial disease)—which significantly increase morbidity and mortality[2–4].

One of the most prevalent and clinically significant comorbidities in patients with T2DM is hypertension, with a reported prevalence of over 70%. The presence of chronic hyperglycemia contributes to endothelial dysfunction and arterial stiffness, which elevate blood pressure and accelerate cardiovascular complications. This dual burden of T2DM and hypertension often necessitates polypharmacy—multiple medications taken concurrently—which increases the risk of drug-drug interactions (DDIs). These interactions may reduce therapeutic efficacy, trigger adverse effects, and compromise patient safety[5].

According to the International Diabetes Federation (IDF), as of 2019, approximately 463 million people worldwide are living with diabetes, and this number is projected to reach 700 million by 2045 in the absence of effective interventions. In Southeast Asia, the prevalence stands at 11.3%, while Indonesia ranks seventh globally, with over 10 million individuals affected. National data from Riskesdas further emphasize the rising incidence of DM, particularly in relation to advancing age and urbanization[6].

Despite the clinical importance of DDIs in patients with T2DM and hypertension, studies focusing on this issue—especially in private hospital settings in Indonesia—remain scarce. Therefore, this study was conducted to identify and assess the severity of drug interactions in outpatient prescriptions for patients with T2DM and hypertension at Advent Hospital Medan. The findings aim to support evidence-based improvements in clinical pharmacy services and promote safer, more rational pharmacotherapy.

METHODOLOGY

This study is a non-experimental, cross-sectional descriptive study with a retrospective design. It aimed to evaluate the potential for drug interactions in outpatients with diabetes mellitus and hypertension by reviewing prescriptions from administrative, pharmaceutical, and clinical perspectives.

Location and Time of Reasearch

The research was conducted at Advent Hospital Medan, located on Gatot Subroto Street Km 4, Sei Sikambing D, Medan Petisah, Medan City, North Sumatra. Data collection was carried out from October to December 2023, and data processing was conducted in August 2024.

Population and Sampel

The population in this study consisted of all outpatient prescriptions received at Advent Hospital Medan from October to December 2023. Samples were selected purposively, with the inclusion

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criterion being electronic prescriptions containing at least five drugs. Out of a total of 20,431 prescriptions, 191 met the criteria and were included for further analysis.

RESULT AND DISCUSSION

Administrative Aspects Review

To ensure legal and procedural compliance, a review of administrative elements in each prescription was conducted. Table 1 presents the completeness of key administrative components recorded in 191 outpatient prescriptions.

Table 1. Presciption Administrative Completeness Data

Administrative aspects	amount	Percentage
Patient name	191	100 %
Age	191	100 %
Weight	0	0 %
Gender	191	100 %
Doctor's name	191	100 %
Practice license (SIP)	191	100 %
Address	0	0 %
Phone number	0	0 %
Paraf	191	100 %
Prescription date	191	100 %

Based on Table 1, the review of outpatient prescriptions at Advent Hospital Medan revealed that several administrative elements were consistently complete, including patient name, age, gender, doctor's name, practice license (SIP), signature, and prescription date, all of which achieved 100% completeness. Key administrative components such as the doctor's name and license (SIP) are essential to ensure the legitimacy of the prescription and to prevent forgery. The prescription date is also crucial for documenting the validity period and traceability of therapy. However, the absence of patient weight, address, and phone number may limit individualized pharmacotherapy and follow-up[7,8].

Pharmaceutical Aspects Review

According to the Ministry of Health Regulation (Permenkes No. 72/2016), the pharmaceutical review of prescriptions should include the drug name, dosage form and strength, quantity, stability, and compatibility. These components are critical in minimizing the risk of medication errors, with particular emphasis on ensuring the accuracy of the drug name, dosage form, strength, and quantity[9].

The 191 prescriptions reviewed in this study comprised a wide range of medications, both generic and branded, and included various dosage forms such as capsules, tablets, syrups, and suspensions. The results of the pharmaceutical evaluation are presented in Table 2, which shows that all essential pharmaceutical components—drug name, dosage form, strength, quantity, and stability—were fully stated in every prescription, resulting in a 100% compliance rate across all categories.

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Clinical Review of Prescriptions

A clinical review was conducted to evaluate the appropriateness of the prescribed drugs in terms of therapeutic indication, dosage, usage instructions, potential duplication, and drug interactions. These factors are crucial for ensuring that pharmacotherapy is both rational and safe, especially in patients receiving multiple medications[7].

Table 3 presents the evaluation results of 191 outpatient prescriptions categorized by the number of drugs prescribed. Each prescription was assessed for the accuracy of indications, dosage, instructions for use (including method and duration), presence of duplication, and potential drug interactions.

Table 2. Completeness of Pharmaceutical Information in Prescriptions

Pharmacetical aspects	Frequency	Percentage
Drug name	191	100 %
Dosage form	191	100 %
Strength of preparation	191	100 %
Quantity of medicine	191	100 %
Stability	191	100 %

Table 3. Prescription Clinical Completeness Data

No	Amount of Medication	Number of Recipes	Accurate Indication	Accurate Dosage	Rules, How to Use and duration of Use	Duplication	Interaction
1.	Five drugs	41	100 %	100%	100 %	0 %	34,1 %
2.	Six drugs	57	100 %	100%	100 %	0 %	52,6 %
3.	Seven drugs	32	100 %	100%	100 %	0 %	34,3 %
4.	Eight drugs	23	100 %	100%	100 %	0 %	56,5 %
5.	Nine drugs	19	100 %	100%	100 %	0 %	78,9 %
6.	Ten drugs	12	100 %	100%	100 %	0 %	83,3 %
7.	Eleven drugs	4	100 %	100%	100 %	25 %	100 %
8.	Twelve drugs	2	100 %	100%	100 %	0 %	50 %
9.	Thirteen drugs	1	100 %	100%	100 %	0 %	100 %

As shown in Table 3, all prescriptions met clinical standards in terms of indication, dosage, instructions for use, and duration of treatment, with a 100% compliance rate. However, prescriptions containing a higher number of drugs were more likely to involve drug-related problems. One notable case of drug duplication (25%) was identified in a prescription containing 11 drugs. Furthermore, the prevalence of drug interactions increased progressively with the number of medications prescribed—occurring in 34.1% of prescriptions with 5 drugs, 52.6% with 6 drugs, 34.3% with 7 drugs, 56.5% with 8 drugs, 78.9% with 9

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drugs, 83.3% with 10 drugs, 100% with 11 and 13 drugs, and 50% with 12 drugs. Among these identified interactions, 17 were pharmacodynamic and 3 were pharmacokinetic in nature. These findings emphasize the critical need for comprehensive clinical reviews and systematic drug interaction screening, particularly in polypharmacy scenarios, to enhance patient safety and optimize therapeutic outcomes.

Identification of Drug Interactions

A total of 20 clinically relevant drug interactions were identified in the prescriptions analyzed. Each interaction was assessed for its severity and underlying mechanism, whether pharmacodynamic or pharmacokinetic. These interactions predominantly involved antidiabetic agents (e.g., metformin, glimepiride, insulin) and antihypertensive medications (e.g., bisoprolol, candesartan, amlodipine)[10]. The complete list of interactions is presented in Table 4.

Table 4. Drug Interaction Identification Result

Drug Interactions	Severity Level	Interaction Mechanism
Metformin + Glimepirid	Moderate	Pharmacodynamics
Metformin + Acarbose	Minor	Pharmacokinetics
Metformin + Insulin glargine	Moderate	Pharmacodynamics
Metformin + Glibenklamid	Moderate	Pharmacodynamics
Metformin + Nifedipin	Moderate	Pharmacodynamics
Metformin + Furosemid	Moderate	Pharmacokinetics
Metformin + Ramipril	Moderate	Pharmacokinetics
Metformin + Spironolactone	Moderate	Pharmacodynamics
Glimepiride + Ramipril	Moderate	Pharmacodynamics
Glimepiride + Bisoprolol	Moderate	Pharmacodynamics
Bisoprolol + Insulin glargine	Moderate	Pharmacodynamics
Bisoprolol + Valsartan	Moderate	Pharmacodynamics
Bisoprolol + Insulin glulisine	Moderate	Pharmacodynamics
Bisoprolol + Amlodipin	Moderate	Pharmacodynamics
Bisoprolol + Spironolactone	Moderate	Pharmacodynamics
Bisoprolol + Nifedipin	Moderate	Pharmacodynamics
Candesartan + Spironolactone	Mayor	Pharmacodynamics
Candesartan+ Insulin glargine	Moderate	Pharmacodynamics
Candesartan+Insulinglulisine	Moderate	Pharmacodynamics
Glimepirid + Insulin glulisine	Moderate	Pharmacodynamics

The identification of drug interactions revealed several clinically significant combinations, primarily involving antidiabetic and antihypertensive agents. Among these, the combination of metformin and glimepiride demonstrated a moderate pharmacodynamic interaction that increases the risk of hypoglycemia, necessitating regular blood glucose monitoring and possible dose adjustment. Similarly, metformin combined with insulin glargine or glibenclamide also heightened the risk of hypoglycemia due to their synergistic glucose-lowering effects[11]. On the other hand, metformin and acarbose showed a minor pharmacokinetic

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interaction, as acarbose reduces metformin's intestinal absorption by approximately 35%, though it generally does not require major intervention. Notably, the co-administration of metformin and nifedipine enhances metformin's plasma concentration through increased gastrointestinal absorption via OCT1 transporters, representing a moderate pharmacokinetic concern. Additionally, metformin with furosemide may increase the risk of lactic acidosis and hypoglycemia due to mutual alterations in drug plasma levels, calling for intermittent use and careful monitoring[12].

In terms of interaction with renin-angiotensin-aldosterone system (RAAS) inhibitors, metformin and ramipril presented a moderate pharmacodynamic interaction, where ramipril may potentiate metformin's hypoglycemic effect. Conversely, spironolactone combined with metformin may paradoxically raise blood glucose levels and increase the risk of lactic acidosis, especially in renally impaired patients. Glimepiride and ramipril showed a similar risk profile, with ramipril enhancing insulin sensitivity and thereby increasing the likelihood of hypoglycemia. When glimepiride was used with bisoprolol, there was concern over the masking of hypoglycemia symptoms such as tachycardia, complicating early detection of hypoglycemia[13,14].

Among cardiovascular drugs, bisoprolol combined with insulin glargine or insulin glulisine posed a risk of bradycardia and hypotension due to unopposed alpha-adrenergic effects. In combination with amlodipine, bisoprolol may exhibit additive effects on lowering blood pressure and heart rate, with the additional concern of increased bisoprolol bioavailability due to metabolic inhibition. Likewise, the combination of bisoprolol and spironolactone could lead to hypotension, bradycardia, and impaired glycemic control, while bisoprolol with nifedipine showed additive hypotensive effects that may precipitate cardiovascular compromise, although tolerable under cardiac monitoring[15].

A particularly critical interaction was observed between candesartan and spironolactone, categorized as major due to the significantly elevated risk of hyperkalemia—especially in elderly patients or those with renal impairment, diabetes, or heart failure. Meanwhile, candesartan in combination with insulin glargine or insulin glulisine was associated with an increased hypoglycemia risk, necessitating careful dose titration and blood glucose monitoring. Finally, glimepiride and insulin glulisine, when used concurrently, presented a compounded hypoglycemic effect, underlining the importance of gradual dose adjustment and patient education to mitigate risks.

CONCLUSION

This study screened 191 prescriptions for drug interactions in outpatients with diabetes and hypertension at Advent Hospital Medan (Oct–Dec 2023). While administrative and pharmaceutical data were complete, clinically significant interactions were identified, including moderate (metformin–glimepiride, bisoprolol–insulin) and major (candesartan–spironolactone) cases.

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Commonly prescribed drugs included metformin, glimepiride, pioglitazone, bisoprolol, amlodipine, and candesartan. These results highlight the need for regular prescription reviews to ensure safe and effective polypharmacy management.

REFERENCES

1. Ginting, A. N. B., Ginting, C. N., Rusip, G. & Chiuman, L. Antidiabetic Activity of Cep-Cepan Leaf Extract Nanoparticles (Castanopsis costata) in Streptozotocin-Induced White Rat Models. *J. Penelit. Pendidik. IPA* **11**, 64–70 (2025).
2. Alkandahri, M. Y. *et al.* Antidiabetic activity of extract and fractions of Castanopsis costata leaves on alloxan-induced diabetic mice. *Pharmacogn. J.* **13**, (2021).
3. Furman, B. L. Streptozotocin-Induced Diabetic Models in Mice and Rats. *Curr. Protoc.* **1**, e78 (2021).
4. Sari, H., Kaban, V. E., Situmorang, F. R. & Fahdi, F. UJI EFEKTIVITAS ANTIDIABETES KOMBINASI EKSTRAK DAUN MENIRAN (Phyllanthus niruri L.) Dan KELOPAK BUNGA ROSELLA (Hibiscus sabdariffa L.) PADA TIKUS JANTAN PUTIH. *J. Penelit. Farm. Herb.* **2**, 24–28 (2019).
5. Mierza, V., Lau, D. C., Hadjami, D. R., Amelia, T. C. & Ryandha, M. G. Article Review: Study of the Potential of Indonesian Herbal Plants as Antidiabetic in Type 2 Diabetid Patients. *J. Pharm. Sci.* 529–540 (2023).
6. Savych, A. & Milian, I. Total flavonoid content in the herbal mixture with antidiabetic activity. *PharmacologyOnLine* **2**, 68–75 (2021).
7. Choudhry, N. K. *et al.* Medication Adherence and Blood Pressure Control: A Scientific Statement From the American Heart Association. *Hypertension* **79**, (2022).
8. Anders, H.-J., Peired, A. J. & Romagnani, P. SGLT2 inhibition requires reconsideration of fundamental paradigms in chronic kidney disease,'diabetic nephropathy', IgA nephropathy and podocytopathies with FSGS lesions. *Nephrol. Dial. Transplant.* **37**, 1609–1615 (2022).
9. Sudarmi, S. & Hurria, H. Implementation Of Pharmaceutical Service Standards Based On Regulation Of The Minister Of Health Number 73 Of 2016 At Pharmacies In Wara District Palopo City. in *International Conference of Business, Education, Health, and Scien-Tech* vol. 1 2263–2273 (2024).
10. Kithas, P. A. & Supiano, M. A. Hypertension in the geriatric population: a patient-centered approach. *Med. Clin.* **99**, 379–389 (2015).
11. Budi, A. *et al.* Detection of glibenclamide adulteration in herbal remedies for diabetes mellitus using TLC. *Bul. Kedokt. Kesehat. Prima* **3**, 6–10 (2024).
12. Alaofi, A. L. Sinapic acid ameliorates the progression of streptozotocin (STZ)-induced diabetic nephropathy in rats via NRF2/HO-1 mediated pathways. *Front. Pharmacol.* **11**, 1119 (2020).
13. Puri, B. K., Kingston, M. C. & Monro, J. A. Fructose-associated hepatotoxicity indexed by the lactate dehydrogenase isoenzyme LDH-5. *Med. Hypotheses* **124**, 40–41 (2019).
14. Hamrahian, S. M. & Falkner, B. Hypertension in Chronic Kidney Disease. in *Hypertension: from basic research to clinical practice* (ed. Islam, Md. S.) vol. 956 307–325 (Springer International Publishing, Cham, 2016).
15. Uchmanowicz, B., Chudiak, A. & Mazur, G. The influence of quality of life on the level of adherence to therapeutic recommendations among elderly hypertensive patients. *Patient Prefer. Adherence* **Volume 12**, 2593–2603 (2018).