

Evaluation of the Suitability of Antihypertensive Therapy in Type 2 Diabetes Mellitus Patients with Hypertension Comorbidity

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ABSTRACT

Background: Diabetes and hypertension are two chronic diseases that often occur together. The prevalence of hypertension in diabetic patients is twice as high as in the general population, with approximately 69% of adults with diabetes also having hypertension. Cardiovascular disease is the leading cause of death in diabetic patients, and hypertension management plays a crucial role in reducing this risk. Antihypertensive therapy for type 2 diabetic patients with hypertension requires complex treatment strategies.

Objective: This study aims to evaluate the suitability of antihypertensive therapy prescribed to type 2 diabetic patients with comorbid hypertension, comparing it with the guidelines in the 12th edition of the DiPiro therapeutic algorithm in 2023.

Research Methods: This is a descriptive study with a retrospective data collection method, using consecutive sampling. The sample consists of 47 outpatient type 2 DM patients with comorbid hypertension. Variables evaluated include drug indication, drug class, and drug dosage. Data analysis was conducted using Microsoft Excel to calculate percentages of drug therapy suitability.

Results: The evaluation found that the suitability of drug indication was 100%, the suitability of drug class was 65.96%, and the suitability of drug dosage was 100%.

Conclusion: Most type 2 DM patients with comorbid hypertension in this study were male, aged 60-74 years. The study highlights that while the suitability of drug indication and dosage met the recommended standards, the drug class suitability was below 100%. It is recommended that further efforts be made to align the prescribed antihypertensive therapy with the treatment guidelines.

Keywords: Evaluation; Hypertension; Outpatient; Therapy Suitability



INTRODUCTION

Based on the International Diabetes Federation (IDF) report in 2021, the prevalence of type 2 diabetes mellitus continues to increase worldwide, with 537 million adults aged 20 to 79 years suffering from diabetes mellitus that year. This figure is expected to increase to 783 million by 2045. Indonesia ranks fifth among countries with the highest number of diabetes sufferers, reaching 19.5 million people in 2021, and is expected to reach 28.57 million people by 2045. Diabetes mellitus is a major modifiable risk factor for atherosclerotic cardiovascular disease (ASCVD) and is one of the 10 leading causes of disability. High blood pressure is a major risk factor in ASCVD that can be controlled. Hypertension often occurs in patients with diabetes mellitus (Kim *et al.*, 2022).

Diabetes and hypertension are two chronic diseases that often occur together. The prevalence of hypertension in diabetic patients is twice as high as in the general population, with approximately 69% of adults with diabetes also having hypertension. In diabetic patients, there is an increase in the formation of non-enzymatic glycosylation products and sodium retention which causes vascular stiffness and increased blood pressure. In addition to the pathophysiological relationship, these two conditions also have interrelated risk factors and complications. Risk factors include family factors, race, dyslipidemia, and lifestyle. Complications include macrovascular disorders such as stroke, myocardial infarction, peripheral vascular disease, congestive heart failure, and coronary artery disease. Also, there are microvascular complications such as retinopathy, neuropathy, and nephropathy (Baah-nyarkoh *et al.*, 2023).

Hypertension in patients with type 2 diabetes is closely related to increased body fluid volume and peripheral vascular resistance. This condition occurs due to changes in blood vessels and an increase in the amount of body fluid caused by high levels of insulin and blood sugar that occur in insulin resistance. After reaching an advanced stage, peripheral vascular resistance becomes one of the main causes of hypertension in diabetic patients, and complications related to vascular remodeling further worsen the condition. In particular, the adjustment of the afferent artery during diabetic nephropathy increases glomerular pressure, which then leads to further complications (Ohishi, 2018).

Cardiovascular disease is the leading cause of death in diabetic patients. Hypertension management is an important strategy in reducing this risk. Antihypertensive therapy for type 2 diabetic patients with hypertension requires complex treatment. Therefore, it is necessary to evaluate the suitability of antihypertensive therapy to effectively lower blood pressure while minimizing the risk of related complications. Based on the 12th edition of the DiPiro therapeutic algorithm in 2023, four first-line antihypertensive agents, namely ACE inhibitors (ACEi), angiotensin II receptor blockers (ARBs), calcium channel blockers (CCBs), and thiazide-type diuretics, have been shown to reduce cardiovascular events in patients with diabetes. The American Diabetes Association also recommends a minimum blood pressure target of <140/90 mmHg in patients with diabetes to reduce the risk of cardiovascular complications.

This research has not been conducted in Sleman Regency, making it important to evaluate the suitability of therapy with treatment guidelines for patients with type 2 diabetes mellitus (DM) and comorbid hypertension. This study aims to improve therapy quality, contributing to national resilience, particularly in the context of Social and Cultural Resilience, and

promoting Nationalism by reducing morbidity and mortality from complications of type 2 DM and hypertension. The novelty of this research lies in assessing antihypertensive therapy suitability in type 2 DM patients with comorbid hypertension in Sleman. While similar studies have been conducted globally and in other parts of Indonesia, this study fills a local knowledge gap and offers a unique contribution to improving therapy quality in the region. The research aims to evaluate the effectiveness of antihypertensive treatments to better manage both hypertension and diabetes. This study is expected to improve national health outcomes, reduce morbidity and mortality, and contribute to national resilience by addressing the health challenges posed by these chronic diseases.

RESEARCH METHODS

This study is an analytical observational study, where the researchers did not provide any intervention to the research subjects. The research design used is descriptive with a retrospective data collection method. The research samples were selected using the consecutive sampling technique. The study was conducted in the medical records unit of a hospital in Sleman Regency. The inclusion criteria for this study included patients aged over 18 years who were diagnosed with type 2 diabetes mellitus with hypertension comorbidity and had complete medical record data. Meanwhile, the exclusion criteria included patients with incomplete medical record data related to medication use and patients who were pregnant.

Tools and materials

The tools used are worksheets used to record or collect the necessary patient data, therapy guidelines, namely DiPiro, 2023: "Pharmacotherapy a Pathophysiologic Approach", and Microsoft Excel software to process patient data that has been obtained. The research materials used are patient medical records with complete data in the form of patient identity such as name, age, gender, weight, height, and diagnosis and date of examination. Subjective patient data includes complaints, comorbidities, and treatments given such as indications, drug classes, and drug doses received by the patient.

Research procedure

The research procedure starts from literature study, proposal preparation, submission of EC (No. 131/KEP-PKU/VI/2024) and research permit, data collection, data processing, preparation of reports and publication of research.

Data analysis

This research is descriptive, with univariate data analysis processed using Microsoft Excel. The data includes numbers, averages, standard deviations, and percentages of prescription suitability according to therapeutic guidelines. The data presented includes:

- a. Suitability of drugs indication.
- b. Suitability of drugs class or name.
- c. Suitability of drugs dosage.

RESULTS AND DISCUSSION

The sample consisted of 47 patients out of 100 who met the inclusion criteria. The calculated results and obtained data are presented in tabular form. Patient characteristic data collection aimed to identify the demographics and profiles of Type 2 DM patients with comorbid hypertension at Hospital X in Sleman Regency. Patient characteristics included details such as name, age, gender, weight, height, diagnosis, and examination date, which were then categorized by gender and age.

TABLE I. Characteristics of type 2 DM patients with comorbid hypertension

Characteristics of Patients	Frequency (n)	Percentage(%)
Gender		
Male	32	68.09
Female	15	31.91
Total	47	100
Age (Years)		
25-44	6	12.77
45-59	19	40.43
60-74	20	42.55
>74	2	4.26
Total	47	100

Based on Table I, the grouping results show that Type 2 DM patients with comorbid hypertension are more prevalent among males (32 individuals or 68.09%) compared to females (15 individuals or 31.91%). A study by the University of Glasgow, Scotland, cited in Pratiwi *et al.* (2024), also mentioned that males are more susceptible to Type 2 DM, especially those with a Body Mass Index (BMI) exceeding 31.83, classified as obese. Several biological factors, such as higher insulin resistance in males and fat accumulation in certain organs, are the primary reasons why males are at greater risk of developing Type 2 DM and hypertension. The combination of these two conditions—Type 2 DM and hypertension—can exacerbate the patient's condition. Diabetes can damage blood vessels, weaken blood pressure regulation, and increase the risk of cardiovascular complications, which are common among hypertensive patients. Additionally, hormonal factors play a role, as low testosterone levels in males may further elevate the risk of developing both conditions (Pratiwi *et al.*, 2024).

Another study conducted by Aristoteles (2018) revealed a correlation between gender and hypertension, showing that men are more likely to develop hypertension in their late thirties, while women are more prone to it after menopause. Consequently, men with Type 2 DM have a higher likelihood of developing hypertension at a younger age, further compromising cardiovascular health. Gender influences the incidence of hypertension, with men experiencing it more frequently than women, with an approximate 2.29% higher increase in

systolic blood pressure. Men are believed to have lifestyles that tend to elevate blood pressure compared to women. However, after menopause, the prevalence of hypertension in women significantly increases (Putra *et al.*, 2021).

In addition to gender, age groups also influence the prevalence of Type 2 DM with hypertension. The study results indicate that most Type 2 DM patients with hypertension fall within the age range of 60–74 years (42.55%), followed by the 45–59 age group (40.43%). Generally, blood pressure tends to increase with age. This rise in blood pressure is attributed to structural changes in large blood vessels, where the vessel lumen narrows, and the vessel walls become stiffer. Consequently, blood is forced to flow through the narrowed vessels, leading to elevated blood pressure (Telaumbanua & Rahayu, 2021).

The decline in vascular elasticity with age further exacerbates the prevalence of hypertension in diabetic patients. As age increases, physiological functions of the body diminish, leading to a higher incidence of degenerative diseases such as hypertension, diabetes, and cardiovascular diseases. Factors such as reduced vascular elasticity, obesity, endothelial dysfunction, elevated cholesterol levels, and genetic predisposition contribute to an increased risk of hypertension in the elderly (Laurent & Boutouyrie, 2015). In diabetic patients, older age is often associated with neurohormonal changes, such as reduced IGF-1 levels, which decrease glucose uptake due to reduced insulin receptor sensitivity, and increased visceral fat linked to decreased physical activity and lifestyle changes (Sabrini *et al.*, 2022). The increased prevalence of Type 2 DM with hypertension in the elderly is driven by vascular changes over time. Aging leads to intimal thickening, endothelial damage, and reduced availability of Nitric Oxide (NO), a vascular vasodilator. These changes result in vascular stiffness, impaired blood flow, and increased accumulation of calcium and fat, which contribute to hypertension (Akalu & Belsti, 2020).

TABLE II. Profile of antihypertensive drug use based on drug class

Class	Drugs	Frequency (n)	Percentage (%)
ARB	Candesartan	23	29.49
ACEi	Ramipril	4	5.13
	Lisinopril	3	3.85
CCB	Amlodipine	17	21.79
	Nifedipine	6	7.69
	Flunarizine	5	6.41
	Diltiazem	1	1.28
Diuretic			
Loop	Furosemide	7	8.97
Potassium sparing	Spironolactone	4	5.13
Thiazide	Hydrochlorothiazide	1	1.28
Alfa agonist	Clonidine	1	1.28
Beta blocker	Bisoprolol	6	7.69
Total		78	100

The use of antihypertensive drugs in patients with Type 2 Diabetes and hypertension involves selecting therapies based on drug classes, either as monotherapy or combination therapy. Hypertension therapy often begins with monotherapy, as it has been proven to reduce systolic blood pressure by 7–13 mmHg and diastolic pressure by 4–8 mmHg. If the target blood pressure is not achieved within a month, the dosage can be increased, or a

combination of first- and second-line therapies can be administered while minimizing the risk of drug interaction side effects (Polopadang et al., 2021). Based on Table II, the most frequently used class of antihypertensive drugs is CCBs, accounting for 37.17%. Amlodipine, a type of CCB, was the most commonly prescribed drug at 21.79%, followed by ARBs, particularly Candesartan, at 29.49%. According to the 12th edition of DiPiro's (2023), CCBs and ARBs are among the four first-line classes recommended for hypertension in diabetic patients, alongside ACE inhibitors and thiazide diuretics.

TABLE III. Profile of antihypertensive drug use based on usage patterns

Drugs	Frequency (n)	Percentage (%)
Monotherapy		
Candesartan	6	12.77
Ramipril	1	2.13
Lisinopril	2	4.26
Amlodipine	7	14.89
Flunarizine	3	6.38
Spironolactone	1	2.13
Total	20	42.55
Combination		
Candesartan+Furosemide+Amlodipine	1	2.13
Candesartan+Furosemide+Nifedipine	2	4.26
Candesartan+Amlodipine+Bisoprolol	1	2.13
Amlodipine+Bisoprolol+Spironolactone	1	2.13
Amlodipine+Hydrochlorothiazide+Bisoprolol	1	2.13
Amlodipine+Bisoprolol	1	2.13
Ramipril+Amlodipine	1	2.13
Ramipril+Nifedipine	1	2.13
Ramipril+Spironolactone	1	2.13
Lisinopril+Nifedipine	1	2.13
Candesartan+Flunarizine	2	4.26
Candesartan+Diltiazem	1	2.13
Candesartan+Amlodipine	4	8.51
Candesartan+Nifedipine	2	4.26
Candesartan+Furosemide	3	6.38
Candesartan+Bisoprolol	2	4.26

Candesartan+Clonidine	1	2.13
Furosemide+Spironolactone	1	2.13
Total	27	57.45

Based on Table III, monotherapy was used in 22 patients (42.55%), with amlodipine being the most commonly prescribed antihypertensive at 14.89%. Amlodipine, a calcium channel blocker (CCB), is frequently used to treat hypertension in the elderly, as systolic hypertension is more prevalent than diastolic hypertension in this age group. Systolic hypertension poses a greater risk of organ damage in the elderly compared to diastolic hypertension. Data indicate that CCBs like amlodipine are more effective in reducing systolic hypertension in the elderly, thereby lowering the risk of worsening organ damage (Putra *et al.*, 2021).

Amlodipine, widely used in hypertension therapy, is vascular-selective, has a long half-life, and is absorbed slowly, minimizing the risk of sudden blood pressure drops (Nilansari *et al.*, 2020). CCBs are often prescribed for hypertensive patients with coronary artery disease and diabetes mellitus. Their mechanism of action involves inhibiting calcium ion influx into arterial smooth muscle, leading to vasodilation and reduced peripheral resistance. CCBs are recommended for hypertensive patients with diabetes because they help prevent the progression of atherosclerosis, improve heart and kidney function, and reduce the risk of diabetes-related complications. In diabetic hypertensive patients, the use of CCBs can reduce mortality rates. Furthermore, CCBs are considered an ideal antihypertensive choice as they do not affect insulin sensitivity or glucose metabolism in Type 2 diabetes patients (Hapysari *et al.*, 2024).

Apart from CCBs, Candesartan from the ARB class is the second most commonly used antihypertensive monotherapy after CCBs. ARBs are typically prescribed to patients who are intolerant to ACE inhibitors (ACEis). The British Journal of Cardiology (BJC), in its publication on ARBs for hypertension, states that administering Candesartan at a dose of 8–16 mg/day provides additional benefits, such as reducing Body Mass Index (BMI) and Atheroma Mass Index (AMI) in hypertensive patients. This effect supports the use of Candesartan, especially for patients requiring control of additional risk factors related to body mass and cardiovascular conditions. Furthermore, Candesartan has favorable effects on cerebral and myocardial ischemia, making it an excellent choice for early therapy in patients at risk of vascular diseases. ARBs also offer added protection against the risk of stroke progression in diabetic patients, helping to reduce the incidence of complications in this patient group (Helmidanora & Sentat, 2018). The more frequent prescription of ARBs compared to ACEis is partly due to the bothersome side effects of ACEis, especially dry cough, which often occurs at night. A study by Diatmika *et al.* (2018) found that Captopril, an ACE inhibitor, caused dry cough in 76.00% of patients who used it. Beyond hypertension treatment, ARBs are also commonly prescribed for diabetic patients to prevent kidney complications, particularly for those who experience coughing with ACEi use (Kurnianta *et al.*, 2024).

TABLE IV. Suitability of antihypertensive drug

Suitability Indicator	Suitability		Frequency (n)	Appropriateness Percentage
	Suitability	Unsuitability		
Suitability of drugs indication	47	0	47	100%
Suitability of drugs class or name	31	16	47	65.96%
Suitability of drugs dosage	47	0	47	100%

The evaluation of therapy suitability in this study refers to the DiPiro, 12th Edition, 2023 guidelines, covering three main aspects: indication, drug class/name, and dosage.

Evaluation of Indication Suitability

The evaluation of indication suitability for antihypertensive use is based on the precision in prescribing medication aligned with blood pressure ranges specified in the DiPiro therapy guidelines. For antihypertensive treatment in patients with type 2 diabetes mellitus (DM), therapy suitability is determined by the accurate use of antihypertensive drugs based on a documented hypertension diagnosis, where patient blood pressure exceeds >140/90 mmHg. Results in Table IV indicate that all 47 medical records of type 2 DM patients with hypertension comorbidity (100%) showed suitable indication for antihypertensive use. The therapy was deemed suitable if the prescribed medication aligned with the hypertension diagnosis, verified through blood pressure measurements at Hospital X in Sleman Regency during April–November 2023.

Evaluation of Drug Class/Name Suitability

The evaluation of drug class or name suitability in this study refers to selecting therapy classes (either monotherapy or combination therapy) based on the diagnosis recorded in patient prescriptions and compared to the reference literature, DiPiro, 12th Edition, 2023. Table IV shows that among 47 medical records of type 2 DM patients with hypertension comorbidity, drug class/name suitability was achieved in 65.96%. Most patients received therapy from ACE inhibitors (ACEi), ARBs, or CCBs, which are consistent with DiPiro guidelines. However, discrepancies were noted in patients using loop diuretics, either as monotherapy or in combination, which are not recommended by DiPiro for antihypertensive therapy in type 2 DM patients. The guidelines suggest the use of thiazide diuretics for these conditions.

Evaluation of Dosage Suitability

The dosage of antihypertensive drugs was deemed suitable if it fell within the minimum and maximum ranges recommended by the DiPiro, 12th Edition, 2023. This study assessed the dosage by considering two patient characteristics: age and gender. Overdosing, particularly for drugs with a narrow therapeutic index, may lead to adverse effects, whereas underdosing might fail to achieve the desired therapeutic levels (Wycidalesma & Yuswantina, 2021). According to Table IV, the study found that dosage suitability for antihypertensive drugs,

whether in monotherapy or combination therapy, reached 100%, adhering to the DiPiro, 12th Edition, 2023 guidelines.

CONCLUSION

The conclusion of this study highlights that the majority of patients with comorbid type 2 diabetes mellitus and hypertension are male, within the age range of 60-74 years. Additionally, it was found that there is less than 100% alignment in the suitability of the drug class. This indicates a need for further evaluation and potential adjustments to ensure better adherence to optimal therapeutic guidelines, ultimately improving the management of both conditions simultaneously.

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