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Research Article

Evaluation of Antihypertensive Therapy Rationality in Hospitalized Hypertensive Patients with Diabetes Mellitus at South Tangerang City General Hospital

Suny Koswara R[1], Luciana[2], Nurwulan Adi Ismaya[3], Rida Ramadhani [4], Agung Dewantoro[5], Cyntia Wulandari[6]

[1,2,3,4,5]Department of Pharmacy, Stikes Widya Dharma Husada Tangerang, Banten, Indonesia, 15417.
[6]Department of Pharmacy, Universitas Pakuan, Bogor, Indonesia, 16143.

koswarasuny@gmail.com

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ABSTRACT

Hypertension is a chronic condition that frequently coexists with diabetes mellitus and may significantly increase the risk of cardiovascular and renal complications. Evaluating the rational use of antihypertensive drugs is important to ensure appropriate therapy. This study aimed to assess the rationality of antihypertensive drug use in hypertensive patients with diabetes mellitus hospitalized at South Tangerang City General Hospital from October 2024 to March 2025. A descriptive cross-sectional design with retrospective data collection was used based on medical records. Total sampling of 67 medical records met the inclusion and exclusion criteria. The rationality of antihypertensive therapy was evaluated using four parameters: appropriate indication, appropriate patient, appropriate drug selection, and appropriate dosage, based on current clinical guidelines. The results showed that all antihypertensive prescriptions met the criteria for rational drug use across all evaluation parameters, with a rationality rate of 100%. Antihypertensive monotherapy was used in 27 (40.29%) patients while combination therapy was used in 40 (59.71%) patients Calcium channel blockers, especially amlodipine, were the most frequently used agents in monotherapy, while the combination of a calcium channel blocker and an angiotensin receptor blocker, particularly amlodipine and candesartan, was the most common regimen. Drug interactions occurred in 23.8% of patients, with severity classified as moderate (92.6 %), and minor (7.40 %). The most frequent interactions occur between bisoprolol and candesartan. Conclusion: antihypertensive prescribing in this population was rational and support cardiovascular and renal protection in diabetes management ; however drug interactions are still present and need attention to improve therapeutic outcomes.

Keywords: Antihypertensive; diabetes mellitus; evaluation of drug use; rationality drug; South Tangerang Hospital

INTRODUCTION

Hypertension remains one of the most prevalent chronic non-communicable diseases worldwide and is a major modifiable risk factor for cardiovascular morbidity and mortality. Persistent elevation of blood pressure contributes to serious complications, including coronary artery disease, stroke, heart failure, and chronic kidney disease (CKD). In Indonesia, hypertension continues to pose a significant public health burden due to its high prevalence and the challenges associated with long-term treatment adherence and optimal blood pressure control. Effective hypertension management requires not only accurate diagnosis but also rational antihypertensive therapy to achieve therapeutic targets and prevent complications (World Health Organization [WHO], 2023b).

Diabetes is one of the fastest-growing health problems worldwide, with an estimated 537 million people living with diabetes in 2021, with a high mortality rate of 6.7 million among adults and seniors aged 20-79 (Kemenkes RI, 2022). One of the

hallmarks of diabetes mellitus is decreased insulin production, resulting in hyperglycemia (PERKENI, 2021). When blood glucose levels rise in individuals with diabetes mellitus, it can cause blood vessel damage. This occurs because blood sugar oxidizes and reacts with proteins, causing blood vessel walls to become stiff and blocked, leading to hypertension. Approximately 60-80% of people with diabetes mellitus have hypertension, which is a significant risk factor for macrovascular and microvascular problems (Hong et al., 2021).

Inappropriate use of antihypertensive medications can result in various toxicities, therapeutic failure, excessive medical costs due to hypertension, and patient death. To ensure that the antihypertensive medication selection process is always carried out in accordance with guidelines, the use of antihypertensive medications is important. Previous research conducted by Ekaningtyas et al. (2021) found that the evaluation of the appropriateness of antihypertensive medication use yielded 100% correct indication, 100% correct patient, 84.21% correct drug, and 85.71% correct dose (Ekaningtyas et al., 2021). Furthermore, a study by Hasanah and Alrosyidi (2024) found 100% correct indication, 100% correct patient, 72% correct drug, and 100% correct dose (Hasanah et al., 2024).

Drug-related problems (DRPs) are also important concerns in antihypertensive therapy. DRPs include inappropriate drug selection, dosing errors, drug interactions, contraindications, and medication non-adherence. These problems may result in uncontrolled hypertension, increased hospitalization, progression of organ damage, and higher mortality. A recent Indonesian study reported substantial DRP occurrence among hospitalized hypertensive patients, demonstrating that medication-related problems continue to contribute significantly to poor clinical outcomes (Pharmaceutical Care Network Europe, 2020).

Hypertension frequently coexists with diabetes mellitus, creating a particularly high-risk patient population. The coexistence of these conditions markedly increases the risk of macrovascular and microvascular complications, especially cardiovascular disease, nephropathy, retinopathy, and cerebrovascular events. According to the latest American Diabetes Association Standards of Care, patients with diabetes and hypertension should generally achieve a blood pressure target of <130/80 mmHg when safely attainable to reduce cardiovascular and renal complications. Furthermore, the 2023 European Society of Hypertension guideline recommends early combination therapy for patients with significantly elevated blood pressure to improve target attainment and reduce therapeutic inertia (American Diabetes Association, 2024; European Society of Hypertension, 2023).

Antihypertensive selection in diabetic patients requires additional consideration of renal and cardiovascular protective effects. Agents targeting the renin–angiotensin–aldosterone system, such as angiotensin-converting enzyme inhibitors and angiotensin receptor blockers, are often preferred in patients with albuminuria or chronic kidney disease because of their renoprotective benefits. The latest Kidney Disease: Improving Global Outcomes guideline strongly recommends renin–angiotensin system inhibitors in patients with CKD and diabetes to reduce proteinuria and slow disease progression (Kidney Disease: Improving Global Outcomes, 2024).

Despite the clinical complexity of managing hypertensive patients with diabetes mellitus, studies evaluating the rationality of antihypertensive drug use in this specific population remain limited, particularly in Indonesian hospital settings. Most previous studies have focused on general hypertensive populations without specifically evaluating patients with diabetes mellitus and associated comorbidities. This limitation creates a research gap regarding whether antihypertensive prescribing in hospitalized diabetic hypertensive patients is aligned with current evidence-based guidelines (Andriyani et al., 2023). Studies specifically evaluating the appropriateness of antihypertensive selection in hospitalized patients with hypertension and diabetes mellitus remain limited, particularly at South Tangerang City Regional General Hospital. Most Indonesian studies still assess antihypertensive use in patients with hypertension and diabetes mellitus based on older guidelines (e.g., JNC 8, the 2019 Hypertension Consensus, or previous diabetes mellitus guidelines), rather than the latest recommendations. Therefore, this study applies the most recent American Diabetes Association (ADA) 2024/2025 guidelines

Therefore, this study aimed to evaluate the rationality of antihypertensive drug use in hypertensive patients with diabetes mellitus hospitalized at South Tangerang City General Hospital during October 2024–March 2025. The evaluation was conducted based on four rationality parameters, namely

appropriate indication, appropriate patient, appropriate drug selection, and appropriate dosage. The findings of this study are expected to provide evidence regarding prescribing quality and support the optimization of antihypertensive therapy in patients with hypertension and diabetes mellitus.

METHODS

Research Design

This study will use an observational analytical descriptive design with a retrospective approach. The type of research used was descriptive research with a *cross-sectional* approach. The research will examine medical records of hospitalized patients diagnosed with hypertension and diabetes mellitus at South Tangerang City General Hospital during from October 2024 to March 2025.

The primary data source will consist of patients' complete medical records, including patient identification data (name, gender, age, and registration number), antihypertensive therapy details (drug name, dosage, frequency, and route of administration), and blood pressure measurements in patients with hypertension and diabetes mellitus.

Data will be collected systematically using a structured data collection form developed by the researcher. Each patient's medical record will be reviewed individually. First, the diagnosis of hypertension and diabetes mellitus will be verified. Second, the appropriateness of antihypertensive therapy will be assessed. Third, the suitability of the selected drug for the patient will be evaluated. Fourth, the prescribed dose will be compared with the recommended dose in the selected guideline. In addition, potential drug interactions will be assessed by reviewing all concomitantly prescribed medications and identifying clinically significant interactions using a recognized drug interaction reference. Finally, each parameter will be classified as appropriate or not appropriate, and the proportion of rational drug use will be calculated as a percentage.

Population, Sample, and Sampling Techniques

Population

The population consist of all hospitalized patients with hypertension and diabetes mellitus who received at least one antihypertensive drug during the study period

Sample

The sample will be selected using *purposive sampling*. This study included 67 patients who met the inclusion and exclusion criteria. The inclusion criteria may include patients aged 18 years or older, patients with clearly documented diagnoses of hypertension and diabetes mellitus, and patients with complete records for the main study variables. The exclusion criteria may include pregnant patients, patients with incomplete records for the primary variables, and patients hospitalized for less than 24 hours.

Assessment Indicators

The indicators for assessing the rationality of drug use refer to the 2011 Indonesian Ministry of Health Indicators. The rationality of drug use will be evaluated based on *Pharmacotherapy: A Pathophysiologic Approach* by Joseph T. DiPiro, whereas drug interactions will be assessed using *Drug Interaction Handbook*. The assessment criteria include appropriate indication, appropriate patient, appropriate drug, and appropriate dose.

Data Analysis and Research Ethic

The data were analyzed descriptively using Microsoft Excel to determine the number and percentage of rational drug use and potential drug interactions. This study was submitted for ethical review and received ethical approval from University of Jember under ethical clearance letter number 3226/UN30.3/KEPK/DL/2025.

RESULTS AND DISCUSSION

Patient Characteristics

Characteristics Based on Age and Gender

Patient characteristics were first analyzed based on age and gender to describe the demographic profile of hypertensive patients with diabetes mellitus included in this study. The distribution of patients across age groups and the proportion of male and female patients are presented in Table 1.

Based on research results, hypertension and diabetes mellitus in South Tangerang City General Hospital (RSU) patients began to develop at age 25 and were most common in the 56-65 age group, or the late elderly group, with 31 (46.28%) patients. Aging causes blood pressure to rise more easily, due to physiological changes in the patient's body, such as increased peripheral resistance and increased sympathetic nervous system activity (Tri Wasilah et al., 2022).

Table 1. Patient characteristics

Type	No	Criteria	Age (years)	Number of Patients	Percentage (%)
Age	1	Late adolescence	17-25	1	1.49
	2	Early adulthood	26-35	1	1.49
	3	Late adulthood	36-45	5	7.47
	4	Early old age	46-55	14	20.89
	5	Late old age	56-65	31	46.28
	6	Elderly	≥65	15	22.38
Gender	1	Male		29	43.28
	2	Female		38	56.72

Source: Medical records of outpatients at South Tangerang City General Hospital from October 2024 to March 2025.

One of the physical declines commonly experienced by older adults is the deterioration of the cardiovascular system. Aging causes the heart valves to thicken and stiffen, while the heart's ability to pump blood decreases by approximately 1% each year. In addition, the heart rate becomes less responsive to stress, blood vessels lose their elasticity, and blood pressure increases due to greater peripheral vascular resistance. Approximately 60% of older adults experience elevated blood pressure after the age of 75. Strict blood pressure control in the elderly is important to prevent uncontrolled hypertension and reduce the risk of other diseases, such as diabetes mellitus, stroke, and myocardial infarction (Jatiningsih, 2016). Based on the research findings, the majority of patients were women, accounting for 38 patients (56.72%). Women are at a higher risk of developing hypertension than men due to the decline in estrogen production during menopause. Estrogen plays an important role in protecting blood vessels from damage by increasing high-density lipoprotein (HDL) levels. High HDL levels serve as a protective factor against atherosclerosis, which is one of the contributing factors to hypertension. Consequently, women become more susceptible to hypertension (Andriyani et al., 2023).

Blood Pressure Classification

Blood pressure was further classified to determine the severity of hypertension experienced by patients at the time of hospitalization. The distribution of patients according to stage 1 and stage 2 hypertension is presented in Table 2. Based on the study results, most patients were classified as having stage 2 hypertension, with 45 patients, while 22 patients were classified as having stage 1 hypertension. This finding indicates that the majority of hospitalized hypertensive patients with diabetes mellitus experienced more severe blood pressure elevation, suggesting inadequate blood pressure control prior to hospitalization.

The high proportion of patients with stage 2 hypertension may be attributed to several factors, including poor medication adherence, prolonged duration of hypertension, unhealthy lifestyle, and the coexistence of diabetes mellitus. Diabetes mellitus contributes to vascular endothelial dysfunction, arterial stiffness, and increased peripheral vascular resistance, all of which worsen blood pressure control. Chronic hyperglycaemia also accelerates atherosclerosis and nephropathy, which may further increase the severity of hypertension. According to the American Diabetes Association, hypertension is one of the most common comorbidities in patients with diabetes and significantly increases the risk of cardiovascular complications, including stroke, coronary artery disease, and chronic kidney disease.

This result is consistent with the study by Andriyani et al. (2023), which reported that patients with hypertension accompanied by diabetes mellitus were more likely to present with uncontrolled or severe hypertension due to metabolic disturbances and vascular complications. Similarly, a study by European Society of Cardiology and European Society of Hypertension highlighted that patients with diabetes often have more difficult-to-control hypertension because of increased arterial stiffness and impaired renal function.

Table 2. Blood pressure classification

No	Blood Pressure Classification	Blood Pressure (mmHg)	Number of Patients	Percentage (%)
1	Stage 1 hypertension	140-149/90-99	22	32.84
2	Stage 2 hypertension	>160/>100	45	67.16
Total			67	100

Source: Medical records of outpatients at South Tangerang City General Hospital from October 2024 to March 2025.

From the perspective of antihypertensive rationality, the predominance of stage 2 hypertension has important clinical implications. Patients with stage 2 hypertension generally require more aggressive therapy, often involving combination antihypertensive treatment rather than monotherapy, to achieve target blood pressure. According to the International Society of Hypertension guidelines, most patients with blood pressure ≥160/100 mmHg require initial combination therapy to achieve optimal blood pressure control. Therefore, evaluating the rationality of antihypertensive use—including appropriate indication, appropriate patient selection, appropriate drug selection, and appropriate dosage—is essential to ensure effective treatment outcomes and prevent further complications in hypertensive patients with diabetes mellitus.

Overall, the predominance of stage 2 hypertension in this study suggests that blood pressure control among hospitalized hypertensive patients with diabetes mellitus remains suboptimal. This condition emphasizes the importance of early screening, strict blood pressure monitoring, patient education, and rational antihypertensive therapy to reduce morbidity and mortality associated with cardiovascular complications

Characteristics Based on Comorbidities

Hypertensive patients with diabetes mellitus often present with additional comorbid conditions that may influence antihypertensive drug selection and treatment outcomes. The types and frequency of comorbidities identified among the study population are presented in Table 3. Based on the characteristics of patients according to comorbidities, this study found that hypertensive patients with diabetes mellitus had several accompanying diseases. The most common comorbidity was Chronic Kidney Disease, affecting 25 patients. Other frequently observed comorbidities were heart disease, affecting 15 patients, and cerebral infarction (stroke), also affecting 15 patients. These findings indicate that hypertension accompanied by diabetes mellitus is strongly associated with the development of macrovascular and microvascular complications, particularly those involving the kidneys, heart, and brain.

The predominance of Chronic Kidney Disease among the study population may be explained by the close pathophysiological relationship between hypertension, diabetes mellitus, and renal impairment. Chronic hyperglycemia in diabetes mellitus causes glomerular hyperfiltration, thickening of the glomerular basement membrane, and progressive nephron damage. At the same time, uncontrolled hypertension increases intraglomerular pressure and accelerates renal function decline. The coexistence of hypertension and diabetes therefore creates a synergistic effect that substantially increases the risk of kidney damage. According to Kidney Disease: Improving Global Outcomes, hypertension is both a major cause and a consequence of chronic kidney disease, creating a cycle that worsens cardiovascular and renal outcomes.

This finding is consistent with previous studies reporting that chronic kidney disease is one of the most common comorbidities in hypertensive patients with diabetes mellitus. A study by Andriyani et al. (2023) reported that renal impairment frequently occurred in patients with long-standing hypertension and diabetes due to persistent vascular damage. Similarly, research conducted by Afkar et al. (2021) found that chronic kidney disease was the most dominant comorbidity among hospitalized diabetic hypertensive patients, particularly in elderly populations.

Table 3. Characteristics based on comorbidities

No.	Comorbidities	Number of patients	Percentage (%)
1.	Heart disease	15	13.51
2.	Kidney dysfunction	25	22.52
3.	Dyspepsia (indigestion)	7	6.30
4.	Pneumonia (lung inflammation)	9	8.11
5.	Cerebral infarction (stroke)	15	13.51
6.	Urinary tract infection (UTI)	5	4.51
7.	Tuberculosis (TB)	10	9.03
8.	Diabetic neuropathy	8	7.20
9.	Hyperuricemia (high uric acid)	3	2.70
10.	Hypercholesterolemia (high cholesterol)	11	9.01
11.	Prostate (enlarged gland)	1	0.90
12.	Hepatitis (liver inflammation)	2	1.80
	Total	**111**	**100**

Source: Medical records of outpatients at South Tangerang City General Hospital from October 2024 to March 2025.

Heart disease was the second most frequent comorbidity in this study, affecting 15 patients. This finding may be associated with long-term elevated blood pressure and chronic hyperglycemia, both of which contribute to endothelial dysfunction, accelerated atherosclerosis, left ventricular hypertrophy, and coronary artery disease. Persistent hypertension increases cardiac workload, leading to structural and functional cardiac abnormalities over time. Diabetes mellitus further exacerbates this process by promoting inflammation, oxidative stress, and vascular injury. As a result, patients with both hypertension and diabetes have a significantly higher risk of developing cardiovascular disease compared with patients with either condition alone. Hypertension is a risk factor for heart disease, and if left untreated, it can lead to dangerous complications. Hypertension is highly prevalent in adulthood, where high-fat diets and smoking habits can contribute to plaque formation in blood vessels. Diabetes mellitus is also a risk factor for heart disease, resulting in changes in lipid metabolism that lead to increased atherogenesis. Furthermore, people with diabetes develop heart disease more quickly than those without diabetes, as the disease can impair heart function, leading to stiffening of the heart muscle (Lily Marleni1, 2017).

The prevalence of heart disease in this study is comparable to findings reported by Sari et al. (2022), who observed that cardiovascular complications were among the leading comorbidities in hypertensive diabetic patients. Their study suggested that prolonged exposure to elevated blood pressure and poor glycemic control were major contributors to cardiac complications.

In addition, cerebral infarction (stroke) was found in 15 patients, indicating a substantial burden of cerebrovascular complications. Stroke is a well-recognized complication of uncontrolled hypertension and diabetes mellitus. Hypertension is the strongest modifiable risk factor for stroke because elevated blood pressure damages cerebral blood vessels, increases arterial stiffness, and promotes thrombus formation. Hypertension is the most common risk factor for stroke, as it causes unnecessary stress on the blood vessels thickening and deterioration, which can ultimately lead to stroke. When blood vessels thicken, accompanied by increased blood pressure, cholesterol and other fatty substances can damage the artery walls and cause blockages in the brain's arteries. The increased tension in the brain's blood vessels can also weaken the blood vessel walls, which can ultimately cause the blood vessels to rupture and ultimately cause a stroke (Permatasari, 2020).

Diabetes mellitus further increases stroke risk by accelerating atherosclerosis and impairing vascular integrity. The coexistence of these two conditions significantly increases the likelihood of ischemic cerebrovascular events. This finding aligns with research by Prasetyo et al. (2022), which demonstrated a high incidence of stroke among hospitalized hypertensive patients with diabetes mellitus. Their study emphasized that poor blood pressure control and delayed therapeutic intervention were major contributors to cerebrovascular complications.

From the perspective of antihypertensive therapy rationality, the presence of comorbidities such as Chronic Kidney Disease, heart disease, and stroke has important implications for drug selection. Patients

with chronic kidney disease often require antihypertensive agents with renoprotective effects, such as Lisinopril or Losartan, while patients with cardiovascular disease may benefit from specific agents depending on cardiac function and clinical status. Therefore, evaluating the rationality of antihypertensive use—including appropriate indication, appropriate patient selection, appropriate drug selection, and appropriate dosage—is essential to optimize treatment outcomes and prevent further complications.

Overall, the high prevalence of chronic kidney disease, heart disease, and stroke in this study suggests that hypertensive patients with diabetes mellitus represent a high-risk population with complex therapeutic needs. These findings highlight the importance of early detection, comprehensive comorbidity management, and rational antihypertensive therapy to reduce morbidity and mortality.

Distribution of Antihypertensive Drug Use

Antihypertensive therapy in this study was classified into single-drug and combination regimens to describe the prescribing patterns applied at South Tangerang City General Hospital. The complete distribution of antihypertensive drug classes, drug names, and the number of patients receiving each regimen is presented in Table 4.

Based on the study findings, among patients receiving monotherapy, the most commonly prescribed antihypertensive class was the calcium channel blocker (CCB), specifically Amlodipine, used in 14 patients (19.89%). In combination therapy, the most frequently prescribed regimen was the combination of a calcium channel blocker and an angiotensin II receptor blocker (ARB), specifically Amlodipine and Candesartan, used in 16 patients (23.88%). This finding suggests that CCB-based therapy plays a major role in the management of hypertensive patients with diabetes mellitus in this study population. Based on the 2019 PERHI Consensus, the target blood pressure in hypertensive patients with diabetes mellitus is <130/<80 mmHg for those aged under 65 years, and 130–139/70–79 mmHg for those aged 65 years and over, provided that tolerated by patients. The combination of ARBs and CCBs is considered effective because it works through two different mechanisms to lower blood pressure and has protective effects on the kidneys and heart. This is consistent with the theory that patients with stage 2 hypertension are advised to use combination therapy of two or more drugs (Andriyani et al., 2023).

The high utilization of calcium channel blockers, particularly Amlodipine, may be explained by their effectiveness in reducing blood pressure through peripheral vasodilation, favorable safety profile, and good tolerability, especially in elderly patients. Calcium channel blockers reduce vascular smooth muscle contraction by inhibiting calcium influx, thereby decreasing peripheral vascular resistance. This mechanism is particularly beneficial in patients with isolated systolic hypertension or increased arterial stiffness, conditions commonly observed in elderly hypertensive patients and patients with diabetes mellitus. In addition, amlodipine has a long duration of action, allowing once-daily administration and improving medication adherence.

The predominance of CCB use in this study is consistent with previous research. Andriyani et al., (2023) reported that calcium channel blockers were among the most frequently prescribed antihypertensive agents in diabetic hypertensive patients because of their efficacy and relatively minimal metabolic effects. Similarly, research by Sari et al. (2022) found that amlodipine was widely used as first-line antihypertensive therapy in hospitalized patients due to its effectiveness in achieving blood pressure control.

Regarding guideline recommendations, the use of calcium channel blockers is consistent with the latest recommendations from the American Diabetes Association. The ADA Standards of Care recommend that antihypertensive therapy in patients with diabetes may include ACE inhibitors, ARBs, thiazide-like diuretics, or calcium channel blockers as first-line agents, depending on the patient's clinical characteristics and comorbidities. Therefore, the use of amlodipine in this study can be considered rational, particularly in patients without significant albuminuria or advanced chronic kidney disease.

Table 4. Distribution of antihypertensive drug use

Drug Administration Pattern	Drug Class	Drug Name	Number of patients	Percentage (%)
Single Antihypertensive Therapy	ACEi	Ramipril	1	1.49
	ARB	Candesartan	10	14.01
	CCB	Amlodipin	14	19.89
	Beta Blockers	Bisoprolol	2	2.98
Total			27	40.29
Combination Antihypertensive Therapy	ACEi + Diuretik	Ramipril + Furosemid	1	1.49
	ARB + Diuretik	Candesartan + furosemid	2	2.98
	BB + ACEi	Bisoprolol + Ramipril	2	2.98
	BB + ARB	Bisoprolol + Candesartan	1	1.49
	BB + CCB	Bisoprolol + Amlodipin	4	4.97
	BB + Diuretik	Bisoprolol + Furosemid	2	2.98
	CCB + ACEi	Amlodipin + Ramipril	1	1.49
	CCB + ARB	Amlodipin + Candesartan	16	23.88
	CCB+ACEi+ Diuretik	Amlodipin+ Ramipril+ Spironolakton	1	1.49
	CCB+BB+ARB	Amlodipin + Bisoprolol + Candesartan	4	4.97
		Nifedipin + Bisoprolol + Candesartan	1	1.49
	CCB+Diuretik+BB	Amlodipin +Furosemid + Bisoprolol	3	3.47
	Diuretik+ARB+BB	Furosemid + Candesartan + Bisoprolol	4	4.97
	Diuretik+ARB+CCB	Furosemid + Candesartan + Amlodipin	1	1.49
		Furosemid + Candesartan + Nifedipin	1	1.49
Total			40	59.71
Sub Total			67	100

Notes: *Angitensin Converting Enzymes Inhibitor* (ACEi), *Antagonis Angiotensi II* atau *Angiotensi Receptor Blocker* (ARB), *Antagonis Kalsium atau Calsium Channel Blocker* (CCB), *Beta-blockers* (BB).

The dominance of Candesartan in combination therapy also has important clinical significance. ARBs block the action of angiotensin II at the AT1 receptor, resulting in vasodilation, reduced aldosterone secretion, and decreased sodium retention. These effects effectively lower blood pressure while providing additional organ-protective benefits. Compared with other antihypertensive classes, ARBs are especially valuable in patients with diabetes because they provide renoprotective and cardioprotective effects.

One major reason for the frequent use of ARBs in hypertensive patients with diabetes mellitus is renal protection. Patients with diabetes are at high risk of developing diabetic nephropathy due to chronic hyperglycemia-induced glomerular damage.

Activation of the renin–angiotensin–aldosterone system (RAAS) contributes to increased intraglomerular pressure and progressive kidney damage. ARBs such as candesartan reduce intraglomerular pressure, decrease proteinuria, and slow the progression of renal dysfunction. According to the American Diabetes Association and Kidney Disease: Improving Global Outcomes guidelines, ACE inhibitors or ARBs are strongly recommended for patients with diabetes who have albuminuria, reduced estimated glomerular filtration rate (eGFR), or chronic kidney disease.

Renal protection is particularly important in this study because Chronic Kidney Disease was identified as the most common comorbidity, affecting 25 patients. The high prevalence of CKD indicates that renal function preservation should be an essential consideration in antihypertensive selection. In patients with Chronic Kidney Disease (CKD) , blood pressure management aims not only to achieve target blood pressure but also to delay renal disease progression and reduce cardiovascular risk. Therefore, antihypertensive regimens containing ACE inhibitors or ARBs are generally preferred unless contraindications such as hyperkalemia, bilateral renal artery stenosis, or severe acute kidney injury are present.

The frequent use of the combination of Amlodipine and Candesartan can also be explained by the complementary mechanisms of these drugs. Amlodipine primarily reduces peripheral vascular resistance through vasodilation, whereas candesartan suppresses RAAS activity and provides renal protection. Combining these two classes improves blood pressure control while minimizing adverse effects such as reflex tachycardia or peripheral edema. This combination is particularly useful in patients with stage 2 hypertension, where monotherapy is often insufficient to achieve target blood pressure.

These findings are supported by research conducted by Prasetyo et al. (2022), which showed that combination therapy involving CCB and ARB was frequently used in hypertensive patients with diabetes and chronic kidney disease due to superior blood pressure control and organ protection. Similar results were reported by Afkar et al. (2021), who found that combination therapy provided better achievement of therapeutic targets in patients with multiple comorbidities.

From the perspective of antihypertensive rationality, the predominance of CCB and ARB therapy in this study suggests that drug selection was largely appropriate for the clinical characteristics of the patients, especially considering the high prevalence of diabetes mellitus and chronic kidney disease. The selection of antihypertensive agents should not only focus on lowering blood pressure but also on preventing target organ damage and improving long-term clinical outcomes.

Overall, the findings indicate that the use of calcium channel blockers and angiotensin II receptor blockers in this study was clinically rational and aligned with current evidence-based guidelines. The presence of chronic kidney disease further strengthens the importance of renal-protective antihypertensive therapy, particularly RAAS inhibitors, in optimizing treatment outcomes among hypertensive patients with diabetes mellitus.

Distribution of Antidiabetic Drug Use

In addition to antihypertensive therapy, antidiabetic medications were also evaluated to provide a complete picture of pharmacological management in this patient population. The distribution of antidiabetic drug therapy used by patients is presented in Table 5. Based on the results of the study, it was found that 43 (64.17%) patients used a single antidiabetic drug, and the most commonly used drug was metformin, with 18 (26.86%) patients. Metformin is a biguanide antidiabetic drug used as first-line therapy in patients with type 2 diabetes mellitus. Indications for administering metformin include type 2 diabetes patients whose blood glucose levels are not controlled through diet and exercise interventions alone, especially in patients with a body mass index (BMI) ≥25 kg/m² (overweight or obese), because metformin has additional effects in the form of weight loss and increased insulin sensitivity without increasing the risk of hypoglycemia. This drug is also used in patients with insulin resistance, metabolic syndrome, or high fasting insulin levels. Metformin can be given alone or in combination with other oral antidiabetic drugs if glycemic control has not been achieved. Metformin works by lowering blood sugar levels without causing hypoglycemic reactions, therefore metformin is more Used in patients with diabetes mellitus. Metformin is also safe for use in combination with antihypertensive drugs of the ACEI, ARB, CCB, and diuretic classes (Andriyani et al., 2023).

Table 5. Distribution of antidiabetic drug use

Therapeutic Class	Drug Name	Number of Patients	Percentage (%)
Single-Agent Antidiabetic Therapy	Metformin	18	26.9
	Novorapid (Aspart)	11	16.4
	Gliquidon	3	4.5
	Levemir (Detemir)	2	2.9
	Humalog (Lispro)	2	2.9
	Lantus (Glargine)	5	7.5
	Glimepirid	2	2.8
Total		43	64.17
Combination Antidiabetic Drug Therapy	Metformin + Glimepirid	3	4.5
	Novorapid (Aspart)+ Levemir (Detemir)	4	6.1
	Novorapid (Aspart) + Lantus (Glargine)	10	15.2
	Humalog (Lispro) + Lantus (Glargine)	3	4.5
	Akarbose + Metformin	2	2.9
	Apidra (Glulisine) + Lantus (Glargine)	2	2.9
Total		24	35.83
Sub- Total		67	100

Source: Primary Data (October 2024 – March 2025).

Meanwhile,combination antidiabetic drugs were used in 24 (35.83%) patients, with the most commonly used drugs being novorapid (aspart) + lantus (detemir) in 10 (14.92%). The combination antidiabetic drug, novorapid (aspart) + lantus (detemir), is safe and effective for use in diabetic patients with comorbid hypertension because it does not increase blood pressure, does not interact actively with antihypertensive drugs of the ACEI, ARB, or CCB classes, and does not increase the risk of stroke, heart attack, or heart failure.

Evaluation of Antihypertensive Medication Use in Hypertensive Patients with Diabetes Mellitus

Rationality of Drug Use

Evaluation of antihypertensive medication use is based on appropriate indication, appropriate patient, appropriate drug, and appropriate dosage. Antihypertensive medication use in hypertensive patients with diabetes mellitus is adjusted according to standards, namely the Eighth Joint National Committee on Hypertension (JNC VIII) 2014, the Consensus on Hypertension Management (PERHI 2021), and the Drug Information Handbook (DIH 2013). The distribution of appropriate antihypertensive medication use is shown in Table 6.

Table 6. Evaluation of the rational use of antihypertensive drugs

No	Criteria	Information	Amount	Percentage (%)
1	Right indication	Appropriate	67	100
		Inappropriate	0	0
2	Right patient	Appropriate	67	100
		Inappropriate	0	0
3	Right medication	Appropriate	67	100
		Inappropriate	0	0
4	Right dose	Appropriate	67	100
		Inappropriate	0	0

Table 6 shows that the accuracy of the use of antihypertensive drugs in hypertensive patients with diabetes mellitus is reviewed from the correct indication of 100%, the correct patient 100%, the correct drug 100%, and the correct dose 100%. Medication use is medically appropriate if it meets certain requirements. In this study, the evaluation of medication use included several criteria, namely:

Appropriate Indication

A medication is considered appropriate if it is administered according to the patient's complaint and is based on the doctor's diagnosis. Indication appropriateness in this study was evaluated using the 2013 Drug Information Handbook (DIH) standard. Indication appropriateness in this study was achieved in 67 (100%) patients, as the antihypertensive medication administered to patients diagnosed with hypertension was in accordance with the established standards. Patients diagnosed with hypertension are those with Systolic blood pressure greater than or equal to 140 mmHg and diastolic blood pressure greater than or equal to 90 mmHg.

Blood pressure is divided into several categories. Normal blood pressure is characterized by a systolic pressure of less than 120 mmHg and a diastolic pressure of less than 80 mmHg. Prehypertension is a condition where the systolic pressure is between 120–139 mmHg or the diastolic pressure between 80–89 mmHg, indicating an increased risk of developing hypertension. Stage 1 hypertension is characterized by a systolic pressure of 140–159 mmHg or a diastolic pressure of 90–99 mmHg, and is usually the starting point for lifestyle interventions or medication. Meanwhile, stage 2 hypertension is a more severe condition, with a systolic pressure of ≥160 mmHg or a diastolic pressure of ≥100 mmHg, which requires more aggressive treatment to prevent serious complications such as stroke, heart disease, and kidney damage. The results of this accurate indication evaluation are in line with Perdana's research (2023) which found 100% accuracy.

Appropriate Patient

Next, the appropriate patient aspect refers to the selection of medication that takes into account the patient's condition and avoids contraindications. Patient appropriateness in this study was evaluated using the Drug Information Handbook (DIH) standard. According to the 2024 DIH, antihypertensive drugs, based on patient comorbidities, include CCBs, ACE inhibitors, and ARBs, which are recommended for diabetic patients. Patients with stroke, heart failure, and patients with kidney disease and diabetes are given ACE inhibitors or ARBs. Patients with heart failure are given beta-blockers (BB), ACE inhibitors/ARBs, and diuretics. Patients with coronary heart disease are given beta-blockers and ACE inhibitors/ARBs. The results showed that most patients with comorbidities such as stroke, kidney failure, and diabetes used amlodipine (CCB), candesartan (ARB), ramipril (ACE inhibitor), bisoprolol (BB), and furosemide (diuretic). According to the Indonesian Heart Association (DIH), beta-blocker drugs such as bisoprolol are not recommended for hypertensive patients with diabetes mellitus, but may be justified in certain conditions, especially if there are additional indications such as a history of myocardial infarction or heart failure. According to the Indonesian Heart Association (DIH) 2024, selective beta-blockers such as atenolol or bisoprolol have a lower risk of impaired glucose control than non-selective beta-blockers. In hospitalized patients, the use of beta-blockers is considered acceptable if under close medical supervision and considering the clinical benefits outweigh the potential risks. The evaluation results based on the patient accuracy aspect in this study indicated that the percentage of antihypertensive medication accuracy was 100% for 67 patients. This patient accuracy was achieved because the medication administered to the patient was appropriate for the patient's condition and did not cause any contraindications. This patient accuracy evaluation result aligns with Abdalla's (2021) study, which found 100% accuracy.

Appropriate Medication

Next, the appropriate medication aspect refers to the selection of appropriate medication based on its therapeutic effect and the drug of choice for hypertension with diabetes mellitus. Medication appropriateness in this study was evaluated using the 2014 JNC VIII standards. For example, a 64-year-old patient with blood pressure of 145/90 (stage 1 hypertension) received 10 mg of amlodipine. This aligns with the JNC VIII standard, which states that stage 1 hypertension patients aged 60 years and over should receive monotherapy, such as a CCB/thiazide. Another patient with blood pressure of 160/90 (stage 2 hypertension) aged 50 years received combination therapy, namely amlodipine 10 mg and candesartan 8 mg. This aligns with the JNC VIII standard, which states that stage 2 hypertension patients of all ages should receive combination therapy with a CCB/thiazide and an ACE inhibitor/ARB, or, if necessary, a CCB+thiazide+ACE inhibitor/ARB. Based on the medication accuracy aspect, this study found that 67 (100%) patients received the correct dose and frequency of antihypertensive medication according to established standards. The results of this

medication accuracy evaluation align with the study by Perdana (2023) which found 100% accuracy.

Correct Dosage

Furthermore, the aspect of dosage accuracy refers to the appropriateness of the prescribed medication dose, based on the single-use dose and the daily frequency of administration for patients diagnosed with hypertension. If the antihypertensive medication prescription falls within the minimum dose range and the recommended daily dose, the prescription is considered appropriate. The dosage is also adjusted to the patient's condition, including age, body weight, and specific disorders. Dosage accuracy in this study was evaluated using the 2021 PERHI standards. Based on the 2021 PERHI guidelines, patients with hypertension and diabetes mellitus with comorbidities and impaired kidney function require medication dosage adjustments. For example, ramipril is given at a dose of 2.5-10 mg, candesartan at a dose of 8-32 mg, and bisoprolol at a dose of 2.5-10 mg. The doses listed in this study are Amlodipine 5-10 mg, Candesartan 8-16 mg, Bisoprolol 2.5-5 mg, Ramipril 5 mg, Furosemide 20-40 mg, which are in accordance with the initial dose and dose range according to PERHI 2021. For example, a patient with blood pressure of 163/100 (stage 2 hypertension) aged 50 years with comorbid chronic kidney failure received candesartan 16 mg 1 x 1 drug therapy. This is in accordance with PERHI 2021, namely the use of candesartan drugs with a dose of 4 mg-32 mg per day. The results of the evaluation based on the aspect of dosage accuracy in this study stated that the percentage of patients with antihypertensive drugs was obtained at 67 (100%) patients, because the antihypertensive drugs given to patients diagnosed with hypertension were in accordance with the standards used. The results of this appropriate dose evaluation are in line with Perdana's (2023) study which obtained 100% accuracy.

Antihypertensive Drug Interactions

The drug interactions in this study are antihypertensive drug interactions (Table 7) as seen from patient medical records and adjusted to literature studies based on Drug Interactions Stocley 10th Edition. About 16 prescriptions (23.8%) had the potential for drug interactions, and almost half of them did not have drug interactions, with 51 prescriptions (76.1%). The results of this study are in line with research conducted by Setyoningsih (2022) that found that 73.2% of the 41 patients received polypharmacy, and 75.6% experienced drug interactions.

Table 7. Number of antihypertensive drug interactions

Information	Amount	Percentage (%)
Interaction Occurs	16	23.8
No Interaction Occurred	51	76.1
Total	67	100

Analysis of drug interactions in the use of antihypertensive drugs based on severity at South Tangerang City Hospital in December 2024, adjusted using the Drugs Interaction Checker (Drugs.com). Refer to table 8 Drug interactions Table 8 indicates that the predominant interaction observed in this study was of moderate severity, comprising 92.6% of all interactions. The concomitant administration of bisoprolol and candesartan may lead to a pharmacodynamic interaction characterized by additive antihypertensive effects. This interaction has the potential to increase the incidence of hypotension, dizziness, and bradycardia; therefore, routine monitoring of blood pressure and heart rate is warranted during combination therapy.

Table 8. Drug interactions based on severity

No	Severity	Drug Combination	Amount	Percentage (%)
1	*Minor*	Amlodipine +	2	7.40
2	*Moderate*	Bisoprolol + Candesartan	8	92.6
		Bisoprolol + Furosemide	5	
		Furosemide + Candesartan	6	
		Amlodipine + Furosemid	2	
		Candesartan + Nifedipine	2	
		Bisoprolol + Nifedipine	1	
		Ramipril + Bisoprolol	1	
	Total		27	100

CONCLUSION

The evaluation of the rational use of antihypertensive medications demonstrated that all prescriptions met the criteria for the correct indication, correct patient, correct drug, and correct dosage, with an appropriateness rate of 100% for each parameter. These findings indicate that antihypertensive prescribing practices at South Tangerang City General

Hospital were consistent with established clinical guidelines and reflected a high level of prescribing accuracy.

Despite the appropriate selection and prescribing of antihypertensive therapy, potential drug interactions were identified, with moderate interactions being the most frequently observed. Although these interactions do not necessarily require discontinuation of therapy, they may increase the risk of adverse clinical outcomes, such as excessive blood pressure reduction, dizziness, electrolyte disturbances, or other clinically significant effects. Therefore, routine monitoring, individualized patient assessment, and appropriate clinical management are essential to ensure the safety and effectiveness of pharmacotherapy, particularly in patients with multiple comorbidities and polypharmacy.

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CONFLICT OF INTEREST

All authors declared that there was no conflict of interest.

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