

Evaluation Of Antihypertensive Drug Use On Therapy Effectiveness Based On Patient Characteristics And Adverse Drug Reactions

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Hypertension is a chronic disease that requires long-term management to prevent cardiovascular complications, and antihypertensive therapy success is influenced by both patient characteristics and drug safety. This study aimed to describe patient characteristics, antihypertensive drug use, adverse drug reactions, and treatment effectiveness among outpatients at Baptis Batu Hospital. An analytical observational study with a prospective cross-sectional design was conducted using purposive sampling, yielding 95 eligible patients. Data were obtained from medical records and structured interviews; ADRs were assessed using the Naranjo Algorithm and Therapy effectiveness was defined as a reduction in blood pressure of $\geq 20/10$ mmHg based on the PERHI (2021) criteria. Data were analyzed descriptively and using the Chi-Square test ($\alpha = 0.05$). Most patients were female (67.4%), aged < 65 years (58.9%), receiving combination therapy (76.8%), and experiencing polypharmacy (65.3%), with amlodipine and candesartan the most frequently prescribed combination. Therapy was effective in 71 patients (74.7%), and ADRs occurred in 33 patients (34.7%). ADR occurrence was significantly associated with therapy effectiveness ($p = 0.002$). The study described patient characteristics, antihypertensive drug use, ADR occurrence, and therapy effectiveness among outpatients at Baptis Batu Hospital. ADR occurrence was significantly associated with therapy effectiveness ($p = 0.002$). These findings support individualized antihypertensive treatment and continuous ADR monitoring to optimize therapy effectiveness and safety.



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Hypertension remains one of the most extensively studied global public health problems, yet it continues to pose a major challenge because of its contribution to cardiovascular morbidity and mortality. The World Health Organization estimates that more than 1.28 billion adults aged 30–79 years

worldwide live with hypertension, most of them in low- and middle-income countries. Because hypertension is often asymptomatic, it is frequently called a silent killer, and can progress to serious complications such as stroke, heart failure, and chronic kidney disease [1]. In Indonesia, hypertension

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prevalence among adults was 30.8% in 2023, a slight decrease from 34.1% in 2018 [2,3]; however, the gap between prevalence based on physician diagnosis and direct blood pressure measurement remains large among the elderly, indicating that many cases are still undiagnosed [2]. This makes the evaluation of antihypertensive therapy success not merely drug availability a relevant, cross-disciplinary issue for clinical pharmacy, medicine, and health policy.

The success of antihypertensive therapy is conceptually influenced by two main factors: patient characteristics (age, sex, polypharmacy, and regimen type) and drug safety, reflected in the incidence of adverse drug reactions (ADRs) [4]. Current literature, however, presents an inconsistent picture of how strongly each factor contributes. Several systematic reviews report that antihypertensive prescribing patterns in Indonesia are relatively uniform, dominated by calcium channel blockers (CCBs) and angiotensin receptor blockers (ARBs), with generally appropriate use [5,6]. Studies in elderly populations found that age and comorbidities were associated with drug selection, but blood pressure target achievement was not always reported [7]. More notably, one observational study found no significant difference in effectiveness between two pharmacologically distinct antihypertensive classes [8], while an electronic medical record-based study in another country reported statistically significant blood pressure reductions with both monotherapy and combination therapy, yet only 35–47% of patients achieved guideline-recommended targets [9]. These discrepancies suggest that statistical significance does not always translate into clinical efficacy, and that antihypertensive effectiveness is difficult to generalize without considering the local population and clinical context.

ADRs may affect the effectiveness of antihypertensive therapy and are therefore important to consider when evaluating treatment outcomes. One study in a population with characteristics similar to this study reported no significant difference in blood pressure target achievement between patient groups [10], contradicting the common clinical

assumption that ADRs reduce adherence and, consequently, therapeutic efficacy. This discrepancy between empirical findings and clinical assumption represents a research gap that warrants further investigation using standardized, replicable causality instruments.

To address this gap, ADRs in this study were assessed using the Naranjo Algorithm, a quantitative instrument comprising ten structured questions that is widely used in pharmacovigilance, including in regional ADR evaluations [11]. The algorithm classifies the certainty of a drug–reaction causal relationship into four categories (definite, probable, possible, doubtful), increasing objectivity relative to purely subjective clinical judgment. Because all study variables patient characteristics and ADRs as predictors, and therapy effectiveness as the outcome were categorical, associations were tested using the Chi-Square test, a widely used and readily interpretable non-parametric method.

To date, local data that systematically combine patient characteristics, ADRs based on the Naranjo Algorithm, and antihypertensive therapy effectiveness in outpatients particularly at mid-sized hospitals such as Baptis Batu Hospital remain very limited. This study addresses that gap by providing hospital-based pharmacoepidemiological evidence from an Indonesian outpatient setting that combines descriptive patient- and drug-utilization profiling with a structured, validated ADR causality assessment, an approach that has not previously been reported for this population. Accordingly, this study aims to describe patient characteristics, antihypertensive drug utilization patterns, ADR occurrence, and therapy effectiveness, and to analyze the relationships between these variables using the Chi-Square test, thereby providing local evidence that enriches and clarifies the mixed findings reported in the existing literature.

Results and Discussion

Characteristics of Hypertension Patients

The characteristics of the 95 hypertensive outpatients are presented in Table 1

Table 1. Characteristics of Hypertension Patients.

Patient Characteristics	Category	Frequency (n)	Percentage (%)
Gender	Man	31	32.6
	Woman	64	67.4
Age	< 65 years	56	58.9
	≥ 65 years	39	41.1
Polypharmacy	No polypharmacy	33	34.7
	Polypharmacy	62	65.3
Use of Antihypertensive Drugs	Single	22	23.2
	Combination	73	76.8
Comorbidity	Hypertension with Heart	61	64.2
	Hypertension with non-cardiac	34	35.8

Among the 95 outpatients with hypertension included in this study, most patients were female (67.4%) and aged <65 years (58.9%). The higher proportion of female patients may reflect differences in healthcare-seeking behavior and population characteristics. This finding differs from studies reporting higher proportions of men, indicating that sex distribution may vary across settings [11]. All patients had at least one comorbidity, with cardiac comorbidity being the most common (64.2%). The presence of comorbidities may increase treatment complexity because antihypertensive selection must consider cardiovascular benefit, safety, and potential drug interactions [10].

The high use of combination antihypertensive therapy (76.8%) and polypharmacy (65.3%) may reflect the need to manage hypertension together with multiple comorbid conditions. Combination therapy is generally used when a single drug is insufficient to achieve blood pressure control, while polypharmacy may result from concurrent treatment of comorbidities [4,12]. Amlodipine and candesartan were among the most frequently used agents; their complementary mechanisms and the cardiovascular

comorbidity profile may explain their frequent use [4,18,19].

For non-cardiovascular comorbidities, treatment selection may also consider potential effects on other organ systems. For example, NSAID use in osteoarthritis may reduce antihypertensive effectiveness and increase renal risk [40,41], while CCB use may be considered carefully in patients with GERD because it has been associated with reflux oesophagitis [41–43].

Overview of Adverse Drug Reactions (ADRs) of Antihypertensive Drugs

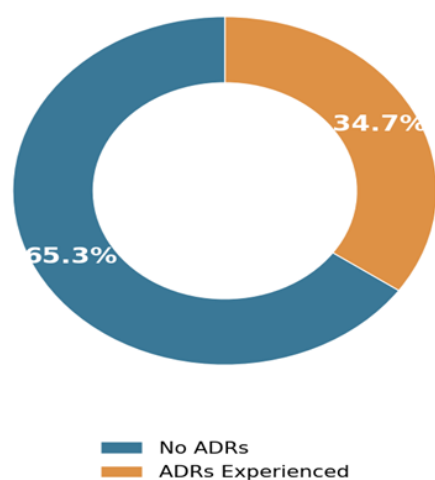
The occurrence of ADRs according to antihypertensive regimen is presented in Table 2 and Figure 1. Among 95 patients, 33 (34.7%) experienced ADRs and 62 (65.3%) did not. Peripheral edema was mainly observed in CCB-containing regimens, while frequent urination and hyperglycemia occurred in regimens containing diuretics. Shortness of breath and weakness were observed in some beta-blocker-containing regimens. This pattern is consistent with the known pharmacological effects of these drug classes [16,17,22–25].

Table 2. Overview of Adverse Drug Reactions (ADRs) of Antihypertensive Drugs

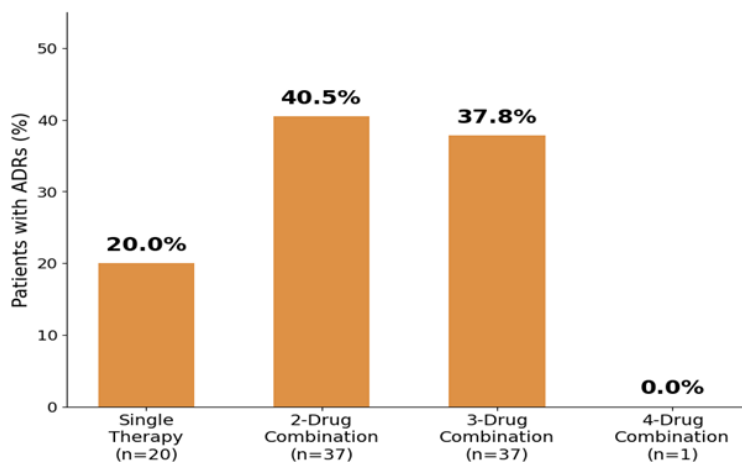
Antihypertensive Drug Regimen	Number (n)	No Adverse Drug Reactions (ADRs) n (%)	There are Adverse Drug Reactions (ADRs) n (%)	Adverse Drug Reactions (ADRs) Experienced
Single Therapy				
CCB	11	7 (63.6%)	4 (36.4%)	Edema (swelling in the legs), cough
ARB	9	9 (100%)	-	-
Combination Therapy of 2 Drugs				
CCB + ARB	25	17 (68%)	8 (32%)	Edema (swelling of the legs)
BB + ARB	5	3 (60%)	2 (40%)	Shortness of breath (bronchospasm), hyperglycemia, weakness
BB + ACE-I	2	1 (50%)	1 (50%)	Shortness of breath (bronchospasm)
ARB + Diuretic	5	1 (20%)	4 (80%)	Frequent urination, hyperglycemia
Combination Therapy of 3 Drugs				
CCB + BB + Diuretic	1	-	1 (100%)	Shortness of breath (bronchospasm)
CCB + BB + ARB	18	12 (66.7%)	6 (33.3%)	Frequent urination, hyperglycemia, edema (swelling of the legs), shortness of breath (bronchospasm)
CCB + ARB + Diuretic	16	10 (62.5%)	6 (37.5%)	Edema (swelling of the legs), frequent urination
BB + ARB + Diuretic	2	1 (50%)	1 (50%)	Frequent urination
4-Drug Combination Therapy				
BB + ARB + Diuretic	1	1 (100%)	-	-
Total	95	62 (65.3%)	33 (34.7%)	

Figure 1. Overview of Adverse Drug Reactions (ADRs) of Antihypertensive Drugs

A. Overall ADR Occurrence (n = 95)



B. ADR Occurrence by Regimen Type



Overview of the Effectiveness of Antihypertensive Therapy

In this study, an assessment of the effectiveness of antihypertensive therapy was conducted to determine the success of drug use in achieving blood pressure targets in hypertensive patients. This analysis aimed to describe the proportion of patients who successfully achieved their therapy targets and those who did not achieve them after receiving antihypertensive treatment. Furthermore, effectiveness results were presented based on the therapy regimen used to provide an

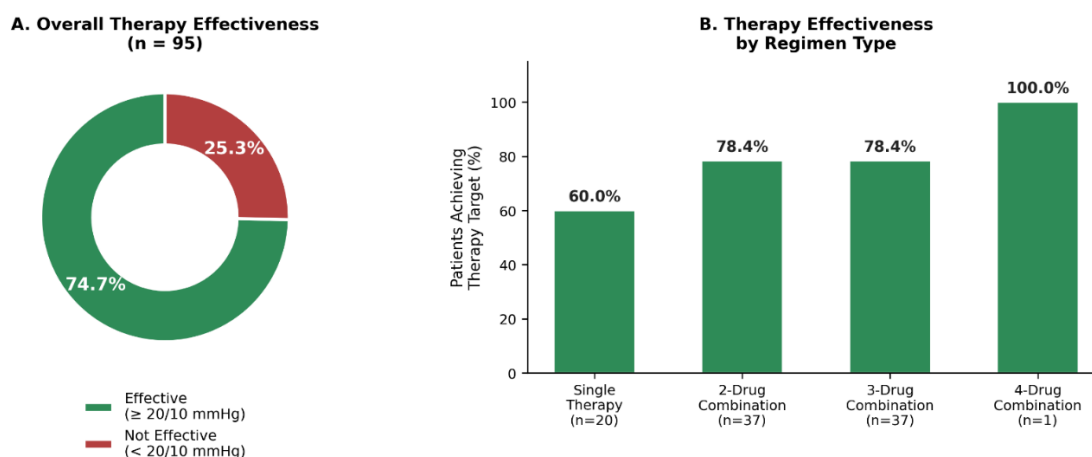
overview of the success of therapy in each treatment group. The results of this analysis are presented in the following Table 4.3 and Figure 4.3.

Among 95 patients, 33 (34.7%) experienced ADRs and 62 (65.3%) did not. Peripheral edema was mainly observed in CCB-containing regimens, whereas frequent urination and hyperglycemia occurred in regimens containing diuretics. Shortness of breath and weakness were observed in some beta-blocker-containing regimens. These findings are consistent with the known pharmacological effects of the respective drug classes [16,17,22–25].

Table 3. Overview of the Effectiveness of Antihypertensive Therapy

Antihypertensive Drug Therapy Regimen	Number (n)	BP decrease < 20/10 mmHg n (%)	BP decrease ≥ 20/10 mmHg n (%)
Single Therapy			
CCB	11	6 (54.5%)	5 (45.5%)
ARB	9	2 (22.2%)	7 (77.8%)
Combination Therapy of 2 Drugs			
CCB + ARB	25	5 (20%)	20 (80%)
BB + ARB	5	1 (20%)	4 (80%)
BB + ACE-I	2	1 (50%)	1 (50%)
ARB + Diuretic	5	1 (20%)	4 (80%)
Combination Therapy of 3 Drugs			
CCB + BB + Diuretic	1	-	1 (100%)
CCB + BB + ARB	18	5 (27.8%)	13 (72.2%)
CCB + ARB + Diuretic	16	3 (18.75%)	13 (81.25%)
BB + ARB + Diuretic	2	-	2 (100%)
4-Drug Combination Therapy			
BB + ARB + Diuretic	1	-	1 (100%)
Total	95	24 (25.3%)	71 (74.7%)

Figure 2. Overview of the Effectiveness of Antihypertensive Therapy



The results indicate that most patients achieved effective antihypertensive therapy, with 71 patients (74.7%) meeting the blood pressure reduction criterion. The high proportion of target achievement may be related to individualized regimens and the frequent use of combination therapy, particularly CCB-containing regimens, which provide complementary blood-pressure-lowering mechanisms [4]. This proportion was higher than the 35–47% target achievement reported by Khan et al. [9], although differences in population and clinical context should be considered. Adherence, duration of hypertension, lifestyle, and sodium intake, which were not evaluated in this study, may also have contributed to unsuccessful outcomes [13].

4.1.4 Relationship between Patient Characteristics and Therapy Effectiveness

Based on the Chi-square test results in Table 4.4, there was no significant relationship between sex ($p > 0.05$), age ($p > 0.05$), polypharmacy ($p > 0.05$), comorbidity ($p > 0.05$), or antihypertensive regimen type ($p > 0.05$) and therapy effectiveness. This indicates that patient characteristics alone did not. The results of the analysis of the relationship between the chi-square test of patient characteristics and the effectiveness of therapy obtained are as follows.

determine blood pressure target achievement in this study, likely because each patient received a different type, dose, or combination of antihypertensive drugs tailored to their clinical condition, hypertension severity, and comorbidities therapy was individualized rather than uniform across characteristic groups. Accordingly, male and female patients, those aged < 65 and ≥ 65 years, patients with or without polypharmacy, and patients receiving single or combination therapy showed no significant differences in achieving blood pressure reduction targets [10]. In the polypharmacy group, the medications used were not exclusively antihypertensives but also included therapy for comorbidities, which may explain why polypharmacy did not directly affect antihypertensive effectiveness. Combination therapy is also generally given to patients with more difficult-to-control blood pressure, while single therapy is given to patients with milder initial presentations. This individualized adjustment of therapy to each patient's clinical needs is the most likely explanation for the absence of a significant relationship between patient characteristics and therapy effectiveness in this study [4].

Table 4. Relationship between Patient Characteristics and Therapy Effectiveness

Variables	Category	BP decrease < 20/10mmHg n (%)	BP decrease $\geq$ 20/10mmHg n (%)	p-value
Gender	Man	10 (32.3%)	21 (67.7%)	0.275
	Woman	14 (21.9%)	50 (78.1%)	
Age	< 65 years	15 (26.8%)	41 (73.2%)	0.682
	≥ 65 years	9 (23.1%)	30 (76.9%)	
Polypharmacy	No Polypharmacy	9 (27.3%)	24 (72.7%)	0.742
	Polypharmacy	15 (24.2%)	47 (75.8%)	
Use of Antihypertensive Drugs	Single	8 (36.4%)	14 (63.6%)	0.172
	Combination	16 (21.9%)	57 (78.1%)	
Comorbidity	Hypertension with Heart	12	49	0.514
	Hypertension with Non-Cardiac	9	25	

Relationship of Adverse Drug Reactions (ADRs) to Therapy Effectiveness

This analysis was conducted to determine whether there was a relationship between the occurrence of Adverse Drug Reactions (ADRs) and the effectiveness of therapy

Table 5. Analysis of the Relationship between Adverse Drug Reactions (ADRs) and Therapy Effectiveness

Adverse Drug Reactions (ADRs)	BP decrease < 20/10mmHg n (%)	BP decrease ≥ 20/10mmHg n (%)	Total	p-value
No Adverse Drug Reactions (ADRs) (< 9)	22 (35.5%)	40 (64.5%)	62	0.002
There are Adverse Drug Reactions (ADRs) (≥ 9)	2 (6.1%)	31 (93.9%)	33	

The Chi-square test results indicate a significant relationship between ADR occurrence and therapy effectiveness ($p < 0.05$). Patients who experienced ADRs tended to achieve their blood pressure reduction targets more often than patients who did not, which may be because most ADRs observed in this study were consequences of the same pharmacological mechanisms that also produce the antihypertensive effect [14]. The most common ADR was peripheral edema associated with CCB use, both as monotherapy and in combination; its occurrence may therefore reflect that the drug's pharmacological effect is occurring as expected, which is also associated with more frequent target achievement. Similarly, bradycardia with bisoprolol and increased urinary frequency with furosemide are ADRs that arise from the same mechanisms that contribute to the antihypertensive effect. These findings do not indicate that ADRs make therapy more effective; rather, they show a statistically significant association between ADR occurrence and therapy effectiveness [15].

Discussion

The patient profile showed a predominance of female patients, patients aged < 65 years, cardiac comorbidities, combination therapy, and polypharmacy. The higher proportion of women may reflect differences in healthcare-seeking behavior and population characteristics. This sex distribution differs from some studies reporting higher

proportions of men, indicating that patient composition may vary across settings [11].

Combination therapy was common, with amlodipine and candesartan among the most frequently used drugs. Amlodipine lowers peripheral vascular resistance through calcium-channel blockade, while candesartan inhibits the angiotensin II AT1 receptor and may provide cardiovascular and renal protection [4,18,19]. The frequent use of these agents is consistent with the cardiovascular comorbidity observed in this population.

The two-, three-, and four-drug regimens indicate that treatment was adjusted to individual clinical needs. The most common two-drug combination, amlodipine plus candesartan, provides complementary blood-pressure-lowering mechanisms and is consistent with PERHI recommendations [4]. The single four-drug regimen consisted of bisoprolol, furosemide, spironolactone, and valsartan, reflecting individualized treatment for a complex clinical condition.

ADRs occurred in 34.7% of patients, while most patients did not experience ADRs. Peripheral edema was the most common ADR and is consistent with dihydropyridine CCB use. Kiani et al. [22] also reported a dose-dependent increase in peripheral edema with amlodipine. Other observed ADRs, including bradycardia or weakness with bisoprolol and frequent urination with furosemide, are

consistent with the pharmacological actions of these drugs [16,17,23–25].

The study also showed different treatment patterns across comorbidity groups. Patients with CAD commonly received amlodipine, candesartan, and furosemide, whereas candesartan-based regimens were common among patients with diabetes. These patterns are consistent with the need to address cardiovascular risk, fluid status, and renal protection in patients with multiple comorbidities [27–34]. Overall, the findings support treatment selection based on the clinical condition rather than the number of comorbidities alone.

For non-cardiovascular comorbidities, treatment selection also considered potential effects on other organ systems. For example, NSAID use in osteoarthritis may reduce antihypertensive effectiveness and increase renal risk [40,41], while GERD may influence the choice between ARB- and CCB-based therapy [41,42]. These considerations highlight the importance of individualized treatment in patients with multiple conditions.

Therapy was effective in 71 patients (74.7%). This proportion was higher than the 35–47% target achievement reported in the electronic medical record study by Khan et al. [9], although differences in population and clinical context should be considered. The higher achievement observed with combination therapy is consistent with the principle that complementary mechanisms can provide greater blood-pressure reduction [4,51].

No significant relationship was found between sex, age, polypharmacy, comorbidity, or antihypertensive regimen type and therapy effectiveness. In contrast, ADR occurrence was significantly associated with therapy effectiveness ($p = 0.002$). The higher proportion of target achievement among patients with ADRs should not be interpreted as ADRs causing better therapy outcomes; rather, the finding represents a statistical association that may reflect shared pharmacological mechanisms of efficacy and ADRs [14,15]. These findings emphasize

the need for individualized therapy and continuous ADR monitoring.

Research Limitations

This study has several limitations that should be considered when interpreting the results. First, the cross-sectional observational design describes associations between variables at a single point in time and cannot establish causal relationships between patient characteristics or ADR occurrence and antihypertensive therapy effectiveness. ADRs were assessed through direct patient interviews using the Naranjo Algorithm. To minimize recall bias, patients were interviewed during the data collection period using structured questions regarding their symptoms, the onset and duration of complaints, and the medications used. The interview findings were also cross-checked with available medical records and medication data to support the assessment. This approach helped ensure that the information used in the Naranjo assessment was based on both patient-reported complaints and available clinical data. Third, this study did not account for all factors that can influence antihypertensive therapy effectiveness, such as treatment adherence, physical activity, diet, and other lifestyle factors.

Conclusion

Most patients in this study were female, aged < 65 years, had cardiac comorbidities, received combination antihypertensive therapy, and experienced polypharmacy. Therapy was effective in 71 patients (74.7%). Sex, age, polypharmacy, comorbidity, and antihypertensive regimen type were not significantly associated with therapy effectiveness. In contrast, ADR occurrence was significantly associated with therapy effectiveness ($p = 0.002$), with a higher proportion of target achievement observed among patients with ADRs. The most common ADRs included peripheral edema, shortness of breath, and frequent urination with hyperglycemia. These findings support individualized antihypertensive treatment and continuous ADR monitoring.

Materials and Methods

Research design and population

This study used an analytical observational design with a prospective cross-sectional approach, conducted at the Internal Medicine and Cardiology Clinics of Baptis Batu Hospital between April and May 2026. The study population comprised outpatients aged ≥ 30 years with a diagnosis of hypertension undergoing antihypertensive therapy. Samples were selected using non-probability, purposive sampling, based on inclusion criteria (age ≥ 30 years, uncontrolled blood pressure $> 130/80$ mmHg, complete medical record data, patients provided written informed consent before participating in the interview, and at least 3 months of antihypertensive therapy) and exclusion criteria (incomplete data, unwillingness to be interviewed, hypertensive emergency, or already-controlled hypertension).

Data collection

Data were obtained from two sources: secondary data from patient medical records and primary data. ADRs were assessed through direct patient interviews using a structured data collection checklist and the Naranjo Algorithm. The use of a standardized checklist ensured consistent data collection across participants and helped minimize recall and interviewer-related bias. Data collected included patient characteristics (age, sex, polypharmacy, antihypertensive regimen type), blood pressure values during therapy, and ADR occurrence.

Assessment of Adverse Drug Reactions (ADRs)

ADRs were assessed using the Naranjo Algorithm, comprising 10 questions used to determine the likelihood of a causal relationship between a drug and a reaction. Scores were categorized as definite, probable, possible, or doubtful, and grouped as ADR-positive if the total score was ≥ 9 and ADR-negative if < 9 .

Assessment of therapy effectiveness

Antihypertensive therapy effectiveness was assessed based on changes in the patient's blood pressure during treatment, as recorded in the medical record. Therapy effectiveness was assessed during one study visit by comparing the patient's blood pressure measurement at the time of data collection with the blood pressure value recorded three months earlier in the medical record. Therapy was categorized as effective if a reduction of $\geq 20/10$ mmHg in systolic/diastolic blood pressure was achieved compared with the measurement three months earlier. Therapy was categorized as ineffective if the reduction did not reach $\geq 20/10$ mmHg.

Statistical analysis

Data were analyzed descriptively and analytically using SPSS. Categorical data were presented as frequencies and percentages. The Chi-Square test was used to analyze the relationship between patient characteristics and ADR occurrence with antihypertensive therapy effectiveness, given that most variables were nominal and categorical. A p-value < 0.05 was considered statistically significant.

Research ethics

This research received approval from Baptis Batu Hospital under permit number 426/20/IV/RSBB_DIR/2026, and ethical clearance from the Ethics Committee of the Department of Psychology, University of Muhammadiyah Malang (No. E.6.m/543/KE-FPsi-UMM/III/2026). Patient confidentiality was maintained throughout the study, and data were processed only in aggregate form for statistical analysis.

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