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ORIGINAL RESEARCH

EVALUATION OF ANTIHYPERTENSIVE DRUGS USE IN ISCHAMIC STROKE PATIENTS USING THE ATC/DDD METHOD AT KOJA REGIONAL GENERAL HOSPITAL, JAKARTA

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Abstract

Background: Ischemic stroke accounts for approximately 87% of all stroke cases, making it the most prevalent subtype compared with hemorrhagic stroke. The Indonesian Neurological Association recommends the use of antihypertensive therapy in patients with ischemic stroke.
Purpose: This study aimed to quantify the utilization of antihypertensive drugs using the Anatomical Therapeutic Chemical/Defined Daily Dose (ATC/DDD) methodology in ischemic stroke inpatients at Koja District Hospital, Jakarta, between January and December 2022.
Methods: A descriptive, retrospective design was employed, reviewing the medical records of 114 ischemic stroke inpatients who met the inclusion criteria. Data collected included sociodemographic characteristics, antihypertensive drug utilization, and DU-90% profiling. Data analysis was performed using Microsoft Excel.
Results: Over the study period, the total length of stay was 633 patient-days. The highest consumption in DDD/100 patient-days was observed for amlodipine (57.78), followed by captopril (27.99), candesartan (13.14), and ramipril (4.36). Other agents showed lower levels of utilization. The DU-90% segment consisted of amlodipine, captopril, candesartan, and ramipril.
Conclusion: Amlodipine, captopril, candesartan, and ramipril were the primary drugs within the DU-90% utilization segment. These findings provide important insights for formulary management and rational drug use in ischemic stroke therapy.

Background

Stroke remains a leading cause of morbidity and mortality worldwide, with ischemic stroke accounting for approximately 87% of all stroke cases, making it the predominant subtype compared to hemorrhagic stroke. The burden of ischemic stroke is particularly concerning in low- and middle-income countries, where limited access to specialized care and preventive strategies exacerbates outcomes. Effective management of modifiable risk factors, particularly hypertension, plays a critical role in reducing morbidity, disability, and recurrence rates associated with ischemic stroke. The Indonesian Society of Neurologists emphasizes the use of antihypertensive therapy as a standard recommendation in the management of ischemic stroke, both for acute care and secondary prevention.

Rational drug use is an essential component of stroke management, ensuring that patients receive appropriate therapy in terms of choice, dosage, and duration. The Anatomical Therapeutic Chemical/Defined Daily Dose (ATC/DDD) methodology, developed by the World Health Organization, provides a standardized approach to quantifying and comparing drug,.

utilization across healthcare settings. This methodology enables healthcare professionals and policymakers to evaluate prescribing patterns, identify potential irrational use of medicines and improve formulary decision-making. Applying ATC/DDD analysis in ischemic stroke management is particularly relevant in resource-limited hospital settings, where optimizing cost-effective yet evidence-based therapy remains a priority.

Despite the high prevalence of ischemic stroke and the clear guideline recommendations on antihypertensive therapy, studies evaluating actual prescribing patterns in Indonesian hospitals remain limited. Koja District General Hospital, located in Jakarta, serves as a referral center for stroke patients and provides an opportunity to assess real-world antihypertensive drug utilization. Understanding the prescribing trends and identifying the most frequently used antihypertensive agents through the DU 90% method may provide valuable insights for formulary stewardship and clinical decision-making. Furthermore, such evidence is essential to ensure alignment with clinical guidelines, optimize patient outcomes, and contribute to the broader effort of improving stroke care in Indonesia

Method

This observational, descriptive study employed a retrospective review of medical records from ischemic stroke inpatients at Koja District Hospital between January and December 2022. Data were extracted from the hospital's medical record room from March to May 2023. A purposive (non-random) sampling method identified 114 of 121 total ischemic stroke patients meeting inclusion criteria. Collected variables included sociodemographic data, antihypertensive drug utilization, and DU-90% profiling. Data were analyzed using Microsoft Excel.

Results

Table 1. Patient Gender Distribution

Gender	F (n=114)	Percentage (%)
Man	71	62,3
Women	43	37,7

Among the 114 ischemic stroke patients included in this study, the majority were male (62.3%), whereas female patients accounted for 37.7%. This finding is consistent with epidemiological evidence suggesting that men are at higher risk of developing ischemic stroke compared to women, particularly in middle to older age groups.

Table 2. Patient Age Distribution

Age	F (n=114)	Percentage (%)
15 – 25	1	0,87
26 – 35	1	0,87
36 – 45	15	13,1
46 – 55	30	26,3
56 – 65	43	37,7
66 – 70	15	13,1
71 – 75	6	5,2
> 75	3	2,6

The age distribution of the patients revealed that ischemic stroke predominantly occurred in older adults. The largest proportion was observed in the age group of 56–65 years (37.7%), followed by 46–55 years (26.3%) and 36–45 years (13.1%). Only a small fraction of patients were below 35 years of age (1.74%). This supports the well-established association between increasing age and higher stroke incidence.

Table 3. Comorbidities among Ischemic Stroke Patients

Comorbidities	**F (n=114)**	**Percentage (%)**
Hypertension	81	71,05
Dyslipidemia	52	45,61
Diabetes Mellitus	21	18,42
Hypercholesterolemia	14	12,28
Coronary Heart Disease	11	9,64
Gout	8	7,017
Chronic Kidney Failure	2	1,75
Other Diseases (epilepsy, GERD, prostate, schizophrenia, asthma)	7	6,14

Hypertension was the most prevalent comorbidity, reported in 71.05% of patients, followed by dyslipidemia (45.61%) and diabetes mellitus (18.42%). Other comorbidities included hypercholesterolemia (12.28%), coronary heart disease (9.64%), gout (7.02%), chronic kidney disease (1.75%), and other conditions such as epilepsy, gastroesophageal reflux disease, prostate disorders, schizophrenia, and asthma (6.14%). The predominance of cardiovascular and metabolic disorders highlights their strong role as risk factors for ischemic stroke.

Table 4. Length of Stay Distribution and Total Patient-Days

Length of Stay (Days)	**Number of Patients**	**Total Number of Days of Stay / LOS (Days)**
1-3	17	45
4-6	61	306
7-9	36	282
Total	114	633

The majority of patients (53.5%) were hospitalized for 4–6 days, contributing to 306 total patient-days. Patients with a length of stay between 7–9 days accounted for 36 cases (31.6%) with 282 patient-days, while 17 patients (14.9%) were hospitalized for 1–3 days (45 patient-days). Overall, the total number of patient-days was 633, with an average length of stay (LOS) of approximately 5.55 days per patient. This reflects a moderate duration of hospitalization, likely influenced by the severity of stroke and the presence of comorbidities.

Table 5. ATC Classification of Antihypertensive Agents

Antihypertensive Drug Class	**Drugs name**	**ATC Code**
Diuretik	Furosemide	C03CA01
	Hydrochlorothiazide	C03AA03
	Spironolactone	C03DA01
β-Bloker	Bisoprolol	C07AB07
	Carvedilol	C07AG02
ACE-Inhibitor	Captopril	C09AA01
	Ramipril	C09AA05

Antihypertensive Drug Class	Drugs name	ATC Code
ARB	Candesartan	C09CA04
	Irbesartan	C09CA06
	Losartan	C09CA01
CCB	Amlodipine	C08CA01
	Nifedipine	C08CA05

Antihypertensive agents prescribed to ischemic stroke patients were classified according to the Anatomical Therapeutic Chemical (ATC) system. The drugs belonged to five major classes: diuretics (furosemide, hydrochlorothiazide, spironolactone), β-blockers (bisoprolol, carvedilol), ACE inhibitors (captopril, ramipril), angiotensin receptor blockers (candesartan, irbesartan, losartan), and calcium channel blockers (amlodipine, nifedipine). This indicates that the pharmacological management adhered to guideline-recommended antihypertensive therapies for secondary stroke prevention.

Table 6. Antihypertensive Utilization (DDD/100 Patient-Days)

Antihypertensive Drugs	Total Number of DDD Usages	DDD/100 Days of Treatment (mg/100 days)
Amlodipine	145	57,78
Captopril	34,5	13,75
Candesartan	33	13,14
Ramipril	11	4,36
Losartan	9	3,58
Furosemide	6,5	2,57
Irbesartan	3	1,18
Nifedipine	3	1,18
Spironolactone	2,33	0,90
Hydrochlorotiazid	2	0,78
Bisoprolol	1,75	0,63
Carvedilol	0,33	0,05

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Table 7. DU-90% Profile for Antihypertensive Use

Drug Name	% Usage	% Kumulatif	DU 90%
Amlodipine	57,78	57,78	90%
aptopril	13,75	71,56	
Kandesartan	13,14	84,7	
Ramipril	4,36	89,06	
Losartan	3,58	92,64	10%
Furosemide	2,57	95,21	
Irbesartan	1,18	96,39	
Nifedipine	1,18	97,57	
Spironolactone	0,90	98,47	
Hydrochlorotiazid	0,78	99,25	
Bisoprolol	0,68	99,93	
Carvedilol	0,07	100	

The Drug Utilization 90% (DU-90%) analysis demonstrated that five drugs—amlodipine (57.78%), captopril (13.75%), candesartan (13.14%), ramipril (4.36%), and losartan (3.58%)—accounted for 90% of total antihypertensive use. This concentrated prescribing pattern indicates a rational drug utilization approach, with the majority of therapy focused on a limited number of evidence-based agents. Such findings suggest alignment with clinical practice guidelines and support the rationality of antihypertensive prescribing in this patient population.

Discussion

This study aimed to assess the quantity of antihypertensive drug use based on the Anatomical Therapeutic Chemical/Defined Daily Dose (ATC/DDD) method in inpatients with ischemic stroke at Koja District General Hospital, Jakarta. Data were collected retrospectively, with the sample consisting of patients diagnosed with primary ischemic stroke who received antihypertensive therapy and met the inclusion criteria. A total of 121 patients were initially identified, of whom 114 met the inclusion criteria.

According to Table 1, patient demographic characteristics showed that 71 patients (62.3%) were male and 43 (37.7%) were female, indicating that the majority of patients with ischemic stroke receiving antihypertensive therapy were male. This finding aligns with a study by Endang et al. (2020) in Ternate, which also reported that males were more affected than females (62% vs 38%). These findings are consistent with Indonesia's Basic Health Research (RISKESDAS, 2018) data, which indicated a higher prevalence of stroke among men. Contributing factors may include lifestyle habits such as smoking, which promotes plaque accumulation and atherosclerosis. Additionally, psychological stress can act as a risk factor for stroke by triggering hormone release that can elevate blood pressure, increase blood viscosity, and potentially cause cerebral vessel rupture (Susilawati & HK, 2018).

The higher incidence of stroke in men is also linked to the presence of testosterone, which elevates LDL cholesterol levels, thus increasing the risk of cardiovascular diseases. Conversely, estrogen in premenopausal women is known to have a protective effect against atherosclerosis, which may explain the lower prevalence among females (Laily, 2017).

In Table 2, the age group most affected was 56–65 years (43 out of 114 patients), indicating that older adults are more vulnerable to ischemic stroke. Aging leads to vascular changes, including narrowing of vessel lumen and loss of elasticity, which raise blood pressure and increase the risk of atherosclerotic plaque rupture and arterial blockage. Nonetheless, stroke

can still occur in individuals under 40 years of age, particularly due to unhealthy lifestyle factors, such as high-fat diets, physical inactivity, and chronic stress (Ramadhaeni *et al.*, 2018). The duration of living with stroke ranged from 1 to 10 years, with an average of 3 years. Stroke onset after age 50 typically correlates with reduced life expectancy due to various risk factors and declines in quality of life, especially when lifestyle habits are not well managed (Budi & Syahfitri, 2018).

Based on Table 3, hypertension was the most common comorbidity among ischemic stroke patients (81 patients, 71.05%), confirming its role as a major risk factor. Both systolic and diastolic hypertension significantly increase stroke risk by causing vascular damage, promoting atherosclerosis, and increasing the likelihood of cerebral artery blockage (Kabi et al., 2015). Dyslipidemia was also prevalent (45.6%), characterized by elevated LDL and triglycerides, and decreased HDL levels. High LDL leads to arterial plaque formation, contributing to atherosclerosis (Pakpahan *et al.*, 2022). Diabetes mellitus, another notable comorbidity, increases stroke risk by causing thickening of cerebral blood vessels, reducing vessel lumen and impairing cerebral perfusion, leading to brain infarction (Letelay *et al.*, 2019).

As shown in Table 4, the total length of stay (LOS) was 633 days, with an average hospitalization of 6 days per patient. Most ischemic stroke patients are hospitalized for 1–14 days, which is shorter than hemorrhagic stroke cases that often require 14–21 days (Nirmalasari et al., 2020). This is because ischemic stroke, typically due to atherosclerotic blockage, often results in hemiparesis that can improve with prompt treatment. In contrast, hemorrhagic strokes tend to cause more severe symptoms, including loss of consciousness, requiring longer care (Othadinar *et al.*, 2019). LOS is a crucial variable for calculating antihypertensive drug use in DDD/100 patient-days. Factors affecting LOS include disease severity, prior medication use, and adverse drug reactions (Dewi *et al.*, 2019).

According to Table 5, antihypertensive drugs are categorized under the cardiovascular system in the ATC classification system developed by WHO. Drug utilization evaluation (DUE) helps assess both quantity and quality of drug use. The ATC/DDD system, recommended by WHO, was used to assess the defined daily dose (DDD) of each drug, based on total usage during hospitalization (Andrajati & Retnosari, 2022).

From Table 6, the quantity of antihypertensive use was calculated using standard ATC/DDD procedures. Drugs were grouped by pharmacological class, and DDD values were derived by dividing the total drug usage (mg) by the WHO-assigned DDD for each agent. Then, DDD/100 patient-days was calculated by dividing the total DDD by LOS (in days) and multiplying by 100 (Kemenkes, 2017).

The four most commonly used antihypertensive agents (in DDD/100 patient-days) were Amlodipine 57.78, Captopril 13.75, Candesartan 13.14, Ramipril 4.36. These findings are consistent with prior studies, such as one conducted in RSUD S. K. Lerik Kupang (2018), where Calcium Channel Blockers (CCBs) were the most frequently prescribed. Similarly, in Koja Hospital (2022), CCBs particularly amlodipine dominated usage. CCBs act by blocking calcium influx, leading to vascular smooth muscle relaxation and effective blood pressure reduction. Amlodipine, specifically, is vasoselective, has low oral bioavailability, a long half-

life, and slow absorption, making it ideal for stroke prevention without abrupt hypotension (Fadhilla & Permana, 2020).

Among ACE inhibitors, captopril was the second most used and ramipril the fourth. ACE-Is lower blood pressure by inhibiting angiotensin II formation and reducing aldosterone secretion. They also increase bradykinin, contributing to vasodilation. These agents are preferred due to their low metabolic side effects during long-term therapy (Putri *et al.*, 2019). Candesartan, an ARB, was the third most used agent. It is an angiotensin II receptor blocker (type 1) with proven benefits in limiting ischemic stroke damage and improving outcomes (Tandi *et al.*, 2018).

Amlodipine remains the most widely used due to its superior stroke prevention compared to other classes (Octasari & Oktaviani, 2019), and its pharmacokinetic profile. CCBs relax cardiac muscle and reduce calcium influx, thus enhancing vasodilation. Combining CCBs with ARBs has shown significant antihypertensive efficacy (Dipiro *et al.*, 2015).

According to Table 7, the Drug Utilization (DU) 90% analysis indicated that the following drugs made up 90% of antihypertensive use: amlodipine, captopril, candesartan, and ramipril. The DU 90% metric was calculated by ranking each drug's DDD/100 patient-days contribution and determining the cumulative percentage. These data reflect the most commonly prescribed drugs in clinical practice.

The DU 90% profile at Koja Hospital in 2022 showed some variation from other studies. For instance, research by Ni Putu (2020) in Kupang identified amlodipine and captopril in the DU 90% segment, while candesartan and ramipril were not included. This indicates interregional differences in antihypertensive prescribing patterns.

Conclusion

Male patients aged 56–65 years with hypertension are at greatest risk for ischemic stroke requiring antihypertensive therapy. Overall antihypertensive consumption was highest for amlodipine (57.78 DDD/100 patient-days), followed by captopril, candesartan, and ramipril. These four drugs comprised the DU-90% segment, offering evidence for targeted stewardship.

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