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Cost-Effective Analysis of Aspirin and Clopidogrel Therapy in Hospitalized Ischemic Stroke Patients at Mataram City Hospital

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A B S T R A C T

Ischemic stroke is one of the diseases with the highest death cases in Indonesia. So stroke patients often need further treatment and long-term rehabilitation. To determine the cost-effectiveness and therapy of aspirin and clopidogrel in ischemic stroke patients by looking at the GCS score of hospitalization at Mataram City Hospital, and to determine the most cost-effective therapy based on ACER and ICER. The research method used was observational descriptive and data collection was carried out retrospectively through patient medical records and financial details data. The sample met the inclusion criteria of 78 people, the sample was analyzed quantitatively by the Independent sample t-test analysis method. The results showed that the total cost of treatment for ischemic stroke patients treated with antiplatelets was the highest in the VIP class clopidogrel group of Rp 5,400,015 and VIP class aspirin Rp 4,982,370 The increase in the highest GCS score of aspirin in class ll was 2.84 and clopidogrel class lll was 2.45. The most cost-effective ACER values of all antiplatelet treatment classes are aspirin VIP class Rp 2,129,218, class l Rp 1,785,451, class ll Rp 1,700,509, class lll Rp 1,380,574 and ICER value in class l Rp -1,993,315 and class lll Rp -1,555,950. The ACER scores of all treatment classes showed that aspirin had the lowest scores. Based on sensitivity analysis and tornado diagrams, clopidogrel showed higher results so that aspirin was more cost-effective than clopidogrel. The use of aspirin antiplatelets was more cost-effective than clopidogrel from all direct medical cost data of ischemic stroke patients

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INTRODUCTION

Non-hemorrhagic stroke or ischemic stroke is the blockage of blood vessels that causes blood flow to the brain to be partially or completely stopped and is the most common type of pathology that accounts for 80-88% of all stroke cases, while hemorrhagic stroke accounts for about 12-20% of cases (Hankey, 2020). Of these cases, stroke is a high-growth disease according to research (Zhang et al., 2023) Stroke is the second highest cause of death and long-term disability in the world, especially in developed and developing countries with aging populations, one example in Asia is China stroke is the first cause of death. Prevalence of stroke by data World Stroke Organization shows that every year there are 13.7 million new cases of stroke, and about 5.5 million deaths occur due to stroke (Mutiarasari, 2019).

Seeing the high prevalence of events, rational therapy is needed. The goals of acute stroke treatment include reducing neurological symptoms, reducing mortality and morbidity, preventing secondary complications in limbs and neurological dysfunction, and preventing stroke recurrence (Powers et al., 2018). Treatment for ischemic stroke patients involves a wide variety of therapies, including the use of antiplatelet drugs such as aspirin and clopidogrel. Both of these drugs work by inhibiting blood clotting and preventing blood clots that can clog blood vessels in the brain. Ischemic stroke occurs when blood flow to the brain is blocked, usually due to a blockage by a blood clot (thrombus). These thrombus is formed from the aggregation of platelets, which are small blood cells that gather and stick to each other. However, the use of antiplatelet drugs also has a lot of costs, so it is necessary to conduct a cost-effectiveness analysis (Kasner et al., 2021).

According to the cost of health services, stroke costs the highest at 2.56 trillion rupiah in 2018. Stroke is included in the category of cardiovascular diseases with the category of catastrophic diseases, which are diseases that require high costs in treatment and have complications that can endanger life. For example, in stroke, heart, cancer, kidney failure and diabetes mellitus. The number of stroke patients every year has increased so that the cost of health services automatically increases and can also have a major impact on the country's socio-economic development. If the choice of medication is not right, it can cause a longer stay in the hospital, so that it can cause complications of other diseases and eventually an increase in treatment costs. Consideration of the use of a drug in the treatment of a disease in addition to meeting the requirements for effectiveness, safety also takes into account the pharmacoeconomic aspect (Ministry of Health of the Republic of Indonesia, 2018).

It is necessary to conduct an economic analysis related to health services. A comprehensive way to determine the economic influence of alternative drug therapies or other health interventions is by pharmacoeconomic analysis in the form of Cost Effectiveness Analysis (CEA). Cost analysis is usually used to find out the average direct medical cost. This analysis can estimate the additional cost of an output or outcome, as there is no measure of the amount of money or clinical outcome that describes the value of the outcome. Cost Effectiveness Analysis (CEA) is an economic evaluation method that can be used for decision-

making in choosing the best alternative (Pichon-Riviere et al., 2023) Parameters that can be used to measure the effectiveness of therapy are by using Parameters Glasgow Coma Scale (GCS) is a neurological scale used to objectively assess a person's degree of consciousness. It was first introduced in 1974 by Graham Teasdale and Bryan J. Jennett, professors of neurosurgery at Institute of Neurological Sciences, University of Glasgow. GCS consists of 3 examinations, namely the assessment of eye-opening response (eye opening), best motor response (Best Motor Response), and the best verbal response (best verbal response). Each component of GCS and the sum of GCS scores are very important, therefore, GCS scores must be written correctly, for example: GCS 10, has no meaning, so it must be written as: GCS 10 (E2M4V2). The highest score indicates that the patient is conscious (Mentis Compos), namely GCS 15 (E4M6V5), and the lowest score indicates a comma (GCS 3 E1M1V1) (Wuysang, 2015).

THEORETICAL REVIEW

Definition of Stroke

Stroke causes brain damage that occurs suddenly, progressively, and rapidly as a result of non-traumatic disturbances in cerebral blood circulation. This disturbance can suddenly cause symptoms such as unilateral paralysis of the face or limbs, impaired speech, slurred speech, changes in consciousness, visual disturbances, and findings from follow-up (control) examinations (Utama & Nainggolan, 2022). Stroke can be classified into two types: ischemic stroke and hemorrhagic stroke. Ischemic stroke is caused by a lack of blood supply to the brain, whereas hemorrhagic stroke occurs due to the rupture of one or more blood vessels in the brain, resulting in bleeding. Neurological deficits occur when the blood vessels supplying the brain are obstructed due to fatty deposits lining the vessel walls, known as atherosclerosis, which can cause obstruction in the form of cerebral thrombosis (Setiawan, 2021).

Epidemiology

In the United States, stroke is the third leading cause of death, with a mortality rate of 146,664 deaths. Stroke is also the third leading cause of death in Indonesia, with 138,268 deaths, accounting for 9.7% of total deaths. A study conducted between 1990 and 2010 in 28 countries reported an increase in stroke incidence from 250.55 per 100,000 person-years to 257.96 per 100,000 person-years, while prevalence changed from 434.86 per 100,000 people to 393.38 per 100,000 people. The increase in stroke incidence and prevalence occurred in developing countries with low- to middle-income levels. In low- to middle-income countries, the incidence of stroke increased from 252 per 100,000 person-years in 1990 to 282 per 100,000 person-years in 2010, along with an increase in prevalence from 360 per 100,000 people to 394 per 100,000 people (Saraswati & Khariri, 2021).

Etiology

Based on etiology, stroke is classified into hemorrhagic stroke and ischemic stroke. The differences between these two types of stroke include treatment methods, risk factors, and pathology. Ischemic stroke is caused by

obstruction of the cervical or cerebral arteries, resulting in death of brain tissue due to impaired blood flow to certain areas of the brain. Atherosclerosis is one of the risk factors for ischemic stroke and is characterized by thickening of the arterial walls due to cholesterol deposition. Thrombus formation, hypercholesterolemia, and free radicals contribute to the development of atherosclerosis (Haiga et al., 2022).

METHODOLOGY

Study design

The design of this study is observational descriptive with a quantitative approach using patient medical record data. This research was conducted at the Mataram City Hospital from May 2023 to May 2024.

Population and sample

The population in this study is all ischemic stroke patients in the Mataram City Hospital inpatient period May 2023 – May 2024. The sample of this study is patients who meet the predetermined inclusion criteria. In this study, the inclusion criteria are inpatients with the main diagnosis of ischemic stroke, treated with aspirin and clopidogrel who have medical record data, financial data, complete GCS scores and use BPJS financing. While patients who are forced to go home or go home of their own volition, patients who die, patients who receive antiplatelet combination therapy are included in the exclusion criteria.

Study instruments

In this study, a data collection sheet or case record form (CRF) is used to record and collect medical record data of ischemic stroke patients who undergo hospitalization at the Mataram City Hospital. This data collection sheet contains variables required in the study, such as patient demographic data (age, gender), clinical data (diagnosis, length of hospitalization), treatment data (type of antiplatelet used - aspirin or clopidogrel, dose, and length of use), as well as cost data (drug costs, hospitalization costs, supporting examination costs, and total cost of treatment).

Data collection

Data were collected retrospectively using the total sampling technique. The data was first compiled into primary data and processed using SPSS statistical software 26.

Data Analysis

The analysis of test data with the help of using the SPSS program was carried out to find out whether there was a meaningful difference in the variables in the cost of the aspirin and clopidogrel antiplatelet selection group, then a data distribution test was carried out to measure the data had a normal distribution using the Kolmogorof-Smirnov non-parametric test, where if the result of the normal data distribution was $P>0.05$, then the test was continued with theThe independent test to measure the data had a significant or not difference in the average therapeutic effectiveness and total cost paid in the selection group of antiplatelet aspirin and clopidogrel, but if the result of the data distribution was abnormal which was $P<0.05$, then the Mann Whitney test was continued. To see the cost effectiveness between the two treatment groups, it can be calculated using the formula:

$$\text{ACER} = \frac{\text{Rata} - \text{rata biaya terapi obat}}{\text{Efektivitas (100 \%)}}$$

$$\text{ICER} = \frac{\text{Biaya obat A} - \text{Biaya obat B}}{\text{Efektivitas obat A} - \text{ Efektivitas obat A}}$$

RESEARCH RESULTS AND DISCUSSION

Table 1. The distribution of ischemic stroke patients in the Mataram City Hospital inpatient for the period May 2023-May 2024 is based on the age and gender of each antiplatelet group.

	Antiplatelets			
Age	**Aspirin**	**Clopidogrel**	**N**	**Percentage (%)**
31-54		10	10	13
55-60	6	20	26	33
>60	10	32	42	54
Total	16	62	78	100
Man	11	39	50	64
Woman	5	23	28	36
Total	16	62	78	100

Remarks: n = number of patients
Source : raw data processed

Table 2. Comorbid distribution of ischemic stroke patients in Mataram City Hospital inpatient period May 2023-May 2024.

Risk factors	**n**	**%**
No *comorbidities*	26	33
Hypertension	31'	40
Hypertension + DM	7	9
Heart failure	2	3
DM	5	6
DM + hypertension + heart failure	3	4
Heart failure + hypertension	4	5
Total	78	100

In table 1 The study shows that ischemic strokes are more common in the elderly group, especially over 60 years old. This is consistent with the findings of Riskesdas 2013 which noted that the prevalence of stroke increases significantly with age, reaching 67% at the age of ⩾75 years. This increased risk is associated with degenerative processes that affect the structure and function of blood vessels. Judging from gender, men are more at risk of ischemic stroke than women. Some studies show the incidence of ischemic stroke in men is 1.25 times higher. This is due to modifiable risk factors such as smoking, hypertension, and high cholesterol that are more common in men. Interestingly, women before menopause have a neuroprotective effect due to the hormone estrogen, so they have a lower risk of stroke between the ages of 40-75 years. However, after the age of 75, the risk of stroke in women increases by up to 50% compared to men (Sultradewi Kesuma et al., 2019).

Research reveals hypertension as the most important comorbid in ischemic stroke patients. This is supported by data that shows hypertension ranks first as a risk factor for stroke, with a prevalence of 64% of total cases.

A study at the Sukoharjo Regional General Hospital found that the proportion of hypertension in the acute phase stroke was 45.9%. In low-income countries, despite the lower prevalence of risk factors, stroke patients have the highest hospital mortality rates, likely due to delays in treatment and disparities in health management systems. The findings of the study confirm the importance of hypertension as a key indicator of ischemic stroke risk, underscoring the need for proper management and prevention (Wajngarten & Silva, 2019).

Table 3. Use of antiplatelets in ischemic stroke patients

Antiplatelets	VIP n (%)	Class l n (%)	Class ll n (%)	Class lll n (%)	Total n (%)
Aspirin	3 (25)	3 (18,75)	6 (27,28)	4 (14,29)	16 (20,51)
Clopidogrel	9 (75)	13 (81,25)	16 (72,72)	24 (85,71)	62 (79,49)
Total	12 (100)	16 (100)	22 (100)	28 (100)	78 (100)

Based on the results of table 3, the study revealed the pattern of antiplatelet use in ischemic stroke patients in various treatment classes. Clopidogrel dominated the use of antiplatelets in all classes, with the highest percentage in class III (85.71%), followed by class I (81.25%), class II (72.72%), and VIP class (75%). Clopidogrel is widely chosen for its effectiveness in preventing recurrence of strokes. The drug works by inhibiting P2Y12 receptors on platelets, preventing aggregation and the formation of blood clots. Its pharmacokinetics support use, with 50% bioavailability and half-life allowing for once-daily administration Clopidogrel works by inhibiting the activity of enzymes that platelets need to stick together and form blood clots. By inhibiting this platelet aggregation process, the risk of blockage of blood vessels that can trigger a stroke can be reduced (Rakhmawati et al., 2019). Recommendations from American Heart Association/American Stroke Association supports the use of clopidogrel in the secondary prevention of ischemic stroke, based on Level A evidence from randomized clinical trials. MATCH studies and Cochrane Collaboration meta-analyses also confirmed the effectiveness and safety of this drug, particularly in patients with multiple risk factors or who are intolerant to aspirin. Aspirin is still used, but in a much lower percentage across all treatment classes, ranging from 14.29% to 27.28%. This study shows a clear clinical trend towards clopidogrel as the antiplatelet of choice in ischemic stroke management.

Table 4. GCS (Glasglow Coma Scale) profile on the use of aspirin and clopidogrel based on GCS category in patients with ischemic stroke of first upon admission to hospital

GCS Categories	Aspirin n	%	Clopidogrel n	%	Total n	%
15-14 (mentis compos)	2	9,52	19	90,48	21	100
13-12 (apathetic)	10	28,57	25	71,43	35	100
11-10 (somnolent)	4	18,19	18	81,81	22	100

Based on Table 4, this study analyzed the Glasgow Coma Scale (GCS) score in ischemic stroke patients, referring to the study (Ojaghihaghighi et al., 2017) which shows a GCS score range between 8-15. Patients were grouped into three categories of consciousness based on GCS scores: compos mentis (score 15-14), apathy (score 13-12), and somnolent (score 11). In the clopidogrel group, the distribution of patients showed that the majority were in the apathetic category with 25 (71.43%) patients, followed by 19 (90.48%) patients with composite mentions, and 18 (81.81%) patients with somnolent. In contrast, in the aspirin group, the composition of patients was dominated by the apathy category with 10 (28.57%) patients, somnolent 4 (18.19%) patients, and compos mentis only 2 (9.52%) patients. These significant differences illustrate the variation in ischemic stroke patients' levels of consciousness upon admission to hospital, with clinical manifestations that develop over several hours, including symptoms of gradual headaches and neurological disorders such as aphasia and hemiparesis.

Table 5. Change in the average GCS score of aspirin and clopidogrel group patients in the Mataram city hospital inpatient period May 2023-May 2024

Treatment room	Antiplatelets	Initial GCS	GCS End	Δ GCS Score	P	P
VIP Class	Aspirin	12.33±0.54	14.67±0.57	2,34	0,457	1,000
	Clopidogrel	13±1.41	14.67±0.50	1,67	0,278	1,000
Class l	Aspirin	12.66±0.57	14.33±0.57	1,67	0,871	0,071
	Clopidogel	12.84±1.81	14.84±0.37	2	0,772	0,259
Class ll	Aspirin	11.83±1.16	14.67±0.51	2,84	0,436	0,362
	Clopidogrel	12.37±1.50	14.37±0.51	2	0,390	0,377
Class lll	Aspirin	12.50±1.29	14.75±0.50	2,25	0,754	0,870
	Clopidogrel	12.25±1.48	14.70±0.46	2,45	0,742	0,884

Table 5 of the Glasgow Coma Scale (GCS) score in ischemic stroke patients from two main perspectives. At hospital admission, there was no significant difference in the initial GCS score between the aspirin and clopidogrel groups ($p>0.05$), which could be due to variations in the patient's state of consciousness and severity. During treatment, all patients experienced an increase in GCS scores to reach 14-15 at the end of treatment. Measurements were taken over 4 days, with 4 daily measurements, referring to a study by Dyker & Lees (1998) that showed the possibility of an improvement in consciousness in the first 72 hours. Although there was variation in the increase in GCS scores in different treatment classes, the statistical test showed no significant difference between the two therapy groups ($p=0.359$). The highest increase in GCS score occurred in the aspirin group in treatment class II (2.84), while in the clopidogrel group the highest increase was in treatment class III (2.45), indicating the variability of therapy response in ischemic stroke patients.

Table 6. Average cost of VIP class direct medical

Direct medical expenses	Antiplatelets		
	Aspirin	Clopidogrel	P *value*
Emergency Room	IDR 221,722	IDR 352,199	0,909
Medical rehabilitation poly	IDR 506,917	IDR 471,667	

Clinical Pathology Laboratory	IDR 308,581	IDR 629,133	
Hospitalization/room fees	IDR 2,912,840	IDR 2,822,984	
radiology.	IDR 505,058	IDR 509,889	
Other drug costs	IDR 518,815	IDR 607,163	
Antiplatelets	IDR 8,437	IDR 6,980	
Average Total Per Patient (Rp)	IDR 4,982,370	IDR 5,400,015	

Table 7. Average cost of direct medical class 1

Direct medical expenses	**Antiplatelets**		
	Aspirin	**Clopidogrel**	**P *value***
Emergency Room	IDR 224,813	IDR 343,348	0,614
Medical rehabilitation poly	IDR 273,466	IDR 417,089	
Clinical Pathology Laboratory	IDR 461,121	IDR 460,757	
Hospitalization/room fees	IDR 1,127,384	IDR 1,032,410	
radiology.	IDR 540,333	IDR 654,849	
Other drug costs	IDR 350,632	IDR 722,782	
Antiplatelets	IDR 3,955	IDR 8,263	
Average Total Per Patient (Rp)	IDR 2,981,704	IDR 3,639,498	

Table 8. Average cost of direct medical class II

Direct medical expenses	**Antiplatelets**		
	Aspirin	**Clopidogrel**	**P *value***
Emergency Room	IDR 340,833	IDR 269,318	0,584
Medical rehabilitation poly	IDR 305,980	IDR 343,881	
Clinical Pathology Laboratory	IDR 608,574	IDR 489,179	
Hospitalization/room fees	IDR 2,168,015	IDR 1,094,202	
radiology.	IDR 733,341	IDR 598,109	
Other drug costs	IDR 665,110	IDR 851,019	
Antiplatelets	IDR 7,593	IDR 8,355	
Average Total Per Patient (Rp)	IDR 4,829,446	IDR 3,654,063	

Table 9. Average Cost of Direct Medical Class III

Direct medical expenses	**Antiplatelets**		
	Aspirin	**Clopidogrel**	**P *value***
Emergency Room	IDR 434,902	IDR 226,972	0,771
Medical rehabilitation poly	IDR 335,375	IDR 389,164	
Clinical Pathology Laboratory	IDR 419,704	IDR 575,443	
Hospitalization/room fees	IDR 715,351	IDR 943,785	
radiology.	IDR 737,000	IDR 697,618	
Other drug costs	IDR 457,829	IDR 577,194	
Antiplatelets	IDR 6,130	IDR 7,305	
Average Total Per Patient (Rp)	IDR 3,106,291	IDR 3,417,481	

Based on table 6 To determine the number of resources available, it is necessary to conduct an economic analysis related to health services. A comprehensive way to determine the economic impact of alternative drug therapy or other health interventions is by pharmacoeconomic analysis in the form of Cost Effectiveness Analysis (CEA) (Ref et al., 2018). Based on a comprehensive analysis of data on the comparison of the cost of using aspirin and clopidogrel antiplatelets in ischemic stroke patients in different classes of care (VIP, Class I, II, and III), it can be concluded that there is no significant difference in the average cost of direct care between the two types of therapy across all classes of care. This is indicated by a significance value greater than 0.05 in all groups (VIP: 0.909; Class I: 0.614; Class II: 0.584; Class III: 0.771). Although the cost of clopidogrel is nominally higher than aspirin in most treatment classes, the difference is not statistically significant. The variation in costs that occur is more influenced by individual patient factors such as disease severity, comorbidities, medical support needs, and necessary medical measures, rather than by the selection of antiplatelet type. These findings indicate that from an economic perspective, both antiplatelet options can be considered equally in terms of impact on the total cost of direct medical care, with therapy selection more focused on the patient's individual clinical factors.

Table 10. ACER calculation in VIP class

Antiplatelets	Average Direct medical cost (C) (Rp)	Average GCS (Effectiveness) score (E)(Mean) (%)	ACER (C/E) (Rp)
Aspirin	IDR 4,982,370	2,34 %	IDR 2,129,218
Clopidogrel	IDR 5,400,015	1,67 %	IDR 3,233,542

Table 11. ACER calculation in class l

Antiplatelets	Average Direct medical cost (C) (Rp)	Average GCS (Effectiveness) score (E)(Mean) (%)	ACER (C/E) (Rp)
Aspirin	IDR 2,981,704	1,67 %	IDR 1,785,451
Clopidogrel	IDR 3,639,498	2 %	IDR 1,819,749

Table 12. ICER calculation in class l

Antiplatelets	Average Direct medical cost (C) (Rp)	Average GCS (Effectiveness) score (E)(Mean) (%)	Δ C	ΔE	ICER (ΔC/ ΔE)
Aspirin	IDR 2,981,704	1,67 %	-657.794	0,33	-1.993.315
Clopidogrel	IDR 3,639,498	2 %			

Table 13. ACER calculation in class ll

Antiplatelets	Average Direct medical cost (C) (Rp)	Average GCS (Effectiveness) score (E)(Mean) (%)	ACER (C/E) (Rp)
Aspirin	IDR 4,829,446	2,84	IDR 1,700,509
Clopidogrel	IDR 3,654,063	2	IDR 1,827,031

Table 14. ACER calculation in class lll

Antiplatelets	Average Direct medical cost (C) (Rp)	Average GCS (Effectiveness) score (E)(Mean) (%)	ACER (C/E) (Rp)
Aspirin	IDR 3,106,291	2,25	IDR 1,380,574
Clopidogrel	IDR 3,417,481	2,45	IDR 1,394,890

Table 15. ICER calculation in class lll

Antiplatelets	Average Direct medical cost (C) (Rp)	Average GCS (Effectiveness) score (E)(Mean) (%)	Δ C	ΔE	ICER (ΔC/ ΔE)
Aspirin	IDR 3,106,291	2,25	-311.190	0,2	-1.555.950
Clopidogrel	IDR 3,417,481	2,45			

Based on the cost-effectiveness analysis of the use of aspirin and clopidogrel antiplatelets in various treatment classes (VIP, Class I, II, and III), it can be concluded that aspirin consistently shows lower ACER (Average Cost-Effectiveness Ratio) values than clopidogrel in all treatment classes. In VIP and class II rooms, aspirin is in a dominant position (column G) with higher effectiveness and lower cost, so it does not require ICER analysis. Meanwhile, in classes I and III, although aspirin has a lower cost but also a lower effectiveness (column A), ICER analysis showed negative results (Rp -1,993,315 for class I and

Rp -1,555,950 for class III), which indicates that clopidogrel is not cost-effective compared to aspirin. The relatively small increase in effectiveness in the use of clopidogrel (0.33 units in class I and 0.20 units in class III) was not worth the additional cost required (Rp 657,794 in class I and Rp 311,190 in class III). Thus, from a pharmacoeconomic perspective, aspirin may be recommended as a more cost-effective antiplatelet option for ischemic stroke therapy in all classes of care, given its comparable effectiveness to clopidogrel but at a more affordable cost.

Table 16. VIP grade aspirin sensitivity analysis

Name of the fee	Total fees	+25	-25	difference
Emergency Room	IDR 665,166	IDR 831,457	IDR 498,874	IDR 332,583
Medical rehabilitation poly	IDR 1,520,750	IDR 1,900,938	IDR 1,140,563	IDR 760,375
Clinical Pathology Laboratory	IDR 925,744	IDR 1,157,180	IDR 694,308	IDR 462,872
Inpatient/room fees	IDR 8,738,520	IDR 10,923,150	IDR 6,553,890	IDR 4,369,260
Radiology.	IDR 1,515,173	IDR 1,893,966	IDR 1,136,380	IDR 757,586
Other drug costs	IDR 1,556,446	IDR 1,945,558	IDR 1,167,335	IDR 778,223
Antiplatelets	IDR 25,312	IDR 31,640	IDR 18,984	IDR 12,656
Total	IDR 14,947,111	IDR 18,683,889	IDR 11,210,334	IDR 7,473,555

Table 17. Sensitivity analysis of VIP class clopidogrel

Name of the fee	Total fees	+25	-25	Difference
Emergency Room	IDR 3,169,794	IDR 3,962,242	IDR 2,377,345	IDR 1,584,897
Medical rehabilitation poly	IDR 4,245,000	IDR 5,306,250	IDR 3,183,750	IDR 2,122,500
Clinical Pathology Laboratory	IDR 5,662,199	IDR 7,077,749	IDR 4,246,649	IDR 2,831,100
Inpatient/room fees	IDR 25,406,854	IDR 31,758,567	IDR 19,055,140	IDR 12,703,426
Radiology.	IDR 4,589,000	IDR 5,736,250	IDR 3,441,750	IDR 2,294,500
Other drug costs	IDR 5,464,470	IDR 6,830,588	IDR 4,098,353	IDR 3,732,235
Antiplatelets	IDR 62,823	IDR 78,529	IDR 47,117	IDR 31,412
Total	IDR 48,600,140	IDR 60,750,175	IDR 36,450,104	IDR 25,300,070

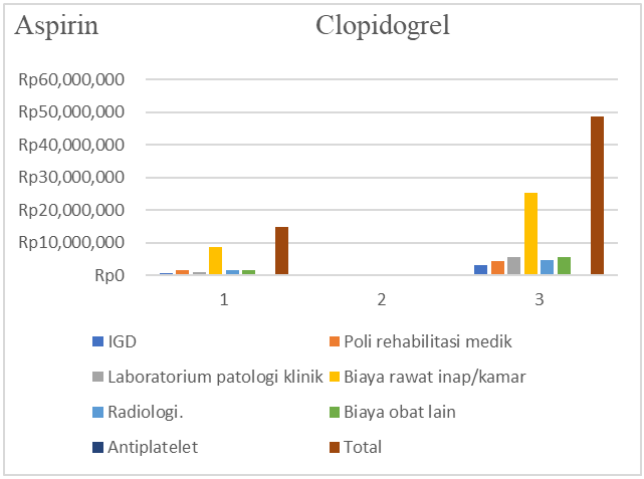


Table 18. Aspirin sensitivity analysis class l

Name of the fee	Total fees	+25	-25	Difference
Emergency Room	IDR 674,438	IDR 843,047	IDR 505,828	IDR 337,218
Medical rehabilitation poly	IDR 820,397	IDR 1,025,496	IDR 615,297	IDR 410,198
Clinical Pathology Laboratory	IDR 1,383,364	IDR 1,729,205	IDR 1,037,523	IDR 691,682
Inpatient/room fees	IDR 3,382,152	IDR 4,227,690	IDR 2,536,614	IDR 1,691,076
Radiology.	IDR 1,621,000	IDR 2,026,250	IDR 1,215,750	IDR 810,500
Other drug costs	IDR 1,051,896	IDR 1,314,870	IDR 788,922	IDR 525,948
Antiplatelets	IDR 11,865	IDR 14,831	IDR 8,899	IDR 5,933
Total	IDR 8,945,112	IDR 11,181,389	IDR 6,708,833	IDR 4,472,555

Table 19. Sensitivity analysis of class l clopidogrel

Name of the fee	Total fees	+25	-25	Difference
Emergency Room	IDR 4,463,519	IDR 5,579,399	IDR 3,347,639	IDR 2,231,760
Medical rehabilitation poly	IDR 5,422,155	IDR 6,777,694	IDR 4,066,616	IDR 2,711,078
Clinical Pathology Laboratory	IDR 5,989,836	IDR 7,487,295	IDR 4,492,377	IDR 2,994,918
Inpatient/room fees	IDR 18,621,330	IDR 23,276,662	IDR 13,965,998	IDR 9,310,665
Radiology.	IDR 8,513,034	IDR 10,641,293	IDR 6,384,776	IDR 4,256,517
Other drug costs	IDR 7,896,163	IDR 9,870,204	IDR 5,922,122	IDR 3,948,082
Antiplatelets	IDR 107,416	IDR 134,270	IDR 80,562	IDR 53,708
Total	IDR 51,013,453	IDR 63,766,817	IDR 38,260,090	IDR 25,506,728

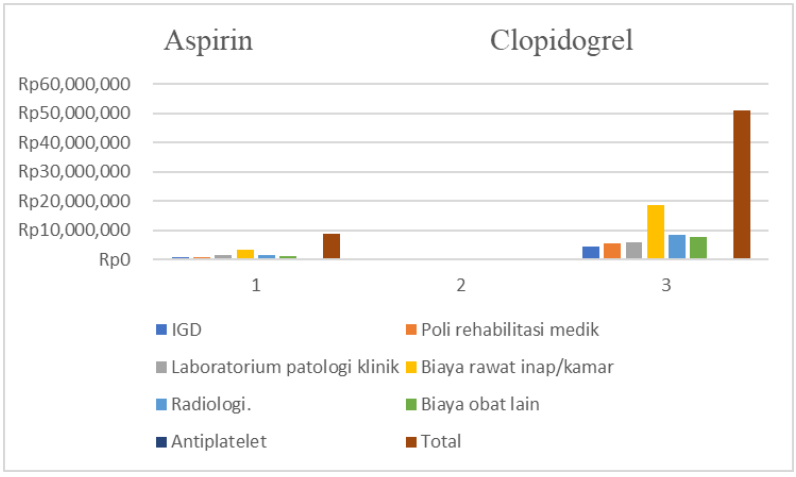


Table 20. Class ll aspirin sensitivity analysis

Name of the fee	Total fees	+25	-25	Difference
Emergency Room	IDR 2,044,999	IDR 2,556,249	IDR 1,533,749	IDR 1,022,500
Medical rehabilitation poly	IDR 1,835,879	IDR 2,294,849	IDR 1,376,909	IDR 917,940
Clinical Pathology Laboratory	IDR 3,651,446	IDR 4,564,308	IDR 2,738,585	IDR 1,825,723
Inpatient/room fees	IDR 13,008,088	IDR 16,260,110	IDR 9,756,066	IDR 6,504,044
Radiology.	IDR 4,400,045	IDR 5,500,056	IDR 3,300,034	IDR 2,200,023
Other drug costs	IDR 3,990,660	IDR 4,988,325	IDR 2,992,995	IDR 1,995,330
Antiplatelets	IDR 45,556	IDR 56,945	IDR 34,167	IDR 22,778
Total	IDR 28,976,673	IDR 36,220,841	IDR 21,732,505	IDR 14,488,337

Table 21. Clopidogrel class ll sensitivity analysis

Name of the fee	Total fees	+25	-25	Difference
Emergency Room	IDR 4,309,095	IDR 5,386,369	IDR 3,231,821	IDR 2,154,548
Medical rehabilitation poly	IDR 5,502,095	IDR 6,877,619	IDR 4,126,571	IDR 2,751,048
Clinical Pathology Laboratory	IDR 7,826,862	IDR 9,783,578	IDR 5,870,147	IDR 3,913,431
Inpatient/room fees	IDR 17,507,233	IDR 21,884,041	IDR 13,130,425	IDR 8,753,617
Radiology.	IDR 9,569,746	IDR 11,962,183	IDR 7,177,310	IDR 4,784,873
Other drug costs	IDR 13,616,299	IDR 17,020,374	IDR 10,212,224	IDR 6,808,150
Antiplatelets	IDR 133,678	IDR 167,098	IDR 100,259	IDR 66,839
Total	IDR 58,465,008	IDR 73,081,262	IDR 43,848,757	IDR 29,232,506

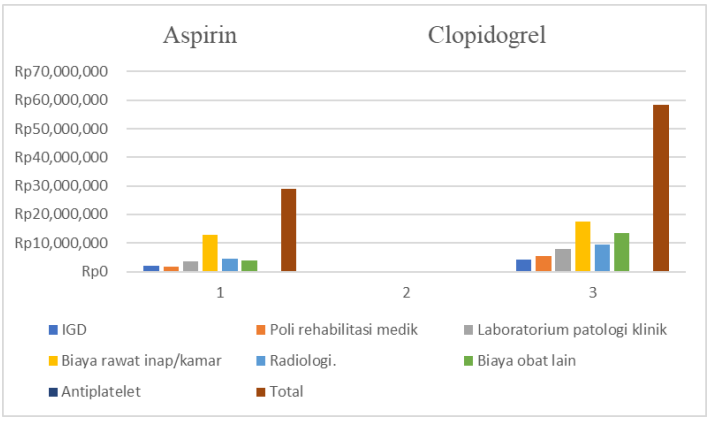
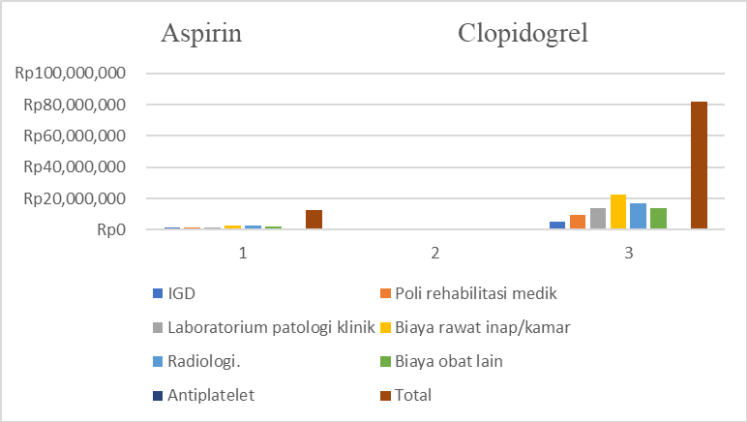


Table 22. Aspirin sensitivity analysis of class lll

Name of the fee	Total fees	+25	-25	Difference
Emergency Room	IDR 1,739,609	IDR 2,174,511	IDR 1,304,707	IDR 869,805
Medical rehabilitation poly	IDR 1,341,500	IDR 1,676,875	IDR 1,006,125	IDR 670,750
Clinical Pathology Laboratory	IDR 1,678,814	IDR 2,098,518	IDR 1,259,111	IDR 839,407
Inpatient/room fees	IDR 2,861,402	IDR 3,576,752	IDR 2,146,052	IDR 1,470,701
Radiology.	IDR 2,948,000	IDR 3,685,000	IDR 2,211,000	IDR 1,474,000
Other drug costs	IDR 1,831,315	IDR 2,289,144	IDR 1,373,486	IDR 915,658
Antiplatelets	IDR 24,521	IDR 30,651	IDR 18,391	IDR 12,261
Total	IDR 12,425,161	IDR 15,531,451	IDR 9,318,872	IDR 6,252,582

Table 23. Sensitivity analysis of clopidogrel class lll

	Total fees	+25	-25	Difference
Name of the fee	IDR 5,447,318	IDR 6,809,148	IDR 4,085,489	IDR 2,723,659
Medical rehabilitation poly	IDR 9,339,935	IDR 11,674,919	IDR 7,004,951	IDR 4,669,968
Clinical Pathology Laboratory	IDR 13,810,629	IDR 17,263,286	IDR 10,357,972	IDR 6,905,315
Inpatient/room fees	IDR 22,650,840	IDR 28,313,550	IDR 16,988,130	IDR 11,325,420
Radiology.	IDR 16,742,829	IDR 20,928,536	IDR 12,557,122	IDR 8,371,414
Other drug costs	IDR 13,852,658	IDR 17,315,823	IDR 10,389,494	IDR 6,926,329
Antiplatelets	IDR 175,322	IDR 219,153	IDR 131,492	IDR 87,661
Total	IDR 82,019,531	IDR 102,524,415	IDR 61,514,650	IDR 41,009,766



Based on table 16 Sensitivity analysis in pharmacoeconomics studies is an important method to evaluate data uncertainty by considering the variation in the value of cost parameters in the lower and upper value ranges of 25% % (Fatin et al., 2019). This method uses a threshold as a reference to determine whether a health technology can be categorized as cost-effective or not (Ulfah et al., 2022).

The visualization of the results of one-way sensitivity analysis is generally presented in the form of a tornado chart, where the position of the cost variable in the diagram reflects the degree of impact, with the variable having the greatest impact placed at the top of the chart and decreasing according to the magnitude of the impact. The sensitivity analysis was conducted by calculating a cost variation of ±25% for each category of cost details which included emergency room, medical rehabilitation poly, clinical pathology laboratory, inpatient/room, radiology, other drugs, and antiplatelets. The results of this analysis are visualized in the form of a tornado chart, where the length of the diagram is directly proportional to the magnitude of the expense or expense. Based on the analysis, hospitalization/room costs were identified as the most sensitive parameter to change, caused by variations in the duration of treatment between patients. In the context of ischemic stroke treatment, the aspirin group showed better outcomes by considering treatment effectiveness and cost factors as components that have a significant influence on disease management.

CONCLUSIONS AND RECOMMENDATIONS

Based on the results of the study, it can be concluded that aspirin shows better cost-effectiveness compared to clopidogrel in the therapy of ischemic stroke patients in all classes of care. This is evidenced by lower ACER aspirin values in all classes, starting from the VIP class (Rp 2,129,218), class I (Rp 1,785,451), class II (Rp 1,700,509), to class III (Rp 1,380,574). The increase in GCS scores in the aspirin group also showed quite good results, with the highest increase in class II of 2.84. In terms of treatment costs, aspirin consistently showed a lower total cost than clopidogrel in almost all classes of treatment. ICER analysis which showed negative values in class I (Rp -1,993,315) and class III (Rp -1,555,950) indicated that the use of aspirin was more profitable in terms of cost and effectiveness. These results were supported by sensitivity analysis and tornado diagrams that showed that clopidogrel had higher values, thus reinforcing the conclusion that aspirin is a more cost-effective option in antiplatelet therapy for ischemic stroke patients.

Recommendation:

1. For future research, further studies are recommended using other antiplatelet agents and therapeutic outcomes such as platelet aggregation. In addition, studies with longer durations are needed to obtain larger sample sizes.
2. For hospitals, this study is expected to serve as a source of scientific information regarding the cost profile and therapeutic outcomes of ischemic stroke treatment and to be used as a consideration in determining more effective treatment strategies.

FURTHER STUDY

Future studies should involve larger, multicenter populations to improve generalizability. Prospective designs with longer follow-up and the use of QALYs or DALYs are recommended to assess long-term cost-effectiveness. Inclusion of indirect costs, subgroup analyses, and evaluation of medication adherence and adverse events are also suggested to provide a more comprehensive economic evaluation of aspirin and clopidogrel therapy in ischemic stroke patients.

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