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Evaluating Economic Outcomes: Single-Use Aspirin vs. Aspirin-Clopidogrel in Ischemic Stroke Patients Based on Barthel Index Scores

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ABSTRACT: Ischemic stroke is a catastrophic disease that causes large costs in Indonesia. The high prevalence of stroke results in increased morbidity and mortality rates, which will impact the socioeconomic status of stroke patients. Cost Effectiveness Analysis (CEA) is a method in pharmaco-economics that aims to make decisions regarding the rational choice of therapy and evaluate the economic impact on ischemic stroke patients. This study aims to determine the Incremental Cost Effectiveness Ratio (ICER) value of antiplatelet therapy in the aspirin-clopidogrel combination group and the single aspirin group in ischemic stroke patients treated at the Regional General Hospital. Dr. M. Djamil Padang. The clinical parameter observed was the Barthel Index (BI) value. This research is a descriptive study with retrospective data collection using medical record data and the Hospital Management Information System (SIMRS) at RSUD Dr. M.Djamil Padang. The cost data shows the total direct medical costs incurred in treating ischemic stroke. Based on the results obtained, the Incremental Cost Effectiveness Ratio (ICER) value is IDR (-) 401,302. 71 per 1% increase. In this study it can be concluded that the aspirin-clopidogrel combination has better cost effectiveness than aspirin alone.

Keywords: **cost-effectiveness analysis; stroke ischemic; aspirin; clopidogrel; ICER .**

Introduction

Stroke is a nervous system disorder that occurs due to a blockage of blood vessels, which disrupts blood flow and causes blood vessels to rupture, causing bleeding [1]. Rupture of the arteries leading to the brain results in the sudden death of brain cells due to lack of oxygen [2]. According to the WHO (World Health Organization), stroke is characterized by acute clinical manifestations that occur due to neurological dysfunction in the brain, spinal cord, and retina, either partially or completely, that persist for ≥ 24 hours or cause death due to vascular disorders Currently, the prevalence of stroke continues to increase sharply. According to the WHO (World Health Organization), stroke is the second leading cause of death and the third highest cause of disability globally. If there is no good treatment, the number of stroke patients will continue to increase and even double. Indonesia is one of the countries with the most stroke sufferers in Asia and fourth in the world. In general, the highest death rate due to stroke, 70%, occurs in countries with low-income ranges due to stroke disability. Conversely, in countries with high income ranges, the death rate from stroke tends to decrease to 42% [3].

According to Riskesdas data (2018) the prevalence of stroke in Indonesia has increased to 10.9% from previously only 7% [4,5]. The Riskesdas report for West Sumatra Province (2018) states that West Sumatra is included in the 10 provinces with the most stroke sufferers with a distribution of the age group >75 years with a predominant male gender. Based on the doctor's diagnosis of the general population, stroke characteristics in West Sumatra reached 1.08% or around 2,553,200 patients [4,5].

Based on data released by the AHA (American Heart Association) 87% of all types of stroke are classified as ischemic strokes, while 13% are classified as Stroke hemorrhagic [6]. Ischemic stroke is a condition caused by a

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clot in the blood vessels in the brain, while hemorrhagic stroke is caused by bleeding in the brain [7,8]. One of the therapies for ischemic stroke is antiplatelet. Broadly speaking, this drug works as a platelet anti-aggregator. Antiplatelet aggregation plays an important role in the treatment of ischemic stroke, so therapy is needed to intervene in platelet function in treatment. such as aspirin, clopidogrel, ticipolin or dipyridamole [6,9]. Antiplatelet administration is proven to reduce at least 68% of recurrent strokes in the incidence of ischemic stroke to 24% [9].

Various clinical studies to compare the effectiveness of antiplatelet administration as a stroke prevention therapy have been carried out. Several studies have shown that single aspirin is more effective than clopidogrel [10,11]. Several trials have tested the efficacy and safety of clopidogrel and aspirin versus aspirin in preventing recurrent stroke in ischemic stroke [12–14]. A meta-analysis from 2018 found that an aspirin-clopidogrel combination given within 24 hours of an ischemic stroke also reduced the risk of recurrent stroke [15]. On the other hand, recent studies have looked at the potential for aspirin-clopidogrel combination therapy in ischemic stroke patients and from the results found there are still many insignificant data [16,17].

The high prevalence of stroke, length of stay and increased morbidity and mortality in stroke will have an impact on the socio-economic burden that must be borne by ischemic stroke patients [18]. According to the (BPJS) Health Social Security Administering Body (2020) the cost of Indonesian Health Insurance Services reached 4 trillion rupiah in 2016-2018 [19]. In fact, stroke is included in the 4 groups of catastrophic diseases that incur the highest costs in Indonesia. The costs incurred reached around 2.5 trillion [19].

The large number of BPJS participants who have suffered strokes has resulted in high JKN costs that must be incurred in treating strokes in Indonesia. The burden of JKN costs for stroke has continued to increase since 2014-2016. In 2014 for stroke, the JKN cost was IDR 813,392,575,975 then increased in 2015 to IDR 1,131,104,070,060 until in 2016 this increase in value reached IDR 1,171,127,754,410 [20,21].

Therefore, in order to obtain economical health services, an analysis related to the field of pharmaco-economics is needed [22,23]. The method used is Cost Effectiveness Analysis (AEB). In this Cost-Effectiveness Analysis, the total cost will be compared with the effects of two or more treatment options [24]. The aim is to assist in analyzing rational therapy selection decision-making and evaluating the economic impact of using combined and single antiplatelets in ischemic stroke patients [10]. So we get a therapy that has better cost effectiveness for ischemic stroke patients.

In Fitriani's research (2021) it was stated that based on the calculation of the Incremental Cost-Effectiveness Ratio value for single aspirin therapy and the aspirin-clopidogrel combination, the RIEB value was IDR (-).864,636 for the PT parameter and IDR (-).474,315 for the APTT parameter. So the results show that single aspirin therapy has better effectiveness and lower costs compared to the combination of aspirin-clopidogrel [10]. However, there are differences in several other previous studies, this is because the economy is always changing from time to time [25–27]. Meanwhile, there is still a Barthel index (BI) value, beside APTT that can be used as a reference unit for the effectiveness of antiplatelet therapy in cases of ischemic stroke. Barthel Index is an assessment tool that measure stroke patient's ability to complete daily living activity [28,29].

Based on the description of the problems that occur, it is necessary to consider additional research to prove that using the Cost Effectiveness Analysis (AEB) method in the use of single aspirin antiplatelet therapy or the combination of aspirin-clopidogrel in ischemic stroke patients has a better cost effectiveness in BI score.

Method

Research Design, Target Population

Research conducted at Dr. M Djamil Padang. The research was conducted in February 2023-April 2023. This observational research design used a study-based approach [22] using medical record data. The data collection technique was carried out retrospectively on the medical records of ischemic stroke inpatients. Sampling was carried out by purposive sampling, where 97 patient data were obtained for further analysis. This study compared aspirin alone with the aspirin-clopidogrel combination

Inclusion and Exclusion Criteria

The inclusion criteria for this study were BPJS participants with a diagnosis of inpatient ischemic stroke, both men and women aged >18 years, patients who received aspirin-clopidogrel combination antiplatelet therapy or aspirin alone, who had Barthel Index (BI) data and medical cost data. long. Meanwhile, the exclusion criteria for inpatient ischemic stroke patients with incomplete and unclear medical record data, patients who died while being treated were excluded from this study.

Table 1. Characteristic sosiodemographic of stroke ischemic patients

Characteristics Sociodemography	Aspirin (n=48)		Aspirin-Clopidogrel Combination (n=49)		Number of Patient		*p value*
	n	%	n	%	n	%	
Age Group							
15-24 years	0	0	0	0	0	0	
25-34 years	0	0	3	6.1	3	3.1	
35-44 years	2	4.2	4	8.2	6	6.2	
45-54 years	12	25.0	8	16.3	20	20.6	0.320[a]
55-64 years	22	45.8	23	46.9	45	46.4	
65-75 years	9	18.8	9	18.4	18	18.6	
>75 years	3	6.3	2	4.1	5	5.2	
Gender							
Male	23	47.9	28	57.1	51	52.6	0.480[a]
Female	25	52.1	21	42.9	46	47.4	
Last Education							
Low	7	14.6	6	12	13	13.4	
Medium	31	64.6	26	53.1	57	58.8	0.313[a]
High	10	20.8	17	34.7	27	27.8	
Work							
Not Working	20	41.7	17	34.7	37	38.1	0.619[a]
Working	28	58.3	32	65.3	60	61.9	

[a] Chi-square

Perspective, Time Horizon, and Index Year

The cost perspective in this research was the hospital perspective (health care perspective) where the costs used are medical costs paid to the hospital. The sample for this study was a population of patients registered with BPJS who were diagnosed with ischemic stroke in January-December 2021 who met the inclusion and exclusion criteria. The time horizon is set at one year with the index year 2021.

Currency and Discount Rate

The currency used is Rupiah (IDR). Because it is in the same fiscal year, no discount cost and effect was applied in this study [30].

Cost-Effect Variables

The variable costs used here are direct medical costs such as administration costs, inpatient costs, supporting costs, and drug costs obtained from Hospital Information and Management System (SIMRS). Meanwhile, the influencing variable is the Barthel Index (BI) score [15,28].

Data Analysis

Data were analyzed by calculating effectiveness based on therapy results, initial values before treatment and after treatment on the Barthel Index (BI) score. For each dependent variable, a normality test was carried out first. Parametric data with two dependent variables were tested

Table 2. Effectiveness of aspirin single therapy and aspirin-clopidogrel combination in ischemic stroke patients

Effect Parameters	Aspirin			Aspirin-Clopidogrel			*p value*
	Mean	95% CI		Mean	95% CI		
		Lower	*Upper*		*Lower*	*Upper*	
BI difference	10.0 ± 11.43	6.67	13.32	11.22 ± 11.43	7.93	14.50	0.691 [b]

[b] Mann-Whitney

Table 3. Analysis of direct medical costs using the combination of aspirin-clopidogrel and aspirin in inpatient type ischemic stroke patients at RSUP Dr. M Djamil Padang Year 2021

Antiplatelet type	Total	Average direct medical costs (IDR)	*p value*
Aspirin	48	11,109,062	0.109
Aspirin-Clopidogrel	49	10,617,671	

using T test [31]. For non-parametric data that has two variables was tested using Mann-Whitney, while more than two variables was tested using Kruskal-Wallis, while categorical variables was tested with Chi-square [31]. The result of a p-value < 0.05 is declared to have a significant effect. Next, a cost-effectiveness analysis was carried out by calculating the ICER value with the total direct cost as cost parameter and Barthel index as effect parameter.

Results and Discussion

Sosiodemographic Characteristic

The sociodemographic data of ischemic stroke patients is presented in Table 1. The educational level of ischemic stroke sufferers is divided into three categories, namely low (no school, elementary school), medium (middle school, high school), high (academy and college). The largest number of hospitalized ischemic stroke sufferers in this study were patients with a high school education level of 58.8%. Meanwhile, the level of higher education was 27.8%. And the percentage of patients with a low school education level was less (13.4%), this is in line with research conducted by Patricia *et al.* where 58% of 75 ischemic stroke patients had a high school education. In sociodemographic features, it was found that there were no significant differences between recipients of aspirin alone and the aspirin-clopidogrel combination [32]. It can be assumed that there is no relationship between sociodemographic characteristics and the type of antiplatelet received. Education level considers the incidence of ischemic stroke. A person's level of education can determine a person's attitude towards healthy behavior. Higher education is associated with extensive knowledge, so that someone with a high level of education is believed to be able to prevent and control the symptoms that appear with appropriate treatment [33].

Effect Parameter

The effectiveness of antiplatelet therapy observed in this study was the result of therapy in the form of the Barthel Index (BI) score for ischemic stroke patients before and after receiving treatment [29,34].

Table 2 shows the effectiveness of aspirin therapy and the aspirin-clopidogrel combination on the Barthel index value in ischemic stroke patients. From the results obtained, the therapeutic effectiveness of patients who received the aspirin-clopidogrel combination was not much different from patients who received aspirin alone. In the analysis of differences in mean parameters of the Battle Index (BI) effect parameters, a p value of 0.691 (>0.05) was obtained. This value does not indicate a significant difference in the results of the two aspirin-clopidogrel combination therapies received by the patient.

Cost Analysis

In cost analysis, cost parameters and effect parameters will be calculated to obtain the ICER value. The average cost provided in Table 3.

In this study, medical cost analysis was conducted from a healthcare perspective. The calculated costs are the direct medical costs of patients who received aspirin alone and aspirin-clopidogrel combination therapy. Based on research results, the average direct medical cost of single aspirin therapy is IDR 11,109,062. For aspirin-clopidogrel combination therapy IDR 10,617,671. In this study, the sample used was a combination of aspirin-clopidogrel with various brands, causing the total direct treatment costs in the aspirin and combination groups to be very different. Statistically, there is no significant difference between these two costs (p>0.05) (Table 3).

Table 4. ICER values for effect parameters

Antiplatelet	Number of Patients	Cost (IDR)	Effect (%)	*ICER*
Aspirin	48	11,109,062	10.00	IDR (-) 401,302.71 / %
Aspirin-Clopidogrel	49	10,617,671	11.22	

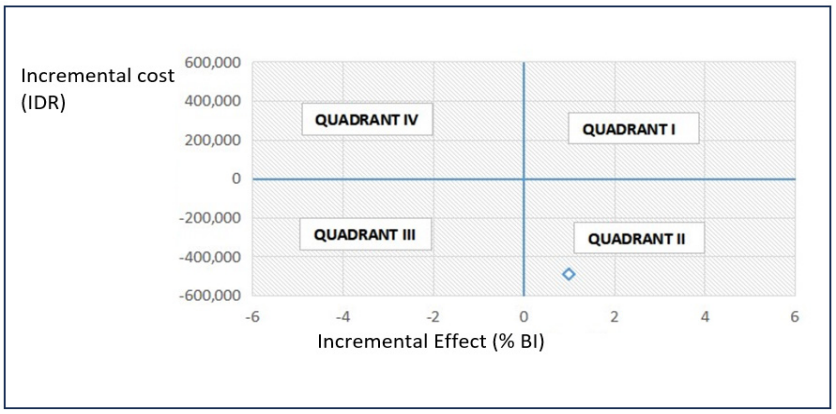

Figure 1. Cost-effectiveness diagram of Incremental cost effectiveness ratio of using aspirin-clopidogrel combination compare to single-used aspirin

Incremental Cost-Effect Ratio (ICER)

Antiplatelet cost effectiveness analysis in this study was calculated using the Incremental Cost-Effectiveness Ratio (ICER) value that provided in Table 4. The average effectiveness and direct costs of treatment are included in the ICER formula. The incremental cost value in the form of direct medical costs is compared with the effect score value (Barthel Index).

The effectiveness of using aspirin alone and the aspirin-clopidogrel combination assessed in this study was seen from the Barthel Index (BI) score effect parameter. Based on research, it was found that the average direct medical costs for each therapy group were IDR 11,109,062 and the aspirin-clopidogrel combination IDR 10,617,671. The ICER value is obtained using the formula. It was found that the ICER value in ischemic stroke patients was IDR (-) 43,257.46 for every 1% increase in BI value. This figure means that each cost is IDR (-). 401,302,71 use of the aspirin-clopidogrel combination will increase the Barthel Index score by 1%.

The cost-effectiveness diagram for the parameter effect of Barthel Index (BI) is as shown in Figure 1.

The value-added effect will be included as the x-axis. Meanwhile, the difference in average direct medical costs between the aspirin-clopidogrel groups remained the same, namely IDR (-) 491,391 and entered as the y-axis. This value means that the costs in the aspirin-clopidogrel combination antiplatelet therapy group were smaller than those in the single aspirin therapy group. The effectiveness resulting from the use of the aspirin-clopidogrel combination group was greater than the effectiveness of the aspirin alone group. Based on the ICER value obtained, the ICER value is in the quadrant (quadrant 2), this can be interpreted as aspirin-clopidogrel combination antiplatelet therapy having (high effectiveness at low cost) [10].

In the context of ischemic stroke, which occurs when blood flow to a part of the brain is blocked, the Barthel Index is important for several reasons. The first is functional assessment. The Barthel Index provides a quantitative measure of a person's functional status. After an ischemic stroke, patients often experience varying degrees of impairment in motor skills and activities of daily living [28,29]. The Barthel Index helps healthcare professionals gauge the level of assistance a person requires to carry out essential tasks. Second, by tracking changes in Barthel Index scores over time allows healthcare providers to assess the effectiveness of interventions and monitor the progress of stroke survivors. Improved Barthel Index scores typically indicate enhanced functional independence and recovery [29].

Next, the Barthel Index provides a standardized and objective means of communication among healthcare professionals. It helps in documenting a patient's baseline functional status, setting realistic goals for rehabilitation, and communicating progress to the patient, their family, and other members of the healthcare team [34,35].

Strength and limitation

This research has the advantage of taking into account direct medical costs both based on packages and based on claim costs. Meanwhile, this study also has limitations, including confounding factors that can influence the evaluation of the effectiveness of therapy, such as the patient's clinical condition, comorbidities, patient compliance with treatment, and the patient's lifestyle, which are not all recorded in the patient's medical record. Apart from that, the results of this study also do not represent other health service providers because the

research subjects were only limited to ischemic stroke patients at RSUD Dr. M Djamil Padang. It is hoped that further research can be carried out using a prospective cohort design by controlling other confounding variables and conducted at several different health service providers.

Conclusion

The Incremental Cost-Effective Ratio (ICER) of Barthel Index (BI) in this study is IDR 401,302.71 for every 1% increase in the BI score. The three RIEB values are in the second quadrant, where the aspirin-clopidogrel combination group has better effectiveness than the aspirin alone group.

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