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FACTORS ASSOCIATED WITH ADMINISTRATION OF ANTIPLATELET THERAPY ON NEUROLOGICAL DEFICITS NIHSS SCORE IN ACUTE ISCHEMIC STROKE

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Abstract

Stroke is the highest cause of death in the world. Antiplatelet therapy is one of the important therapies in acute ischemic stroke patients. Antiplatelet works by inhibiting platelet aggregation. In the implementation of antiplatelet therapy administration, it was found that (26.9%) administration was done more than 6 hours since the doctor's program. To find out quantitative outcomes in stroke patients, the NIHSS examination was carried out. To determine the factors related to antiplatelet administration to the NIHSS score in acute ischemic stroke patients at "X" Hospital Yogyakarta. This study uses the correlation method with a retrospective approach. Documentation studies (secondary data) were used in collecting data. The number of samples was 64 respondents from a total population of 465 patients with an ischemic stroke diagnosis. The probability sampling technique was used with a simple random sampling technique in taking the sample. Of the total sample of 82 respondents, 64 samples passed for analysis. Non-parametric Spearman test was used for analysis. These results suggest that within the scope of this study, the timing, type, and dosage of antiplatelet therapy did not show a significant impact on the severity of stroke symptoms as measured by NIHSS scores among the patients studied at "X" Hospital in Yogyakarta.

Keywords: acute ischemic stroke; antiplatelet therapy; NIHSS

1. Introduction

An ischemic stroke interrupts the blood supply to the brain, resulting in a sudden loss of brain function (Brunner & Suddath, 2013). Ischemic stroke is also defined as a stroke caused by an infarction (clarified by radiological investigations, pathology, or other evidence indicating ischemia of the brain, spinal cord, or retina) (Keputusan Menteri Kesehatan Republik Indonesia, 2019).

WHO (World Health Organization) stated that in 2012, the country's risk profile was 21%. This figure indicates that stroke is the highest cause of death, and this rate has not changed significantly since 2000, so it can be concluded that stroke management is not optimal and requires special attention (Keputusan Menteri Kesehatan Republik Indonesia, 2019). The Ministry of Health noted that around 63.7% of post-stroke patients, in the long term, could not live independently. In Indonesia, it is estimated that in one year, 500,000 people will have a stroke, and around 25% of it, or 125,000 people, will die due to strokes, and the rest, about 375,000, will have mild or severe disabilities. The stroke events are 200 per 100,000 of the population. The ischemic stroke events are higher than hemorrhagic stroke, which is two-thirds of the total stroke events (Nurul, 2019). According to Basic Health Research data (2019), the prevalence of stroke in Indonesia reaches 10.9 out of 1000 population, while 200 are recurrent strokes.

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According to the national data, the majority of strokes in Indonesia in 2018 among residents aged ≥15 years was around 10.9% or about 2,120,362 people, based on a doctor's diagnosis. The province with the highest prevalence of stroke in Indonesia is East Kalimantan (14.7%) followed by the Special Region of Yogyakarta (14.6%), while Papua (4.1%) and North Maluku (4.6%) are provinces with the lowest prevalence. (Kemenkes RI, 2018). At "X" Hospital in 2021 cases of patients with a Stroke Infarction diagnosis are in second place after Corona Virus Infection with a total of 295 people out of a total of 545 patients with a Stroke diagnosis.

Emergency management of patients with acute ischemic stroke can be carried out in several ways: intravenous thrombolysis (rTPA), intra-arterial thrombolysis, and mechanical thrombectomy (Keputusan Menteri Kesehatan Republik Indonesia, 2019). For intravenous thrombolysis, intra-arterial thrombolysis and mechanical thrombectomy, there are several criteria that must be met by the patient. The hospital must also have supporting equipment and a Stroke Unit room for monitoring post-operative patients. For patients who cannot perform Thrombolysis and Mechanical Thrombectomy, the patient will receive Antiplatelet therapy if there are no contraindications. Antiplatelet therapy is often used in ischemic stroke patients to prevent recurrent attacks. AHA/ASA guidelines recommend antiplatelet therapy as the cornerstone of anti thrombolytic therapy to prevent secondary ischemic stroke and should be used in non cardioembolic stroke patients. Aspirin antiplatelet therapy at a dose of 50 to 325 mg/day initiated between 24 and 48 hours after completion of alteplase has also been shown to reduce death and long-term disability. (Dedi et al., 2023) At "X" Hospital in 2021 only 3 patients can undergo intravenous thrombolysis (rTPA) out of 295 patients with a diagnosis of infarction or ischemic stroke. From a preliminary study in the Stroke Unit Room of "X" Hospital in April 2022, data was obtained that out of 26 infarction or ischemic stroke patients receiving antiplatelet therapy, 7 patients (26.9%) received antiplatelet therapy more than 6 hours since the neurologist program. And of the 26 ischemic stroke patients, 15 patients (57.7%) received antiplatelet therapy in the transit room and inpatient room since the neurologist program in the emergency room.

Antiplatelet is a drug to inhibit thrombus formation in the arterial system by inhibiting platelet aggregation (Aenulyaqin et al., 2022). Antiplatelet therapy in patients with acute ischemic stroke can reduce brain lesions, the risk of re- stroke will decrease thereby reducing the risk of death and increasing long-term stroke outcomes (Sandercock, et al., 2014 dalam Gofir, 2020). Antiplatelet therapy is expected to reduce mortality and long-term disability.

The golden period recommended on ischemic stroke patients according to Fassbender is 3 to 4.5 hours (Arif et al., 2019).

According to Widi (2013), providing appropriate and fast therapy is an important key in reducing deaths and neurological deficits caused by stroke patients. So providing therapy past the Golden Period can result in permanent neurological damage (Arif et al., 2019)). According to the Minister of Health (2019) in the PNPK Stroke Management, patients with acute ischemic stroke are given aspirin at a dose of 160-325 mg within 24 to 48 hours after the attack. (Arif et al., 2019), while according to AHA (2018), recommends administering antiplatelet aspirin in acute ischemic stroke within 24 hours after stroke onset. Thus, it is very important to pay attention to the time, dose and type of antiplatelet therapy given to ischemic stroke patients. In providing antiplatelet therapy to acute ischemic stroke patients, doctors can vary, both in dose and type, this is due to several considerations. Several factors that influence a doctor's decision to provide antiplatelet therapy are guidelines, age, and systolic blood pressure level at the time of infection and hypertension. (Liu et al., 2022)

One of the tests to determine disability or neurological deficits in stroke patients is the NIHSS (National Institute of Health Stroke Scale) examination. NIHSS is one of the measurement tools to determine the outcome of a stroke quantitatively. Apart from being used to assess the degree of neurological deficits, the NIHSS is also used to facilitate communication between subjects and medical personnel, evaluate, determine treatment, predict stroke subject outcomes, determine initial prognosis and complications as well as necessary intervention (Maharani et al., 2021). In addition to being used by modern neurologists, the NIHSS is also used by more than 500,000 certified health care professionals using a web-based platform. The NIHSS is also the gold standard for assessing the severity of stroke (Lyden, 2017).

2. Method

This study correlation study with a retrospective approach. The population in this

study were all patients with a medical diagnosis of ischemic stroke at Yogyakarta "X" Hospital during the treatment period from January 2021 to May 2022 a total of 465 patients. In this study, from a population of 465 patients, the researchers took samples using the probability sampling technique with the simple random sampling technique and by calculating the number of samples using the Slovin formula, namely 82 respondents. After collecting data from 82 respondents, there were 64 that could be used as samples, the rest was unusable due to incomplete data, the patient deceased, the patient was bleeding so he did not get antiplatelet therapy, and the patient received thrombolysis therapy.

The univariate analysis performed includes the characteristics of the respondents' age and sex, as well as all the variables assessed, namely time of antiplatelet therapy administration, type of antiplatelet therapy administration, dose of antiplatelet administration and NIHSS score in patients with acute ischemic stroke. Meanwhile, bivariate analysis was performed on the independent variables of each of the factors related to the administration of antiplatelet therapy (time, type and dose) with the dependent variable, namely the NIHSS score. Bivariate analysis was performed using the non-Parametric Spearman test.

3. Result and Discussion

Characteristics of respondents based on age and gender of antiplatelet therapy.

Tabel 1. Characteristics of respondents based on age and gender of antiplatelet therapy
January 1, 2021 – May 31, 2022 (n=64)

Characteristics	n	Percentage (%)
Age (years old)		
Early adulthood (26-35)	0	0
Late adulthood (36-45)	6	9,4
Early elderly (46-55)	10	15,6
Late elderly (56-65)	18	28,1
Seniors (>65)	30	46,9
Gender		
Female	24	37,5
Male	40	62,5

Source : (primary data, 2022)

The results of the study from 64 respondents showed almost half results in the elderly age group (46.9%) while none of the early adult age group (0%). This study shows that the increasing age, the higher the stroke event is. This result is in accordance with the theory of Hutagalung S.M, (2019) which says that increasing age will increase the risk of stroke, due to the increasing accumulation of plaque accumulation in blood vessels (Hutagaluh, 2019). The results of this study are in accordance with the results of the prevalence of stroke patients in the 2018 Basic Health Research, namely almost half (45.3%) in the age range 65 to 74 years and half (50%) aged over 75 years, while in the age range 35-44 years, 45 -54 years, 25-34 years and 15-24 years there is a small portion. Meanwhile, research conducted by (Apriani Novi, Sinurat Puji Pinta O., 2020). found that the majority (55.3%) of patients had strokes at the age of 55-64 years.

The results of the study based on gender showed that the majority of respondents were male (62.5%). Men are more at risk of stroke because many men have smoking habits, where the nicotine and carbon monoxide contained in cigarettes can lower oxygen levels in the blood, damage blood vessel walls and trigger blood clots. (Hutagaluh, 2019). The results of research conducted by Novi Apriani, et al, (2020) showed that the research respondents were mostly women (52.6%) (Apriani Novi, Sinurat Puji Pinta O., 2020). However, it is different from the research conducted at RSUD Dr. Chasan Boesoirie, Ternate, ischemic stroke affects many male patients, namely 62% (Syahti, 2020).

Characteristics of respondents based on the timing, type, and the dose of antiplatelet therapy

Tabel 2. Characteristics of respondents based on timing, type, and the dose of antiplatelet therapy
January 1, 2021 – May 31, 2022 (n = 64)

Characteristics	n	Percentage (%)
Timing of antiplatelet administration	34	53,1
≤ 24 hours	16	25
>24 hours to ≤ 48 hours	14	21,9
>48 hours		
Type of antiplatelet administration		
Clopidogrel	3	4,7
Aspirin	56	87,5
Clopidogrel dan aspirin	5	7,8
Dosage of antiplatelet administration		
≤ 100mg/day	**25**	**39,1**
>100mg/day to ≤ 200mg/day	**37**	**57,8**
>200mg/day	**2**	**3,1**

Source : primary data, 2022)

The results showed that the majority (53.1%) of antiplatelet therapy given to acute ischemic stroke patients at "X" Hospital Yogyakarta (53.1%) was ≤ 24 hours after onset, while a small proportion were given >24 hours to ≤ 48 hours from onset (25 %) and administration > 48 hours

from onset (21.9%). This shows that most of the acute ischemic stroke patients at Yogyakarta "X" Hospital have received immediate therapy (≤ 24 hours). Antiplatelet therapy can reduce the risk of death and improve the outcome of stroke patients, namely by reducing the area of brain damage caused by ischemic and also reducing the occurrence of re-ischemic stroke by 25% by administering antiplatelet less than 48 from stroke attacks (Mutiarasari, 2019).

The results showed that almost all of the antiplatelet administration in patients with acute ischemic stroke at Yogyakarta "X" Hospital (87.5%) was of the aspirin type, and a small proportion were given the type of clopidogrel (4.7%) while the combination of clopidogrel and aspirin was 7.8 %. These results are the same as a study conducted by Hasanah Isra (2020), the most antiplatelet therapy given to ischemic stroke patients at the Bukit tinggi National Stroke Hospital in 2019 was the use of single aspirin (90%), single clopidogrel 4.4% and a combination of aspirin and clopidogrel 5 .5% (Isra, 2020). Aspirin is a prodrug with a fast onset of action compared to clopidogrel (Kurniasari, 2017). The Minister of Health (2019) in the National Guidelines for Medical Services (NGMS) for Stroke Management states that patients with acute ischemic stroke are given aspirin at a dose of 160-325 mg within 24 to 48 hours after the attack (Keputusan Menteri Kesehatan Republik Indonesia, 2019).

The results showed that most of the doses (57.8%) of antiplatelet therapy in patients with acute ischemic stroke at "X" Yogyakarta Hospital were >100 mg/day to ≤ 200 mg/day, and a small proportion (3.1%) with doses >200 mg /day.

Most of the administration of antiplatelet therapy to acute ischemic stroke patients at Yogyakarta "X" Hospital with doses > 100 mg/day to ≤ 200 mg/day is in accordance with the recommendations of the Minister of Health (2019) which states in the PNPK Stroke Management, that patients with ischemic stroke acutely given aspirin at a dose of 160-325mg within 24 to 48 hours after the attack (Keputusan Menteri Kesehatan Republik Indonesia, 2019).

Characteristics of respondents based on the initial NIHSS score.

Tabel 3. Characteristics of respondents based on the initial NIHSS score(n=64)

NIHSS Score	n	Percentage (%)
Mild	32	50
Moderate	25	39,1
Moderate to	5	7,8
heavy	2	3,1
Total	64	100

Source : (primary data, 2022)

The results showed that half of the acute ischemic stroke patients at Yogyakarta "X" Hospital initially had a mild NIHSS score of 50%, almost half had a moderate NIHSS score of 39.1%, and a small proportion had a moderate NIHSS score of 7.8. % and with a heavy NIHSS score of 3.10%.

This study is not the same as the results of a study conducted by Wulan, D.R & Erlida, B.A., (2020) at the Ulin Hospital in Banjarmasin that the severity of mild stroke was 5.8%, moderate severity was 38.5%, severe severity was 23.1% and a very severe severity rate of 32.7% (Wulan & Erlida, 2020). According to the results of the NIHSS examination study at Yogyakarta "X" Hospital, half (50%) were carried out > 12 hours (carried out in an inpatient room) by a neurologist. This is possibly due to the lack of knowledge from the officers when the NIHSS examination was carried out.

Correlation between time, type and dose of antiplatelet therapy with the NIHSS score.
The results showed that there was no significant relationship between the time, type and dose of antiplatelet therapy with the NIHSS score, namely:

1. There was no significant relationship (p value > 0.05) between the time of antiplatelet administration and the NIHSS score in acute ischemic stroke patients.
2. There was no significant relationship (p value > 0.05) between the type of antiplatelet therapy and the NIHSS score in patients with acute ischemic stroke.
3. There was no significant relationship (p value > 0.05) between the dose of antiplatelet administration and the NIHSS score in acute ischemic stroke patients.

The results of the study showed that there was no significant relationship between the time of administration of antiplatelet therapy and the NIHSS score in acute ischemic stroke patients due to the administration of antiplatelet therapy which was not given immediately. The results of the study showed that 79.7% of the data obtained for antiplatelet therapy was given > 1 hour from the neurologist program, so there is a possibility that the expected dose target was not achieved. This will hinder efforts to reperfusion cerebral

tissue in the acute stroke phase which is an attempt to reduce disability/neurological deficits in acute stroke patients. In the AHA/ASA (2013) management of ischemic stroke is said to be done immediately, namely 3 hours from the onset of the stroke.

In administering drugs there are 7 principles that must be considered by nurses, namely the right patient, the right drug, the right dose, the right time, the right route/method of administration, the right documentation and the right health education regarding medication (Lestari Siti, 2016). The right time in the principle of drug administration is one of the things that is important for nurses to pay attention to, where nurses must be on time or according to the doctor's program because it is related to the action of drugs that can cause therapeutic effects of these drugs.

According to Widi (2013) prompt and appropriate treatment can reduce death and minimize brain damage caused by ischemic stroke (golden period) (Arif et al., 2019). In this study, it was also found that 35.9% of patients came to the hospital > 24 hours from the onset of symptoms so that efforts to reperfuse cerebral tissue were getting smaller.

There is no significant relationship between the type and dose of antiplatelet therapy administration and the NIHSS score in acute ischemic stroke patients because the initial NIHSS examination was carried out > 12 hours from the time of arrival at the hospital, so there is a possibility that the initial NIHSS results did not match the conditions when the patient arrived. This is inconsistent with the AHA Journals (2017) that an NIHSS score check is required within 12 hours of the patient coming to the hospital (Lyden, 2017). The NIHSS assessment is important from the beginning to the end of the patient while in the hospital, because the results of the NIHSS assessment can be seen how severe or neurological deficits occur in stroke patients (Ambresh & Sanjeeth, 2021). In addition, the NIHSS assessment can also facilitate communication with health workers, determine possible prognoses from the start and complications as well as necessary actions, evaluate, determine treatment, predict the results of examining stroke patients (Maharani et al., 2021).

The American Heart Association (AHA) 2018 recommends that patients who met the criteria for giving rtPA should receive intravenous rtPA, whereas patients who do not meet the criteria for giving rtPA are given antiplatelet therapy for minor strokes (NIHSS < 3 or high risk of TIA) by giving double antiplatelets (aspirin and clopidogrel) started within 24 hours for 21 days with the aim of preventing recurrent stroke within 90 days of the onset of stroke symptoms. Recommendations for the treatment of acute ischemic stroke are given aspirin within 24 hours of stroke onset. Patients with stenosis/severe occlusions in the large intracranial arteries require 75 mg clopidogrel therapy in addition to aspirin for 90 days (Ghofir, 2021).

The second possible cause of the results of the study which showed no significant relationship between the time, type, and dose of antiplatelet therapy with the NIHSS score in acute ischemic stroke patients was due to the type of stroke experienced by the patient whose NIHSS score increased was progressive stroke or in evolution where the patient was still neurological symptoms occur which are increasingly severe (Hutagaluh, 2019).

Other possible causes, according to researchers, are risk factors for blood sugar levels, blood pressure and the size of the lesion that affect the severity of stroke. In stroke patients with Diabetes Mellitus, the area near hypoxia will process glucose, namely anaerobic metabolism to form lactic acid and cause intravascular and extravascular acidosis, which can trigger damage to neurons and vascular tissue (Hermawan, 2022). In patients with hypertension or high blood pressure, there will be autoregulation disorders of changes in systemic blood pressure, namely difficulties in contraction and dilation (Razdiq & Imran, 2020) . The location and area of the brain that is disturbed will affect the severity and severity of the neurological deficit. If blood circulation is disrupted in vital and extensive areas of the brain, it will result in severe neurological deficits and even deat (Santoso et al., 2017). In this study the researchers did not collect data related to blood pressure, blood sugar levels and the size of the lesion so there was no supporting data.

It is hoped that this research will provide an overview of the relationship between antiplatelet therapy and neurological deficits that occur in acute stroke patients. Doctors can consider the time, type and dose in providing antiplatelet therapy to acute stroke patients. Meanwhile, nurses can pay more attention to the timing of administering medication to patients so that patients get optimal results.

In conducting research, researchers have several limitations, those are,

1. The limited number of respondents, this is because the hospital where the research was conducted used neurological deficit assessment by the NIHSS only at the beginning of November 2020.
2. Due to limited research time, researchers did not use cross-sectional research methods.

4. Conclusion and Suggestion

In the study at "X" Hospital Yogyakarta, no significant connections were found between the timing, type, or dosage of antiplatelet therapy and the NIHSS scores in ischemic stroke patients.

Healthcare professionals, especially nurses, are advised to prioritize the timely administration of antiplatelet therapy adhering to the established principles of drug administration. Alongside this, conducting NIHSS examinations immediately upon patient arrival and discharge is recommended, emphasizing the critical role of these assessments in stroke care. Additionally, nurses are encouraged to educate the public about the concept of the "Golden Time" in acute stroke treatment, underscoring the urgency of timely intervention for better outcomes.

For future research endeavors, it's suggested to expand sample sizes to ensure a more comprehensive representation of each variable under assessment. Employing the cross-sectional research method is proposed to align the gathered data more effectively with researchers' expectations. Furthermore, there's a call for investigating the relationship between lesion size, blood pressure, blood sugar levels, and NIHSS scores in stroke patients in future studies, recognizing these factors' potential association with stroke severity.

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