



CORRELATION BETWEEN FLUCTUATION OF BODY TEMPERATURE AND OUTCOME IN ACUTE ISCHEMIC STROKE PATIENTS

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DOI: 10.5281/zenodo.3612057

Abstract

Background: Stroke is one of the leading causes of death and long term disability in the world. Increased body temperature is one of the factors that affects the outcome of stroke.

Objective: To determine the correlation between fluctuation of body temperature and outcome in acute ischemic stroke patients admitted to H. Adam Malik General Hospital, Medan.

Methods: This study used cross sectional design on acute ischemic stroke patients in H. Adam Malik General Hospital, Medan. Non-contrast scan of the head was performed to diagnose acute ischemic stroke. Body temperature was measured on admittance and every two hour within the first 24 hours to assess fluctuation of body temperature and NIHSS to determine outcome. Data analysis was performed using Spearman correlation test.

Results: This study involved 62 acute ischemic stroke patients which consisted of 37 males (59.9%) and 25 females (40.3%), with the mean age of 59 years old and age range of 42-72 years old. There were 54 patients (87.1%) with history of hypertension (HT), 17 patients (27.4%) with diabetes mellitus (DM), 18 patients (29%) with dyslipidemia, 24 patients (38.7%) had smoking habit and 10 patients (16.1%) with coronary heart disease (CHD). There were 41 patients (66.1%) with moderate baseline NIHSS, 40 patients (64.5%) with moderate outcome NIHSS, 11 patients (17.7%) with body temperature fluctuation and 10 patients (16.1%) with death outcome. The result of statistical analysis showed a significant correlation between body temperature fluctuation and outcome in acute ischemic stroke patients ($p = 0.001$).

Conclusion: There was a correlation between body temperature fluctuation and outcome in acute ischemic stroke patients.

Keywords: Acute stroke, ischemic, body temperature fluctuation, outcome.

Introduction

Stroke is one of the cause of death and long term disability in the world. In Indonesia, the national data showed stroke as the highest cause of death (15.4%) in hospitals. The mortality rate caused by stroke in Indonesia, according to 2002 data from WHO, reached 123,684 people and caused disability in 8 per 1000 people in population. In North Sumatera, out of 25 hospitals, the number of female stroke patient was proportional to male patients, with the average age of 29 (20-95) years, and hypertension as the most common risk factor and result of head CT-scan revealed ischemic stroke (53.7%).^{1,2}

Body temperature is a simple, objective, and accurate indicator from a physiological status with little effect from external and psychogenic stimulus compared to other vital signs such as pulse, respiratory rate, and blood pressure. Therefore, body temperature can help in estimating disease severity, source, duration, and effect of therapy. Increased body temperature can be a factor that influence the outcome of stroke.^{3,4}

The mechanism of body temperature increase can cause brain damage, which includes increased metabolism in the penumbra area, increased excitatory amino acid release, free radicals, acidosis, and permeability changes from blood-brain barrier.^{5,6}



Methods

Subjects

The subjects were taken from the population of Haji Adam Malik General Hospital, Medan. The subjects were determined according to non-random consecutive sampling method. The inclusion criteria in this study were ischemic stroke patient confirmed through head CT-scan, ≤ 72 hours onset of attack, and gave permission to participate in the study. The minimum sample size in this study was 62.

Study Design

This is a bivariate analytical study with cross-sectional data collection method using primary data source obtained from acute stroke patients admitted to H. Adam Malik General Hospital who were observed to obtain characteristics of body temperature fluctuation in acute ischemic stroke patient and correlation study was conducted to determine the correlation between body temperature fluctuation in acute ischemic stroke patient and outcome.

Statistical Analysis

The data from this study were processed statistically with the help of SPSS (Statistical Product and Science Service) program version 22.0 for Mac. Spearman test was performed to determine correlation power.

Results

Out of all ischemic stroke patients admitted in H. Adam Malik General Hospital, Medan in August 2018 to September 2019, 62 of them met the inclusion criteria and were involved in this study. The majority of subjects were male (59.7%) with the average year of 59 years and an interval of 42-72 years. The most frequent ethnic was Batak (43.5%), most were high school graduate (43.5%), most occupation was entrepreneur (37.1%). The most risk factor found was hypertension (87.1%). A complete data of subject characteristics is presented in Table 1.

Table 1. Subject characteristics

Characteristics of subjects	Mean (min-max)	n (62)	Percentage (%)
Age (year)	62 (42-72)		
$\geq 40 - 50$		17	27.4
51 - 60		14	22.6
61 - 70		28	45.2
> 71		3	4.8
Gender			
Male		37	59.7
Female		25	40.3
Ethnic			
Batak		27	43.5
Java		22	35.5
Karo		9	14.5
Aceh		4	6.5
Occupation			
State civil apparatus		16	25.8
Housewife		16	25.8
Entrepreneur		23	37.1



INTERNATIONAL JOURNAL OF RESEARCH SCIENCE & MANAGEMENT

Others	7	11.3
Education		
Elementary school	6	9.7
Junior high school	22	35.5
High school	27	43.5
Bachelor's degree	7	11.3
Risk Factors		
Hypertension	54	87.1
Diabetes Mellitus	17	27.4
Dyslipidaemia	18	29
Coronary heart disease	10	16.1
Smoking	24	38.7

According to the characteristics of blood pressure, body temperature, NIHSS score, and outcome, overall systemic blood pressure during admittance had an average of 160 mmHg (140-190 mmHg) and diastolic of 90 mmHg (70-100 mmHg). The average body temperature was 36.6°C (36-28.6°C). Subjects with body temperature fluctuation were comprised of 16.1%. Most NIHSS admission category was moderate (66.1%) with average of 11.2 ± 6.2. Most NIHSS discharged category was moderate (64.5%) with average of 7 (1-33). The outcome of death comprised of 16.1%. Complete data regarding characteristics of blood pressure, body temperature, NIHSS score, and outcome in this study is presented in Table 2.

Table 2. Characteristics of blood pressure, body temperature, NIHSS score, and outcome.

Score Characteristics	Mean	n (62)	Percentage (%)
Blood pressure in			
Systolic	160 (140-190)**		
Diastolic	90 (70-100)**		
Temperature in	36.6 (36-38.6)**		
Temperature fluctuation	1.5 (-1.2-2.9)**		
Yes		11	16.1
No		51	83.9
NIHSS Admission	11.2 ±6.2*		
Mild		14	22.6
Moderate		41	66.1
Severe		7	11.3
NIHSS Discharged	7 (1-33)**		
Mild		10	16.1
Moderate		40	64.5
Severe		12	19.4
Outcome			
Died		10	16.1
Lived		52	83.9



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According to Spearman statistical analysis, there was a correlation between body temperature fluctuation and significant NIHSS discharged with p value < 0.001. Meanwhile, correlation r value obtained was 0.544, which showed moderate correlation power. These results can be seen in Table 3.

Table 3. Correlation between body temperature fluctuation and NIHSS out

<i>NIHSS Discharged</i>	
Temperature fluctuation	r = 0.544 p < 0.001 n = 62

According to Chi-square correlation test on 62 samples, there was a correlation between body temperature fluctuation and significant outcome with p value < 0.001. These results can be seen in Table 4.

Table 4. Correlation between body fluctuation and outcome.

Fluctuation	Outcome			p
	Died	Lived	Total	
Yes	8	3	11	p < 0.001
No	2	49	51	
Total	10	51	62	

Discussion

This study involved 62 subjects consisted of (59.9%) male with average age of 59 years old and age interval of 42-72 years. The characteristics of age and gender in this study were relevant to a study by Miscbach (2001) who stated that male was 55% more frequently had stroke compared to female with > 45 years of age. Appelros *et al.* (2009) stated that male had incidence ratio of 33% and 41% and higher prevalence compared to female with the age range of 65-74 years for stroke due to strong major risk. Both results above were in line with Rambe *et al.* (2013) who also stated that stroke incidence in male was 33% higher than female, with prevalence 41% higher than female and the average age of subjects was 59 years (age range between 20 to 95 years), and most subjects were within 40-59 years age group (46.5%) and 60-79 years (42.5%).^{1,7,8}

The most common ethnic was Batak (43.5%), which was relevant with Tambunan *et al.* (2019) who stated that Batak people were 87,1% more affected by ischemic stroke than non-Batak people due to consumption of traditional alcoholic drink. Most subjects were high school graduate (43.5%). According to Tambunan *et al.* (2019), education status was associated to stroke. This was in line with knowledge regarding stroke risk factors and how to prevent them. Most subjects were entrepreneur which comprised of 37.1%, whereas low economic status correlated to healthcare access (Smith *et al.*, 2003). There were 87.1% patients with history of hypertension. An epidemiological study revealed that hypertension was found in 50-70% stroke patients according to Rambe *et al.* (2013). Miscbach *et al.* (2001) stated that hypertension is the main risk factor of stroke that comprised of 73.9%.^{1,9}

Based on the characteristics of blood pressure, body temperature, NIHSS score, and outcome in this study, the average systolic blood pressure during admittance was 160 mmHg (140-190 mmHg) and diastolic 90 mmHg (70-100 mmHg). Hypertension causes disturbances in blood vessels in the form of atherosclerosis and fibrinoid necrosis. Atherosclerosis can cause autoregulation problem. Sudden change in blood pressure will decrease perfusion pressure, thus lead to brain tissue ischemic (ischemic stroke) or hyperemia, edema, and hemorrhage



INTERNATIONAL JOURNAL OF RESEARCH SCIENCE & MANAGEMENT

(hemorrhagic stroke). Fibrinoid necrosis causes microaneurysm, thus sudden increase in blood pressure can cause blood vessel rupture (hemorrhagic stroke).^{11,12}

The average body temperature during admittance was 36.6°C (36-38.6°C). Subjects who were affected by body temperature fluctuation consisted of 16.1%. Around 50% of stroke patients will undergo body temperature increase which is related to stroke severity, extension of lesion, mortality, and neurological outcome. Increased body temperature is recommended as a marker for patient outcome and should be confirmed that it was not because of an infection (Wrotek *et al.*, 2011). In severe stroke, tissue necrosis can increase body temperature due to inflammatory mediators circulating in the blood, such as PGE₂.¹³

The most common category of NIHSS admission was moderate with 66.1% and average 11.2 ± 6.2. The most common category of NIHSS discharged was moderate with 64.5% and average of 7 (1-33). Stroke severity was measured with NIHSS, which is a strong outcome predictor. Baseline NIHSS changes compared to when the patients were discharged or died affected outcome, which was expressed by Woters *et al.* (2018) who stated that 369 patients who participated in the study had OR 0.82; 95% CI 0.77-86 on functional outcome. Similar study by Sablot *et al.* (2011) also stated that NIHSS > 22 gave predictions on physical dependence and death caused by severe neurological deficit.^{15,16}

Death outcome in this study was 16.1%. This was relevant to Greer *et al.* (2008), whereas fever or increased body temperature in stroke patient significantly associated to poor outcome, with RR 1.4 on mortality, 1.3 on GCS, 1.9 on BI, 2.2 on mRS, 1.4 on Canadian stroke scale, 2.8 on intensive care duration and 3.2 on hospital stay.¹⁷

According to Spearman correlation analysis, there was a correlation between body temperature fluctuation and significant NIHSS discharged with p value < 0.001. Furthermore, the obtained correlation r value was 0.544, which showed moderate correlation power. Around 50% of stroke patients will undergo body temperature increase, which is related to stroke severity, extension of lesion, mortality, and neurological outcome. Increased body temperature is recommended as a marker of patient outcome and should be ruled out from infection (Wrotek *et al.*, 2011). In severe stroke, tissue necrosis can increase body temperature caused by inflammatory mediators circulating in the blood such as PGE₂ (Reith *et al.*, 1997). PGE₂ induction in the brain started the process of set-point increase in the hypothalamus. Although PGE₂ is important in the occurrence of fever, it is not a neurotransmitter. Therefore, PGE₂ release from hypothalamus endothelium will trigger PGE₂ receptor in glial cells, which will cause rapid release from cyclic adenosine 5-monophosphate (cyclic AMP), which is a neurotransmitter. This cyclic AMP will cause thermoregulator set-point increase in the hypothalamus (Batubara, 2011).^{13,18}

According to Chi-square correlation test, there was a correlation between body temperature fluctuation and significant outcome with p value < 0.001. The mechanism of body temperature increase can cause brain damage which include increased metabolism around the penumbra area, increased excitatory amino acid release and free radicals, acidosis and permeability change from blood-brain barrier (Batubara, 2011). Fever can give clinical symptoms of loss of consciousness in the form of delirium and stupor. In sensitive individual, a seizure can occur. For every 1°C of change in body temperature, there is a 13% increased consumption of O₂ in the brain which increased calories and liquid needs. The fever is caused by necrosis or change in body temperature regulation center, which is the anterior part of hypothalamus or direct irritation to the hypothalamus. Hypothalamus is supplied by posterior choroidal artery (Greer *et al.*, 2008). Increased body temperature in stroke patient can also be caused by infection process. Wastfelt *et al.* (2018) stated that pneumonia and urinary tract infection are the most common diseases that causes fever in stroke patients and had an effect on patient outcome.^{17,18,19}

Conclusion

This study revealed significant correlation between body temperature fluctuation and NIHSS score of acute ischemic stroke patients with p value < 0.001. Furthermore, the correlation r value obtained was 0.544, which



INTERNATIONAL JOURNAL OF RESEARCH SCIENCE & MANAGEMENT

showed moderate correlation power. There was also a significant correlation between body temperature fluctuation and outcome with p value < 0.001.

Suggestion

Further analysis is needed regarding factors that affected outcome and that considered lesion extension and location in neuroimaging examinations, and other confounding control such as infection in ischemic stroke patients in predicting outcome.

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INTERNATIONAL JOURNAL OF RESEARCH SCIENCE & MANAGEMENT

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