



THE DIFFERENCES OF ANTITHROMBIN III, FIBRINOGEN, AND TROPONIN I LEVELS BETWEEN ACUTE ISCHEMIC STROKE AND ACUTE HEMORRHAGIC STROKE

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Abstract

Introduction: Plasma antithrombin III associated with fibrinogen might help the risk assessment of acute ischemic stroke, but studies that discuss those levels in hemorrhagic stroke are still limited. Troponin I is a cardiac enzyme that has high sensitivity and specificity in the detection of heart injury after stroke. The purpose of this study is to determine the differences of antithrombin III, fibrinogen, and troponin I levels between acute ischemic stroke and acute hemorrhagic stroke.

Method: This study used a descriptive analytic study with a cross sectional design. A total of 52 research subjects, consisting of 26 acute ischemic stroke patients and 26 acute hemorrhagic stroke patients were taken by consecutive non-random sampling method. The blood samples from the subjects that have been diagnosed by history taking, physical examination and head CT scan, were taken for examination of antithrombin III, fibrinogen, and troponin I levels. Data analysis was performed by unpaired T test and Mann-Whitney test.

Results: The median antithrombin III level in the acute ischemic stroke group was 93.00%, while in the acute hemorrhagic stroke group was 101.85% ($p=0.341$). The mean fibrinogen level in the acute ischemic stroke group was 453.46 ± 171.16 mg/dL, while in the acute hemorrhagic stroke group was 399.15 ± 203.02 mg/dL ($p=0.302$). The median troponin I level in the acute ischemic stroke group was 0.00 ng/mL, while in the acute hemorrhagic stroke group was 0.00 ng/mL ($p=0.698$).

Conclusion: There were no significant differences of antithrombin III, fibrinogen, and troponin I levels between acute ischemic stroke and acute hemorrhagic stroke.

Introduction

Neurological deficits in stroke caused by non-traumatic blood circulation disorders. These neurological deficits include weakness of arms or legs, inability to speak, vision changes, loss of consciousness, etc.¹

Plasma antithrombin (AT) III associated with fibrinogen might help the risk assessment of acute ischemic stroke. One control study in China found that antithrombin III level in acute ischemic stroke was lower than in non-stroke patients but the fibrinogen level was higher in acute ischemic stroke than in non-stroke patients.² Another study conducted by Chitsaz et al. found no significant differences of fibrinogen level between ischemic stroke and hemorrhagic stroke.³

It is known that both ischemic stroke and hemorrhagic stroke have a negative effect on cardiac function. Damage to the cardiac muscle can occur after an ischemic stroke in the absence of primary cardiac cause. The basic neuroanatomy of cardiac muscle damage associated with stroke is not yet known.⁴ Troponin I is one of the most sensitive and specific cardiac enzymes as a marker of cardiac damage after ischemic stroke, intracerebral hemorrhage, and subarachnoid hemorrhage.^{5,6,7} Another study conducted by Hasirci et al. found higher troponin I level in acute ischemic stroke patients with anterior circulation involvement compared to acute hemorrhagic stroke patients ($p < 0.05$).⁶

Based on the description above, it is known that there were changes in levels of antithrombin III, fibrinogen, and troponin I in patients with acute ischemic stroke and acute hemorrhagic stroke. Therefore, researchers were



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interested in examining the differences of antithrombin III, fibrinogen, and troponin I levels between acute ischemic stroke and acute hemorrhagic stroke.

Methods

Study Samples

This study recruited patients who were admitted to Adam Malik General Hospital Medan, Indonesia due to acute stroke. A total of 52 research subjects, consisting of 26 acute ischemic stroke patients and 26 acute hemorrhagic stroke patients were enrolled consecutively in this study. The blood samples from the subjects that have been diagnosed by history taking, physical examination and head CT scan, were taken for examination of antithrombin III, fibrinogen, and troponin I levels. This study had been approved by the institutional ethics committee. The inclusion criteria in this study were patients diagnosed with acute stroke (onset ≤ 7 days) who participate in this study as evidenced by signing the research informed consent sheet. Patients with anticoagulant use, pregnancy, liver disease, chronic kidney disease, acute coronary syndrome, and SIRS (Systemic Inflammation Response Syndrome) were excluded from this study.

Study Design

This study used a descriptive analytic study with a cross sectional design to determine the differences of antithrombin III, fibrinogen, and troponin I levels between acute ischemic stroke and acute hemorrhagic stroke. This study was conducted in Adam Malik General Hospital Medan, Indonesia from July 2018 to March 2019. The sampling technique used in this study was consecutive non-random sampling.

Statistical Analysis

To determine the differences of antithrombin III, fibrinogen, and troponin I levels between acute ischemic stroke and acute hemorrhagic stroke, unpaired T test and Mann-Whitney test were performed in this study.

Results

Of the 52 subjects analyzed, 31 (59.6%) male patients and 21 (40.4%) female patients were included in this study. The average age of 52 subjects was 55.52 ± 13.41 years. The median antitrombin III level was 99.55% with minimum level was 15.00% and maximum level was 111.60%. The mean fibrinogen level was $426.30 \text{ mg/dL} \pm 187.93 \text{ mg/dL}$. The median troponin I level was 0.25 ng/mL with minimum level was 0.00 ng/mL and maximum level was 5.02 ng/mL. (Table 1)

Table 1. Demographic Characteristics of Research Subjects

Charateristic	Total Subject n = 52 (%)	Acute Ischemic Stroke n = 26 (%)	Acute Hemorrhagic Stroke n = 26 (%)
Sex - Male - Female	31 (59.6) 21 (40.4)	18 (69.2) 8 (30.8)	13 (50) 13 (50)
Age (Average \pm SD) (year)	55.52 ± 13.41	59.50 ± 9.11	51.54 ± 15.85
AT III Median (min-max) (%)	99.55 (15.00 - 111.60)	93.00 (43.10 - 111.60)	101.85 (15.00 - 111.40)
Fibrinogen Mean \pm SD (mg/dL)	426.30 ± 187.93	453.46 ± 171.16	399.15 ± 203.03
Troponin I Median (min-max) (ng/mL)	0.25 (0.00 - 5.02)	0.00 (0.00 - 5.02)	0.00 (0.00 - 3.73)



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The results of the study using the Mann-Whitney test showed no differences of antithrombin III levels between acute ischemic stroke and acute hemorrhagic stroke with p value = 0.341. (Table 2)

Table 2. The Differences of Antithrombin III Levels Between Acute Ischemic Stroke and Acute Hemorrhagic Stroke

	Median (Minimum - Maximum)	p value
AT III level in acute ischemic stroke (n=26)	93.00% (43.10% – 111.60%)	0.341
AT III level in acute hemorrhagic stroke (n=26)	101.85% (15.00% – 111.40%)	

Mann-Whitney Test

The results of the study using the unpaired T test test showed no differences of fibrinogen levels between acute ischemic stroke and acute hemorrhagic stroke with p value = 0.302. (Table 3)

Table 3. The Differences of Fibrinogen Levels Between Acute Ischemic Stroke and Acute Hemorrhagic Stroke

	Mean ± SD	p value
Fibrinogen level in acute ischemic stroke (n=26)	453.46 ± 171.16 mg/dL	0.302
Fibrinogen level in acute hemorrhagic stroke (n=26)	399.15 ± 203.03 mg/dL	

Unpaired T test

The results of the study using the Mann-Whitney test showed no differences of troponin I levels between acute ischemic stroke and acute hemorrhagic stroke with p value = 0.698. (Table 4)

Table 4. The Differences of Troponin I Levels Between Acute Ischemic Stroke and Acute Hemorrhagic Stroke

	Median (Minimum - Maximum)	p value
Troponin I level in acute ischemic stroke (n=26)	0.00 ng/mL (0.00 ng/mL – 5.02 ng/mL)	0.698
Troponin I level in acute hemorrhagic stroke (n=26)	0,00 ng/mL (0.00 ng/mL – 3.73 ng/mL)	

Mann-Whitney Test

Discussion

The subjects of this study consisted of 52 people with the most sex in stroke patients found in men. Similar results were also found in Chitsaz et al. study, which is from 116 subjects as many as 60 (51.7%) men and 56 (48.3%) women suffered stroke.³ Men have higher risk factors for stroke than women. This is influenced by genetic factor and positive effect of estrogen in cerebral circulation.⁸ The average age of stroke patients in this study was 55.52 ± 13.41 years. Chitsaz et al. found that the average age prevalence was 65.4 ± 16.2 years. The risk factors for stroke increase two times every one decade after 55 years old.^{3,9}

In this study, there were no significant differences of AT III levels between acute ischemic stroke and acute hemorrhagic stroke ($p=0.341$). Singh et al. found decreased AT III biological and immunological activity in acute ischemic stroke compared to control group. In acute hemorrhagic stroke, there were increase in AT III biological and immunological activity compared to control group. Regarding the role of AT III in hemorrhagic stroke, there is a great paucity in literature.¹⁰ Another study conducted by Meng et al. found that the level of AT III was lower in ischemic stroke than in non-stroke group and it can predict the ischemic stroke before positive imaging evidence is obtained. When the ischemic stroke occurs, thrombin will be activated and cause increase consumption of AT III and decrease plasma AT III level rapidly.²



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From the results of this study, there were no significant differences of fibrinogen levels between acute ischemic stroke (453.46 ± 171.16 mg/dL) and acute hemorrhagic stroke (399.15 ± 203.03 mg/dL) with $p = 0.302$. This is in line with the results of Chitsaz et al., where higher fibrinogen levels were found in ischemic stroke compared to hemorrhagic stroke but were not statistically significant ($p = 0.12$).³ Similar results were obtained from the Ziakas et al. study, where no significant differences in fibrinogen levels were found between ischemic stroke and hemorrhagic stroke.¹¹ Meng et al. found that fibrinogen levels in the acute ischemic stroke group were higher than in the non-stroke group ($p < 0.001$), thus predicting the incidence of acute ischemic stroke before positive imaging evidence is obtained. The tendency of thrombosis arises when the blood clotting activity increases and the fibrinolysis system decreases. According to some studies, the blood of thrombotic patients is coagulated faster than normal people. This condition is called hypercoagulability. It turns out that in patients with thrombocytosis, the levels of various clotting factors, especially fibrinogen, factors V, VII, VIII, and X increase.¹² Atherothrombotic syndrome in intracerebral hemorrhage is one of the pathogenesis of vascular disease in the brain. Increased fibrinogen and Willebrand factors are associated with increased risk of brain hemorrhage. It is suspected that higher fibrinogen is associated with a lack of nocturnal declines in blood pressure, a trait that may increase risk of hemorrhagic stroke.¹³

From the results of this study, there were no significant differences of troponin I levels in acute ischemic stroke patients with acute hemorrhagic stroke with $p = 0.698$. This is consistent with the study of Sandhu et al., where there were no significant differences in troponin I levels among ischemic stroke, intracerebral hemorrhage, and subarachnoid hemorrhage.⁷ In another study conducted by Hasirci et al., higher levels of troponin I were found in ischemic stroke patients with anterior circulation involvement compared to hemorrhagic stroke patients ($p < 0.05$).⁶ The differences in results found may be due to different research methods and variations in sampling time. An increase in troponin I levels in the anterior circulation ischemic stroke is probably due to the blood supply from the insular cortex originating from the anterior circulation which causes sympathoadrenal activation, resulting in catecholamine release and damage to the myocardium.⁶ Previous studies showed the hypothalamus as the main center of cardiac dysfunction in patients with subarachnoid and intracerebral hemorrhage. Further research is needed to explain the clinical implications of the examination of troponin I levels in hemorrhagic stroke patients.⁶

Conclusion

In this study, it can be concluded that there were no significant differences of antithrombin III, fibrinogen, and troponin I levels between acute ischemic stroke and acute hemorrhagic stroke.

Suggestion

Further research needs to be performed by standardizing sampling time, thereby reducing research bias.

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