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# Hematocrit as disability predictor 30 days post-ischemia stroke

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## ABSTRACT

**Objective.** Measure whether the hematocrit can be the disability predictor in 30 days post ischemic stroke.
**Methods.** This study is a cohort retrospective using secondary data from medical records of patients with stroke ischemia. The total sample in this study is 54, consisting of group with hematocrit <43% and group with hematocrit >43.5%. Disability is measured with modified Rankin Scale (mRS) which consist of independent group (score 0-2) and dependent group (score 3-5); and Barthel Index score which consist of independent group (score >12) and dependent group (score <12) using Mann Whitney test.
**Results.** The mean age of the population was 60.333+10.97338 which the most age group that suffering from stroke is late elderly (56-65 years old). Majority of subjects is men (70.37%). The mean of hematocrit value 42.62+3.550467%, there are 34 subjects (62.96%) in group with hematocrit <43.5% and 20 subjects (37.04%) in group with hematocrit >43.5%. There are no significant associations between hematocrit and mRS (p-value = 0.735) also BI (p-value = 0.49), but there are significant associations between age (p value = 0.043) and sex (p-value = 0.002).
**Conclusion.** Hematocrit value cannot be used as a predictor of disability 30 days post ischemic stroke.

**Keywords:** hematocrit, disability, stroke

## INTRODUCTION

Stroke is classically characterized as a neurologic deficit associated with focal acute injury to the central nervous system caused by vascular disorders, including cerebral infarction, intracerebral hemorrhage, and subarachnoid hemorrhage [1]. Ischemic stroke is the most common stroke subtype, which is caused by the occlusion of an intracranial artery and causes infarction in the cerebral area [2]. There are several measuring tools for assessing function related to stroke, such as Barthel Index (BI) and modified Rankin Scale (mRS) [3].

The prevalence of ischemic stroke in Indonesia according to Riskesdas in 2018 was 10.9% and D.I. Yogyakarta province is the highest prevalence in Indonesia, it was 14.6% [4]. Stroke is the fifth largest cause of mortality in the United States (US), with an annual incidence ranging from 795,000 to 1,000,000 cases, where ischemic stroke cases account for 87% of all types of stroke [1]. Based on the IHME (Institute for Health Metrics and Evaluation) in 2020, the number of DALYs (Disability-Adjusted Life Years) for stroke in Indonesia was 10.87%, which is the highest number compared to other diseases [5]. Stroke is the most common case of neurological disease in the world's adult population and is the third leading cause of chronic disability. Approximately 74% population with stroke were dependent to other people in living their daily life [6].

Hematocrit is one of body's biomarkers that can show outcomes in stroke patients [6]. Male patients with acute complex strokes might have a poor outcomes due to the presence of extreme hematocrit values or as a result of hematocrit abnormalities including those resulting in reduced oxygen transport, changes in blood viscosity, and inappropriate cerebral autoregulation [7]. The study also said that high hematocrit is associated with the occurrence of ear-

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ly death after stroke. Research conducted by Mutiari [8] also shows that there is an association between high hematocrit and Early Neurological Deterioration (END). High hematocrit causes a change in blood viscosity and reduces blood flow to the brain, so it can cause in decreased oxygen transport and widespread the infarct lesions. Research conducted by Widjiatno [9] stated that there was no association between hematocrit and stroke prognosis as measured by the Gadjah Mada Stroke Algorithm (GMSA).

This study aims to determine whether the hematocrit can be a predictor of ischemic stroke disability 30 days after stroke so that the results of the study can be used as a reference to predict the presence of disability 30 days after stroke with a hematocrit examination.

## METHODS

### Patient characteristics

This study used the cohort retrospective research method with secondary data. The data was collected from medical records in 2018-2020. There are 54 subjects of ischemic stroke patients at Bethesda Hospital Yogyakarta. These number of subjects was obtained from the sample calculation using Openepi software with a minimum sample of 30 subjects. The inclusion criteria in this study included [1] patients aged >18 years, [2] mild or moderate ischemic stroke based on NIHSS, [3] stroke onset <24 hours, [4] laboratory examinations at the time of hospital admission, and [5] patients fully alert based on GCS. Exclusion criteria included incomplete patient data recording.

### Variables

The independent variable of this study was hematocrit. In this study, hematocrit was divided into 2 groups: Hct <43.5% and >43.5%. The dependent variable was disability 30 days post-ischemia stroke. In this study, the measurement of disability 30 days after ischemic stroke was measured using the modified Rankin Scale (mRS) and Barthel Index (BI). The disability scores were divided into 2 groups; independent and dependent. The mRS score in the independent group was 0-2 and the mRS score in the dependent group was 3-5. The BI score in the independent group was >12 and the BI score in the dependent group was <12. Based on prior research, potential covariates that might have association with hematocrit were comorbid disease (hypertension, diabetes mellitus, heart disease, and gastrointestinal disease) and comedication (antihypertension, antidiabetic, antiplatelet, and PPI). So therefore, these two covariates were also measured [3].

### Statistical analysis

All statistical analysis used SPSS 26.0. Basic subject characteristics were measured by using bivariate analysis chi-square test. Association between disability 30 days post-ischemia stroke (mRS and BI) and hematocrit were measured with bivariate analysis by using Mann-Whitney test. To find out whether there is a difference between two variables, we also measured for mean difference mRS score and BI score using Paired T-Test between baseline and 30 days post-ischemia stroke. A significantly result described as p-value <0,05.

## RESULTS

### Basic subject characteristics

This study used 54 data on stroke patients who had their first attack with onset less than 24 hours at the stroke center of Bethesda Hospital, Yogyakarta. The result of basic subject characteristics was shown in Table 1. Hematocrit in patients on admission to the hospital has an average 42.62$\pm$3.550467%. The average has similarities with the research of Widjiatno [9], with the average 41.44 $\pm$ 6.143% and the Yang [10] study, with the average 41.8 $\pm$4.3%. The mean age was 61.1428$\pm$1,366 years with a range of 36-82 years and dominated by the late elderly (56-65 years). Subjects were dominated by men which is 38 subjects (70,37%); while woman only 16 subjects (29,63%). The most common comorbidity was hypertension (51,61%). There are significant association between sex and hematocrit (p-value = 0,002), and age and hematocrit (p-value = 0,043).

### Correlation between mRS and hematocrit

As shown in Table 1, association between mRS and hematocrit was not statistically significant (p-value = 0,735). The mean difference which is comparing baseline and 30 days in group <43,5% and group >43.5% (Table 2) shows -12.27$\pm$4.06 with p-value 0,000.

### Correlation between BI and hematocrit

As shown in Table 1, association between BI and hematocrit was also not statisticaly significant (p-value = 0,49). The mean difference that compares baseline and 30 days in group <43,5% and group >43.5% (Table 2) shows 5.31$\pm$2,17 with p-value 0,000.

## DISCUSSION

In this study, the association between hematocrit and post-ischemic stroke disability with mRS score (p-value = 0.735) and BI score (p-value = 0.49) did not show significant results (p-value > 0.05). The results was similar with Widjiatno's [9] study; which showed that hematocrit had no prognostic value on the clinical performance using the Gadjah Mada Stroke Algorithm (ASGM) in acute infarct stroke pa-

tients (p-value = 0.352). Another research, Hashem's [11] study showed a correlation between hematocrit and stroke clinical outcome (r =-0.545, p-value = 0.0013), as well as Mutiari's study [8] which showed an association between hematocrit and early neurological deterioration (END) (p- value = 0.001) where 17 patients (25%) had END.

In this study, the hematocrit as a predictor of disability 30 days after ischemic stroke had no significant association. It was caused by the variability of the research subject. Variations can be seen from the calculation of the standard deviation which normally ranges from 2. The deviation value is directly proportional to the size of the variation; which was the higher the deviation value, the greater the variation [12]. The standard deviation that was obtained in the independent group mRS was 3.19293 and the non-independent group was 5.76033, and the standard deviation obtained in the independent BI group was 3.21149 and in the non-independent group was 5.98899.

Analysis of the mean difference by using Paired T-Test showed a significant change in Barthel Index and NIHSS scores from baseline to day 30, both in the Hct <43.5% group and in the Hct group > 43.5% (p-value = 0.000). This indicated that there was an average difference between BI and NIHSS on day 1 (baseline) and day 30 post stroke. A negative mean difference indicated that the BI value on the first day was lower than on day 30, which indicates an improvement in ischemic stroke and a positive mean indicates a decrease in the NIHSS average, which means an improvement in stroke as well.

The study by Kellert [13] showed that low post-ischemic stroke hematocrit was associated with poor clinical outcomes (p-value = <0.001). The possible mechanism underlying the relationship between low Hct and smooth muscle function in blood vessels is oxygen delivery along with alteration of Hct and Hb levels which will affect vascular function [14]. Hematocrit has a positive correlation with tissue oxygen tension even in the normal range of hematocrit, which indicates a decrease in Hct can cause a decrease in oxygen supply to tissues.

Research by Yang showed an association between high hematocrit and the incidence of ischemic stroke. The high hematocrit level causes an increase in blood viscosity and peripheral resistance, which causes decreasing of cerebral circulation [10]. Kellert's study showed a high hematocrit level was associated with a poor clinical outcome (p-value = 0.012) [12]. A possible mechanism underlying the association of high Hct with vascular smooth muscle dysfunction was related to hypoxia. Lewis' study [15] showed that patients with erythrocytosis had endothelial dysfunction suggesting that chronic hypoxia may lead endothelial dysfunction with excessive erythrocytosis. Endothelial dysfunction that occurs after a stroke causes oxidative stress, inflammation, increased vascular tone, damage to the blood-brain barrier, and thrombovascular complications in the brain [16].

The El-Solh [17] and Martini [18] studies also showed that Hct was significantly associated with blood viscosity. Blood viscosity regulates wound trauma, which is a trigger for the production of nitric oxide (NO) from the endothelium. In the Martini [18] animal study, elevated Hct can cause increased plasma nitrite or nitrate and cause endothelial nitric oxide synthase (eNOS) failure by increasing blood viscosity. In addition, the high and low blood viscosity due to Hct can also induce low oxygen tension in the tissues. According to the Hagen-Poiseuille law, blood flow depends on the thickness of the blood and the diameter of the blood vessels. Fowler [19] showed that high viscosity causes low cardiac output. This indicated that higher Hct levels may induce tissue oxygen tension with high peripheral vascular resistance and low cardiac output. This also indicated that high levels of Hct may be a factor in vascular dysfunction. The Tohgi study [20] showed that high hematocrit was a risk factor for cerebral infarction when the arteries are too small or are stenotic due to atherosclerosis. Hematocrit is thought to increase atherosclerosis by increasing protein infiltration into the vessel wall, triggering platelet adhesion to the subendothelium and causing blockage of blood flow [9]. Accumulation of atherosclerosis in the subintima arteries causes the formation of platelet clots which will then attract thrombin, fibrin, and erythrocyte debris that can clot into sizes; so the risk of stenosis of the cerebral blood vessel is increased [21].

A significant association was found between hematocrit and sex (p-value = 0.002). This result has been confirmed in other studies. Brown's study [22] found that hematocrit was lower in female, compared with male. Grau's [23] study showed that high hematocrit level tends to happen more in men compared to women (p-value = <0.001). In the Bachman [24] study, high hematocrit in men was associated with high levels of testosterone, which stimulates erythropoietin. The subject of ischemic stroke was dominated by men as many as 38 subjects (70.37%). This is similar with the study of Barker-Collo [25] and Maryanti [26] which showed that the incidence of stroke was more common in men than women. According to the CDC [27], there are several risk factors that cause a high incidence of stroke in men, such as hypertension, smoking habits, overweight and obesity, diabetes, frequent alcohol consumption, and lack of physical activity; while the incidence of stroke in women was found to be less than men, which only occurred in 16 subjects (29.63%).

This is influenced by the presence of the estrogen hormone in women before menopause which is able to provide protection with antiatherogenic effects that cause vasodilation in a. coronary and protects neurons and glial cells [28].

A significant association was also obtained between hematocrit and age. Research conducted by Brown [22] states that the hematocrit increases in adolescence up to 1.5 years afterward, then the hematocrit will decrease with age. The age of the research subjects were dominated by the late elderly (56-65 years). The risk of stroke is low in those under 35 years of age and increases every decade after 55 years of age, which it is influenced by the aging process of advanced glycation end products (AGEs) which can cause a high collagen accumulation so that the tissue becomes stiff and affects vascular elasticity [26]. The Soto-Cámara [29] study showed several risk factors associated with the first stroke in the elderly <75 years, such as hypertension, dyslipidemia, cardiovascular disease, atrial fibrillation, smoking, alcoholic, and sedentary lifestyle (p-value < 0,001).

The most common comorbidity experienced by the subject was hypertension. This is similar to the Simić-Panić [30] study which found that the majority of comorbid cases in ischemic stroke patients were hypertension (51.61%). Remodeling of large and small arteries due to hypertension can reduce the luminal diameter and vasodilatory reserve, causing hypoperfusion and hemodynamic failure. The repetitive mechanical stress during hypertension and the degradation of the elastic fibers in the vessel wall cause stiffness in the arteries. Endothelial dysfunction and damage can increase the risk of atherosclerosis, which can increase the risk of stroke [31].

## CONCLUSIONS

The hematocrit value cannot be used as a predictor of disability 30 days after ischemic stroke. Future researchers are expected to be able to assess the degree of severe stroke, with a longer study period, specific studies on men or women, and controlling for other confounding variables.

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