Association of Serum Uric Acid with Severity of Ischemic Stroke

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Abstract

Serum Uric Acid (SUA) is the end product of nucleotide metabolism. The level of SUA is increased (hyperuricemia) when the balance between the production, for example in people with purine-rich diet, and the disposal of uric acid is disrupted, such as those with kidney problems. The aims of this research was to determine the correlation between SUA and severity of ischemic stroke patients. This was a correlational study with a retrospective cross-sectional study by collecting data from medical records of Ischemic Stroke (IS) patient in Dr. Soetomo General Hospital Surabaya within the period of January 2019 – December 2019, used total sampling technique with inclusion and exclusion criteria. SUA level was taken from the medical records filled at admission. The severity of stroke was measured using NIHSS data obtained during the beginning of the hospital admission. 41 sample of 51 population of patients met the inclusion criteria. The data was analyzed by the Spearman Rank correlation test to determine the correlation between SUA and severity of ischemic stroke. The result showed p-value = 0.897 with a correlation value of 0.021, so, there was a weak correlation between SUA and severity of ischemic stroke patients. The limitation of this study was a single-centered study with a small number of sample limiting its generality. Additional researches with bigger subjects are needed to study about the association of SUA and stroke severity.

Keywords : Ischemic stroke, uric acid, NIHSS

Introduction

Serum Uric Acid (SUA) is the end product of nucleotide metabolism (1). It is synthesized mainly in the liver, intestines and the vascular endothelium as the end product of an exogenous pool of purines, and endogenously from damaged, dying and dead cells (2). In normal concentration, SUA is beneficial for human body as it exerts antioxidant properties which may protect against oxidative stress (3). The level of SUA is increased (hyperuricemia) when the balance between the production, for example in people with purine-rich diet, and the disposal of uric acid is disrupted, such as those with kidney problems (4), Although elevated SUA level has been known to be a major etiological factor of gout (5), studies found conflicting result about its association with stroke, particularly ischemic stroke (IS). Stroke itself is defined as a neurological deficit attributed to an acute focal injury of the central nervous system (CNS) by a vascular cause (6). It is classified as either ischemic (87%), caused by a loss of blood supply to an area of the brain (7), or hemorrhagic (13%), caused by a bleeding into the brain by the rupture of a blood vessel (8–10). Stroke is a major

cause of disability in Indonesia, with a fairly high mortality rate of 28.76% (11), hence it is very important to control the risk factors, particularly the modifiable risk factors, in order to prevent a stroke.

Several studies have found hyperuricemia to be a strong predictor for stroke (12,13), and that hyperuricemia increases the risk for ischemic stroke incidence (14,15). In contrast, other studies found that high SUA level is associated with better stroke outcome (16,17). The study aims to determine the correlation between SUA and severity of ischemic stroke patients, measured with the National Institute of Health Stroke Scale (NIHSS). The study is expected to give a better understanding about the topic in order to prevent and control stroke.

Research Elaborations

This was a correlational research with analytical observation as the research design which aims to analyze the relation between SUA and severity of ischemic stroke. It was a retrospective cross-sectional study by collecting data from medical records of ischemic stroke patient in Dr. Soetomo General Hospital Surabaya within the period of January 2019 – December 2019. This research used total sampling technique as the sampling method. Patients with hemorrhagic stroke, 2nd episode of ischemic stroke, history of malignancy, or presence of infection upon admission, were excluded from this study. SUA level is taken from the medical records filled at admission. The severity of stroke is measured using NIHSS data obtained during the beginning of the hospital admission. The data was analyzed using the Spearman Rank correlation test to determine the correlation between SUA and severity of ischemic stroke.

Results

Among 51 available medical records of ischemic stroke patients at Neurology Department of Dr. Soetomo General Hospital Surabaya within the period of January – December 2019, 41 medical records met the inclusion criteria.

Table 1. Patient Demographic

Variable	Frequency	Percent (%)
Gender		
Male	29	70.7
Female	12	29.3
Age (59.71 ± 12)		
31-40	2	4.9
41-50	8	19.5
51-60	8	19.5
61-70	16	39
Above 70	7	17.1
Ethnicity		
Javanese	34	82.9
Madurese	6	14.6
Other	1	2.4
Education		
Uneducated	9	22
Elementary drop out	4	9.8
Completed elementary school	5	12.2
Completed junior high school	1	2.4
Completed senior high school	16	39
Other	6	14.6
Occupation		
Unemployed	12	29.3
Housewife	6	14.6
Private officer	4	9.8
Entrepreneur	4	9.8

Retiree	2	4.9
Farmer/Fisherman	2	4.9
Laborer/Driver	4	9.8
Other	7	17.1
Marital Status		
Unmarried	2	4.9
Married	35	85.4
Deceased spouse	3	7.3
Other	1	2.4

Table 1 shows the variables of demographic data of ischemic stroke patients in dr. Soetomo General Hospital during the period of January – December 2019 with a total subject of 41 ischemic stroke patients. Mean (±SD) age was 59.71 ± 12 years and 70.7% (n=29) were males. Javanese ethnicity makes up most of the sample with 82.9% (n=34) and about 39% (n=16) achieve education up to senior high school. For the occupation, the most represented category is unemployed with 29.3% (n=12) and 85.4% (n=35) are married.

Table 2. Laboratory findings

Test description	Sample size (N)	Minimum	Maximum	Mean ± SD	Reference range
Blood Pressure					
Systolic (mmHg)	41	110	220	156.9 ± 26.7	< 120
Diastolic (mmHg)	41	70	130	92.4 ± 13.3	< 80
Complete blood count					
Erythrocytes (10^6/µl)	35	1.79	48.8	6.2 ± 7.5	3.5 - 5.9
Leucocytes (10^3/mm^3)	38	4.4	22.9	9.4 ± 3.7	4.5 – 11
Hemoglobin (g/dL)	39	5.2	115	16.5 ± 16.5	12 - 17.5
Hematrocrit (%)	35	16	46	38.6 ± 5.5	36 - 53
Thrombocyte (10^3/µl)	36	130	448	266.6 ± 81.3	150 - 400
Coagulation profile test					
PT (sec)	38	0.8	26.5	11.5 ± 3.7	10 - 13
aPTT (sec)	38	2.8	51.9	26.3 ± 8.1	25 - 35
Lipid examination					
TCHOL (mg/dL)	40	135	326	212 ± 43.3	< 200
LDL (mg/dL)	41	33	236	137.4 ± 41.9	< 130
HDL (mg/dL)	41	23	187	46.6 ± 25.3	> 40
TG (mg/dL)	41	43	510	145.5 ± 92.4	< 150
Blood glucose examination					
RBG (mg/dL)	34	36	565	159.1 ± 108.9	< 200
FBG (mg/dL)	39	61	381	143.3 ± 79.3	< 100
2HPP (mg/dL)	30	62	316	170.8 ± 69	< 140
HbA1c (%)	38	4.1	14.9	9.2 ± 11.7	< 5.7
Liver examination					
SGOT (U/L)	39	6	675	40.0 ± 105.4	5 - 30
SGPT (U/L)	39	12	345	33.6 ± 52.9	4 - 36
Albumin (g/L)	36	3.1	42	4.9 ± 6.3	35 - 50
Kidney examination					
Uric acid (mg/dL)	41	3.1	12.9	5.9 ± 2.2	3.5 - 7.2
BUN (mg/dL)	31	3	65	17.9 ± 12.8	5 - 20
Creatinine (mg/dL)	37	0.4	4.1	1.2 ± 0.7	0.6 - 1.2

Table 2 shows the sample size, minimum, maximum, mean, standard deviation, and reference range of each laboratory variable. Some patients don't have the needed data for the variables, hence unable to be analyzed. Systolic has a mean of 156.9±26.7, with the lowest systolic pressure being 110, and the highest being 220, whereas diastolic has a mean of 92.4±13.3, with lowest diastolic pressure being 70, and the highest being 130. For complete blood count examination, all variables have a mean data that are within the reference range, except for erythrocyte that is slightly higher than the normal range (6.2 ± 7.5). Both total cholesterol (212 ± 43.3) and LDL level (137.4±41.9) also have a

slightly higher mean. Three out of four measures of blood glucose show a higher mean with 143.3±79.3 for FBG, 170.8±69 for 2HPP, and 9.2±11.7 for HbA1c. For liver examination, SGOT has a higher mean of 40.0 ± 105.4, while SGPT and Albumin are within the normal range. All variables of kidney examinations are also within the normal range.

Table 3. Descriptive analysis of SUA and NIHSS

	Serum Uric Acid	NIHSS
Mean	5.973	7.9
Median	5.2	7
Mode	4.9	7
Std. Deviation	2.2088	5.553
Variance	4.879	30.84
Skewness	1.505	1.889
Std. Error of Skewness	0.369	0.369
Kurtosis	2.282	5.357
Std. Error of Kurtosis	0.724	0.724
Minimum	3.1	0
Maximum	12.9	30

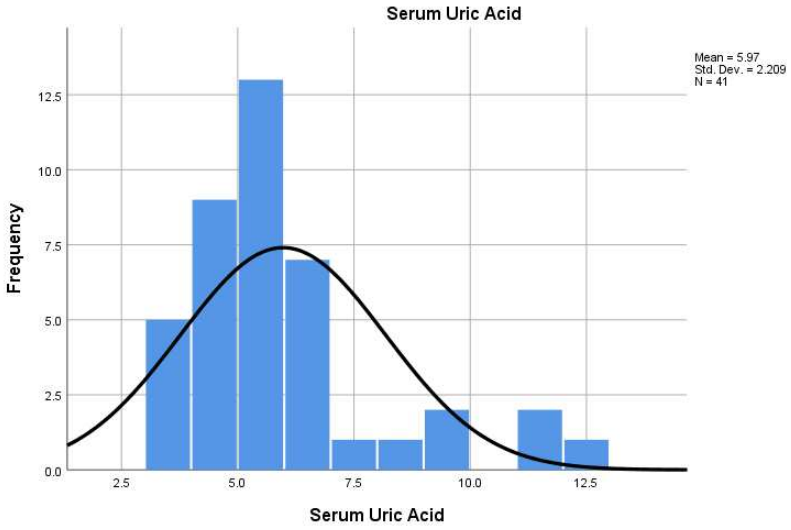

Fig. 1. Distribution of SUA

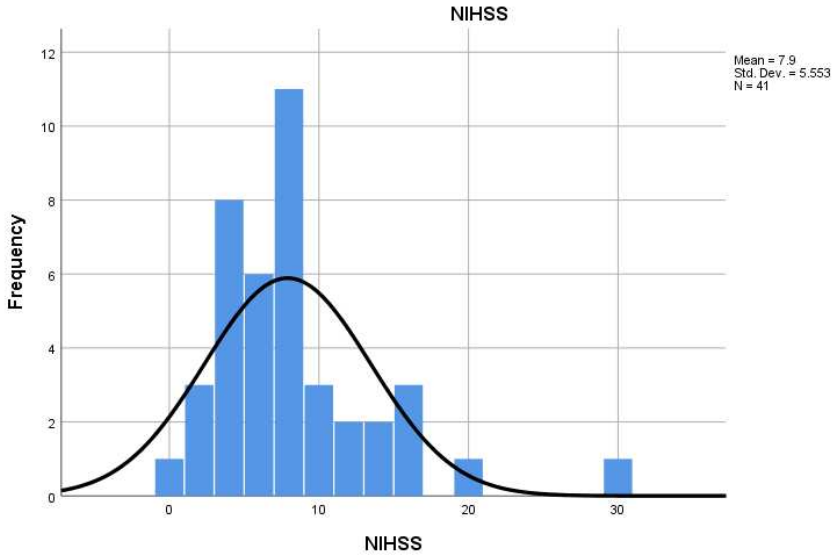

Fig. 2. Distribution of NIHSS

Table 3, Figure 1 and Figure 2 show the descriptive analysis and distribution of SUA and NIHSS among 41 patients. A normality test was performed using the Shapiro-Wilk statistical test for both SUA and NIHSS, resulting in p-value of 0.000 ($p<0.05$) for both variables which indicates abnormal data distribution. Spearman correlation test was used to analyzed the correlation between SUA and NIHSS in order to determine the correlation between two variables. As shown on Table 6, the result showed no statistically significant correlation ($p>0.05$) with a very week correlation value ($r=0.021$) in the positive direction.

Table 6 Correlation test of SUA and NIHSS

		NIHSS
Uric acid	r	0.021
	p	0.897
	n	41

The result of this study showed no statistically significant correlation, between SUA and severity of ischemic stroke, with a very weak correlation value ($r=0.021$) in the positive direction. An important observation in this study is the presence of comorbidity on the subjects. Among 41 patients, there are 25 (60.9%) patients who have a medical history of either hypertension, diabetes mellitus, or dyslipidemia, which is a major risk factor for ischemic stroke and poor outcome.

A literature review was done by Tariq et al. in 2019 about the association of serum uric acid level with ischemic stroke. They found that high uric acid levels are associated with an increased incidence of stroke through activating a cycle

of events involving inflammatory and oxidative mechanism of action which might lead to stroke. Moreover, they also found that hyperuricemia is a strong indicator of negative post stroke functional outcomes (18).

On the contrary, uric acid is also known to have a neuroprotective effect. One study was done by Amaro and Chamorro in 2017 to analyze the impact of uric acid towards stroke patients treated with thrombolysis. They found that increased uric acid levels are associated with better outcome in stroke patients with reperfusion therapies (19). Another study was done by Chamorro in 2004 where they found that the severity of neurological impairment and the volume of infarction in patients with stroke have been found inversely related to the concentration of uric acid, meaning that exogenous administration of uric acid could potentially benefit patients with acute ischemic stroke (20).

The limitation of this study is that it was a single-centered study with a small number of sample limiting its generality, hence the study might not give the best portrayal of the real condition. Moreover, severity of stroke is also majorly affected by other conditions (i.e., hypertension and diabetes mellitus), hence it is hard to individually analyze the effect of uric acid alone.

Conclusion

The objective of the study was to determine the correlation between SUA and severity of ischemic stroke. Based on the results, we found no significant correlation, between SUA and severity of ischemic stroke. Additional researches with bigger subjects are needed to study about the association of SUA and stroke severity.

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Disclosure of conflict of interest

The authors declare no conflicts of interest in the making of this paper.

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