

## THE RELATION OF STROKE PATIENT'S CORTISOL LEVEL TO NATIONAL INSTITUTES OF HEALTH STROKE SCALE CORE ON SPONTANEOUS INTRACEREBRAL HEMORRHAGE: AN OBSERVATIONAL STUDY AT RUMAH SAKIT UMUM DAERAH (REGIONAL PUBLIC HOSPITAL) DR. SOETOMO IN SURABAYA

GIBRAN ADITIARA WIBAWA<sup>1\*</sup>, ASRA AL FAUZI<sup>2</sup>

<sup>1</sup>Department of Faculty of Medicine, Airlangga University, Surabaya, Indonesia. <sup>2</sup>Departement of Neurosurgery, Adhyaksa General Hospital, Jakarta, Indonesia. Email: gibranwibawa@yahoo.com

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### ABSTRACT

**Objective:** The objective of the study was to find out differences in the cortisol level characteristics and National Institutes of Health Stroke Scale (NIHSS) score in the 1<sup>st</sup> and 7<sup>th</sup> days on patients treated at Dr. Soetomo Regional Hospital; thus, it can be the right education for stroke patients.

**Methods:** A prospective observational study was carried out against stroke patients treated in the neurosurgery department on September 2016–March 2017. Evaluation was done to all patients treated at the neurosurgery department. The evaluation process began with basal hormones within the first 24 h and taken at 6:00 and repeated on the 7<sup>th</sup> day to surviving patients. Of all the data obtained, the category scale data are presented by its frequency distribution, while numerical scale data are presented by its descriptive value (average and standard deviation).

**Results:** Of the 17 patients surviving until the 7<sup>th</sup> day, there is a decrease at the average cortisol level on the 1<sup>st</sup> day when compared to the average cortisol level on the 7<sup>th</sup> day with a mean value of 39.67–36.57 and so is the highest cortisol level; it decreases from the 1<sup>st</sup> day of 61.45 to the 7<sup>th</sup> day of 56.70. Meanwhile, in the NIHSS score value, the decrease in score only occurs in the average value on the 1<sup>st</sup> and 7<sup>th</sup> days from an average of 22.82 into 21.41, whereas minimum and maximum scores do not change. With the test result, the cortisol level characteristic gets a score of  $p < 0.05$ ; thus, there is a significant difference.

**Conclusion:** Of the result of observation already carried out on stroke patients treated at Dr. Soetomo Regional Hospital, treatment and education levels for patients who have a risk of stroke factor are very important.

**Keywords:** Stroke, Hemorrhage, National Institutes of Health Stroke Scale, Cortisol

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### INTRODUCTION

Increased stroke patient is one interesting topic that draws the attention of researchers [1]. One type of stroke commonly found is intracerebral hemorrhage (ICH). According to Fathima *et al.* [2] of 70% incidence of ischemic stroke, 20% of cases are ICH. Thus, this case gains much concern, although there are a lot of factors causing a stroke [3].

In the past 2 years, the number of hemorrhage stroke cases at Dr. Soetomo Regional Public Hospital (Rumah Sakit Umum Daerah, RSUD) had significantly increased, which made it a particular concern.

For the past 10 years, the knowledge development of spontaneous ICH (SICH) increasingly changed [4-6], for example, a radiology technique for diagnosing *in vivo* from ICH was found. The ICH occurs when the blood vessel in the brain parenchyma is ruptured. SICH can also happen as the result of a complication of previous lesions, such as vascular malformation or tumor, which is categorized as secondary SICH. When ICH occurred, blood vessels in the brain parenchyma ruptured. This causes an acute illness and gives effect to stroke patients where their cortisol levels are increased. Cortisol levels give an indication of the disease severity and its recovery phases. Cortisol may also be referred to as a short-term prognostic sign from the functional outcome and mortality. The same thing can be occurred in stroke patients who have an experience where cortisol levels increased in 7 days after the occurrence of stroke.

Referring to Barugh *et al.* [7] the increased cortisol after related with subordination, disability, and mortality. However, there is insufficient

evidence to draw conclusion that this relation does not depend on the severity of stroke.

One of the commonly used measuring tools to assess severity degree of a stroke is National Institutes of Health Stroke Scale (NIHSS). NIHSS and NIHSS modified have superiority in assessing the neurological deficit compared to other measuring tools [8,9]. By understanding the relationship between the increased level of cortisol and NIHSS scorer to acute stroke patients on the first 7 day, then, the pattern of handling stroke sufferers can be optimal. Also, a predict recovery of ambulation and upper limb function after 6-month stroke by age and NIHSS models as [10].

### RELATED WORK

Until now, the topic of handling stroke patients has become very interesting. Hence, many researchers want to improve performance with a variety of methods [11-14]. SICH is a multi-factorial and etiological disease, and it is the second most occurring kind of stroke after ischemic stroke with the percentage of 10–20% of all kinds of stroke cases. According to Ikram *et al.* [15], hypertension is the dominant factor that affects the ICH occurrence. It corresponds to research in Japan, which has been issued by Aguilar and Freeman [16].

The understanding of axis hypothalamic-pituitary-adrenal activation during acute condition, which causes the increasing of cortisol serum concentration, is often connected to the severity level of diseases and prognosis. If a patient successfully passes the acute phase but experiences an elongation in a recovery process, a prolonged critical

period may occur [17]. The case of increasing cortisol level on the first 7 days after the stroke is very high.

Cortisol can be used as a prognostic factor of short-term functional ability and death to a patient in China who suffers from an acute ischemic stroke. Studies on the relationship between neuroendocrine change and SICH are not strong enough and still cause conflict [18]. Some studies state that there is a change of the cortisol level in a stroke patient but not specifically for ICH [19].

The increase of the cortisol level is related to symptoms of confusion and poor output of a post-stroke patient. Hypercortisolism is also related to an initial cognitive dysfunction after the occurrence of ischemic stroke. The fluctuative change of the cortisol level affects the increase of death rate after the ischemic stroke [20]. During the acute ischemic stroke, a stress response may occur, and catecholamines increase is proven to be related to the stroke severity level and final output [21]. Death on an acute stroke patient is related to the increase of cortisol serum level while S-Cortisol is related to the stroke severity level [22].

**RESEARCH METHOD**

This research is conducted using an analytic observation method while the samples used are all ICH patients of RSUD Dr. Soetomo that have fulfilled inclusion criteria.

17 patients (9 females and 8 males, Table 1) who were treated by a team of neurosurgeons at RSUD Dr. Soetomo from August 2016 to June 2017 had fulfilled an inclusion and exclusion criteria to form a study group in this research. The sample size is taken using a correlation formula:

$$n = \{ (Z\alpha + Z\beta) / (0,5 \ln [(1+r)/(1-r)]) \}^2 + 3 \tag{1}$$

Then,

$$\alpha = 0.05 \rightarrow Z_\alpha = 1.96 \tag{2}$$

$$\beta = 0.20 \rightarrow Z_\beta = 0.84 \tag{3}$$

The exclusion criteria are of age <17 years old and no >60 years old, having an endocrine disorder, sustaining an extracranial injury, experiencing hemorrhage caused by aneurysm/avm, and having a metabolic disorder. An initial computed tomography scan examination is applied to the patients to diagnose the ICH. The volume measurement is made based on the ABC/2 technique, and it is possible that the intraventricular hemorrhage is scored using the Graeb scheme. Following flowchart is shown in Fig. 1.

Hypothesis:

The levels of cortisol on day 1 and 7 are different

- Sig. >0.05 = H<sub>0</sub> accepted,
- Sig. <0.05 = H<sub>0</sub> is rejected

The NIHSS score of days 1 and 7 is different

- Sig. >0.05 = H<sub>0</sub> accepted,
- Sig. <0.05 = H<sub>0</sub> is rejected

Relationship between cortisol levels day 1 with mortality.

Evaluation of basal hormone is applied to all patients within the first 24 h of being hospitalized. A blood sample is taken at 6.00 a.m. on the following day and is repeated on the 7<sup>th</sup> day only for the patients who survive. The normal level of cortisol hormone is 5–25 mgm dl/1.

The clinical condition of the patients is measured using NIHSS. The measurement is conducted when the patients come and on the 7<sup>th</sup> day. The NIHSS score has been directly evaluated by researchers. All data have been tabulated and analyzed.

**RESULTS**

This research is conducted for 6 months by collecting the medical record data of the patients from the period of September 2016 to March 2017

at RSUD Dr. Soetomo. The collected data are the data of the acute ICH stroke patients. The population collected is 17 patients. The data are divided into the inclusion and exclusion data, as many as 17 patients and 9 patients with characteristics as presented the Table 1.

Table 1 shows the total and percentage of research samples based on age and gender between female and male from the period of September 2016 to March 2017 at RSUD Dr. Soetomo.

The cortisol level of each patient is examined on the 1<sup>st</sup> and the 7<sup>th</sup> days. Table 2 shows the cortisol examination result on the 1<sup>st</sup> and the 7<sup>th</sup> days.

From the data above, it can be seen that the average value of cortisol on the 1<sup>st</sup> day is quite high, which is 39.67 from 17 samples. On the other hand, on the 7<sup>th</sup> day, it can be seen that the cortisol level decreases to the average of 36.57 and the maximum level acquired by the patients also decreases. The maximum value on the 1<sup>st</sup> day is 61.45 with p<0.05. It means that there is a significant difference on the cortisol level of day 1 and the cortisol level of day 7.

After acquiring the cortisol level of each patient from day 1 to day 7, the next thing to do is to test the different NIHSS score from each patient from day 1 to day 7. The examination result can be seen from Table 3.

The NIHSS score of the 17 patients has total value of 22.82 with the p (paired t-test) level of 0.165. The value has slightly decreased on the 7<sup>th</sup> day to 21.41. However, there is no change in the maximum value of NIHSS, which is 36. There is also no change in the minimum value, which is 5 in the NIHSS score.

On the other hand, the result of different characteristic examination between the NIHSS score on the 1<sup>st</sup> day and the 7<sup>th</sup> day is p>0.05, which means the characteristic of NIHSS score on the 1<sup>st</sup> day with the cortisol level on the 7<sup>th</sup> day is the same. Table 4 shows the change in NIHSS score from the observed patient.

Regarding the data above, most patients did not experience changes NIHSS score day-1 and day-7. There was one patient who

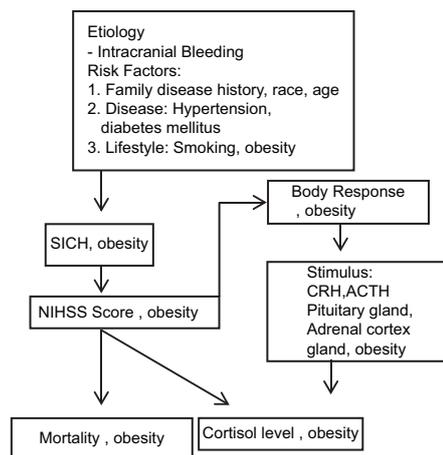


Fig. 1: Flowchart

Table 1: Characteristics of patients

Character	Characteristics	Percentage
Age (n=17)	Mean±SD	51.64±6.56
	Minimum	43
	Maximum	60
Gender (n=17)	Male	47.05
	Female	52.95

Table 2: Test of different levels of cortisol on day 1 until day 7

Take time	n	Mean±SD	Minimum	Maximum	p (paired t-test) Sig. (2-tailed)
Day 1	17	39.67±16.16	5.01	61.45	Sig. 0.019
Day 7	17	36.57±13.58	6.70	56.70	

Table 3: Test of different NIHSS score day 1 and day 7

Day	n	Mean±SD	Minimum	Maximum	p (paired t-test)
1 <sup>st</sup>	17	22.82±9.44	5	36	0.165
7 <sup>th</sup>	17	21.41±9.92	5	36	

NIHSS: National Institutes of Health Stroke Scale

Table 4: NIHSS score data change day 1 and day 7

NIHSS day 1 <sup>st</sup>	NIHSS day 7 <sup>th</sup>				???
	Light (%)	Medium (%)	Weight (%)	Very heavy (%)	
Light	2 (11.76)	-	-	-	2 (11.76)
Medium	-	2 (11.76)	-	-	2 (11.7)
Weight	-	1 (5.88)	5 (29.4)	-	6 (35.29)
Very heavy	-	1 (5.88)	-	6 (35.29)	7 (41.17)
Total	2	4	5	6	17 (100)

NIHSS: National Institutes of Health Stroke Scale

Table 5: Correlation of the cortisol levels and NIHSS score (Pearson test)

	K-1	K-7	N-1	N-7
K-1				
Pearson correlation	-	0.96	0.717	0.619
Sig. 2 Tailed	-	0.00	0.01	0.01
K-7				
Pearson correlation	0.96	-	0.721	0.669
Sig. 2 Tailed	0.00	-	0.01	0.03
N-1				
Pearson correlation	0.717	0.721	-	0.916
Sig. 2 Tailed	0.01	0.01	-	0.00
N-7				
Pearson correlation	0.619	0.669	0.916	-
Sig. 2 Tailed	0.01	0.03	0.00	-

NIHSS: National Institutes of Health Stroke Scale

experienced improvement from the weight group to moderate, and one patient experienced improvement from very heavy group to moderate.

The NIHSS score of the 17 patients has the total value of 22.82 with the p (paired t-test) level of 0.165. The value has slightly decreased on the 7<sup>th</sup> day to 21.41. However, there is no change in the maximum value of NIHSS, which is 36. There is also no change in the minimum value, which is 5 in the NIHSS score.

On the other hand, the result of different characteristic examination between the NIHSS score on the 1<sup>st</sup> day and the 7<sup>th</sup> day is  $p > 0.05$ , which means the characteristic of NIHSS score on the 1<sup>st</sup> day with the cortisol level on the 7<sup>th</sup> day is the same. The subsequent relationship of cortisol levels to NIHSS score on day 1 and day 7 is as follows as presented in Table 5.

Seen on several lines above, the significance can be determined by Sig line (2-tailed). If the value is Sig (2-tailed)  $< 0.05$ .

The most of patients did not experience any changes of NIHSS Score on day 1 and day 7, but there was one patient who experienced

improvement from the weight group to moderate and one patient experienced improvement from very heavy group to moderate. It is likely that stroke patients with greater initial symptom severity tends to have an unfavorable prognosis while the difference of cortisol levels with the output number using independent test is as follows as presented in Table 6.

The results of the data above show that there is no difference among the average value of cortisol the 1<sup>st</sup> day in the group of patients died and alive ( $p > 0.05$ ), the average 7<sup>th</sup> day cortisol in the group died and alive ( $p > 0.05$ ), and the mean NIHSS score day to-1 in the group of patients died and alive ( $p > 0.05$ ). However, there was a difference between the mean 7<sup>th</sup> day NIHSS score in the death and live patient group ( $p < 0.05$ ). After obtaining a cortisol level with NIHSS score, next, correlation of NIHSS score to mortality on day 1 and day 7 by contingency coefficient (Cramer's V) method is presented in Tables 7 and 8.

Based on the data of correlation test of NIHSS day-1 with mortality using contingency coefficient (Cramer's V) obtained contingency coefficient of 0.556 and significance level of 0.055, which means there is no significant relationship between NIHSS score day 1 with mortality. As for the 7<sup>th</sup> day of contingency coefficient of 0.634 and significance level of 0.010, it means that there is a significant correlation between the score of NIHSS day-7 and mortality. NIHSS has a high predictive ability to output in stroke patients at different times after the onset of symptoms.

## CONCLUSION

SICH is one of the processes, which is caused by the pathological disorder previously experienced by a patient. The variable of cortisol level on the day 1, cortisol level on day 7, NIHSS score on the day 1, NIHSS on the day 7, and mortality correlates with one another with various strength. However, if each variable of the cortisol level and NIHSS score is correlated to the mortality, only NIHSS score on the day 7 and mortality is statistically significant. The high death rate in this study is due to the high infection cases at RSUD Dr. Soetomo. The deaths of all deceased patients are caused by lung infection with various microbiological culture results.

Table 6: Difference cortisol level with output number

Var.	Outcome	n	Mean±SD	Minimum	Maximum	p (2 tailed)
K-1	Life	4	32.85±18.25	8.40	50.80	Sig. 0.351
	Die	13	41.77±15.64	5.01	61.45	
K-7	Life	4	28.78±13.35	12.54	45.20	Sig. 0.199
	Die	13	38.97±13.22	6.70	56.70	
N-1	Life	4	15±11.57	5	26	Sig. 0.055
	Die	13	25.23±7.67	13	36	
N-7	Life	4	9±4.61	5	13	Sig. 0.001
	Die	13	25.23±7.67	13	36	

NIHSS: National Institutes of Health Stroke Scale

Table 7: Correlation of NIHSS score and mortality day

NIHSS - day 1	Outcome		Coefficient Cramer's V=0.669, p=0.055 (%)
	Life (%)	Die (%)	
Light	2 (100)	0 (0)	2 (100)
Medium	0 (0)	2 (100)	2 (100)
Weight	1 (16.6)	5 (83.4)	6 (100)
Very heavy	1 (14.3)	6 (85.7)	7 (100)
E	4 (23.5)	13 (76.5)	17 (100)

NIHSS: National Institutes of Health Stroke Scale

Table 8: Correlation of NIHSS score and mortality day 7

NIHSS - day 7	Outcome		Coefficient Cramer's V=0.820, p=0.010 (%)
	Life (%)	Die (%)	
Light	2 (100)	0 (0)	2 (100)
Medium	2 (50)	2 (50)	4 (100)
Weight	0 (0)	5 (100)	5 (100)
Very heavy	0 (0)	6 (100)	6 (100)
E	4 (23.5)	13 (76.5)	17 (100)

NIHSS: National Institutes of Health Stroke Scale

#### AUTHOR(S) CONTRIBUTION

Both the authors contributed equally to this manuscript.

#### CONFLICTS OF INTEREST

The author(s) declare(s) that there are no conflicts of interest regarding the publication of this article.

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