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### RELATIONSHIP BETWEEN ACUTE KIDNEY INJURY WITH MORTALITY IN HOSPITALS IN ACUTE STROKE PATIENTS

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**Keywords:** Acute Kidney Injury, Acute Stroke, Mortality.

#### Abstract

**Background:** Acute kidney injury (AKI) is associated with increased mortality in various clinical conditions. AKI is a free predictor for early mortality or long-term mortality after acute stroke.

**Methods:** Descriptive study on acute stroke patients with AKI during April 2019 - July 2019. AKI diagnosis is based on the Kidney Disease Improving Global Outcomes (KDIGO) criteria.

**Results:** There was no significant relationship between AKI and Mortality value  $p = 0.669$ . No significant relationship was found between blood sugar levels and mortality in acute stroke patients with a  $p$  value = 0.158. There was no significant relationship between leukocytes and mortality in acute stroke patients with a value of  $p = 0.172$ . No significant relationship was found between electrolytes and mortality in acute stroke patients with a value of  $p = 0.652$ .

**Conclusion:** There is no relationship between acute kidney injury and hospital mortality in acute stroke patients.

#### Introduction

Stroke remains a major health problem and it is estimated that there are 700,000 strokes that occur annually in the United States, which cause 160,000 deaths annually, with 4.8 million stroke survivors today.<sup>1</sup> Ischemic cerebrovascular disease is ranked at the top in between the leading causes of death and long-term disability in all developed countries. Preventive measures targeted at major risk factors have reduced the incidence of stroke and mortality rates to date. However, no specific therapy has been developed and proven, which if given immediately after the onset of an acute stroke, will succeed in reducing the level of brain tissue damage and increasing functional outcome<sup>2</sup>.

Acute Kidney Injury (AKI) is defined as sudden damage to kidney function due to increased serum creatinine, decreased urine output, or both<sup>3</sup>. Acute renal failure (ARF) is a syndrome characterized by a sudden decrease in GFR (Glomerular Filtration Rate) with azotemia. Because the onset of ARF is often not visible clinically, it is difficult to study the disease, and there are no national studies of ARF. To date, the incidence and death of ARF is demonstrated from most single data<sup>4</sup>.

Acute kidney injury is associated with increased mortality in various clinical conditions. They examined the incidence, predictors and long-term effects on overall mortality and cardiovascular events after stroke. In addition, kidney dysfunction in patients with symptoms of coronary heart disease or acute stroke has been associated with an increased risk of death and cardiovascular comorbidity. Acute kidney injury is a common complication after an acute stroke. More than a quarter of patients develop AKI in the first 2 days after a stroke. They showed that AKI was a free predictor for early mortality or long-term mortality after acute stroke, after adjusting for chronic kidney disease (CKD) and other factors. In addition, patient survival is only a short time (30 days), and no data are available for new cardiovascular events. Their findings do not reinforce the results of previous studies, but provide additional data for factors that can predict AKI<sup>5</sup>.

#### Method

##### Study sample

All patients with ischemic and hemorrhagic strokes in the acute phase that have been established by history, physical examination, neurological examination and CT examination Head scenarios, kidney function, blood sugar levels, electrolytes are examined by Cobas 6000, which is treated at the Integrated Inpatient Hospital



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(RA4) and Stroke Corner, then taken consecutively and fulfilling the inclusion criteria and there are no exclusion criteria, after that seen dead or not on the 14th day.

### Study design

This research is analytic descriptive with cross sectional data collection method with the data source obtained is primary data from all patients with acute ischemic stroke and acute hemorrhagic stroke who were hospitalized in the Department of Neurology Department FK-USU / H. Adam Malik Hospital Medan.

### Statistical analysis

Research data have been analyzed statistically with the help of the Windows SPSS (Statistical Product and Science Service) computer program. Data analysis and presentation were carried out as follows: To see the demographic characteristics of ischemic stroke and acute phase hemorrhagic stroke patients in the Neurology inpatient room at H. Adam Malik General Hospital Medan, descriptive analysis was used. To see the mortality rate in hemorrhagic stroke with AKI and ischemic stroke with AKI in the Neurology inpatient room at Haji Adam Malik General Hospital Medan, descriptive analysis was used. Chi Square test was used to see the relationship between Acute Kidney Injury and Increased Mortality in Hospitals in Acute Stroke Patients in the Neurology inpatient room at Haji Adam Malik Hospital Medan. Chi Square test was used to see the relationship between blood sugar levels and mortality in acute stroke patients in the Neurology inpatient room at Haji Adam Malik Hospital Medan.

### Result

From all acute stroke patients with AKI treated in the integrated inpatient hospital of H. Adam Malik General Hospital Medan in March 2018 until July 2019, there were 56 patients with acute stroke with AKI who fulfilled the inclusion and exclusion criteria and were included in the study.

Based on the characteristics of 56 research subjects, the average age of 54 - 63 years was 28 subjects (50%), the age range 45 - 53 years was 12 subjects (21.4%), the age range of 64 - 73 years was 10 subjects (17.9% ), and the age range of 74 - 90 years was 6 subjects (10.7%). Research subjects were 34 male subjects (60.7%), and 22 female subjects (39.3%). The education level of research subjects was divided into high school by 30 subjects (53.6%), junior high school by 17 subjects (30.4%), elementary school by 5 subjects (8.9%), undergraduate by 4 subjects (7.1%). Respondents' occupations were divided into private sector by 25 subjects (44.6%), housewives by 10 subjects (17.9%), civil servants by 9 subjects (16.1%), farmers by 7 subjects (12.5%) , retired as many as 5 subjects (8.9%). Risk factors for research subjects with hypertension were 47 subjects (83.9%), hypertension with diabetes myelitus by 8 subjects (14.3%), hypertension with hypercholesterolemia by 1 subject (1.8%). The ethnicity of the research subjects were 25 subjects (44.6%) batak, 13 subjects (23.2%) karo, 12 subjects (21.4%) Javanese, 4 subjects mandailing (7.1) %), and Malay ethnicity as many as 2 subjects (3.6%). Mortality in the study subjects was 50 subjects (89.3%) who did not die and 6 subjects (10.7%) died. Blood Sugar Levels In the study subjects, normal blood sugar levels were 49 subjects (87.5%) and hyperglycemia as many as 7 subjects (12.5%). Leukocytes in the research subjects, normal leukocytes were 36 subjects (64.3%) and those with leukocytosis were 20 subjects (35.7%). Sodium in the research subjects contained hyponatremia in 38 subjects (67.9%) and normal sodium in 18 subjects (32.1%). Potassium in the study subjects were 53 potassium normal (94.6%) and hypokalaemia in 3 subjects (5.4%). Chloride in the study subjects contained normal chloride in 54 subjects (96.4%) and hypochloremia in 2 subjects (3.6%). For complete data on the characteristics of the subjects of this study are presented in table 1.



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Table 1. Characteristics of Research Subjects

Characteristics of respondents	n(56)	Persentase (%)
<b>Age</b>		
45 – 53	12	21,4
54 – 63	28	50,0
64 – 73	10	17,9
74 – 90	6	10,7
<b>Sex</b>		
Male	34	60,7
Female	22	39,3
<b>Education</b>		
Master	4	7,1
High School	30	53,6
Junior High School	17	30,4
Elementary School	5	8,9
<b>Occupation</b>		
Farmer	7	12,5
Government Employees.	9	16,1
Employer	25	44,6
Housewife	10	17,9
Retired	5	8,9
<b>History of Disease</b>		
Hypertension	47	83,9
Hypertension. + Diabetes mellitus	8	14,3
Hypertension.+ Hyperolesterolemia	1	1,8
<b>Race</b>		
Batak	25	44,6
Karo	13	23,2
Jawa	12	21,4
Mandailing	4	7,1
Melayu	2	3,6
Meninggal		
No	6	10,7
Yes	50	89,3
<b>Blood Glucose Level</b>		
Normal	49	87,5
Hyperglycemia	7	12,5
<b>leukocytes</b>		
Normal	36	64,3
Leukocytosis	20	35,7
<b>Sodium</b>		
Hyponatremia	38	67,9
Normal	18	32,1
<b>Potassium</b>		
Hypokalemia	3	5,4
Normal	53	94,6
<b>Chloride</b>		
Hypochloride	2	3,6
Normal	54	96,4



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Based on the mortality characteristics of the research subjects who participated in this study, it was found that died in the research subjects were 6 subjects (10.7%) and did not die as many as 50 subjects (89.3%). There were 4 subjects who died in ischemic stroke and 2 subjects in hemorrhagic stroke. Based on statistical analysis Fisher exact test was used due to the non-fulfillment of the requirements of the chi square test (count expected > 20%), it was found that the results were not significant with a p value of 0.669. Table 2.

*Table 2 Relationship between Acute Kidney Injury (AKI) and mortality in acute stroke.*

	Mortalitas		P value
	Yes	No	
<b>Hemorrhagic Stroke + AKI</b>	4	24	0,669
<b>Ischemic Stroke + AKI</b>	2	26	

*Fisher's exact test*

Based on the characteristics of blood sugar levels in acute stroke patients who took part in the study were obtained subjects with normal blood sugar levels of 49 subjects (87.5%) and subjects with hyperglycemia of 7 subjects (12.5%). Subjects with normal blood sugar levels that died obtained 4 subjects and 45 subjects did not die. Subjects with impaired blood sugar levels died as many as 2 subjects and as many as 5 subjects did not die. From the statistical analysis results, the exact fisher test was used which showed insignificant results with p value of 0.158. Table 3

*Table 3 The relationship between blood sugar levels and mortality in acute stroke patients*

	Mortalitas		P value
	Yes	No	
<b>Normal blood sugar levels</b>	4	45	0,158
<b>Abnormal blood sugar levels</b>	2	5	

*Fisher's exact test*

Based on the characteristics of leukocytes in the respondents who participated in this study it was found that respondents with normal leukocytes were 36 subjects (64.3%) and subjects with leukocytosis were 20 subjects (35.7%). Subjects with disturbed leukocytes died as many as 4 subjects and 16 subjects did not die. In subjects with normal leukocytes, 2 subjects died and 34 subjects did not die. From the statistical analysis Fisher exact test was used which showed insignificant results with a p value of 0.172. Table 4

*Table 4 The relationship between leukocytes and mortality in acute stroke patients*

	Mortalitas		P value
	Yes	No	
<b>Normal leukocytes</b>	2	34	0,172
<b>Abnormal leukocytes</b>	4	16	

*Fisher's exact test*

Based on the characteristics of electrolytes (sodium, potassium, chloride) respondents who participated in the study found respondents with hyponatremia of 38 subjects (67.9%) and subjects with normal sodium as many as 18 subjects (32.1%), respondents with normal potassium were 53 subjects (94.4%) and subjects with hypokalaemia were 3 subjects (5.4%), respondents with normal chloride were 54 subjects (96.4%) and subjects with normal chloride were 2 subjects (3.6%). Subjects with electrolytes disturbed obtained as many as 5 subjects who died and 33 subjects did not die. In subjects with normal electrolytes, there were 1 subjects who died and



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17 subjects did not die. From the statistical analysis, the fisher exact test was used and the results were not significant with a p value of 0.652. Table 5

*Table 5 the relationship between electrolytes and mortality in acute stroke patients*

	Mortalitas		P value
	Yes	No	
<b>Electrolyte Disturbed</b>	5	33	0,652
<b>Normal Electrolytes</b>	1	17	

*Fisher's exact test*

### Discussion

In this study, it was found that the most age range was at age 54 - 63 years as many as 28 subjects (50.0%). Rambe et al (2013) which mention the highest number of subjects in the age group 40 - 59 years (46.5%) and 60 - 79 years (42.5%). Another relevant study by Sidhran et al (2009) mentions that the median age of 541 stroke patients is 67 years, as many as 77% are aged  $\geq 60$  years and 3.8%  $\leq 40$  years. In this study found 34 male subjects (60.7%), more than 22 female subjects (39.3%). The results of this study are relevant to previous studies by Tsagalis (2009) mentioning the characteristics of male gender patient data of 244 subjects (61%)<sup>5,6,7</sup>.

Based on the results of a cross tabulation test between types of stroke AKI patients with mortality obtained, hemorrhagic stroke patients with AKI mortality of 4 subjects and non-mortality of 24 subjects. Whereas in ischemic stroke patients the mortality was 2 subjects and the non-mortality were 26 subjects. Descriptive on the comparison of the number of deaths of stroke patients with AKI it can be concluded that patients with hemorrhagic stroke have a higher mortality rate than ischemic stroke. But statistically, no significant relationship was found because  $p > 0.05$ . This is not in line with research by Khatri et al (2014) mentioning mortality in ischemic stroke in 70 subjects (13%) and mortality in hemorrhagic stroke in 268 subjects (32%). AKI is associated with an increase in hospital mortality in ischemic stroke (odds) ratio (OR) 3.08, 95% CI [1.49-6.35], but not intracerebral hemorrhage (OR) 0.82, 95% CI [1.18-3.77]. kidney function is only checked once upon admission, which is more accurate when kidney function is examined as long as the patient is hospitalized, and can be used as a comparison of the patient's kidney function In the study of Khatri et al (2014) all cases of intracerebral hemorrhage were included in the study and did not take into account the extent of whether or not bleeding, whereas in this study extensive bleeding was calculated / excluded. There are risk factors not cited in this study such as heart failure, where in the research of kathri et al (2014) heart failure as one of the factors a significant cause of death in stroke<sup>3</sup>.

Based on the results of a cross tabulation test between blood sugar levels and mortality in patients with acute stroke obtained subjects with normal blood sugar levels that died obtained 4 subjects and subjects with impaired blood sugar levels who died as many as 2 subjects. Statistically, no significant relationship was found with the value of  $p = 0.158$ . This study is not in line with Al-Weshahy (2017) mentions 60.7% of men with an average age of  $62.9 \pm 10.5$  years. Patients with hyperglycemia had a higher incidence than controls (19.5% vs 0%,  $p = 0.03$ ). NIHSS was statistically higher than control ( $14.9 \pm 5.9$  vs,  $7.8 \pm 3.5$   $p = .000$ ). The mortality and hospitalization rates in the hospital were higher than controls (65.9% vs 5.0%  $p < 0.001$  and  $12.5 \pm 9.1$  vs  $3.0 \pm 4.2$  days,  $p < 0.001$ ). NIHSS (National Institutes of Health Stroke Scale) score, and 30-day mortality higher in hyperglycemic stress compared with diabetics ( $17 \pm 5.1$  vs  $12.7 \pm 6.1$   $p = 0.018$  and 85.7% vs 45%  $p = 0.006$ ). Predictors of death for 30 days were a history of hypertension ( $p = 0.04$ ), NIHSS 10 (91% sensitivity and 100% specificity) and blood sugar levels at admission  $> 223$  mg / dl (63% sensitivity and 96% specificity). In conclusion, hyperglycemia is associated with poor outcomes in acute stroke. History of hypertension, blood sugar level  $> 223$  mg / dl and NIHSS  $> 10$  are predictors of stroke severity. In the Al-Weshahy study (2017) the patients studied had an NIHSS value  $> 10$  and a blood sugar level at admission  $> 223$  mg / dl. Where patients in the Al-Weshahy study patients included moderate to severe stroke who participated in the study and patients with hyperglycemia which were predictors of the severity of the stroke that caused death. In this study the NIHSS value was not calculated and the blood sugar levels of the patients at admission were not all with hyperglycemia so there was no significant relationship between blood sugar levels and mortality in acute stroke<sup>8</sup>.



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Based on the results of the cross tabulation test between leukocytes and mortality in patients with acute stroke, there were 4 subjects with disturbed leukocytes who died as many as 4 subjects and 16 subjects who did not die. In subjects with normal leukocytes, 2 subjects died and 33 subjects did not die. Where not found a significant relationship with the value of  $p = 0.172$ . This study is in line with Zia (2012) stating the value of the Hazard ratio for mortality for 1 year is 1.7 (95% CI: 1.02-2.8) and 0.9 (95% CI: 0.5-1, 8). Where the relationship between total leukocyte values is not significant with the death rate for 1 year in stroke patients<sup>9</sup>.

Based on the results of the cross tabulation test between electrolytes and mortality in acute stroke patients, it was found that subjects with normal electrolytes died by 1 subject and 17 subjects did not die. In subjects with electrolytes disturbed, there were 5 subjects who died and 33 subjects did not die. Where no significant relationship was found with the value of  $p = 0.652$ . This study is in line with Kembuan (2014) stating there is no significant relationship between the electrolyte disturbed by the severity of the stroke with a  $p$  value  $> 0.005$ <sup>10</sup>.

### Conclusion

An insignificant result was found a relationship between acute kidney injury and mortality in acute stroke patients with a  $p$  value of 0.669. An insignificant result was found a relationship between blood sugar levels and mortality in acute stroke patients with a  $p$  value of 0.158. An insignificant result was found an association between leukocytes and mortality in patients with acute stroke with a  $p$  value of 0.172. An insignificant relationship was found between electrolytes and mortality in acute stroke patients with a  $p$  value of 0.652. The mortality rate of acute hemorrhagic stroke with AKI is higher than that of acute ischemic stroke with AKI.

### Suggestion

Further research is needed regarding the factors that influence mortality, namely confounding control such as aspiration, cardiac arrest, nosocomial infection, follow-up of blood sugar levels, leukocytes, electrolytes during treatment in acute stroke with AKI. Also seen are factors affecting mortality in stroke such as heart failure, extensive bleeding.

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