


The Association of Nutrition Status Towards The Outcome of Acute Ischemic Stroke Patients with Type-2 Diabetes Mellitus

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ABSTRACT

Introduction: Stroke is a sudden-onset neurologic deficit and having a type 2 diabetes increases the risk of stroke twice as much. In addition to affecting physical and mental abilities, stroke can also lead to a decline in nutritional status. Malnutrition is associated with poor functional outcomes in all stroke subtypes. The Controlling Nutritional Status (CONUT) score is an objective nutritional marker and could reflect malnutrition due to its comprehensive assessment of nutritional status. This study aims to find the association between nutritional status towards the outcome of acute ischemic stroke patients with type 2 diabetes.

Method: This was an observational analytic study with prospective cohort design using primary data collected consecutively from patients with both acute ischemic stroke and type 2 diabetes mellitus who were hospitalized in the Stroke Corner Room, Intensive Care Unit (ICU) and inpatient ward of Haji Adam Malik General Hospital who met the inclusion criteria. The nutritional statuses of patients were measured using the CONUT score and patients outcomes were measured by mRS score. Spearman correlation test was used to assess the association between nutritional status and outcome of acute ischemic stroke patients with type 2 diabetes mellitus.

Results: There were 43 patients who met the inclusion criteria where the majority of patients were male 22 people (51.2%), in the age group 51-65 years 23 people (53.5%) with a mean age of 57.93 + 10.01, was a housewife 15 people (34.9%) and Bataknese 27 people (62.8%). The majority of patients in this study had mild malnutrition with a total of 15 people (34.9%) and a median CONUT score of 3 (0-11) and poor outcome as many as 29 people (67.4%) with mRS score median 4 (0-6). The result of Spearman correlation test showed a significant correlation between nutritional status and the outcome of acute ischemic stroke patients with type 2 diabetes mellitus with a moderate correlation.

Conclusion: There was a significant correlation between nutritional status and the outcome of acute ischemic stroke patients with type 2 diabetes mellitus with a moderate correlation


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INTRODUCTION

Stroke is a sudden-onset neurological deficit that affects 33 million people annually in the world and more than half of them are experienced in developing countries [1]. According to the Global Burden of Disease (GBD), stroke is the second leading cause of death and disability in the world after coronary heart disease [2].

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In 2012, the World Health Organization (WHO) stated that 6.7 million people died from stroke. Based on Riset Kesehatan Dasar (Riskesdas) in 2018, stroke is the leading cause of death in Indonesia [3].

Stroke is characterized by neurological deficits associated with acute focal injury of the central nervous system (CNS) by vascular causes, including cerebral infarction, intracerebral hemorrhage (ICH), and subarachnoid hemorrhage (SAH). Ischemic stroke is an episode of neurological dysfunction caused by focal cerebral, spinal or retinal infarction [4].

The presence of diabetes mellitus (DM), hypertension, and dyslipidemia are known to be major risk factors for stroke [5]. Having a history of type 2 DM increases the risk for ischemic stroke by two times. In addition, the prognosis of stroke in DM is worse, including higher disability rates and slower recovery. Patients with type 2 DM have a 20% higher risk of mortality or showing worse neurological deficits than patients without type 2 DM [5].

In addition to affecting physical and mental abilities, stroke can also lead to a decline in nutritional status. Nutritional status after stroke can negatively impact functional recovery and mortality rates. Nutritional deficits are found to be around 6-31% before stroke and tend to worsen during hospitalization [6].

Malnutrition is a common condition among patients suffering from stroke, and is often associated with micronutrient and micronutrient deficiencies, unhealthy behaviors and low socioeconomic status. Diabetes mellitus on admission is known to be associated with a 58% increased risk of malnutrition. In addition, diabetes mellitus is also known to be associated with dysphagia, which directly interferes with the patient's nutritional intake [7].

Several studies have reported the effect of malnutrition on the severity or prognosis of ischemic stroke patients. Shiga et al. reported that the prevalence of malnutrition ranged from 8% to 34% in acute ischemic stroke patients [8]. As based on the results of Coban's analysis, of 318 patients with acute stroke, the prevalence of stroke patients who experienced malnutrition was 66.1% in patients aged > 65 years, and 12.2% of patients aged < 65 years [9]. Naito et al. showed that malnutrition was associated with poor functional outcomes in all stroke subtypes [10].

The Controlling Nutritional Status (CONUT) score is an objective nutritional marker consisting of albumin concentration, lymphocyte count, and total cholesterol. CONUT scores are obtained from blood tests and reflect malnutrition due to the comprehensive assessment of nutritional status [11]. Cai et al. reported the risk of malnutrition assessed by Nutritional Risk Screening Tool 2002 (NRS-2002) and CONUT can predict poor clinical outcome at 3 months in acute ischemic stroke patients [12].

Based on the description above, the researchers are interested in conducting research on the association of nutritional status towards the outcome of acute ischemic stroke patients with type 2 DM.

METHOD

This was an observational analytic study with a prospective cohort design using primary data collected consecutively from patients with acute ischemic stroke with type 2 diabetes mellitus who were hospitalized in the stroke corner room, intensive care unit (ICU) and inpatient ward of Haji Adam Malik General Hospital in October 2021 - September 2022 with the aim of finding the association between nutritional status towards the outcome of acute ischemic stroke patients with type 2 diabetes mellitus.

Subjects who participated in the study were patients who met the inclusion criteria, which are acute ischemic stroke patients with type 2 DM based on medical history, physical examination, neurological examination, laboratory examination and CT-scan examination and agreed to participate in this study by signing informed consent. The exclusion criteria in this study were patients with factors that could affect the CONUT score such as sepsis, nosocomial infection, acute and chronic renal failure, impaired liver function, and chronic diseases such as malignancy, HIV/AIDS, and tuberculosis and patients who could not be followed-up on day 14 after the onset of acute ischemic stroke.

CT scan examination in this study used X-Ray CT System, Hitachi brand W 450 series. Lymphocyte levels were measured using SYSMEC XN-1000, total cholesterol levels were measured using Architect c6000,

and albumin levels were measured using Architect c8000. After these three levels were measured, the CONUT score was calculated by summing up the scores of albumin, total cholesterol and lymphocyte levels, as categorized by the CONUT score. CONUT score was calculated on the first day. Stroke outcome was assessed on day 14 after the onset of acute ischemic stroke using the MRS score.

Univariate analysis in this study was conducted to analyze the demographic characteristics of subjects. Numerical variables are presented by displaying the mean, standard deviation, median, (minimum-maximum).

Bivariate analysis in this study was conducted to analyze the relationship between the research variables, in this case to determine the association between nutritional status and the outcome of acute ischemic stroke patients with type 2 DM, the Spearman correlation test was used.

RESULTS

Characteristics of Study Subjects

In table 1, 22 people were male (51.2%) and 21 people (48.8%) were female. There were 12 people (27.9%) who aged 36- 50 years old , 23 people (53.5%) aged 51-65 years old, 7 people (16.3%) aged 66-80 years old, and 1 person aged ≥ 81 years (2.3%) with an overall average age of 57.93 ± 10.01 years. In this study, patients had various occupations, patients who were housewives amounted to 15 people (34.9%), civil servants amounted to 6 people (14%), self-employed amounted to 8 people (18.6%), private employees amounted to 4 people (9.3%), farmers amounted to 2 people (4.7%), military / police amounted to 3 people (7%), and retirees amounted to 6 people (14%).

The majority of patients in this study were Batakese (27 people (62.8%)), followed by Javanese (8 people (18.6%)), Aceh ethnicity 5 people (11.6%), Padang ethnicity 2 people (4.7%) and Nias 1 person (2.3%). Glycemic status in this study obtained a median HbA1c value of 8.3 (5.3 - 17.9)%.

Table 1. Characteristics of research subjects

| Demographics of stroke patients | Mean \pm SD | n = 43 (%) |
|---------------------------------|-------------------|-------------------|
| Gender | | |
| • Male | | 22 (51.2) |
| • Female | | 21 (48.8) |
| Age Group | 57.93 \pm 10.01 | |
| • 36-50 | | 12 (27.9) |
| • 51-65 | | 23 (53.5) |
| • 66-80 | | 7 (16.3) |
| • ≥ 81 | | 1 (2.3) |
| Occupation | | |
| • Housewife | | 15 (34.9) |
| • Civil servant | | 6 (14) |
| • Self-employed | | 8 (18.6) |
| • Private employee | | 4 (9.3) |
| • Farmer | | 2 (4.7) |
| • Military / police | | 3 (7) |
| • Retiree | | 6 (11.6) |
| Ethnicity | | |
| • Aceh | | 5 (11.6) |
| • Batak | | 27 (62.8) |
| • Jawa | | 8 (18.6) |
| • Padang | | 2 (4.7) |
| • Nias | | 1 (2.3) |
| Glycemic Status | | |
| • HbA1c | | 8.3 (5.3 – 17.9)% |

Characteristics of Nutritional Status of Study Subjects

The albumin level of patients in this study were classified based on the category of CONUT score , in which there were 18 patients (41.9%) with albumin levels >3.5 g/dL , 6 patients (14%) with albumen levels of 3-3.49 g/dL , 2.5-3 g/dL numbered 11 people (25.6%), and 8 people (18.6%) with albumin levels <2.5 g/dL. The cholesterol level of patients in this study is divided based on the category of CONUT score, where it is

known that there were 21 patients (48.8%) with cholesterol levels >180 mg/dL, 11 people (25.6%) with cholesterol levels 140-180 mg/dL, 7 people with cholesterol levels 100-139 mg/dL (16.3%), and 4 people with cholesterol levels <100 mg/dL (9.3%). The lymphocyte level of patients in this study were also divided based on the CONUT score category, where it was known that patients with lymphocyte levels ($103/\mu\text{L}$) >1.6 amounted to 25 people (58.1%), 1.2-1.59 amounted to 9 people (20.9%), 0.8-1.19 amounted to 6 people (14%), and <0.8 amounted to 3 people (7%) (Table 2).

In this study, it is known that the patients' CONUT score show the interpretation of their nutritional statuses, where it is known that 11 patients (25.6%) had normal nutritional status, 15 patients (34.9%) had mild malnutrition, 10 patients (23.3%) had moderate malnutrition, and 7 patients (16.3%) had severe malnutrition.

Table 2. Descriptive Characteristics of Nutrition Parameters and Nutrition Status of Study Subjects

| Patient's nutritional status | n = 43 (%) |
|--|------------|
| Albumin (g/dL) | |
| • ≥ 3.5 | 18 (41.9) |
| • 3-3.49 | 6 (14) |
| • 2.5 -3 | 11 (25.6) |
| • < 2.5 | 8 (18,6) |
| Cholesterol (mg/dL) | |
| • > 180 | 21 (48.8) |
| • 140-180 | 11 (25.6) |
| • 100-139 | 7 (16.3) |
| • < 100 | 4 (9.3) |
| Limfosit ($\times 10^3/\mu\text{L}$) | |
| • $\geq 1,6$ | 25 (58.1) |
| • 1.2-1.59 | 9 (20.9) |
| • 0.8-1.19 | 6 (14) |
| • < 0.8 | 3 (7) |
| Status nutrition | |
| • Normal | 11 (25.6) |
| • Mild malnutrition | 15 (34.9) |
| • Moderate malnutrition | 10 (23.3) |
| • Severe malnutrition | 7 (16.3) |

In this study, the Shapiro-Wilk test was used to see the normality of these parameters because the sample size was <50 people. From table 3. it was found that albumin and cholesterol parameters were normally distributed ($p>0.05$) but lymphocyte parameters and CONUT score were not normally distributed ($p<0.05$). In this study, the mean albumin was 3.18 ± 0.76 g/dL and the mean cholesterol was 177.13 ± 54.44 mg/dL. For lymphocytes and CONUT score, the median was $1.8\times 10^3/\mu\text{L}$ (0.66-20.8) and 3 (0-11).

Table 3. Characteristics of Nutrition Parameters of Study Subjects

| Nutrition parameter | Mean \pm SD | Median | Minimum | Maksimum | p value |
|--|-------------------|--------|---------|----------|---------|
| Albumin (g/dL) | 3.18 ± 0.76 | 3.1 | 1,6 | 4,9 | 0.889* |
| Cholesterol (mg/dL) | 177.12 ± 54.43 | 178 | 67 | 283 | 0.577* |
| Lymphocyte ($\times 10^3/\mu\text{L}$) | | 1.8 | 0.66 | 20.8 | 0.000* |
| CONUT score | | 3 | 0 | 11 | 0.001* |

*Shapiro-Wilk test

Outcome Characteristics of the Study Subjects

Based on table 4. it was found that the majority of patients in this study had a poor stroke outcome with a total of 29 patients (67.4%) and obtained a median mRS score of 4 (0-6).

Table 4. Characteristics of Stroke Outcome of Study Subjects

| | Outcome stroke | n=43(%) |
|------|----------------|------------|
| Good | | 14 (32,6%) |
| Poor | | 29 (67,4%) |

Table 5. Characteristics of mRS Score of Study Subjects

| Outcome parameter | Median | Minimum | Maksimum | <i>p value</i> |
|-------------------|--------|---------|----------|----------------|
| mRS Score | 4 | 0 | 6 | 0,011* |

*Shapiro-Wilk test

Association between Nutritional Status towards Stroke Outcome

Statistical analysis tests were carried out on 43 research samples in assessing the relationship between nutritional status and the outcome of acute ischemic stroke patients with type 2 diabetes mellitus. In this study, the CONUT score data to assess nutritional status with the mRS score to assess stroke outcome had been tested for normality ($p < 0.05$) and it was shown that none of the data were normally distributed, so the correlation test used in this study was the Spearman correlation test.

Based on the Spearman correlation test in table 6. This study shows that there was a significant and unidirectional relationship between nutritional status and outcome of acute ischemic stroke patients with type 2 diabetes mellitus with moderate correlation strength ($r = 0.57$, $p < 0.001$). There was a unidirectional relationship between the two variables, thus it can be interpreted that the more severe the malnutrition condition, the worse the outcome of acute ischemic stroke patients with type 2 diabetes mellitus is.

Table 6. Association between Nutritional Status towards Stroke Outcome

| | Stroke Outcome (mRS score) |
|-------------------------------------|--|
| Nutritional status (CONUT score) | $r = 0,570$ $p < 0.001$ $n = 43$ |

Note: Spearman correlation test

DISCUSSION

Characteristics of Acute Ischemic Stroke Patients with Type 2 Diabetes Mellitus

Based on demographic data, the majority of the subjects of this study were male with 22 patients (51.2%). These results differ from study by Rambe et al. (2013) which found that women were more at risk of strokes (52.7%) and study by Ritarwan et al. (2016) which also found that more women had ischemic stroke (55.1%) [13-14]. The reason behind this result is that the subjects in the study were ischemic stroke patients with type 2 diabetes mellitus, where the prevalence of diabetic patients is higher in men than women [15].

Cerebral ischemia triggers a cascade of pathological events such as excitotoxicity, cell necrosis, apoptosis, inflammation, blood-brain barrier damage, etc., ultimately culminating in cellular dysfunction and death. Although much progress has been made in tracing the molecular pathways of pathological processes such as excitotoxicity, oxidative stress, inflammation, and apoptosis after ischemic stroke, there is still no effective therapy. However, evidence is emerging to suggest that gender differences occur in certain aspects of these pathological cascades, including in the activated molecular pathways, leading to cell death and various aspects of peripheral and brain inflammatory responses, despite gender being overlooked in most experimental studies [16].

A number of studies report gender differences in mortality and morbidity after ischemic stroke. Typically, stroke affects women at an older age than in men. Therefore, they are more likely to contribute to most stroke-related deaths and disability. Data on gender differences in mortality rates after ischemic stroke are conflicting with some studies reporting higher in-hospital mortality rates in women, whereas others report no difference in mortality rates between genders either in-hospital or at 3 months after ischemic stroke.

However, the general consensus is that women have worse functional outcomes, compared to men, after ischemic stroke [16].

Most patients in this study were in the age range of 51-65 years with a total of 23 patients (53.5%). This is in accordance with study by Pranata (2020) which found that most stroke patients were in the age range of 51-<66 years with 18 subjects (35.6%) [17]. Study by Apriani et al. (2020) also found that acute ischemic stroke patients were in the age range of 55-<65 years (55.3%) [18]. Aging is the most powerful non-modifiable risk factor for stroke incidence, which doubles every 10 years after age 55. With age, the micro- and macrocirculation of the brain undergoes structural and functional changes. Age-related microcirculatory changes are thought to be mediated by endothelial dysfunction and impaired cerebral autoregulation and neurovascular coupling. Aging is therefore associated with several apparent changes in intracranial and extracranial cerebral arteries that may predict the risk of a future stroke event [19].

The majority of patients in this study were housewives with 15 patients (34.9%). The same results were also found in the study by Rambe et al. (2012) which found that the most common type of occupation in stroke patients was housewives as many as 200 patients (35.6%) and study by Barus et al. (2021) which found the majority of jobs as housewives [20]. The majority of patients were Batakese with 27 patients (62.8%). These results are in accordance with research by Apriani et al. (2020) which found that the majority of stroke patients were Batakese with a total of 25 patients (65.8%) [18].

In this study, the patient's glycemic status was obtained with a median HbA1c value of 8.3 (5.3 - 17.9) %. Measurement of HbA1c in every ischemic stroke patient is very important. Higher blood HbA1c levels leads to a more serious neurological disorders and a worse prognosis after three months. Long-term high blood glucose, as well as high blood HbA1c can cause large vessel lesions and microangium, and cause the oxygen dissociation curve to the left, resulting in oxygen dissociation barrier, nerve tissue ischemia and hypoxia [21]. Patients with HbA1c > 6.5 have higher NIHSS scores. Thus, HbA1c affects the severity of ischemic stroke and was found to be statistically significant. The study conducted by Das et al. showed that hyperglycemia is a poor prognostic marker in stroke [22].

Nutritional Parameter Characteristics of Acute Ischemic Stroke Patients With Type 2 Diabetes Mellitus

In this study, nutritional parameters such as albumin, cholesterol and lymphocytes were grouped according to the criteria of the CONUT score. For the nutritional status of patients, grouped based on the scoring of the CONUT score. The majority of patients in this study belonged to the group of patients with albumin levels >3.5 g/dL with a total of 18 people (41.9%) and the average overall albumin level in this study was 3.19 + 0.76 g/dL. This is in line with research by Manickam et al. (2019) and research by Gaurav et al. (2014) which also obtained an average albumin level of >3.5 g/dL [23,24]. The majority of ischemic stroke patients have albumin levels > 3.5g/dL and have a good outcome. The albumin value in the results of this study is a factor that plays a role among cholesterol and lymphocyte values on the CONUT score.

It is well known that serum albumin plays an important role in the clinical outcome of vascular diseases. The neuroprotective effect of albumin is due to various properties of albumin such as anti-inflammatory and antioxidant effects, as well as inhibition of thrombosis in the microcirculation. Albumin also reduces hematocrit levels and also plays an important role in erythrocyte aggregation. Other neuroprotective effects of albumin in stroke include preventing thrombosis and preventing leukocyte adhesion in the early reperfusion phase [23].

Experimental studies in mice by Belayev et al. presented by Manickam et al. showed high-dose albumin therapy, if administered within 2 to 4 hours after stroke onset, was highly effective in improving neurological status and reducing infarct volume as well as reducing brain swelling [23].

The results of a study by Kasundra et al. indicated that higher serum albumin levels are associated with a better short-term prognosis. Therefore, serum albumin levels can be used as an indicator of short-term prognosis [83]. The study by Nair et al. also supports the fact that high serum albumin levels are associated with better functional outcome after acute ischemic stroke [25].

The majority of patients with good outcomes have lower NIHSS scores, low mRS scores, high albumin and small infarct volumes. This is in line with the results in this study where the majority of patients with high albumin levels had a good outcome. According to Manickam et al. not only serum albumin but infarct volume also plays a role in the final outcome of stroke patients [23].

The majority of patients in this study belonged to the group of patients with cholesterol levels >180 mg/dL with a total of 21 people (48.8%) and the average total cholesterol level was 177.13 ± 54.44 mg/dL. In this study, patients with dyslipidemia with cholesterol-LDL values ≥ 140 mg/dl, triglycerides ≥ 150 mg and or cholesterol-HDL < 40 mg/dl were still included as research subjects but the patient's dyslipidemia status was not analyzed.

The average cholesterol in this study is in line with research by Koton et al. (2012) which obtained the overall average patient cholesterol of 195.3 ± 48.3 mg/dL and Markaki et al. (2014) who got the overall average patient cholesterol of 177.88 ± 46.4 mg/dL [26,27]. Research by Koton et al. (2012) and Markaki et al. (2014) stated that high cholesterol levels are associated with better acute ischemic stroke outcomes. The key mechanism of stroke pathophysiology can induce a systemic catabolic imbalance accompanied by disruption of metabolic efficiency and degradation of body tissues. Low cholesterol is associated with a complex set of conditions related to sarcopenia and inflammation. Low cholesterol levels can also lead to a reversal of stroke risk factors, in line with the obesity paradox after a stroke [26].

In addition, the neuroprotective properties of cholesterol have been reported in animal studies. Cholesterol has a free radical neutralizing effect which may limit the extent of ischemic damage. Hypercholesterolemic mice appear more resistant to lethal hypoxia, and cholesterol levels have been correlated with survival of mice that have been exposed to hypoxic conditions. Downregulation of vascular endothelial growth factor has been proposed as the cause of such survival [26]. However, in this study, the majority of patients with high total cholesterol levels had a poor outcome because the majority of them were malnourished.

The majority of the patients in this study belonged to the group of patients with lymphocyte levels > $1.6 \times 10^3/\mu\text{L}$ with a total of 25 people (58.1%), with a median overall lymphocyte level of $1.8 \times 10^3/\mu\text{L}$ (0.66-20.8). In acute ischemic stroke, tissue hypoxia induces an inflammatory reaction in the brain parenchyma. The pathophysiological process after stroke onset is known to be caused by leukocyte infiltration and release of inflammatory mediators. This contributes to neuronal death or apoptosis [28].

Several experiments in mice have shown that increased lymphocyte levels upregulate the anti-inflammatory cytokine interleukin (IL)-10 and suppress proinflammatory cytokines, including IL-6 and tumor necrosis factor (TNF)- α , thus inducing a protective effect on nerves. Research by Juli et al. (2021) reported that low lymphocyte levels were associated with poor neurological outcome based on the NIHSS scale. Therefore, lymphocytes as a subtype of leukocytes play an important role as a mediator and can be used as a predictor of neurological outcome [28]. In this study, the majority of patients had high lymphocyte levels, but the majority of them had a poor outcome. This is because the majority of patients with high lymphocyte levels experienced malnutrition.

Association between Nutritional Status towards The Outcome of Acute Ischemic Stroke Patients with Type 2 Diabetes Mellitus

The majority of patients in this study were patients with mild malnutrition, with a total of 15 people (34.9%) and had a poor outcome with a total of 29 patients (67.4%). This study also found a significant unidirectional relationship between nutritional status and the outcome of acute ischemic stroke patients with type 2 diabetes mellitus with moderate correlation strength ($r = 0.57$, $p < 0.001$). This is in line with study by Naito et al. (2020) which reported that there is a relationship between nutritional status and ischemic stroke outcome [10]. Study by Cai et al. (2020) also reported that the risk of malnutrition obtained from the CONUT score can predict poor outcomes in acute ischemic stroke patients [12].

Assessment of nutritional status using the CONUT score has several advantages. First, the CONUT score can be calculated from three blood test parameters: serum albumin, lymphocytes and total cholesterol

levels. These three parameters are objective indicators that can be easily measured from blood samples, thus making the CONUT score efficient and reliable. Secondly, in a study by Cai et al., it was reported that more patients were at risk of malnutrition when assessed using the CONUT score compared to the NRS-2002 score, indicating that the CONUT score has better sensitivity [12].

In the study by Akimoto et al. the CONUT score and GNRI (Geriatric Nutritional Risk Index) score were used as tools to assess malnutrition. However, in their study, only the CONUT score served to assess the prognosis of patients after an acute ischemic stroke event [29]. Several previous studies reported that the GNRI score is associated with poor prognosis and showed good ability in predicting patient prognosis after hospital discharge. However, these studies evaluated the outcome three months after the acute ischemic stroke event, whereas in the study by Akimoto et al. the patient's prognosis was assessed at the time of hospital discharge, which is usually 5 to 181 days from the first day of hospital admission; which is shorter than the aforementioned studies. Therefore, they concluded that the CONUT score may function better than the GNRI score in predicting the short-term prognosis of acute ischemic stroke patients [29].

The reason why there is a difference between the outcome analysis between these two scores is because the CONUT score includes lymphocyte levels in its evaluation. Lymphocyte levels are considered to be a factor indicating depression of the immune system, and a decrease in lymphocyte levels can lead to an infection such as pneumonia. In a study by Akimoto et al, patients who were assessed for malnutrition with the help of the CONUT score suffered more pneumonia, so it can also be concluded that the CONUT score can be useful in predicting pneumonia complications in stroke patients [88]. In the management of stroke patients, clinicians often do not consider nutritional support in stroke patients, so the nutritional status of patients is often neglected [30]. Approximately 6-31% of nutritional deficits are found before stroke and tend to worsen during hospitalization. One way to overcome nutritional problems in stroke patients is by providing oral nutritional supplementation [6]. In the study by Barus et al. (2021), there is a significant difference in energy intake between the treatment group given oral nutritional supplementation and the control group ($p=0.012$) [30].

The limitations of this study are; it does not analyze factors that can affect the nutritional status of acute ischemic stroke patients including age, gender, smoking, history of drinking alcohol; comorbid diseases that can affect the nutritional status of patients such as anemia, hypertension, dyslipidemia, coronary heart disease, atrial fibrillation and neurological deficit conditions such as decreased consciousness, dysphagia, aphasia and the use of NGT tubes in patients. This study also did not analyze other factors that may affect stroke outcome such as the patient's glycemic status and infarct volume, lesion area, lesion location or stroke subtype. In addition, the study time was relatively short at 14 days after stroke onset where previous studies assessed the outcome of acute ischemic stroke within 3 months after the onset of ischemic stroke.

CONCLUSION

There is a significant association between nutritional status towards outcome of acute ischemic stroke patients with type 2 diabetes mellitus with moderate correlation strength ($r = 0.57$, $p < 0.001$).

DECLARATIONS

Ethics approval and consent to participate. Permission for this study was obtained from the Ethics Committee of Universitas Sumatera Utara and H. Adam Malik General Hospital..

CONSENT FOR PUBLICATION

The Authors agree to publication in Journal of Society Medicine.

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COMPETING INTERESTS

None.

AUTHORS' CONTRIBUTIONS

All authors significantly contribute to the work reported, whether in the conception, study design, execution, acquisition of data, analysis, and interpretation, or in all these areas. Contribute to drafting, revising, or critically reviewing the article. Approved the final version to be published, agreed on the journal to be submitted, and agreed to be accountable for all aspects of the work.

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REFERENCE

1. Bender M, Jusufovic E, Railic V, Kelava S, Tinjak S, Dzevdetbegovic D, et al. High burden of stroke risk factors in developing country: the Case Study of Bosnia-Herzegovina. *Mater Sociomed*. 2017; 29(4):277-9.
2. Zhang FL, Guo ZN, Wu YH, Liu HY, Luo Y, Sun MS, et al. Prevalence of stroke and associated risk factors: a population based cross sectional study from northeast China. *BMJ Open*. 2017; 7(9):1-11.
3. Kementerian Kesehatan RI Badan Penelitian dan Pengembangan. Hasil utama riset kesehatan dasar Tahun 2018. Kementerian Kesehatan Republik Indonesia. 2018; 1–100.
4. Sacco RL, Kasner SE, Broderick JP, Caplan LR, Connors JJ, Culebras A, et al. An updated definition of stroke for the 21st Century: a statement for healthcare professionals from the American Heart Association/American Stroke Association. *AHA Journals*. 2013; 44(7):2064–89.
5. Tziomalos K, Dimitriou P, Bouziana SD, Spanou M, Kostaki S, Angelopoulou SM, et al. Stress hyperglycemia and acute ischemic stroke in hospital outcome. *Metabolism Journal*. 2017; 67:99–105.
6. Foley N, Teassel R, Marina R, Wiener J, Finestone H. Nutritional interventions following stroke. *Neurorehabilitation and Neural Repair*. 2018; 1–42.
7. Corrigan ML, Escuro AA, Celestin J, Kirby DF. Nutrition in the stroke patient. *Nutrition in Clinical Practice*. 2011; 26(3):242–52.
8. Shiga Y, Nezu T, Hosomi N, Aoki S, Nishi H, Naito H, et al. Effect of tooth loss and nutritional status on outcomes after ischemic stroke. *Nutrition*. 2019;5-14.
9. Çoban E. Malnutrition Rate in Stroke Patients on Admission. *Med Bull Sisli Etfal Hosp*. 2019; 53(3):272–275. doi: 10.14744/SEMB.2018;81994.
10. Naito H, Hosomi N, Nezu T, Kuzume D, Aoki S, Morimoto Y, et al. Prognostic role of the controlling nutritional status score in acute ischemic stroke among stroke subtypes. *Journal of the Neurological Sciences*. 2020;416:1-6.
11. Xiang W, Chen X, Ye W, Li J, Zhang X, Xie D. Prognostic nutritional index for predicting 3-month outcomes in ischemic stroke patients undergoing thrombolysis. *Frontiers in Neurology*. 2020; 11:1–7.
12. Cai ZM, Wu YZ, Chen HM, Feng RQ, Liao CW, Ye SL, et al. Being at risk of malnutrition predicts poor outcomes at 3 months in acute ischemic stroke patients. *European Journal of Clinical Nutrition*. 2020; 74(5):796–805.
13. Rambe AS, Fithrie A, Nasution I dan Tonam. Profil pasien stroke pada 25 rumah sakit di Sumatera Utara 2012 survei berbasis rumah sakit. *Neurona*. 2013;30(2).
14. Ritarwan K, Yenita Y. Nilai Prognostik Parameter Fibrinogen dan Uji Reliabilitas terhadap Outcome Stroke Iskemik Akut. 2017;2(2):11.
15. Nordström A, Hadrévi J, Olsson T, Franks PW, Nordström P. Higher Prevalence of Type 2 Diabetes in Men Than in Women Is Associated With Differences in Visceral Fat Mass. *J Clin Endocrinol Metab*. 2016;101(10):3740-3746. doi:10.1210/jc.2016-1915

16. Gibson CL. Cerebral Ischemic Stroke: is Gender Important?. *J Cereb Blood Flow Metab.* 2013;33(9):1355–61.
17. Pranata H, Sinurat PPO, Batubara CA. Hubungan Rasio Neutrofil Limfosit dan High Sensitivity C-Reactive Protein Dengan Keparahan Dan Outcome Pada Pasien Stroke Iskemik Akut. Universitas Sumatera Utara. 2022.
18. Apriani N, Sinurat PPO, Kadri A. Changes in platelet aggregation and nihss after anti-platelet therapy for acute ischemic stroke patients at H.Adam Malik General Hospital Medan. *IJRSM.* 2020;7(8):45–50.
19. Yousufuddin M, Young N. Aging and ischemic stroke. *Aging.* 2019 (9):2542–4.
20. Barus LI, Fithrie A, Batubara CA. Perbandingan Asupan Nutrisi dan Keparahan pada Pasien Stroke Iskemik Akut dengan dan Tanpa Pemberian Suplementasi Nutrisi Oral. Tesis. Universitas Sumatera Utara. 2021.
21. Patibandla S, Appikatla T, Jayasingh K. Study of the severity of stroke at the time of presentation in diabetic patients correlating with glycemic control. *Int J Adv Med.* 2017;4(2):396-400.
22. Das PP. Glycemic status in acute stroke in relation to its severity and outcome. *Journal of Medical Science and clinical Research.* 2019;7(3):1122– 30.
23. Manickam S, Franklin J, Petchiappan V, Menon S. A Study of Serum Albumin Levels in Acute Ischemic Stroke and its Correlation with Clinical Outcome. *IJCMR.* 2019;6(3).
24. Kasundra G, Sood I. Prognostic Significance Of Serum Albumin Levels In Acute Ischemic Stroke. 2014; 5(4).
25. Nair R, Radhakrishnan K, Chatterjee A, Gorthi SP, Prabhu VA. Serum Albumin as a Predictor of Functional Outcomes Following Acute Ischemic Stroke. 2018; 10(4).
26. Koton S, Molshatzki N, Bornstein NM, Tanne D, on behalf of the NASIS Investigators. Low Cholesterol, Statins and Outcomes in Patients with First- Ever Acute Ischemic Stroke. *Cerebrovasc Dis.* 2012 ;34(3):213–20.
27. Markaki I, Nilsson U, Kostulas K, Sjöstrand C. High Cholesterol Levels Are Associated with Improved Long-term Survival after Acute Ischemic Stroke. *Journal of Stroke and Cerebrovascular Diseases.* 2014 ;23(1):e47–53.
28. Juli C, Heryaman H, Nazir A, Ang E-T, Defi IR, Gamayani U, et al. The Lymphocyte Depletion in Patients with Acute Ischemic Stroke Associated with Poor Neurologic Outcome. *International Journal of General Medicine.* 2021; 4:1843–51.
29. Akimoto T, Hara M, Morita A, Uehara S, Nakajima H. Relationship between Nutritional Scales and Prognosis in Elderly Patients after Acute Ischemic Stroke: Comparison of Controlling Nutritional Status Score and Geriatric Nutritional Risk Index. *Ann Nutr Metab.* 2021 ;77(2):116–23.
30. López Espuela F, Roncero-Martín R, Zamorano JDP, Rey-Sanchez P, Aliaga- Vera I, Portilla Cuenca JC, et al. Controlling Nutritional Status (CONUT) Score as a Predictor of All-Cause Mortality at 3 Months in Stroke Patients. *Biological Research For Nursing.* 2019 ;21(5):564–70.