Seroja Husada
Jurnal Kesehatan Masyarakat

(2024), 1 (5): 62–72

CORRELATION OF TNF-ALFA INFLAMMATION BIOMARKER LEVELS WITH THE INDONESIAN VERSION OF MONTREAL COGNITIVE ASSESSMENT (MOCA-INA) SCORES IN LAKUNAR ISCHEMIC STROKE PATIENTS

Faishol Hamdani* Jimmy Eko Budi Hartono Dodik Tugasworo** Retnaningsih** Herlina Suryawati** Arinta Puspitawati****

*Neurology Resident of UNDIP Medicine faculty/Dr. Kariadi Hospital, Semarang
**Senior Lecturer in the Neurology Department, UNDIP Medical Faculty /RSUP dr. Kariadi Semarang

SUBMISSION TRACK

Submitted : 19 June 2024
Accepted : 1 May 2024
Published : 2 May 2024

KEYWORDS

TNF-α, cognitive function, MoCA-INA score, lacunar ischemic stroke

CORRESPONDENCE

A B S T R A C T

Background: Tumor Necrosis Factor-Alpha (TNF-α) is a pro-inflammatory cytokine that is responsible for modulation the immune system. TNF-α is another important mediator involved in stroke pathophysiology. Cerebral small vessel disease (CSVD) is a major cause of lacunar ischemic stroke. In stroke there is an increase in TNF-α levels where post-stroke neuroanatomic damage can cause cognitive impairment. Objective: Proving the relationship between TNF-α serum levels on the day 3 of onset and the Moca Ina score on the day 7 of onset, day 30, and the difference in MoCa-INA scores and analyzing the relationship of risk factors cognitive function in lacunar ischemic stroke patients. Methods: An analytical observational study with a prospective cohort approach. Subjects were first-time lacunar ischemic stroke with blood sampling on the day 3 of onset to evaluate TNF-α levels. Cognitive function was examined by the MoCa-INA score which was evaluated on day 7 and day 30. Eta correlation test to connect TNF-α levels with MoCa-INA scores. Bivariate and multivariate analyzes used between the MoCa-INA score and other confounding factors. Results: There was a strong correlation between TNF-α levels on day 3 of onset and MoCA-INA on day 7 (η= 0.972), a very strong correlation was found between TNF-α levels on day 3 of onset and MoCA-INA on day 30 (η= 1,000), and there was a strong correlation between TNF-α levels on day 3 of onset and the difference between MoCA-INA (η=0.905). there is a confounding variable diabetes mellitus that affects the 7th day of MoCA-INA. In the sub-analysis study, the mean serum TNF-α level on cognitive impairment on day 30 was higher than on day 7 with the most dominant domains being visuospatial and executive. Conclusion: There is a strong relationship between serum TNF-α levels and MoCa-INA scores in lacunar ischemic stroke patients, and there is one confounding variable of diabetes mellitus that affects the MoCa-INA score on the 7th day of examination.

BACKGROUND OF STUDY

Stroke is a collection of symptoms due to acute brain function disorders (neurological deficits) both focal and global suddenly more than 24 hours. It is caused by reduced or loss of blood flow to the brain parenchyma, retina, or spinal cord as evidenced by examination of brain imaging. Stroke causes damage to brain tissue which can be characterized by motor, sensory, and cognitive neurologic deficits.[1]

Lacunar ischemic stroke is the most common cause associated with Cerebral small vessel disease (CSVD) which is an intracranial vascular disease based on various pathological and neurological processes, such as syndromes that refer to different clinical manifestations and neuroimaging features caused by structural changes in the vascular parenchyma and brain. In several studies, CSVD is the main cause of loss of function, disability and cognitive decline in the elderly.[2]

Lacunar stroke accounts for up to 25% of all ischemic strokes. Which is a small cavity filled with fluid that is thought to mark the healing stage of a small deep brain infarction. In neuroimaging, a lacunar is a spherical or ovoid fluid-filled cavity, subcortical, with an appearance similar to that of cerebrospinal fluid. They range in size from 3 to 15 mm, which is consistent with a small acute infarction of the deep brain or bleeding within the territory of an arteriole. Lacunar infarcts are usually located in the basal ganglia, internal capsule, thalamus, corona radiata, centrum semiovale and brain stem.

Based on data from the World Health Organization (WHO) in 2016, there were 5.5 million deaths caused by cerebrovascular disease worldwide (2.7 million deaths from ischemic stroke and 2.8 million deaths from hemorrhagic stroke).[3] Eastern Europe, East Asia, as well as parts of Southeast Asia, Central Asia, and Africa have the highest rates of death from stroke.[3] In Indonesia, the prevalence of stroke increased from 7% in 2013 to 10.9% in 2018, and increases with age.[4] Stroke sufferers are mostly found in the age group of 45-54 years, 55-64 years and 65-74 years.[5] According to a 2012 report by the Stroke Foundation of Indonesia, the incidence of stroke in Indonesia per year is 200 out of 100,000 population, around 2.5% die. and the rest have mild or severe disabilities.[6] Based on Riskesdas 2018, there was an increase in the incidence of stroke in Indonesia when compared to Riskesdas 2013 from 7/1000 population to 10.9/1000 population.[7]

Ischemia in the brain triggers the activation of brain cells and peripheral immune cells to activate and play a role in the acute and chronic phases of injury. Many experimental studies have described important responses of microglial cells, infiltrating monocyte-derived macrophages and neutrophils either in relation to either a protective or an adverse effect on brain injury in stroke.

Rapid and precise diagnosis is a very decisive step in the success of stroke patient management. The search for biochemical markers of stroke that can be detected quickly in the blood is very important for the management of acute stroke as well as for post-stroke evaluation. Ideal biochemical markers for diagnosis, monitoring, and prognosis of stroke should meet the following criteria: specific for the brain, detectable in the blood of acute stroke patients, appear early within hours of the attack, peak levels reflect the extent of brain damage, area of the lesion and penumbra, and can predict functional outcomes, one of which is the cytokine Tumor Necrosis Factor-Alpha (TNF-α).[8]

Various biochemical substrates are released in response to conditions that develop inflammatory reactions or pathologies, including inflammation, pain, and cancer. Among those inflammatory cytokines, tumor necrosis factor-alpha (TNF-α) is a well-known pro-inflammatory cytokine that is responsible for the modulation of the immune system. TNF-α is another important mediator involved in stroke pathophysiology.

TNF-α is probably one of the most studied cytokines in the field of stroke research. In an experimental study on rats with middle cerebral artery occlusion. Yang et al, demonstrated that intracerebroventricular injection of antibodies against TNF-α after cerebral artery occlusion significantly decreased infarct volume.[8]

Many studies on the correlation between biomarkers of brain damage and cognition in lacunar ischemic stroke patients have been conducted with varying results, so we are interested in examining this. Based on the description above, a study will be conducted on the relationship between TNF-α levels and clinical outcomes of cognitive function in lacunar ischemic stroke patients.

METHODS OF STUDY

This study is an analytic observational study with a prospective cohort approach. The subjects of this study were acute ischemic stroke patients who were treated at the Inpatient Installation of Dr. Kariadi Semarang in the research period (February 2021 – February 2022) that met the research inclusion criteria. The subjects were acute ischemic stroke patients, as evidenced by an MSCT scan of the head, who came to the hospital in less than 72 hours. And must be first stroke, also minimum have 3 years basic education. The size of the research subjects is determined by consecutive sampling.

We excluded patients with head injury in the last 3 months, suffering from brain tumor, suffering from psychiatric disorders, history of suffering from central nervous system infection. Patients with autoimmune disorders such as rheumatoid arthritis, inflammatory bowel disease and cardiovascular disease. Also patient with aphasia, severe dysarthria, total blindness and total hearing loss.

This study examine serum TNF-α levels of acute ischemic stroke patients on the day 3 then we undergo MoCA-INA test on the day 7 followed by MoCA-INA test on the day 30. Our confounding variable are age, gender, hy pertention, diabetes mellitus, dyslipidemia, obesity status, infarct size, infarct location, education level, and occupation.

The research was asked for approval from the Medical Research Ethics Commission of UNDIP/RSDK with No. 563/EC/KEPK-RSDK/2020.

Statistical analysis was carried out by computer using SPSS for windows version 26. Data analysis included descriptive analysis and statistical analysis. The stages of descriptive statistics are to determine the basic characteristics of research subjects, and analytical statistics to see comparisons, correlations and treatment effects.

Comparative tests were performed using Pearson Chi Square and Fisher's Exact test for nominal data, and Kruskal Wallis for ordinal data. Data with a 2x2 table if it meets the requirements, the Pearson Chi Square test is carried out, if it does not meet the requirements (expected count < 5), the Fischer's Exact test is carried out. Data with 2x3 and 2x4 tables were tested by Pearson Chi Square. The correlation test of the two variables with numerical and nominal scales was analyzed using the Eta correlation test.

RESULT OF STUDY

Charateristics of Research Subjects

This study used 39 research subjects. The mean age of the research subjects was 59.1 ± 9.40 with the lowest age being 36 years and the highest age being 75 years. Subjects aged > 65 years were 10 (25.6%) and 65 years were 29 (74.4 5%). Gender in the subjects of this study were 26 men (66.7%) and 13 women (33.3%). The education level of the subjects obtained was that 5 subjects had graduated from elementary school (12.8%) followed by 6 subjects from junior high school (15.4%), 20 subjects from high school (51.3%), and 8 subjects graduated from college (20.5%). From the employment data, 12 subjects did not work (30.8%) and 27 subjects worked (69.2%).

Tabel 1. Demography Charateristic of Study Subjects

Variabel	F	%
Gender		
Man	26	66,7
Woman	13	33,3
Age		
> 65 y.o.	10	25,6
65 y.o.	29	74,4
Education		
Elementary school	5	12,8
Junior high school	6	15,4
High school	20	51,3
College	8	20,5

Work		
Doesn't work	12	30,8
Working	27	69,2

Of the 39 subjects, most of them suffered from hypertension, there were 34 subjects (87.2%) and 5 subjects (12.8%) didn't suffered from hypertension. There were 10 subjects (25.6%) who suffered from DM and 29 subjects (74.4%) didn't suffered from DM. Many subjects suffered from dyslipidemia namely 37 subjects (94.9%) and 2 subjects did not suffered from dyslipidemia (5.1%). Patients who suffered from obesity are only 6 subjects (15.4%) compared to those who didn't suffered as many as 33 subjects (84.6%).

Based on the size and extent of the infarct, the subjects were divided into 2 groups, namely single lacunar as many as 8 subjects (20.5%), lacunar ≥ 2 as many as 31 subjects (79.5%). From the location of the infarct, the subjects were divided into 3 groups: 11 subjects (28.2%) non-dominant hemisphere, 8 (20.5%) dominant hemisphere and 20 (51.3%).

Tabel 2. Clinical Charateristic of Study Subjects

Variabel		F	%
Hypertension			
	Yes	34	87,2
	No	5	12,8
DM			
	Yes	10	25,6
	No	29	74,4
Dyslipidemia			
	Yes	37	94,9
	No	2	5,1
Obesity			
	Yes	6	15,4
	No	33	84,6
Infarct size and area			
	Single Lacunar	8	20,5
	Lacunar ≥ 2	31	79,5
Infarct location			
	Non-dominant hemisphere	11	28,2
	Dominant hemisphere	8	20,5
	Mixture	20	51,3

Relationship between day 3 onset of TNF-α and MoCA-INA

We use the correlation formula Eta (η), this coefficient is used in simple correlation analysis for nominal variables with interval variables. Parameters to state the size of the correlation, value 0.70 – 1.00 = strong correlation between two variables, value 0.40 – 0.69 = moderate correlation between two variables, value 0.20 – 0.39 = weak correlation between two variables. A value of 0.01 – 0.19 = there is no correlation or can be ignored between two variables, and value of 0.0 = There is no correlation between two variables.[9]

From the data above, the correlation of TNF-α levels on the day 3 of onset with MoCA-INA on the day 7 has a statistical test coefficient of eta (η) 0.972 indicating that there is a strong correlation between the two variables. The correlation between TNF-α levels on the day 3 of onset and MoCA-INA on the day 30 has a statistical test coefficient of eta (η) 1,000, indicating that there is a strong correlation between the two variables. The correlation between TNF-α levels on the day 3 of onset and the difference between MoCA-INA has an eta statistic test coefficient (η) of 0.905, indicating a strong correlation between the two variables.

Table 3. The results of the Eta correlation test the relationship of TNF-α onset on day 3 to MoCA-INA

Variabel	MoCA-INA		
	H+7	H+30	Selisih
	η	η	η
TNF-α	0,972	1,000	0,905

The relationship between confounding variables on MoCA-INA

Comparative tests were performed using Pearson Chi Square and Fisher's Exact test for nominal data, and Kruskal Wallis for ordinal data. Data with a 2x2 table if it meets the requirements, the Pearson Chi Square test is carried out, if it does not meet the requirements (expected count < 5), the Fischer's Exact test is carried out. Data with 2x3 and 2x4 tables were tested by Pearson Chi Square.

From the results of the tests, it was found that there was no significant relationship between age and MoCA-INA on the day 7 (p=0.480), day 30 (p=0.289), nor to the difference between MoCA-INA (p=0.400). There was no significant relationship between sex and MoCA-INA on the day 7 (p=0,276), day 30 (p=0,407) nor to the difference between MoCA-INA (p=0,284). There was no significant relationship between hypertension and MoCA-INA on the 7th day (p=0.600), the 30th day (p=0.436), and the difference between MoCA-INA (p=0.655). There was a significant relationship between DM and MoCA-INA on the day 7 (p=0,050), but there was no significant relationship on the day 30 (p=0,733) and the difference between MoCA-INA (p=0,400). There was no significant relationship between dyslipidemia and MoCA-INA on the day 7 (p=0,595), day 30 (p=0,197), or the difference between MoCA-INA (p=0,150). There was no significant relationship between obesity and MoCA-INA on the day 7 (p=0,365), day 30 (p=0,498), and the difference between MoCA-INA (p=0,597). There was no significant relationship between infarct size and extent of MoCA-INA on the day 7 (p=0.611), day 30 (p=0.383), and the difference between MoCA-INA (p=0.508). There was no significant relationship between infarct location and MoCA-INA on the day 7 (p=0.432), day 30 (p=0.241), and the difference between MoCA-INA (p=0.215). There was no significant relationship between education level and MoCA-INA on the day 7 (p=0,637), day 30 (p=1,000), and the difference between MoCA-INA (p=0,361). There was no significant relationship between work on the the day 7 of MoCA-INA (p=0,560), 30th day (p=0,640), and the difference between MoCA-INA (0,320).

There is one confounding variable that has a good effect on the 7th day of MoCA-INA, there is Diabetes Mellitus, but there is no confounding variable that has an effect on the 30th day of MoCA-INA and on the difference between MoCA-INA.

Table 4. Relationship between confounding variables and MoCa-INA
Strength of correlation of serum TNF-α levels with domains in cognitive impairment

Variables	MoCA-INA		
	7th Day	30th Day	Difference Score

	There is a Disturbance	Normal	P	There is a Disturbance	Normal	P	There are Changes	No Changes	P
Age			0,480£			0,289£			0,400£
>65 y.o	3 (30%)	7 (70%)		0 (0%)	10 (100%)		10 (100%)	0(0%)	
≤65 y.o	11 (37,9%)	18 (62,1%		4 (13,8%)	25 (86,2%)		26 (89,7%)	3 (10,3%)	
Gender			0,276£			0,407£			0,284£
Male	8 (30,8%)	18 (69,2%)		2 (7,7)	24 (92,3%)		23 (88,5%)	3 (11,5%)	
Female	6 (46,2%)	7 (53,8%)		2 (15,4%)	11 (84,6%)		13 (100%)	0 (0%)	
Hypertension			0,600£			0,436£			0,655£
Yes	12 (35,3%)	22 (64,7%)		3 (8,8%)	31 (91,2%)		31 (91,2%)	3 (8,8%)	
No	2 (40%)	3 (60%)		1 (20%)	4 (80%)		5 (100%)	0 (0%)	
DM			**0,050*£**			0,733£			0,400£
Yes	1 (10%)	9 (90%)		1 (10%)	9 (90%)		10 (100%)	0 (0%)	
No	13 (44,8%)	16 (55,2%)		3 (10,3%)	26 (89,7%)		26 (89,7%)	3 (10,3%)	
Dyslipidemia			0,595£			0,197£			0,150£
Yes	13 (48,1%)	24 (88,8%)		3 (8,1%)	34 (91,9%)		35 (94,6%)	2 (5,4%)	
No	1 (50%)	1 (50%)		1 (50%)	1 (50%)		1 (50%)	1 (50%)	
Obesitas			0,365£			0,498£			0,597£
Yes	3 (50%)	3 (50%)		0 (0%)	6 (100%)		6 (100%)	0 (0%)	
No	11 (33,3%)	22 (66,7%)		4 (12,1%)	29 (87,9%)		30 (90,9%)	3 (9,1%)	
Infarct size and area			0,611£			0,383£			0,508£
Single Lakunar	3 (37,5%)	5 (62,5%)		0 (0%)	8 (100%)		7 (87,5%)	1 (12,5%)	
Lakunar ≥ 2	11 (35,5%)	20 (64,5%)		4 (12,9%)	27 (87%)		29 (93,5%)	2 (6,5%)	
Infark location			0,432Σ			0,241Σ			0,215Σ
Non dominan hemisfer	3 (27,3%)	8 (72,7%)		0 (0%)	11 (100%)		9 (81,8%)	2 (18,2%)	
Dominan Hemisfer	3 (37,5%)	5 (62,5%)		1 (12,5%)	7 (87,5%)		8 (100%)	0 (0%)	
Mixture	8 (40%)	12 (60%)		3 (15%)	17 (75%)		19 (95%)	1 (5%)	
Education			0,637Σ			1,000Σ			0,361Σ

Elamantary school	1 (20%)	4 (80%)		0 (0%)	5 (100%)		5 (100%)	0 (0%)	
Junior high school	2 (33,3%)	4 (66,7%)		0 (0%)	6 (100%)		5 (83,3%)	1 (16,7%	
High school	8 (40%)	12 (60%)		3 (15%)	17 (85%)		20 (100%)	0 (0%)	
College	3 (37,5%)	5 (62,5%)		1 (12,5%)	7 (87,5%)		6 (75%)	2 (25%)	
Worrk			0,560$^{£}$			0,640$^{£}$			0,320$^{£}$
Doesn’t work	4 (33,3%)	8 (66,7%)		1 (8,3%)	11 (91,7%)		12 (100%)	0 (0%)	
Working	10 (37%)	17 (63%)		3 (11,1%)	24 (88,9%)		24 (88,9%)	3 (11,1%)	

This study found 14 subjects had cognitive impairment on the day 7 of onset (MoCA-INA <26) from the 40 subjects that studied, then there were 4 subjects with cognitive impairment on the day 30 of onset.

In this study, the most disturbed domains on the day 7 of MoCA-INA examination were memory 64.3%, language 57.1%, and attention 42.8%. While the disturbed domain on the day 30 of MoCA-INA examination could not be assessed because only 4 patients were disturbed and all of them were multidomain.

Table 5. Different domain test on cognitive impairment (MoCA-INA score <26) with TNF-α levels

Domain	N	%	TNF-α		
			Mean ± SD	Median (Min-Maks)	P
Memory					
Onset day 7	9	64,3	134,8 ± 148,0	75,2 (6,1 – 467,1)	0,947
Onset day 30	4	100	311,6 ± 280,2	311,3 (6,1 – 617,7)	-
Visuospatial					
Onset day 7	2	14,3	298 ± 239	298 (129 –467,1)	0,144
Onset day 30	1	25	467,1	467,1	0,655
Attention					
Onset day 7	6	42,8	160,5 ± 179,2	90,8 (6,1 – 467,1)	0,796
Onset day 30	2	50	236,6 ± 325,9	236,6 (6,1 – 467,1)	0,439
Language					
Onset day 7	8	57,1	183,9 ± 228,9	69,6 (6,1 – 617,7)	0,699
Onset day 30	3	75	363,6 ± 318,6	467,1 (6,1 – 617,7)	0,655
Executive function					
Onset day 7	3	27,3	291 ± 169,4	277 (192 – 467,1)	0,052
Onset day 30	1	25	467,1	467,1	0,655

DISCUSSION

In this study, the serum levels of TNF-α of 37 subjects in this study have increased. Acute stroke not only causes a local inflammatory response in the ischemic brain but also triggers a systemic immune response. Following ischemia, there is release of pro-inflammatory agents such as TNF-α into the systemic circulation, leading to activation of peripheral immune cells. This over-activation leads to exhaustion of mature leukocytes, which provokes the recruitment of immature leukocytes that are unable to respond properly to brain damage.

The increase in serum TNF-α levels is caused by neuronal damage followed by leakage of the blood-brain barrier. TNF-α concentrations increase in stroke patients immediately 6-12 hours after onset, levels increase within 24-48 hours and decrease slowly between 72-144 hours after stroke onset.

The results of this study are in accordance with the results of previous studies, namely: those conducted by Jiang C et al (2017), on 96 patients with acute ischemic stroke. There was an increase in serum TNF-α levels on days 1, 3 and 7 from the onset of stroke.[5] Another study conducted by Shakoori et al (2014), a study at 2 hospitals in Pakistan, in stroke patients >24 hours onset during June 2011 to December 2011, total of 131 patients with ischemic stroke 93 patients and hemorrhagic stroke 38 patients. There was a significant increase in serum levels of TNF-α and IL-10 in all stroke patients.[6]

Subjects in this study obtained a median MoCA-INA score that was less than normal (<26) indicating that in acute ischemic stroke there will be a decline in cognitive function. As research conducted by Sachdev et al (2006), that 58% of stroke survivors have cognitive impairment and a quarter are dementia.[10] A cross-sectional study in the UK also found that the prevalence of cognitive impairment was highest within the first month after the onset of ischemic stroke.[11]

Cerebral small vessel disease is associated with cerebral amyloid angiopathy, which is caused by deposits of amyloid-β in the walls of cerebral blood vessels. Cerebral amyloid angiopathy is common in the pathology of Alzheimer's disease, but can also be seen in aging conditions that can be found in autopsy studies of patients. Pathological amyloid angiopathy is associated with impaired episodic memory and decreased perceptual speed in Alzheimer's patients.[12] In addition, abnormal decreases in cerebral blood flow (CBF) have been identified in VCI caused by CSVD. Decreased perfusion in the temporal and frontal lobes of the hippocampus, thalamus and insula correlates with the degree of cognitive impairment. The functional relationship between the left thalamus and the posterior cingulate cortex indicates the severity of cognitive impairment. The frontal lobe and other subcortical locations play an important role in the pathogenesis of VCI due to CSVD.[13]

TNF-α onset on the day 3 had a strong relationship with MoCA-INA day 7 (η) 0.972, so H0 was rejected. TNF-α had a strong relationship with MoCA-INA at the day 30 (η) 1,000, so H0 was rejected. Then TNF-α also has a strong relationship with the difference in MoCA-INA (η) 0.905, so H0 is rejected.

Research conducted by Mu L et al, stated that increased levels of inflammatory markers including TNF-α were associated with decreased cognitive function in patients with cerebral small vessel disease (CSVD).[14] However, in another study conducted by Kulesh et al, on 92 ischemic stroke patients and 14 healthy patients as controls were examined for inflammatory markers IL-1, IL-6, IL-10 and TNF-α on the day 4 and the day 21 and cognitive evaluation was performed between day 7 and day 14. In cognitive impairment, there was a significant increase in the inflammatory markers IL-1β and IL-10 in CSF, while the IL-6 marker was significantly increased in serum compared to normal patients. And there was only a slight increase in serum

TNF-α levels in cognitively impaired patients compared to stroke patients with normal cognitive.[15]

In our study, there were 39 subjects with lacunar stroke. In the cognitive function domain analysis, it was found that patients with executive and visuospatial domain disorders had higher TNF-α serum levels than those in other domains. Meanwhile, the most disturbed on the day 7 of MoCA – INA assessment were memory (64.3%), language (57.1%) and attention (42.8%). Research by Arboix A et al (2013), in a quantitative systematic review (12 cross-sectional study) of specific domains in lacunar infarction stroke reported the most domains of disturbances being attention or working memory and executive function, as well as disorders of other additional domains such as memory, language, and visuospatial. Classical cognitive impairment in lacunar infarct stroke is a more dominant memory disorder accompanied by impaired attention and executive function, in acute stroke conditions, episodic memory domain disorders are found as the main neuropsychological sign.[16]

In this study, there was no correlation between cognitive impairment in each domain and serum TNF-α levels, but from 5 affected subjects there were differences in the amount of TNF-α levels with multi-dominant cognitive impairment compared to single cognitive disorders.

In this study, serum TNF-α levels were found to be higher in patients with cognitive impairment on the day 30 of onset than on the day 7 of onset, so that TNF-α serum levels can be one of the prognostic factors for clinical outcome of cognitive function in lacunar ischemic stroke patients.

In this study we have not found any relationship between our confounding factors and MoCA-INA score except DM on the day 7. This is supported by several previous studies which are influenced by many factors in the process of pathological stroke development.

RESEARCH LIMITATION

This study has several limitations, including the head CT scan is only performed when the patient is admitted, we may need undergo head CT scan more than once to ascertain the location and extent of the infarct. We also have relatively small number of subjects. More studies with larger sample sizes are warranted.

CONCLUSION

There was an increase in serum levels of TNF-α on day 3 of onset in 95% of study subjects. There are strong relationship between TNF-α levels and cognitive function as measured using MoCA-INA at stroke onset day 7, strong relationship between TNF-α levels and cognitive function as measured by MoCA-INA at stroke onset on the day 30, strong relationship between TNF-α levels and improvement in cognitive function as measured by the difference between MoCA-INA onset on the day 30 and the day 7 on onset. There is a relationship between the confounding factors of diabetes mellitus and the MoCA-INA score on the day 7 of onset. And no significant relationship between each domain in cognitive impairment with the Moca – INA score on the 7th and 30th day of onset. Also there is a difference in the mean serum levels of TNF-α levels, higher on the 30th day of onset cognitive impairment compared to the 7th day.

CONFLICTS OF INTEREST

The authors declare no conflict of interest.

ACKNOWLEDGMENTS

This research was suppposted by Dr Kariadi Hospital in Semarang, the Department of Neurology Medical School, University of Diponegoro.

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