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ultrasonography

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**1**  
**Correlation Between Blood Glucose And Low-Density Lipoprotein Level With Pulsatility Index Of Intracranial Arteries Evaluated By Transcranial Color-Coded Duplex Ultrasonography**

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**ABSTRACT**

**1**  
Introduction : Pulsatility index (PI) measures the vascular resistance distal to the examined artery. PI of intracranial arteries may predict the future cerebrovascular event. High blood-glucose and low-density lipoprotein (LDL) level are the known risk factor for atherosclerosis. However, there were few studies which describe the correlation of the two in Indonesia. This study aimed to analyze the correlation between plasma blood-glucose and low-density lipoprotein (LDL) level and PI of intracranial arteries (right and left anterior cerebral arteries, right and left middle cerebral arteries, right and left posterior cerebral arteries, right and left vertebral arteries, and basilar artery) examined by transcranial color-coded duplex ultrasonography (TCCD)

Methods : This study is a Cross Sectional Study Design in Dr. Kariadi Hospital within Januari until December 2018. Forty-eight patients (n = 48) who underwent a TCCD examination were tested for blood-glucose and LDL level. Normality of the data were tested using Saphirowilk, then the correlation tested using Spearman's rank correlation test.

Results : There were significant correlation between both blood-glucose or LDL level with PI of intracranial arteries (all p < 0.05).

Conclusions : blood glucose and LDL level is associated with PI of intracranial arteries.

Keywords : blood-glucose, low density lipoprotein, pulsatility index, vascular resistance, ischemic stroke.

## Introduction

Ischaemic stroke accounts for about 80% of all stroke cases. The mortality and morbidity leaves a burden for human productivity. The prevention strategies to reduce the burden have been developed. Yet, screening modality for brain vessels have not been so popular, especially in developing country.

<sup>1</sup> High blood-glucose and low-density lipoprotein (LDL) level are the known risk factor for atherosclerosis. The association of the two with cerebrovascular event have been well-recognized.<sup>(1)</sup> Having blood glucose and LDL level in control have been the most popular prevention strategy, yet no one knows what have been happened with the vasculature. While MRI-and CT scan- based angiography have been a well-known methods to evaluate intracranial arteries, their high-cost and availability issue may become a challenge in developing countries. Alternatively, transcranial Doppler (TCD) ultrasonography provides cost-effective examination to evaluate physiological disorder of intracranial vasculatures.

<sup>1</sup> Pulsatility index (PI) measures the vascular resistance distal to the examined artery. PI of intracranial arteries may predict the future cerebrovascular event. Lower PI may indicate lower resistance of the vascular beds with higher diastolic flow. On the opposite, higher PI may indicate higher resistance beds with lower diastolic flow. Some vascular condition, such as lipohyalinosis and atherosclerosis may narrow the lumen of distal arteries which increases the resistance of the vascular beds. Such condition may uprise PI of the examined artery using Transcranial Color-Coded Duplex Ultrasonography (TCCD).<sup>(2)</sup>

TCD examination may provide valuable screening modality for those who have uncontrolably high blood glucose and/or LDL level. However, there were few studies which describe the correlation of the blood glucose and LDL level with PI in Indonesia. This study aimed to analyze the correlation between plasma blood-glucose and low-density lipoprotein

(LDL) level and PI of intracranial arteries (right and left anterior cerebral arteries, right and left middle cerebral arteries, right and left posterior cerebral arteries, right and left vertebral arteries, and basilar artery) examined by transcranial color-coded duplex ultrasonography (TCCD).

#### Materials and Methods

This cross sectional study was conducted in drKariadi Hospital within Januari until December 2018. Subjects of the study were patients who underwent a TCCD examination, and recruited consecutively. The inclusion criterias were (1) patient aged 40 to 80 year old, (2) patient who underwent TCCD examination, (3) the patient should be willing to participate in this study. The exclusion criterias were (1) patient who had controlled blood glucose and LDL level by medications for the last one year, (2) patient who had history of any cerebrovascular event.

Prior to examination, informed consent was obtained from all of the participants. Blood samples of patients matched with those criterias were obtained intravenously prior to the TCCD examination and tested for blood glucose and LDL level. We took TCCD examination for following arteries: (1) Anterior Cerebral Artery – right (ACA-R) and left (ACA-L); (2) Middle Cerebral Artery – right (MCA-R) and left (MCA-L); (3) Posterior Cerebral Artery – right (PCA-R) and left (PCA-L); (4) Vertebral Artery – right (VA-R) and left (VA-L); and (5) Basilar Artery (BA). All arteries were examined using each appropriate acoustic windows.

All of the data were obtained and recorded. SPSS version 21.00 was used to calculate the statistics analysis. Normality of the data were tested using Saphiro-Wilk, then the correlations were tested using Spearman's rank correlation test. Statistically significant was defined as  $p < 0.05$ .

## Results

There were 48 patients who were willing to participate in the study, with 22 of them were male (45.83%) and 26 were female (54.17%). Blood glucose, LDL level, obtained from laboratory examination, and all PI of intracranial arteries, obtained by TCCD, are showed in Table I.

Tabel I. Demographic profiles of all subjects

No	Variables	mean	±	SD	n	(%)
1	Age	59.25	±	9.690		
2	Sex					
	Male				22	(45.83%)
	Female				26	(54.17%)
3	Glucose	199.4167	±	63.185		
4	LDL	177.38	±	29.152		
5	PI					
	ACA – R	1.47	±	0.453		
	ACA – L	1.24	±	0.370		
	MCA – R	1.43	±	0.520		
	MCA – L	1.27	±	0.237		
	PCA – R	1.35	±	0.302		
	PCA – L	1.22	±	0.344		
	VA – R	1.32	±	0.412		
	VA – L	1.22	±	0.391		
	BA	1.29	±	0.361		

LDL = Low Density Lipoprotein; PI = Pulsatility Index; ACA = Anterior Cerebral Artery; MCA = Middle Cerebral Artery; PCA = Posterior Cerebral Artery; VA = Vertebral Artery; BA = Basilar Artery; R annotation indicate right arteries, while L indicate left arteries.

We analysed the correlation of each PI with both blood-glucose and LDL level. There were statistically significant correlation between blood-glucose or LDL level with PI of intracranial arteries (all  $p < 0.05$ ). The analysis results are provided in Table II. The graphs of correlation between each artery's PI and blood glucose (Fig. 1) and LDL (Fig. 2) level are also presented.

Table II. Corellation analysis of each PI with both blood-glucose and LDL level

No	Artery	Blood Glucose		LDL	
		p	r	p	r
1	ACA-R	<0.001*	0.587	0.001*	0.456
2	ACA-L	<0.001*	0.496	0.037*	0.303
3	MCA-R	0.003*	0.419	0.013*	0.355
4	MCA-L	0.004*	0.412	<0.001*	0.495
5	PCA-R	0.006*	0.390	0.042*	0.295
6	PCA-L	0.031*	0.312	0.039*	0.299
7	VA-R	0.046*	0.290	0.027*	0.319
8	VA-L	0.035*	0.305	0.003*	0.414
9	BA	0.003*	0.419	0.048*	0.287

\*p value is significant

LDL = Low Density Lipoprotein; PI = Pulsatility Index; ACA = Anterior Cerebral Artery; MCA = Middle Cerebral Artery; PCA = Posterior Cerebral Artery; VA = Vertebral Artery; BA = Basilar Artery; R annotation indicate right arteries, while L indicate left arteries.

## Discussion

This study show us the correlation of blood glucose and LDL level with increased resistance of intracranial arteries. These findings support that risk factors, blood glucose and LDL, have role in the process of narrowing intracranial blood vessel lumen, as measured by increased PI, which predict the future cerebrovascular events. TCD has demonstrated the association between various risk factors and small vessel disease.<sup>(3)</sup> This relationship also has been confirmed by MRI findings including periventricular hyperintensity, deep white matter hyperintensity, lacunar disease, and pontine hyperintensity.<sup>(2)</sup> Pathologically, the small vessel disease is resulted from processes such as stretching, necrosis, calcification, fibrosis, and hypertrophy of endothelium and smooth muscle cells.<sup>(4)</sup> Lipohyalinosis and atherosclerosis may result from increased blood glucose and LDL level.

Park et al demonstrated that PI was significantly higher in diabetic patients ( $p < 0.05$ ) and also, in diabetic patient, was higher in patients with insulin resistance than in patients who still insulin sensitive ( $p < 0.05$ ). Their study also found an association between higher PI and longer duration of diabetes ( $R = 0.264$ ,  $p = 0.025$ ).<sup>(5)</sup> Lee et al in 2007 also found that diabetic patient with complication had higher PI than diabetic patient without complication ( $p <$

0.001).<sup>(6)</sup> These findings and ours confirm that blood glucose may contribute in small vessel disease of intracranial arteries.

Jeon et al found that PI was significantly higher in patients with hyperlipidemia (total cholesterol level >220 mg/dL or low-density lipoprotein cholesterol level >160 mg/dL.) (p = 0.003).<sup>(7)</sup> However, Farhoudi et al found that resistance index rather than PI was significantly higher in patients with higher level of LDL (180 mg/dL).<sup>(8)</sup> Our findings support that LDL level is associated with PI in the way of higher LDL level contribute in higher PI.

Other than blood glucose and LDL level, PI of intracranial arteries also found to be related with age<sup>(3,7,9)</sup>, hypertension<sup>(10)</sup>, obesity<sup>(11)</sup>, and angiopathy<sup>(9)</sup>. All of these findings suggest that TCD maybe a valuable assessment in reassuring people with such risk factors to evaluate intracranial small vessel disease.

Our study had some limitations. Our study obtained data from cross-sectional point of view, which limit the progression observation of the intracranial small vessel disease in associated with increased blood glucose and LDL level. This study design may lack in seeing long term status of blood glucose and LDL level of the study participants. However, we pushed our best to select participants who had not taken medication for controlling their blood glucose and LDL level to simulate the condition. Our study also may have small size of participants. This may affect the reflection of larger population.

## Conclusions

This study shows that **blood glucose and LDL level** is associated with **PI of intracranial arteries**. In the perspective of ischaemic stroke prevention, it is motivated to all patients with uncontrolled blood glucose and LDL level to be screened using TCD examination. Further

study is encouraged to have larger sample size. We also need to observe in population with controlled blood glucose and LDL level to see if the preventive strategy of ischaemic stroke also affect the parameters of TCD.

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Figure Legends

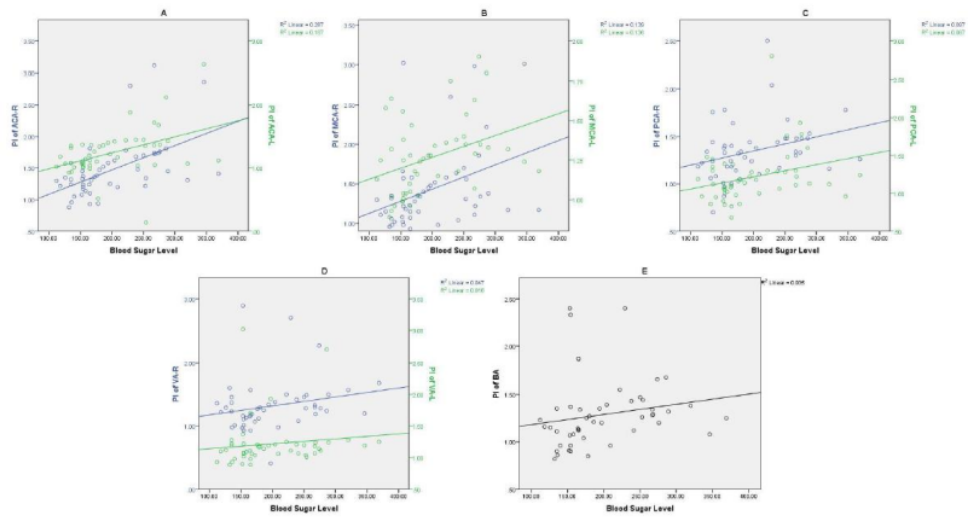


Figure 1. Correlation between each chartery's PI and blood glucose level

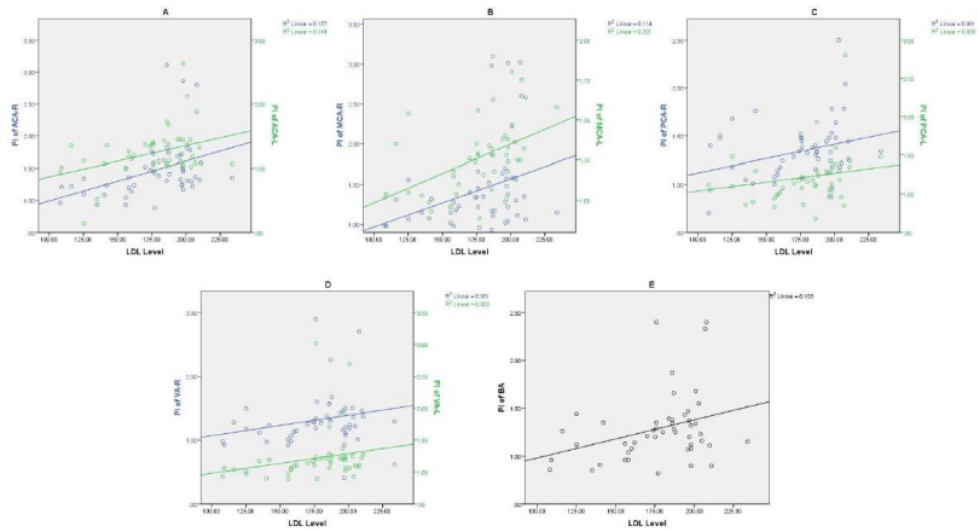


Figure 2. Correlation between each chartery's PI and LDL level

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