ORIGINAL ARTICLE

The Relationship of Blood Glucose and LDL Level with Pulsatility Index of Cerebral Arteries Examined by Transcranial Color-coded Duplex Ultrasonography

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ABSTRACT

Introduction: Diabetes mellitus and dyslipidemia is the most common risk factors for stroke and are associated with atherosclerosis, which promote the incidence of stroke. The pulsatility index (PI) by transcranial color-coded duplex ultrasonography (TCCD) evaluates the vascular resistance of the distal of cerebral artery and can predict the cerebrovascular disease like stroke. The aim of the study is to correlate blood glucose and LDL level with PI of cerebral arteries evaluated by TCCD. **Methods:** The cross sectional study design was performed in 48 patients from January-December 2018 who performed TCCD and were tested for blood glucose and LDL level. Saphiro-Wilk test was performed to analyze the normality of the data then Spearman's rank correlation test was used to evaluate the correlation of the variables. **Results:** There were significant correlation of blood glucose and LDL level with PI of cerebral arteries (all $p < 0.05$). **Conclusion:** Blood glucose and LDL level are correlated with the PI of cerebral arteries.

Keywords: Blood glucose, Ischemic stroke, LDL, Pulsatility index, Vascular resistance

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INTRODUCTION

Ischemic stroke accounts for about 80% of all stroke cases. The mortality and morbidity leaves a burden for human productivity (1–3). There are many risk factors that are associated with stroke, modifiable and non-modifiable. The modifiable stroke risk factors are hypertension, diabetes mellitus, dyslipidemia, obesity, and many more. The non-modifiable stroke risk factors are relatively few; including genetic, age, and gender (1,2). Diabetes mellitus and dyslipidemia is the most common risk factors for stroke and are associated with atherosclerosis, which promote the incidence of stroke (4). Diabetes mellitus is a metabolic disorder characterized by the presence of high blood glucose level due to the dysfunction of insulin secretion or impairment of insulin action (5). Dyslipidemia is a lipid metabolism disorder, including an increase in cholesterol levels an increase in low density lipoprotein (LDL) level, an increase in triglyceride levels and a decrease in high density lipoprotein (HDL) level (6). The association of the two with ischemic stroke have been well-recognized (7).

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. 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 cerebral MRI-and CT scan-based angiography have been a well-known methods to evaluate cerebral 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 cerebral vasculatures (8–10). The pulsatility index (PI) by TCD evaluates the vascular resistance of the distal of cerebral artery and can predict the cerebrovascular disease like stroke. 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) (8,10).

TCD examination with PI may provide valuable screening modality for those who have uncontrolably increase in blood glucose and/or LDL level but there were minimal studies that correlate blood glucose and LDL level with PI. The aim of the study is to correlate blood glucose and LDL level with PI of cerebral arteries evaluated by TCCD.

MATERIALS AND METHODS

This study was an analytical observational study using cross sectional approach at Dr. Kariadi General Hospital from January to December 2018. This research had been getting Ethical Clearance of Health Research Ethics Committee of the Faculty of Medicine Diponegoro University/Dr. Kariadi Hospital.

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. TCCD examination was performed 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. Saphiro-Wilk test was performed to analyze the normality of the data then Spearman's rank correlation test was used to evaluate the correlation of the variables. Statistically significant was defined as $p < 0.05$.

RESULTS

There were 48 patients who were included in this study with the mean of age was 59 years, 22 of them were male (45.83%) and 26 of the subjects were female (54.17%). Table I showed the result of blood glucose, LDL level, and all PI of intracranial arteries. The mean of of blood glucose level was 199.4167 mg/dL and the mean of LDL level was 177.38 mg/dL.

Tabel I : Demographic profiles of all subjects

No	Variables	Min	Median	Max	mean	±	SD	n	(%)
1	Age	41	58	80	59.25	±	9.690		
2	Sex								
	Male							22	(45.83%)
	Female							26	(54.17%)
3	Glucose	112	177	369	199.4167	±	63.185		
4	LDL	108	186	234	177.38	±	29.152		
5	PI								
	ACA – R	0.88	1.355	3.11	1.47	±	0.453		
	ACA – L	0.14	1.175	2.63	1.24	±	0.370		
	MCA – R	0.93	1.305	3.02	1.43	±	0.520		
	MCA – L	0.89	1.255	1.90	1.27	±	0.237		
	PCA – R	0.70	1.330	2.50	1.35	±	0.302		
	PCA – L	0.68	1.150	2.80	1.22	±	0.344		
	VA – R	0.41	1.260	2.89	1.32	±	0.412		
	VA – L	0.89	1.140	3.02	1.22	±	0.391		
	BA	0.82	1.240	2.40	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.

There were statistically significant correlation between blood glucose or LDL level with PI of cerebral 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 were also presented. The PI of right anterior cerebral artery (ACA-R), left anterior cerebral artery (ACA-L), right anterior cerebral artery (MCA-R), left anterior cerebral artery (MCA-L), and basilar artery (BA) had the moderate correlation with blood glucose level (r: 0.41-0.7) with the highest correlation was ACA-R (r: 0.587); while right posterior cerebral artery (PCA-R), left posterior cerebral artery (PCA-L), right vertebral artery (VA-R), left vertebral artery (VA-L) had the weak correlation with blood glucose level (r: 0.21-0.4). The PI of ACA-R, MCA-L, and VA-L had the moderate correlation with LDL level (r: 0.41-0.7) with the highest correlation was MCA-L (r: 0.495); while the others had the weak correlation (r: 0.21-0.4).

DISCUSSION

This study showed the correlation of blood glucose and LDL level with increased resistance of cerebral arteries. These findings support that risk factors, blood glucose and LDL, have role in the process of narrowing cerebral blood vessel lumen, as measured by increased PI, which predict the future cerebrovascular disease.

TCD has demonstrated the association between various risk factors and small vessel disease (11). This relationship also has been confirmed by MRI findings including periventricular hyperintensity, deep white matter hyperintensity, lacunar disease, and pontine hyperintensity (10). Pathologically, the small vessel disease is resulted from process such as stretching, necrosis, calcification, fibrosis, and hypertrophy of endothelium and smooth muscle cells. Lipohyalinosis and atherosclerosis may result from increased blood

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.

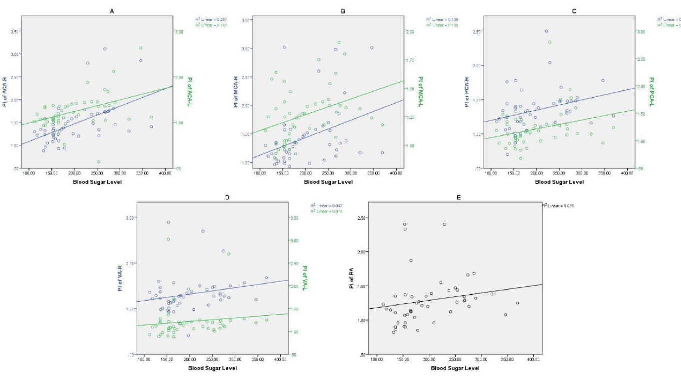

Fig. 1 : Correlation between each artery's PI and blood glucose level

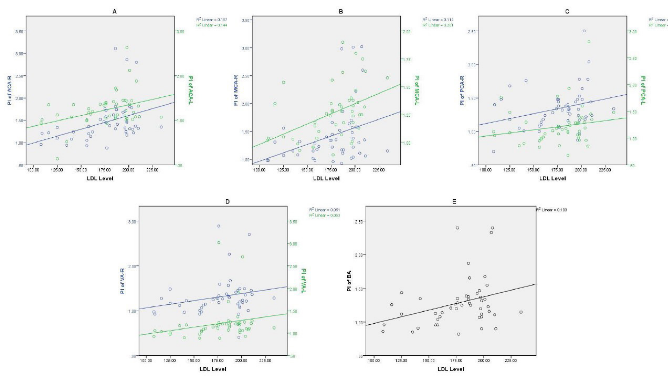

Fig. 2 : Correlation between each artery's PI and LDL level

glucose and LDL level (12).

Park et al. (2008) demostrated that PI was significantly increase in patient with high blood glucose ($p < 0.05$) and also, in diabetic patient, PI was higher in patients with insulin resistance than in patients who still insulin sensitive ($p < 0.05$). Their study also found association between higher PI and longer duration of diabetes ($r = 0.264$, $p = 0.025$) (13). Lee et al. (2007) also found that diabetic patient with complication had higher PI than diabetic patient without complication ($p < 0.001$) (14). These findings confirm that blood glucose may contribute in small vessel disease of cerebral arteries.

Jeong et al. (2018) found that PI was significantly higher in patients with dyslipidemia (total cholesterol level >220 mg/dL or low-density lipoprotein cholesterol level >160 mg/dL) ($p = 0.003$) (15). However, Farhoudi et al found that resistence indeks rather than PI was significantly higher in patients with higher levels of LDL (180 mg/dL) (16). 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 cerebral arteries also found to be related with age, hypertention, obesity, and angiopathy (11,15–19). All of these findings suggest that TCD may be a valuable assessment in reassuring people with such risk factors to evaluate cerebral 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 cerebral 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.

CONCLUSION

This study show that blood glucose and LDL level are correlated with PI of cerebral 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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