The difference in the prevalence of periodontitis degrees between ischemic stroke with diabetes mellitus and prediabetes mellitus

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ABSTRACT

Background: Stroke is a cerebrovascular disease caused by atherosclerosis. Oral health and atherosclerosis may be associated with cerebrovascular disease. Some studies proved the association between chronic infectious diseases, including periodontal tissue disease with stroke risk factors. Diabetes Mellitus has a risk of microvascular complications that are pathologically related to periodontal disease. This study compares the degree of periodontitis between ischemic stroke with diabetes mellitus and ischemic stroke with prediabetes mellitus.

Methods: This study is an observational analytic study with a cross-sectional design. The subjects of this study were infarct stroke patients with diabetes mellitus and prediabetes mellitus in the inpatient ward of Kariadi Hospital Semarang, who met the inclusion and exclusion criteria. The study was conducted from January to March 2020. Infarct stroke was assessed by using head CT scan, while diabetes mellitus using blood glucose with 2 hours postprandial blood glucose and HbA1c, and periodontal disease using MMI (Miller's Mobility Index). The data were analyzed with chi-square correlation test and logistic regression test. The results were significant if the p-value <0.05.

Results: This study was conducted to 42 ischemic stroke patients with diabetes mellitus and prediabetes mellitus. All of the cases also had hypertension. The prevalence of severe periodontitis in DM-hypertension was (OR=0.66; 95% CI=0.12-0.354) compared to prediabetes-hypertension. The chances of severe periodontitis in the age of 61-70 years (OR=2.626; 95% CI=0.473-14.587) compared to the age 51-60 years, dyslipidemia (OR=0.392; 95% CI=0.076-2.016) compared to non dyslipidemia, obesity (OR=2.346; 95% CI=0.382-14.428) compared to non-obesity, smoking (OR=1.768; 95% CI=0.371-8.425) compared to non-smokers.

Conclusion: in this study, all cases of diabetes mellitus and prediabetes mellitus were suffered along with hypertension. The prevalence of severe periodontitis in prediabetes-hypertension patients increased compared to hypertensive-DM patients. There was an increased possibility of severe periodontitis in the risk factors groups of age 61-70 years, obesity, and smoking.

INTRODUCTION

Stroke is currently being a public health problem in most countries, both in developed and developing countries. Stroke is a cerebrovascular disease that can be caused by atherosclerosis. The risk factors for cerebrovascular disease include smoking, diabetes mellitus, obesity, hypercholesterolemia, and hypertension. Nowadays, the concerns to study on the effects of oral health and atherosclerosis is increasing, which is associated with cerebrovascular disease. Periodontitis is one of the examples which associated with stroke. Several studies have shown the association between chronic infectious diseases, including periodontal tissue disease with stroke risk factors.[1]

Prediabetes is one of the manifestations of metabolic syndrome which is the early sign/condition of diabetes mellitus. The history of prediabetes begins with risk factors such as increasing age, obesity, body fat distribution, lack of physical activity, and hyperinsulinemia associated with type 2 diabetes. Prediabetes is a hidden threat because it can induce health problems without symptoms. If this condition is not managed properly, it will cause severe diseases in the future. Prediabetes can increase the risk of type 2 diabetes and other cerebrovascular diseases.[2]

Diabetes mellitus is a risk factor for ischemic stroke characterized by hyperglycemia due to relative or absolute deficiency of insulin, especially in patients aged less than 65 years with increased levels of HbA1c. The incidence of stroke is two-fold higher in diabetic patients than in non-diabetic patients. People with a history of diabetes mellitus are at risk for microvascular complications that are pathologically related to periodontal

disease.[3]

Epidemiological studies determined that approximately 14% of the population had periodontitis. The percentage of periodontitis increased in the United States population, representing 47.2% of those over 30 years old. This prevalence continued to increase to 70.1% at the age over 65, and 5% - 15% had severe form in the adult population. Men showed worse periodontal status than women (56.4% vs 38.4%), as well as lower levels of education and income (66.9%). The prevalence increased along with diabetes mellitus, smoking, and obesity as risk factors for the development of periodontal disease.[4]

Glucose levels in gingival crevicular fluid (GCF) in uncontrolled diabetes mellitus were higher than in controlled diabetes mellitus patients. This resulted in the biofilm and plaque layer content on the tooth surface, which serves as a place for bacteria to attach. Various kinds of bacteria will reproduce better because of adequate food intake, causing the development of caries and periodontal disease.[5]

Diabetes mellitus can cause several manifestations in the oral cavity including gingivitis and periodontitis, loss of gingival attachment, increased degree of tooth unsteadiness, xerostomia, alveolar bone resorption and tooth loss. In this study, the emphasis will be on periodontitis, which is a chronic infectious disease associated with risk factors for ischemic stroke and diabetes mellitus, namely hypertension, dyslipidemia, obesity, and smoking which will be analyzed further to prevent recurrent stroke.[6]

METHOD

This study was a cross sectional study conducted in the inpatient ward of Kariadi Hospital Semarang from January to March 2020.

The subjects have fulfilled and met the following inclusion criteria: 1) The patients agreed to participate in the study (informed consent), 2) The first time patients had ischemic stroke with diabetes mellitus at the aged 50-70 years, 3) The first time patients had ischemic stroke with prediabetes mellitus at the aged of 50-70 years; and the subject did not have the following exclusion criteria: 1) Ischemic

stroke patients with diabetes mellitus or prediabetes mellitus who have lost more than half of the total number of teeth (20 teeth), 2) Ischemic stroke patients with diabetes mellitus or prediabetes mellitus suffering from periodontal abscess, 3) Ischemic stroke patients with diabetes mellitus who experienced the decreased level of consciousness, 4) Recurrent ischemic stroke patients.

The dropout criteria is: 1) Patients whose progress was unknown/could not be contacted both patients and their families, during the specified follow-up time, 2) Ischemic stroke patients who died before the completion of the study.

The research for study subjects was carried out in the emergency department. When the patient first arrived, informed consent, history taking, neurological

Table 1. The Characteristics of study subjects

Variable	Ischemic Stroke		p
	DM	Prediabetes	
Age			
51 – 60	9 (42.9)	6 (28.6)	0.334
61 – 70	12 (57.1)	15 (71.4)	
Gender			
Male	15 (71.4)	12 (57.1)	0.334
Female	6 (28.6)	9 (42.9)	
Hypertension			
Yes	21 (100)	21 (100)	
No	0 (0)	0 (0)	
Dyslipidemia			
Yes	13 (61.9)	10 (47.6)	0.352
No	8 (38.1)	11 (52.4)	
Obesity			
Yes	16 (76.2)	13 (61.9)	0.317
No	5 (23.8)	8 (38.1)	
Smoking			
Yes	13 (61.9)	12 (57.1)	0.753
No	8 (38.1)	9 (42.9)	
Periodontitis			
Severe	16 (76.2)	5 (23.8)	0.001
Mild	5 (23.8)	16 (76.2)	

Table 2. Periodontitis in diabetes mellitus-hypertension and prediabetes-hypertension (HT)

Variable	Periodontitis		PR	p
	Severe	Mild		
Diabetes-HT	16 (76%)	5 (24%)	3.3	0.001*
Prediabetes-HT	5 (24%)	16 (76%)		

*Significant (p<0.05)

Table 3. Results of multivariate logistic regression analysis on periodontitis and risk factors affecting DM subjects

Variable	Adjusted OR	95% CI		p
		Min	Max	
Diabetes mellitus-hypertension	0.066	0.012	0.354	0.002
Age	2.626	0.473	14.587	0.270
Dyslipidemia	0.392	0.076	2.016	0.262
Weight	2.346	0.382	14.428	0.357
Smoking	1.768	0.371	8.425	0.475

*Significant (p<0.05)

examination, head CT scan, and 4 ml of venous blood sampling were performed at the emergency room/ inpatient ward of Kariadi Hospital, Semarang. The blood sample was examined in the central laboratory of Kariadi Hospital Semarang, then a research questionnaire was filled out, and assessed by Miller's Mobility Index (MMI).

All data were statistically analyzed using the SPSS for Windows version 20 program. It was conducted in two stages. The first stage was the descriptive statistics stage to determine the basic characteristics of the subjects. The second stage was the multivariate analysis stage to determine the most significant risk factor that could affect the clinical outcome of patients using logistic regression methods.

RESULTS

At the end of the study, 42 subjects were obtained to be analyzed. The demographic characteristics of patients associated with diabetes mellitus and prediabetes mellitus can be seen in Table 1.

Univariate Analysis

Diabetes mellitus patients aged 51-60 years were 9 patients (42.9%) aged and 12 patients (57.1%) aged 61-70. Male diabetes mellitus patients were 15 patients (71.4%) and 6 patients (28.6%) were female.

Based on risk factors, diabetes mellitus patients who had hypertension were 21 (100%) patients, 0 (0%) had no hypertension, 13 patients (61.9%) had dyslipidemia, 8 patients (38.1%) did not have dyslipidemia, 16 patients (76.2%) had obesity, 5 patients (23.8%) were not obese, 13 patients (61.9%) were smokers, and 8 patients (38.1%) were non-smokers (Table 1).

Meanwhile, based on periodontitis characteristics, 16 diabetes mellitus patients (76.2%) had severe periodontitis and 5 patients (23.8%) had mild periodontitis. There were no any significant differences statistically between two groups in the characteristics of age, gender, risk factors for hypertension, dyslipidemia, obesity and smoking. However, there were significant differences in the periodontitis subjects (p = 0.001) (Table 1).

All cases of diabetes mellitus and prediabetes mellitus were both suffered along with hypertension. Therefore, for the next discussion, the subjects would be divided into the DM-hypertension and prediabetes-hypertension groups.

The analysis to compare the degree of periodontitis in DM-Hypertension (HT) and prediabetes-hypertension groups can be seen in Table 2. The results showed that the possibility of experiencing severe periodontitis cases in DM-HT was 3.3 times higher than prediabetes-HT.

Multivariate analysis

Multivariate analysis was conducted to determine the effect of diabetes mellitus risk factors simultaneously on the degree of periodontitis. The analysis used a logistic regression test consisting of five variables, namely DM-HT (p=0.002, OR=0.066), aged 61-70 years (p=0.270, OR=2.626), dyslipidemia (p=0.262, OR=0.392) , obesity (p=0.357, OR=2.346), smoking (p=0.475, OR=3.597). The analysis to see the relationship of each diabetes mellitus risk factor that played a role in periodontitis can be seen in Table 3.

The result of multivariate analysis showed that there were 3 risk factors for diabetes mellitus wich considered to have an effect on severe periodontitis, namely 61-70 years of age (p = 0.270, OR=2.626; 95% CI 0.473–14.587), obesity (p=0.357, OR=2.346; 95% CI 0.382-14.428), and smoking (p=0.475; OR=3.597; 95% CI 0.371-8.425). The OR of the subjects aged 61-70 years old was 2.6, which showed that people aged 61-70 years had a risk of suffering from severe periodontitis 2.6 times higher than mild periodontitis, compared to the subjects aged 51-60 years after controlled with variable DM-HT, dyslipidemia, obesity, and smoking. The OR of obesity was 2.3, which showed that obese people had a 2.3 times higher risk of suffering from severe periodontitis than non-obese after being controlled with DM-HT, age, dyslipidemia, and smoking variables. Meanwhile, the OR of smoking was 1.7, which showed that people who smoke had a risk of suffering from severe periodontitis 1.7 times higher than mild periodontitis compared to those who did not smoke after being controlled with DM-HT, age, dyslipidemia, and obesity variables (Table 3).

DISCUSSION

Age is an irreversible risk factor. As people get older, the risk of experiencing diabetes mellitus also increases that could increase the incidence of ischemic stroke as well. In a study conducted in Iowa, Switzerland by Robert, showed that people with diabetes mellitus at age >60 increased 3 times more than those aged <55 years old. Age >65 years, it is often associated with diabetes mellitus because in elderly, the body's function is physiologically decreased and leads to a decrease in insulin secretion or resistance so that the body's ability to control high blood glucose levels is not optimal.[7]

The respondents in this study were 71.4% male. The results of this study were contradicted with the theory which stated that women were more at risk of diabetes than men, because physically they had greater chance of the increase of body mass index, menstrual cycle syndrome, as well as menopause, which caused the fat easily accumulated obstructing glucose transport into the cell. This might be due to the fact that this study found more male subjects than female.[8]

Hypertension is one of the risk factors for diabetes mellitus which can cause ischemic stroke. Subjects who suffered from hypertension with diabetes mellitus or prediabetes mellitus were 100%. In this case, all subjects suffered from hypertension. Blood pressure increased due to the changes in endothelial function in type 2 diabetes mellitus patients. Uncontrolled blood sugar levels can lead to various complications in type 2 diabetes mellitus patients. One of the complications that often occurs is macroangiopathy, which is complication in large blood vessels that affects blood pressure change. Insulin resistance and hyperinsulinemia in diabetes mellitus patients can increase peripheral vascular resistance and vascular smooth muscle contractility through an over-response to norepinephrine and angiotensin II. This condition causes an increase in blood pressure through physiological feedback mechanism and the renin-angiotensin-aldosterone system.[9]

The amount of subjects who suffered from dyslipidemia were more than non-dyslipidemia as many as 13 (61.9%) and 8

(38.1%), respectively. A study conducted by Jisieke-Onuigbo et al. showed that the number of dyslipidemia was 90.7% out of 108 patients treated with type 2 diabetes. Cholesterol HDL reduction was the highest abnormality (62%) followed by hypertriglyceridemia (56.5%), hypercholesterolemia (53.7%), and hyper-LDL (44.4%). This was in accordance with the theory which stated that insulin defects and hyperglycemia were the underlying causes of lipoprotein abnormalities or dyslipidemia in type 2 diabetes, including the increased level of triglycerides (TG) and low density lipoprotein (LDL), and decreased level of high-density lipoprotein (HDL).[10]

The subjects who suffered from obesity were 16 patients (76.2%) and non-obese were 5 patients (23.8%). Obese individuals had higher risk of experiencing diabetes mellitus than a non-obese individuals. Based on the theory, insulin adiponectin decreases in obese condition. In insulin resistance, glucose production increased and glucose use decreased increasing blood sugar levels.[11]

Subjects who smoked were more than non-smoker subjects, 13 (61.9%) and 8 (38.1%) patients, respectively. Theoretically, oxidative stress induced by substances in cigarettes can increase epinephrine and norepinephrine level. The release of these hormones will affect the sympathetic nervous system and accelerate the rate of gluconeogenesis and glycogenolysis.[12]

The subjects with severe periodontitis had higher amounts than subjects with mild periodontitis, as many as 16 subjects (76.2%) and 5 subjects (23.8%). The results showed that diabetes mellitus and prediabetes mellitus groups with periodontitis were significantly different (p=0.001).[13]

All cases of diabetes mellitus and prediabetes mellitus in this study were both accompanied by hypertension. A study conducted in an outpatient internal medicine clinic in two major hospitals in Jordan on periodontal status, which showed that periodontal disease was more severe in type 2 diabetes mellitus patients. The severity of periodontal disease was significantly higher in patients

with diabetes >5 years than ≤ 5 years. Diabetes mellitus was a predisposing factor that accelerated periodontal tissue damage initiated by microbial agents and vascular changes. The periodontal tissue would experience a lack of oxygen blood supply, causing an increase in the growth of anaerobic bacteria which resulted in the decrease of tissue defense and function, thus lead to periodontal tissue infection.[14]

The multivariate analysis reported that 61-70 years in diabetes mellitus patients was significantly associated with severe periodontitis after controlling for DM-HT, dyslipidemia, obesity, and smoking. Obesity in patients with diabetes mellitus increased the risk of suffering from severe periodontitis after controlling DM-HT, dyslipidemia, and smoking. Linden, et al. examined the association between obesity and periodontitis in Europe in the 60-70 years who had a BMI> 30 (kg/m²) with a prevalence of 10.1% (OR=1.77; 95% CI=11.24-2.53) and (p-value=0.004) compared to non-obese with a prevalence of 6.3%.[15,16]

Meanwhile, smoking in diabetes mellitus patients increased the risk of suffering from severe periodontitis after being controlled with DM-HT, dyslipidemia, and obesity.

This study has several limitations, for example, this was a cross sectional study. In this study, all cases of diabetes mellitus were accompanied by hypertension, which could lead to bias or changes in the analysis. Based on these limitations, further study is needed to obtain practical clinical use.

CONCLUSION

In this study, all cases of diabetes mellitus and prediabetes mellitus were suffered along with hypertension. The prevalence of severe periodontitis in prediabetes-hypertension is increased compared to DM-hypertension patients. This is probably because hypertension in prediabetes mellitus is stronger in influencing the incidence of severe periodontitis. There was an increased possibility of experiencing severe periodontitis in patients with risk factors of 61-70 years of age, obesity, and smoking

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