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RESEARCH

HBA1C LEVELS IN TYPE 2 DIABETES MELLITUS PATIENTS WITH AND WITHOUT INCIDENCE OF THROMBOTIC STROKE

(Kadar HbA1c Pasien Diabetes Melitus Tipe 2 dengan dan Tanpa Kejadian Strok Infark Trombotik)

Dafina Balqis1, Yudhi Adrianto2, Jongky Hendro Prayitno3

ABSTRACT

Stroke has been stated as one of the leading cause of mortality globally. Association between the incidence of stroke with diabetes have long known. Specifically, duration of diabetes and glycemic control, which monitored through HbA1c levels, has shown its relation with incidence of stroke and other cardiovascular diseases. This study is to determine the difference of HbA1c levels between type 2 diabetes mellitus patients with and without the incidence of thrombotic stroke. The method used in this study is analytic retrospective using patients’ medical records for 3.5 years. This study collected data of HbA1c levels from 443 type 2 diabetes mellitus patients then compared means of HbA1c levels between type 2 diabetes mellitus patients with incidence of thrombotic stroke (n=74) and without incidence of thrombotic stroke (n=369). The comparison of HbA1c levels were also done separately between males and females. This study found the average HbA1c levels were high on both sample groups (10.49%±2.53% for group with incidence of thrombotic stroke and 10.44%±2.8% for group without incidence of thrombotic stroke) with comparison of means p>0.05. Comparison which done separately on males and females also showed similar results with p>0.05. In conclusion, HbA1c levels in both study groups were equally high and there was no significant difference in HbA1c levels found in patients with type 2 diabetes with and without incidence of thrombotic stroke.

Key words: Stroke, diabetes mellitus, HbA1c, cardiovascular disease

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INTRODUCTION

Diabetes Mellitus (DM) is a metabolic disease mainly characterized by hyperglycemia condition. Metabolic deregulation associated with diabetes can cause secondary pathophysiology on various organ systems, causing various complications. In vascular system, diabetes can give microvascular complications, such as peripheral vascular disorders, nephropathy, neuropathy, and diabetic retinopathy, as well as macrovascular complications, such as coronary heart disease and stroke. Diabetes Mellitus, moreover, has been declared as one of the risk factors for stroke. Stroke is a clinical disorder characterized by a decrease in neurological function that occurs suddenly at intervals of 24 hours. This is caused by the resistance of blood flow to the brain, leading to the death of cells in the tissues involved. Stroke, consequently, is a common cause of death in the world and the leading cause of death in many countries in Southeast Asia. In Indonesia, there were 300 of the 100,000 deaths caused by stroke with the incidence of stroke per 1000 people. Chronic hyperglycemia that occurs in people with diabetes, furthermore, can induce bad adaptation to the endothelium, thus contributing in the development of atherosclerosis in macrovascular complications. Some of the key mechanisms that have a role in the occurrence of atherosclerosis as the effects of hyperglycemia are an increased flow of glucose in the polyol pathway, AGE formation, activation of protein kinase C (PKC) and oxidative stress. In addition, HbA1c reflects the mean of plasma glucose level for 2–3 months. HbA1c is a superior parameter in diagnosing and monitoring the blood glucose of patients with DM. Glycated hemoglobin together with the duration of diabetes and hypertension is positively associated with arterial stiffness in atherosclerosis. Thus, this research aimed to determine differences in HbA1c levels among patients with type 2 diabetes mellitus with and without thrombotic infarct stroke.

METHODS

This research was a retrospective analytical study using secondary data from medical records. Data used was collected from Lamongan Muhammadiyah Hospital, which has an integrated medical record system. Thus, all medical records of patients in this hospital were completely recorded in accordance with the medical record number, so the data collection could be facilitated easily. The number of population selected for this research was 2494 patients with type 2 diabetes as recorded in 3.5 years, i.e., from January 2012 to June 2015. The entire population was then filtered with several inclusion criteria. First, the patients had to be aged between 45–80 years old. Second, the patients had to have complete data of age, blood pressure, lipid profile (total cholesterol, HDL cholesterol, LDL cholesterol and triglycerides) and HbA1c. The age range of 45–80 years had been selected since it is more common in male patients up to 80 years and then becomes equally prevalent in male and female patients who suffer the first ischemic stroke. The sharp decline in the prevalence of diabetes in male patients is after the age of 70 years old, whereas in female patients the prevalence declines after the age of 80 years. The rest of the samples was filtered by excluding patients who were anemic, so the final number of the samples were 443 people. These samples were then divided into two groups, namely type 2 diabetes patients with stroke and type 2 DM patients without stroke.

HbA1c levels used for the group with the incidence of thrombotic infarct stroke in this research were HbA1c levels when stroke attack and HbA1c levels prior the stroke. Meanwhile, HbA1c levels used for the group without thrombotic infarct stroke were the medical records of patients with type 2 DM from January 2012 to June 2015.

![Figure 1. Schematic of sampling.](image-url)
last HbA1c levels. The entire samples of HbA1c levels then were determined by chromatography based HPLC assay in the laboratory of Muhammadiyah Hospital, Lamongan.

Finally, all data taken from samples were presented descriptively. Next, a normality test, Kolmogorov-Smirnov test was conducted. A homogeneity test then was also performed using Lavene test on the entire samples. After having found that HbA1c variables were normally distributed and had a homogeneous variance, a comparison test. The t test was conducted using two independent samples.

RESULTS AND DISCUSSION

The number of samples was 443 patients with type 2 diabetes. Those samples were divided into two groups, type 2 diabetes patients with thrombotic infarct stroke (n=74) and type 2 diabetes patients without thrombotic infarct stroke group (n=369). Characteristics of the samples are shown in Table 1 and 2.

Table 1. Characteristics of the research sample group with thrombotic infarct stroke

<table>
<thead>
<tr>
<th>Variables</th>
<th>Data Convergence</th>
<th>Normality</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>57.03±7.94</td>
<td>p&gt;0.05</td>
</tr>
<tr>
<td>HbA1c (%)</td>
<td>10.49±2.53</td>
<td>p&gt;0.05</td>
</tr>
<tr>
<td>Systolic BP (mmHg)</td>
<td>167.61±33.45</td>
<td>p&gt;0.05</td>
</tr>
<tr>
<td>Diastolic BP (mmHg)</td>
<td>90.28±18.46</td>
<td>p&gt;0.05</td>
</tr>
<tr>
<td>Total Cholesterol (mg/dL)</td>
<td>213.29±59.37</td>
<td>p&gt;0.05</td>
</tr>
<tr>
<td>HDL- Cholesterol (mg/dL)</td>
<td>35.67±7.96</td>
<td>p&gt;0.05</td>
</tr>
<tr>
<td>LDL- Cholesterol (mg/dL)</td>
<td>133.72±47.02</td>
<td>p&gt;0.05</td>
</tr>
<tr>
<td>Triglyceride (mg/dL)</td>
<td>176.5 (Median)</td>
<td>p&gt;0.05</td>
</tr>
<tr>
<td></td>
<td>124 (Mode)</td>
<td></td>
</tr>
</tbody>
</table>

Table 2. Characteristics of the research sample group without thrombotic infarct stroke

<table>
<thead>
<tr>
<th>Variables</th>
<th>Data Convergence</th>
<th>Normality</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>56.36±6.74</td>
<td>p&lt;0.05</td>
</tr>
<tr>
<td>HbA1c (%)</td>
<td>10.44±2.8</td>
<td>p&gt;0.05</td>
</tr>
<tr>
<td>Systolic BP (mmHg)</td>
<td>150.14±34.41</td>
<td>p&gt;0.05</td>
</tr>
<tr>
<td>Diastolic BP (mmHg)</td>
<td>84.88±18.15</td>
<td>p&gt;0.05</td>
</tr>
<tr>
<td>Total Cholesterol (mg/dL)</td>
<td>199.76±67.29</td>
<td>p&gt;0.05</td>
</tr>
<tr>
<td>HDL- Cholesterol (mg/dL)</td>
<td>34.97±13.06</td>
<td>p&gt;0.05</td>
</tr>
<tr>
<td>LDL- Cholesterol (mg/dL)</td>
<td>122.97±52.11</td>
<td>p&gt;0.05</td>
</tr>
<tr>
<td>Triglyceride (mg/dL)</td>
<td>187 (Median)</td>
<td>p&gt;0.05</td>
</tr>
<tr>
<td></td>
<td>234 (Mode)</td>
<td></td>
</tr>
</tbody>
</table>

The homogeneity of the samples then was examined in each variable using Lavene test. The entire sample showed a homogenous variance in HbA1c variables with p=0.154 (p>0.05). Meanwhile, the variables of HDL cholesterol and triglycerides showed non-homogeneous data (p<0.05).

The mean of HbA1c levels in type 2 diabetes patients with stroke incidence was 10.49±2.53, while the mean in type 2 diabetes patients without stroke was 10.44±2.8. The results of t-test on two independent samples showed no significant difference in HbA1c between the group of type 2 diabetes patients with thrombotic infarct stroke and the group of type 2 diabetes patients without thrombotic infarct stroke (p=0.871). Similar results were also obtained in two independent samples after t test was performed separately on the samples of male patients (p=0.617) and female patients (p=0.490). The mean HbA1c levels in both male and female patients can be seen in Figure 2.

Figure 2. The mean of HbA1c levels in the research samples based on sex.

These results are supported by the results of Veterans Affairs Diabetes Trial (VADT) stating that intensive glucose control could not lower the incidence of cardiovascular disease in 1791 people with type 2 diabetes mellitus.14 However, after the results of the study were reviewed together with the various results of other studies, it can be concluded that tight blood sugar control for many years can reduce the risk of cerebrovascular disease.15

The insignificant comparative results of HbA1c levels is also incompatible with a large observational research showing the increased risk of progressive on the incidence of cardiovascular disease, stroke, coronary heart disease and total mortality due to
elevated levels of HbA1c. It is also contrary to a theory stating that uncontrolled hyperglycemia—marked with high HbA1c levels—may increase the incidence of cardiovascular disease. Chronic hyperglycemia can increase AGE levels in the circulation and trigger a variety of signaling processes in the body. Vascular conditions, such as arterial stiffness and adhesion as well as platelet aggregation caused by AGES can lead to stroke, myocardial infarction, heart failure and entirely death.

If the characteristics of the samples were observed, furthermore, it is known that there was no difference in the two groups since a variety of other independent variables can lead to stroke, such as blood pressure samples. Low blood pressure (<110/65 mmHg) or high one (≥160/100 mmHg) is known to be associated with the incidence of stroke in patients with type 2 diabetes mellitus. In both groups, the mean of systolic BP reached more than 160 mmHg, positively associated with the incidence of stroke.

Additionally, the lipid profile of the research samples may also affect the incidence of stroke in patients with type 2 diabetes mellitus patients. Type 2 diabetes mellitus patients commonly experience diabetic dyslipidemia characterized by elevated levels of triglycerides, reduced levels of HDL and increased sdLDL that can cause endothelial dysfunction and thickening of the tunica media. Non-HDL cholesterol levels, on the other hand, are associated with an increased risk of stroke incidence and mortality related to diabetes. Summary of various researches suggests that decreased levels of LDL cholesterol in patients with type 2 diabetes may reduce the risk of stroke.

The results of this research showed that there was no difference in the mean of HbA1c levels between in type 2 diabetes mellitus patients with thrombotic infarct stroke and in type 2 diabetes mellitus patients without thrombotic infarct stroke. This comparison was conducted since there was a difference in the incidence of stroke between male and female patients. The incidence of stroke was higher in male patients with type 2 diabetes than in female ones. These results differ from prospective studies suggesting a positive correlation between levels of HbA1c and the risk of stroke in female patients with type 2 diabetes mellitus. The increased risk of stroke and cardiovascular disease in female patients with diabetes is expected because of the tendency for them to reach the high Body Mass Index (BMI) triggering diabetes.

Nevertheless, this research still has some limitations, including the design of research using secondary data. Medical records had made the researchers less flexibility in choosing the samples due to limited knowledge of the written data. Therefore, it was too hard to maximize the homogeneity of the samples. This research also had not collected data on the genetic history of cardiovascular disease, smoking and BMI yet, which could also be able to determine the incidence of cardiovascular complications in patients with type 2 DM.

In addition, the results of this research still have not paid attention to the patient’s history of various antidiabetic treatment, anti-hypertensive drugs, or drugs for dyslipidemia. The effect of those various therapies actually can also affect the incidence of cardiovascular disease in diabetes patients.

Taking a level of HbA1c, not the average one, furthermore, can also influence the absence of differences in levels of HbA1c in both groups. This value could be obtained when the patient was first diagnosed, so the value was likely to be high. Similarly, a research conducted by Litwak, et al with large samples used only one value of HbA1c to predict the incidence of complications of diabetes. Macrovascular complications actually will occur once faced with high HbA1c levels for many years. Hence, for similar further research, it would be better if the blood sugar control variables are obtained through the mean of HbA1c levels since fluctuations in levels of HbA1c can be potential predictors of cardiovascular disease incidence.

CONCLUSION AND SUGGESTION

In conclusion, the results of this research show that there is no difference in HbA1c levels between type 2 diabetes patients with thrombotic infarct stroke and type 2 diabetes patients without thrombotic infarct stroke. The mean of HbA1c levels in both groups is equally high. Similar results are also found in a separate test between male and female genders. This research also finds that the incidence of thrombotic infarct stroke as one of the macrovascular complications of type 2 diabetes does not only rely on blood sugar control, but also other factors affecting endothelial dysfunction, such as lipid profile and blood pressure.

However, this research still has not directly compared a wide range of other risk factors affecting endothelial dysfunctions. Thus, further researches are needed to compare the various other risk factors in order to provide complete information about the variables that need to be controlled by the patients to prevent complications.
Finally, this research indicates that type 2 diabetic patients in have high HbA1c levels. Therefore, medical apparatus must conduct further efforts to improve patients’ adherence to have routine treatment and take regular medication to control their blood sugar levels.

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