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Relationship between Atherogenic Index of Plasma with HbA1c Levels in Type 2 Diabetes Mellitus Patients

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ABSTRACT

Type 2 Diabetes Mellitus (T2DM) is a global health problem due to an increasing prevalence and incidence. HbA1c as a parameter for glycemic control is still above the desired target of 7%. Atherogenic Index of Plasma (AIP) is predicted to be an indicator of cardiovascular disease risk in T2DM. Dyslipidemia in T2DM patients showed a result of increased triglyceride and decreased HDL cholesterol levels. This study aimed to determine the relationship between HbA1c and AIP, triglycerides, and HDL cholesterol in T2DM patients. An analytical observational study using a cross-sectional method on 74 DMT2 patients who underwent HbA1c and lipid profile examinations in January-March 2020. Atherogenic index of plasma was calculated by the logarithmic equation (triglycerides/HDL cholesterol). Data were analyzed by SPSS 25.0. The relationship between HbA1c with AIP, triglycerides, and HDL cholesterol using the Pearson correlation test. Atherogenic index of plasma (0.25±0.25) and triglycerides (211.92±146.09 mg/dL) were found to be higher in the poor glycemic control group (HbA1c > 7%) than AIP (-0.04±0.20) and triglycerides (108.96±38.96 mg/dL) in the good glycemic control group ($p < 0.05$). HDL cholesterol (40.08±12.64 mg/dL) was found to be higher in the poor glycemic control group than HDL cholesterol (52.28±18.12 mg/dL) in the good glycemic control group ($p < 0.05$). There was a significant positive correlation between HbA1c and AIP ($r=0.411$, $p=0.000$), HbA1c with triglycerides ($r=0.418$, $p=0.000$), and a significant negative correlation between HbA1c and HDL cholesterol ($r=-0.233$, $p=0.046$). Insulin resistance can cause lipid metabolism disorders, inflammation, oxidative stress, and coagulation disorders. Maintaining glycemic control and lipid control plays an important role in preventing diabetes complications. There is a significant positive correlation between HbA1c and AIP, HbA1c and triglycerides, and a significant negative correlation between HbA1c and total cholesterol in T2DM patients.

Keywords: Atherogenic index of plasma, HbA1c, HDL cholesterol, type 2 diabetes mellitus, triglyceride

INTRODUCTION

Type 2 Diabetes mellitus (T2DM) is a metabolic disease with hyperglycemic characteristics due to the decrease of insulin secretion by beta cells of the pancreas and/or insulin function due to insulin resistance. T2DM is a world health problem because the prevalence and incidence of this disease keep increasing. Type 2 diabetes mellitus is a developing epidemy that causes individual suffering, impacts productivity, decreases human resources, and increases health care bills.[1,2]

The Diabetes Mellitus (DM) population consists of 90% T2DM. International Diabetes Federation (IDF) 2011 reported 336 million people in the world suffering from T2DM and there are 4.6 million deaths each year or one death every seven seconds. This disease infects 12% of the adult population in the United State and more than 25% happens in the age above 65 years old. According to IDF data in 2014, Indonesia is the fifth country in the world, raising two levels compared to 2013 with 7.6 million people with diabetes.[2]

Changes in lifestyle such as consumption of food with high fat and calories combined with lack of physical activity causing excess storage of food and energy in the body are some of the causes of the increase of DM prevalance.[2] T2DM patients have two to four higher risks for cardiovascular disease compared to normal people. Dyslipidemia is a general condition that is related with bad glycemic control in T2DM. Glycemic control targets in Indonesia have still not met goals. HbA1c levels that, which is a glycemic control parameter is still above the desired target at 7%.[3,4]

The Atherogenic Index of Plasma (AIP) is a logarithmically transformed ratio of molar concentrations of triglyceride to HDL cholesterol that can be calculated by inserting the results of triglyceride and HDL concentration in the calculator of atherogenic risk or with a log equation (triglyceride/HDL cholesterol). Atherogenic index of

plasma is predicted as a cardiovascular risk indicator in T2DM and as an atherogenicity marker that is related to atherosclerosis risks to grade the severity of atherogenic dyslipidemia.[5,6]

Hypertriglyceridemia is one of the risk factors for coronary artery disease in T2DM, cardiovascular disease risks increase 18% every time DM patients' HbA1c levels increase 1%. The increase of HDL cholesterol concentration gives protection towards coronary heart disease, meanwhile, a decrease in HDL cholesterol levels especially those that are related to an increase in a triglyceride can increase cardiovascular risks. Maintaining glycemic and lipid control plays an important role in preventing microvascular and macrovascular complications related to DM. A 0.2% decrease in HbA1c concentration is reported to lower 10% mortality.[7,8]

This study is aimed to find the relationship between HbA1c and AIP, triglyceride, and HDL cholesterol in T2DM patients in Sanglah Hospital, Denpasar.

METHODS

This study was an analytic observational study using a cross-sectional method to find the relationship between AIP with HbA1c concentrations in patients with T2DM during January-March 2020. This study uses secondary data from Laboratory Information System (LIS) with 74 subjects. The subjects of this study are the population that fulfills the inclusion criteria. Inclusion criteria for this study are patients who are >18 years old diagnosed with T2DM for at least one year since data collecting and had HbA1c, triglyceride, and HDL cholesterol examined at the same time. Exclusion criteria in this study are anemia, history of kidney disease, history of liver disease, history of cardiac disease, incomplete medical data, and no history of laboratory examinations that support a diagnosis of T2DM, and medical history on the LIS for more than one year. The atherogenic index of plasma was calculated by an online calculator of atherogenic risk with an algorithm (triglyceride/HDL cholesterol). This study was approved by the Ethical Research Committee UNUD Medical Faculty of Sanglah Hospital, Denpasar with article number 2259/UN14.2.2.VII.14/LT/2020.

Research data were analysed statistically with SPSS 25.0. Numeric variables were presented in mean and standard deviation, the categorical variables will then be presented in total and percentage. Pearson correlation analysis was used to evaluate the relationship between HbA1c with AIP, triglyceride, and HDL cholesterol, if the data was not normally distributed, it would be analyzed using the Spearman correlation test. Correlation coefficient (r) between 0.00–0.24 is weak, 0.25–0.49 medium, 0.5–0.74 strong, 0.75–1.00 evaluated as very strong. The values were stated as significant if $p < 0.05$.

RESULTS AND DISCUSSIONS

This study was held throughout January–March 2020 with a total of 74 T2DM patients that fulfill the inclusion criteria, consisting of 37 males and 37 females. The study's sample characteristics according to age and gender do not show a significant difference between the good and poor glycemic control group (HbA1c ≤ 7% and HbA1c > 7%) with a $p > 0.05$ that shows that both groups have homogenous characteristic traits (Table 1).

Table 1. Samples characteristics

Characteristics	Good Glycemic Control (HbA1c ≤7) (n=25)	Poor Glycemic Control (HbA1c >7) (n=49)	p
Age (years old) (mean±SD)	58.39±10.02	62.92±12.80	0.099
Gender (n, %)			
Male	9(36%)	28(64%)	0.085
Female	16(57%)	21(43%)	
HbA1c (%) (mean±SD)	5.35±0.76	9.17±1.88	0.000
Triglyceride (mg/dL) (mean±SD)	108,96±38.96	211,92±146,09	0.000
HDL cholesterol (mg/dL) (mean±SD)	52.28±18.12	40.08±12.64	0.001
Atherogenic index of plasma (mean±SD)	-0.04±0.20	0.25±0.25	0.000

The number of T2DM patients with poor glycemic control 49 (66%) was higher than those with good glycemic control, which were only 25 patients (34%).

Triglyceride concentrations (211.92±146.09 mg/dL) were statistically significantly higher in the poor glycemic control group compared to triglyceride concentrations (108.96±38.96 mg/dL) in the good glycemic control group with a p-value < 0.05. HDL cholesterol concentrations (40.08±12.64 mg/dL) were significantly lower in patients with poor glycemic control compared to patients from the good glycemic control group (Table 1).

HbA1c concentrations were significantly higher in the poor glycemic control group (9.17±1.88 %) with HbA1c levels in the good glycemic control group (5.35+0.76%) with p < 0.05. The atherogenic index of plasma (0.25+0.25) was significantly higher in the poor glycemic control group compared to the group with the good glycemic control group (-0.04+0.20) with a p < 0.05 (Table 1).

Correlation analysis in this study showed a positive significant correlation between HbA1c and AIP (r=0.411, p=0.000, HbA1c with triglycerides (r=0.418, p=0.000), and a negative significant correlation between HbA1c and HDL cholesterol (r= -0.233, p=0.046) (Table 2). These results show that the higher the HbA1c concentrations, the higher the AIP and triglyceride in T2DM patients, and the higher the HbA1c concentration the lower the HDL cholesterol in patients with T2DM.

Table 2. Correlation of HbA1c concentration towards AIP, triglyceride, and HDL cholesterol in T2DM patients

Variable	HbA1c Concentration		
	n	r	p
AIP	74	0.411	0.000*
Triglyceride	74	0.418	0.000*
HDL cholesterol	74	-0.233	0.046*

*significant (p < 0.05)

Lipid profile and serum lipoprotein abnormalities in T2DM can contribute to coronary artery disease risks. Diabetes is linked with higher mortality and morbidity risks than cardiovascular disease. Glycated hemoglobin or HbA1c is the gold standard of glycemic control in the 6–8 week period.[9]

Diabetes mellitus complications can be prevented with good glycemic control. The target for glycemic control in Indonesia is still not fulfilled. HbA1c concentration in DM patients with poor glycemic control are higher compared to patients with good glycemic control. Most DM patients have an HbA1c above 7%, where good glycemic control has an HbA1c of < 7%.[7,8]

Type 2 diabetes mellitus patients with poor glycemic control (49 patients) were higher than patients with good glycemic control (25 patients). Mean HbA1c concentration as also higher in patients with poor glycemic control. The age span of T2DM patients in both male and female were in the 51–60 years old group.[10] The mean age in the group with good glycemic control compared to the poor glycemic control in this study was 58.39+10.02 years old and 69.92+12.80 years old, respectively.

Female patients usually have higher HDL cholesterol levels because males are easily exposed to oxidative stress compared to females that cause T2DM complications.[10,11] The number of female patients with poor glycemic control (43%) in this study was lower than males (64%).

Insulin resistance or deficiency in T2DM can cause lipid metabolism defects, inflammation, oxidative stress, and coagulation disorders. Dyslipidemia in DM patients increases the risk of cardiovascular disease. Dyslipidemia is one of the conditions that are related to poor glycemic control in T2DM. Lipid profile examinations must be done at least once a year and more often when needed. Patients that are deemed with a good lipid profile (LDL < 100 mg/dL, HDL > 50 mg/dL, triglyceride < 150 mg/dL) may have a follow-up examination every two years. Dyslipidemia that is common in DM patients is an increase in triglyceride, a decrease in HDL with a normal or slightly increased LDL.[8,12,13]

Patients with poor glycemic control in this study had higher mean triglyceride levels (211.92±146.09) mg/dL and lower mean HDL cholesterol level (40.08±12.64) mg/dL compared to those with good glycemic control with mean triglyceride levels and HDL cholesterol levels of (108.96±38.96) mg/dL and (52.28±18.12) mg/dL, respectively. This is in line with a study by Panjeta *et al.* in 2018 that had higher triglyceride and lower HDL cholesterol levels in patients with poor glycemic control.[8]

This study found a significant positive correlation between HbA1c and triglyceride (r=0.418, p=0.000). Correlation results were in concordance to Panjeta *et al.* that found a significant positive correlation (r=0.375, p=0.003) between triglyceride and HbA1c levels.8 The higher the triglyceride level, there would be the increase in HbA1c.

HDL cholesterol concentration and HbA1c has a negative significant correlation (r=-0.233, p=0.046) in this study. It is similar to results by Ratnasari *et al.* that also had a significant negative correlation between HDL cholesterol and HbA1c (r=-0.488, p=0.002), meaning the lower the HDL cholesterol levels the higher the HbA1c.[14]

The atherogenic index of plasma as an atherogenicity marker that is linked to the risk of atherosclerosis can be used to assess the severity of atherogenic dyslipidemia. Endothelial dysfunction is widely known as the main cause of atherosclerosis and cardiovascular disease in many populations. In normal conditions, the endothelial maintain normal vascular tonus, thrombocyte activity, leucocyte adhesion, and thrombosis. Patients with good glycemic control had lower AIP than those with poor glycemic control.[15,16]

There is a significant positive correlation between AIP with HbA1c concentration in this study (r=0.411, p=0.000). This result was in concordance with the study by Anjankar *et al.* that was found a significant positive correlation between AIP and HbA1c concentration (r=0.335, p=0.009) in T2DM patients.[9] The higher the HbA1c, the higher the AIP.

Patients with good glycemic control had a mean AIP that was significantly lower than those with poor control. This is similar to a study by Betabun *et al.* in 2015 that found a higher AIP in the group with poor glycemic control.[12]

CONCLUSIONS AND SUGGESTIONS

There is a medium positive significant correlation between HbA1c with AIP and triglyceride with a weak negative significant correlation between HbA1c and HDL cholesterol. This study has certain limitations. The cross-sectional nature of this study precluded any determination of the causal relationship between AIP and the risk of cardiovascular complications in T2DM patients. The value of AIP in clinical practice needs to be further confirmed by prospective follow-up studies.

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