HbA1c as Glycemic Control is Associated with Triglycerides Levels in Type 2 Diabetes Mellitus

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Abstract— Based on WHO data in 2017, around 150 million people suffer from diabetes mellitus worldwide and it is estimated that this number can double by 2025. Most of this increase will occur in developing countries due to population growth, aging, unhealthy diets, obesity and sedentary lifestyle. Type 2 Diabetes Mellitus (DM) is a metabolic disorder that is marked by the rise in blood sugar due to a decrease in insulin secretion by pancreatic beta cells. The causes of microvascular and macrovascular complications in DM are chronic hyperglycemia that is measured by Hemoglobin A1c (HbA1c) as a control, and the risk factors to be proven, namely serum lipid levels, especially triglycerides which increase in dyslipidemia. Therefore hyperglycemia and dyslipidemia should be reduced, so that the number of microvascular and macrovascular complications in DM patients can be slowed down. The purpose of this study is to measure HbA1c as glycemic control were associated with triglycerides levels in type 2 DM. The method used was cross sectional design conducted by taking 90 data patients who performed HbA1c and triglycerides concurrently at Tarakan Hospital in Central Jakarta in 2017. It was found in 80 patients (88.9%) with age above 45 years, the average HbA1c level was 8% which showed poor control and the mean level of triglycerides above the reference was 170 mg/dL. An increase in triglyceride levels as well as an increase in HbA1c levels is a poor indicator of glycemic control. Based on the results of statistical tests, there was a significant correlation (p value = 0,000) between HbA1c and triglycerides with a positive correlation direction (r = 0,594). It can be concluded, the worse the HbA1c control, the higher triglyceride levels in the blood so that patients with diabetes mellitus must carry out glycemic control regularly to prevent complications.

Keyword: HbA1c, Triglycerides, Type 2 DM

1.   INTRODUCTION

Based on WHO data in 2017, around 150 million people suffer from diabetes mellitus worldwide and it is estimated that this number can double by 2025. Most of this increase will occur in developing countries due to population growth, aging, unhealthy diets, obesity and sedentary lifestyle (WHO, 2017). Tarakan Hospital is a type A hospital which is a reference from type B Hospital. Based on the results of the 10 biggest diseases in 2016, DM was the most common disease with the number of patients diagnosed with type 2 DM were 3112 patients. The total of death cases with DM diagnosis in Tarakan Hospital were 150 patients.Type 2 Diabetes Mellitus (DM) is a metabolic disorder characterized by the increase of blood glucose as an effect of insulin decrease secretion by pancreatic beta cells and or insulin dysfunction (Kerner,WdanBruckel,J. 2014). To reduce the incidence and severity of type 2 DM, preventions are performed like lifestyle modification and medication such as hyperglycemic and insulin oral drugs (Fatimah, R.N. 2015, ADA, 2014). One of the causes of the Hyperglycemia comes from carbohydrate intake that can stimulate glycogen formation from glucose, synthesis of fatty acids and cholesterol and accelerate the metabolism of carbohydrates which will directly form triacylglycerol (triglycerides) in the liver (Ekawati, 2012, Rahayuni, 2016).

In uncontrolled DM,microvascular and macrovascular complications can be occured, namely the condition of chronic hyperglycemia which its control is measured through hemoglobin A1c (HbA1c) checkup, and the risk factors that want to be proven, namely serum lipid levels, especially triglycerides which increase in dyslipidemia (Refa and Dewi, 2013, Rahmawati, Natosba and Jaji. 2016).

Hyperglycemia is characterized by an increase in glycohemoglobin which causes an increase in the level of glycosylated hemoglobin (HbA1c). In an effort to prevent chronic complications of DM patients, proper control is needed. Diabetes can be well controlled if lipid levels and HbA1c levels reach the expected level. Measurement of HbA1c levels in the blood is considered important because this examination will produce an average index of blood glucose levels during the age of erythrocytes (Primadana, Pandelaki and Wongkar, 2016).

A study shows that HbA1c is not only useful as a long-term biomarker of glycemic control, but also a good predictor of lipid profiles. Thus, monitoring of glycemic control by using HbA1c can have additional benefit of identifying diabetic patients who are at greater risk of cardiovascular complications (Shivanand, Manjunath and Jeganathan, 2012).

A Research conducted in India showed a positive correlation between HbA1c levels and triglycerides and weak correlation between the examination of cholesterol, LDL and VLDL. (Meenu, Jayendrasinh and Neeta, 2013). Other studies showed significantly that the triglycerides levels are higher than cholesterol levels in diabetes (Shivanand, Manjunath and Jeganathan, 2012).

 The purpose of this study is to measure HbA1c as glycemic control associated with triglycerides levels in type 2 DM.

2. MATERIALS AND METHOD

The study used an analytic and cross sectional observational design by looking at the data from medical records from Tarakan Hospital which is located at JalanKyaiCaringin No.7, Cideng, Gambir, Central Jakarta, DKI Jakarta 10150 during the months of January - June 2018.

The inclusion criterion set for type 2 DM was patients without knowing the patient's diet at all ages and sex, performing HbA1c examination and examining triglycerides at the same time.

Examination **of HbA1c**

HbA1c examination using Capillary Electrophoresis SebiaMinicap Flex-Piercing method was based on the principle of capillary electrophoresis in free solution. The hemoglobin fraction derived from EDTA blood specimens was separated in silica capillaries, by electrophoretic mobility and electro osmotic flow at high stresses in alkaline buffers. During migration, the hemoglobin fraction was directly detected at an absorbance of 415 nm. The internal quality stabilization was done every day. Reference Value: <6.5%.

Examination of triglycerides

Horiba ABX Pentra 400 was used for triglyceride examination. The working principle of the tool based on the white light of a tungsten halogen lamp captured by the first condenser lens, then it underwentreflection from the reflecting mirror and it was sharpened by a second condenser lens, then the light would go through the cuvette and interact with the mixture of reagents and the finished reacting material. The light transmitted from the cuvette was directed and centered by the third condenser lens and then captured by a kind of concave mirror *reflective grating spreads* into monochromatic light and reflects it on PDA detectors (Analogical Pixel Digital).

The GPO-PAP method was used for the examination of triglycerides with fasting serum specimens of 10-12 hours. Triglycerides by the lipoprotein lipase enzyme were converted to glycerol and free amino acids. Glycerol formed was reacted with ATP with the help of the enzyme glycerol kinase to form glycerol-3 phosphate and ADP. Glycerol-3-phosphate was oxidized with the help of glycerol phosphate oxidase enzyme to dihydroxy acetone phosphate and hydrogen peroxide. The hydrogen peroxide formed would oxidize chlorophenol to form pink quinonymin. The color intensity formed was proportional to the level of triglycerides in the serum. Before doing the examination to the patient, they passed through internal quality stabilization process previously. Reference value <150 mg / dL.

Univariate analysis was done to produce frequency distribution and percentage of each variable. Bivariate analysis was performed on two allegedly related variables between each independent variable and the

dependent variable using correlative analysis, namely Pearson correlation test with normal numerical data distribution requirements, with an alternative Spearman correlation test to the data of HbA1c and triglyceride levels.

The research has been through assessment and valuation carefully with the issuance of the Statement of Exemption from Ethical Agreements Number: KEPK-PKKJ3 / 116 / III / 2018. The data obtained in this study have been approved by respondents, namely Tarakan District Hospital through signing informed consent that contains information relating to research objectives, procedures, risks, and other matters related to the research.

3. RESULTS AND DISCUSSION

This research was carried out by taking 90 data from HbA1c and triglyceride examination on patients with type 2 DM status consist of 37 men and 53 women. The age distribution of respondents was between 33 - 82 years. HbA1c levels were in the range of 4.9-15.7% with an average of 8%. The average triglyceride level was 170 mg /dL with a range of 75-369 mg /dL.

Tabel 1. HbA1c Examination Results based on Age Group

	HbA1c							
	Male			Female			Total	
Age (Year)	Good Control < 6.5%	Fair Control 6.5-8%	Poor Control >8%	Good Control < 6.5%	Fair Control 6.5-8%	Poor Control >8%		
	n%	n%	n%	n%	n %	n %	n	%
26-45	2 2,2	1 1,1	1 1,1	1 1,1	0 0,0	5 5,6	10	11,1
46-65	8 8,9	6 6,7	9 10,0	10 11,1	6 6,7	12 13,3	51	56,7
>65	2 2,2	5 5,6	3 3,3	9 10,0	2 2,2	8 8,9	29	32,2
	Total						100	

HbA1c examination results (Table 1) showed the highest results in the 46-65 years age group as many as 51 (56.7%) patients. The dominance of bad control was obtained both in men and women. Poor control results in men as many as 9 (10.0%) and in women as many as 12 (13.3%) patients. The fair category control showed the same results for men and women as many as 6 patients (6.7%). The control of good glycemic control was found in 8 (8.9%) male respondents and 10 (11.1%) female respondents. In the elderly with age> 65 years, there was found 11 (12.2%) of 29 (32.2%) respondents with poor control of HbA1.

Table 2. Triglyceride Examination Based on Age and Gender Group

	Trigliserides									
Age (year)	Male				Female				Total	
	Normal		Abnormal		Normal		Abnormal			
	n	%	n	%	n	%	n	%	n	%
26-45	2	2,2	2	2,2	0	0,0	6	6,7	10	11,1
46-65	12	13,3	11	12,2	11	12,2	17	18,9	51	56,7
>65	6	6,7	4	4,4	9	10,0	10	11,1	29	32,2
	Total								90	100

Triglyceride results were obtained above normal based on the age group and gender (Table 2,) in the age group 46-65 years old male were 11 (12.2%) and female were 17 (18.9%). At the age of> 65 years, there were 4 (4.4%) men and 10 women (11.1%)

Table 3. Results of HbA1c and Triglycerides in Type 2 DM Patients

HbA1c	Triglycerides				Total	
	Normal		Abnormal			
	n	%	n	%	n	%
Good Control	26	28,9	6	6,7	32	35,6
Fair Control	9	10,0	11	12,2	20	22,2
Poor Control	5	5,6	33	36,7	38	42,2
Total					90	100

The results of cross-tabulation of both parameters (Table 3) obtained good control HbA1c results and normal triglyceride levels as many as 26 patients (28.9%) and above normal triglyceride levels as much as 6 (6.7%), whereas in patients with HbA1c poor control 5 patients (5.6%) had normal triglyceride levels and 33 (36.7%) patients who had triglyceride levels above normal.

Table 4. Results of the correlation of HbA1c levels with triglyceride levels
In Type 2 DMPatients

	Spearman's Test		
	N	Sig	Correlation coefficient
HbA1c	90		
		0.000	0.594
Trigliserida	90		

The results of the correlation test (Spearman's) (Table 4) with a confidence level of 95% d, α = 0.05 (5%) obtained sig 0.00 <0.05 meaning there was a correlation between HbA1c levels and triglyceride levels in type 2 DM respondents with the results of the correlation coefficient (r = 0.594). The results showed a positive correlation with the strong relationship between HbA1c and triglycerides. This can be explained through the pathogenesis of type 2 DM during the advanced phase. Where in this phase, excess glucose in the blood is stored in the form of fat, especially triglycerides. Therefore, if glycemic control is bad, it will cause an increase in blood glucose levels. Furthermore, glucose is converted to triglycerides, resulting in an increase in triglyceride levels (Priyadi and Saraswati, 2012).

The high prevalence of type 2 DM is caused by irreversible factors such as gender, age, and genetic factors (Fatimah,R.N, 2015) and factors that can be changed such as bad habits in eating, lack of physical activity and obesity (Manaf, 2014). In diabetes that has β-cell disorders, insulin release cannot compensate for glucose load. Besides the progressive decrease in β-cell function, first phase insulin secretion also does not occur in patients with type 2 diabetes. This condition causes sufficient insulin secretion to reduce glucose levels in peripheral tissue such as fat tissue and muscle tissue (Tjandrawinata, R, 2016).

The description obtained that women experience in DM more than men. If this is associated with blood fat, theoretically fat levels in adult men average is 15-20% of total body weight, whereas in women is

around 20-25%. The increase in blood fat levels in women with a greater body mass index is higher than in men. Besides, the daily activities and lifestylecontribute to become one of the risk factors for DM type 2 . The increase of the risk of DM in women 3-7 is times higher than men (Jelantik and Haryanti, 2014), (Setyorini and Wulandari, 2017). There were 80 (88.9%) respondents with age ≥ 45 years and the effect of aging on the incidence of type 2 diabetes occurred due to changes in pancreatic beta cells which caused changes in insulin secretion. It is caused by the changes in glucose metabolism in old age (Betteng, PangemanandanMayulu, 2014).

The results also showed that there was still poorer control of HbA1c than other controls. Poor HbA1c levels can lead to complications and Diabetes Control and Complication Trial (DCCT). United Kingdom Prospective Diabetes Study (UKPDS) revealed that every 1% decrease in HbA1c would reduce the risk of death from diabetes by 21%. HbA1c levels with poor control but triglyceride results are still in normal conditions. This is likely to occur because patients have diabetes mellitus less than 10 years. Thecomplications usually occur within 10 to 15 years after diagnosis is made.

The combination of examination results also obtained good control HbA1c levels but triglyceride results is above normal. It is likely to occur due to obesity, increased calorie, intake, high-fat and low-carbohydrate diet, lack of exercise, and genetic factors. Drugs such as hormonal contraception, corticosteroids can also affect triglyceride levels in the blood (Fauziah and Suryanto. 2012). Cross-tabulation also showed good control of HbA1c and had a normal triglyceride value of 26 (28.9%) and normal triglycerides of 6 (6.7%). Results of poor control of HbA1c occured in 5 patients (5.6%) who had normal triglyceride values and 33 (36.7%) patients who had triglyceride values above normal.

Based on the results of statistical analysis, the relationship between HbA1c levels and triglyceride levels showed a strong correlation between HbA1c and triglycerides in type 2 DM patients. These results were consistent with the results of previous studies that the incidence of dyslipidemia in type 2 DM patients commonly found was increased levels of LDL, decreased HDL and increased triglycerides. Research conducted by Priyadi and Saraswati (2012), (Loie, PandelakidanMandang. 2014) showed a significant correlation between HbA1c and triglycerides in type 2 DM. Research by Meenu, Jayendrasinh and Neeta (2013) concluded that there was a significant relationship between HbA1c and triglycerides. High glucose levels could stimulate glycogen formation in the liver and muscle tissue and were also stored in fat tissue in the form of triglycerides.

The theoretical correlation between HbA1c and triglycerides is that insulin secretion causes an increase in lipase sensitive hormones which will cause lipolysis and eventually cause the release of fatty acids and glycerol into the blood circulation.It will cause an increase in free fatty acids, so that if there is excessive amounts, it will be taken to the liver to fat metabolism that will be converted into phospholipids, cholesterol and triglycerides. It results in an increase in cholesterol and triglycerides in the blood, then it will be transported to the circulation through lipoproteins namely LDL and HDL (Wahab, Novitasari and Fitria, 2015).

Clinically, laboratory evaluation of type 2 diabetes mellitus is examined by fasting glucose levels, 2 hours after TTGO and HbA1c. To prevent the occurrence of complications in type 2 diabetes mellitus, lipid profiles such as triglycerides, total cholesterol, HDL and LDL are examined, the examination can be done every two years (PERKENI, 2015). The limitation of this study is that the diet cannot be known to the patient and there is no supporting data such as the patient's IMT data, the duration of the patient's disease and the medication consumed by the patient. Therefore, it is beyond the control of the researcher.

4. CONCLUSION

This research shows the influence of peer education on adolescents about health education of HIV AIDS prevention efforts. There are significant differences in the mean scores on differences in knowledge between peer education methods and lecture methods, even though both methods can increase the level of knowledge about HIV AIDS before and after intervention. The suggestions for this research are collaboration between the health office and schools to innovate related to modification of health education by implementing peer education methods as well as monitoring and evaluating the health education that has been conducted.

5. ACKNOWLEDGEMENT

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