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Correlation of HbA1C and Lipid Profile Levels in Type 2 Diabetes Mellitus Patients at M Yunus Hospital

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Abstract: The lipid profile in type 2 diabetes mellitus patients is highly dependent on the HbA1c value. Poor HbA1c values accompanied by insulin resistance are associated with hypertriglyceridemia, decreased HDL levels, and sometimes followed by increased LDL levels. The aims of this study were to determine the correlation between HbA1c and lipid profile of type 2 diabetes mellitus patients. This research was an analytic observational study with a cross sectional design with prospective method for 2 months. The total sample of 35 patients seeking treatment at the Polyclinic Internal M Yunus hospital. Based on the results, total cholesterol levels (158.83 ± 23.96; 201,51 ± 44.95; p=0.032), triglyceride (111.16 ± 48.06; 156.69 ± 76.07; p=0.169), LDL (80.83 ± 22.69; 121.96 ± 42.82; p=0.030), HDL (43.50 ± 34.24; 13.75 ± 7.62; p= 0.026) lower in type 2 DM patients with controlled glycemic control compared to those without control. There was no significant difference in triglyceride levels between on two groups (111.16 ± 48.06; 156.69 ± 76.07; p=0.169). There was a significant correlation between total cholesterol levels r=0.364; p=0.032), HDL (r=-0.377; p=0.026); LDL (r=0.367; p=0.030) with HbA1c levels. Type 2 diabetes mellitus patients with good glycemic control had significantly lower total cholesterol, triglyceride, and LDL levels compared to type 2 diabetes mellitus patients with poor glycemic control.

Keywords: HbA1c, lipid profile, type 2 diabetes mellitus

1. Introduction

Diabetes mellitus (DM) is a global health problem, and the number of sufferers is increasing every year (Wahab *et al*., 2015). Diabetes mellitus is one of the chronic diseases that attack the pancreas due to not being able to produce enough insulin so that the body cannot process and use insulin effectively. This causes hyperglycemia which is one of the causes of multi-organ failure such as kidneys, nerves, heart, and blood vessels (Sumampouw and Halim, 2019). Patients with diabetes mellitus have a risk of developing dyslipidemia. Dyslipidemia is the stage of accelerating the formation of atherosclerosis that plays a role in cardiovascular disease (Wahab *et al.*, 2015).

Indonesia currently ranks 6th as a country that has the number of diabetes patients aged 20-79 years, amounting to 8.5 billion people in 2017, and is expected to increase to 14.1 billion people in 2035 (World Health Organization, 2016). Based on data from Bengkulu Provincial Health Office in 2018, stated that the number of people with diabetes mellitus reached 19.353 people. It is known that Bengkulu City is ranked first in the number of diabetes mellitus sufferers in Bengkulu Province. The prevalence of diabetes mellitus in Bengkulu City is 1.108 people in

2015, 1.129 people in 2016, 3.155 people in 2017 and 3.334 people in 2018. These data show that number of diabetics has increased significantly so monitoring is still very much needed. Meanwhile, non-communicable disease shows an increasing trend from time to time. According to the results of Basic Health Research (Riskesdas), there is a tendency to increase the prevalence of PTM such as diabetes, hypertension, stroke, and joint disease. This phenomenon is predicted to continue (Kementerian Kesehatan RI, 2018).

Glycemic control monitoring using HbA1c examination aims to see the blood glucose levels of the last 120 days. The American Diabetes Association (ADA) states that glycemic control is said to be good (controlled) if it has a value of < 6.5%, glycemic control is 6.5% -8%, and glycemic control is said to be bad (uncontrolled) if it has a value of > 8%. Glycemic control can determine the progression of diabetes mellitus (Wahab *et al.,* 2015). Glycemic control has an impact on serum lipid levels. Increased fat levels often occur in patients with poor glycemic control (Firdayanti *et al.,* 2017). In theory, the relationship between HbA1c with lipid profile occurs when insulin function decreases resulting in the increased lipase-sensitive hormone that will cause lipolysis so that it will release fatty acids and glycerol which will be carried to the blood circulation, consequently, free fatty acids increase so that if in excess amounts will be taken to the liver for fat metabolism which will be converted into phospholipids, cholesterol, and triglycerides resulting in increased cholesterol and triglycerides. It is then transported to the circulation via lipoproteins namely LDL and HDL (Wahab *et al.,* 2015). Overall HbA1c and lipid profile examinations according to standard laboratory procedures. HbA1c levels and lipid profiles obtained were the results of blood biochemical tests that were examined at the same time.

2. Materials and Methods

This type of study is an analytical observational study with a cross-sectional design with prospective patient data collection. This study was conducted at Dr. M Yunus Hospital Bengkulu. Sampling was carried out for 2 months based on the results of an examination of the lipid profile and data from the patient's medical record. This research has received ethical approval from Health Research Ethics Committee University of Jember, Faculty of Nursing with No. 140/UN25.1.14/KEPK/2022.

The population in this study were patients diagnosed with Type 2 diabetes who underwent treatment at the Internal Medicine Poly of Dr. M Yunus hospital during the two months of the study. The study sample was all populations that met the inclusion criteria. Inclusion criteria in this study were outpatients with Type 2 DM who underwent treatment at the Internal Medicine Poly Dr. M Yunus Hospital Bengkulu, male and female (not pregnant and breastfeeding) , geriatric and non-geriatric, patients with HbA1c data on medical records, lipid profile examination (total cholesterol, HDL, LDL, and triglyceride), and patients in a conscious state. The sampling technique is done by purposive sampling method, sampling techniques are taken based on the inclusion criteria. The calculation of sample size is calculated using the formula.: $n= Z^2xPxQ/d^2$ (n= sample size; Z=standard deviation (if $\alpha = 0.05$ then Z = 1.960); P=proportion

of disease or condition to be sought (if P=0.1 then Q(1-P)=0.9); d2=deviation to population. So the total sample in this study was 35 respondents.

Data collection was carried out at Dr. M Yunus Bengkulu Hospital. Prior to data collection, consent from the respondent must be obtained as proof that the respondent is willing to participate in the research and understands the purpose of the research. Respondents who agreed to participate in the study were examined for lipid profiles in the form of total cholesterol, HDL, LDL, and triglycerides. Data collection was also obtained from the medical records of patients with type 2 DM. Data collected based on the medical records included the patient's identity in the form of the name, age, sex, diagnosis, HbA1c value, and medication profile.

Statistical analysis was carried out by testing the homogeneity of the data followed by comparative and associative analysis. The homogeneity test was carried out using the Levene test, while the comparative test was using the independent T-test. Comparison test of cholesterol, HDL, LDL, triglyceride levels was carried out in the controlled glycemic control group and uncontrolled glycemic control. Pearson's correlation test was also performed to assess the relationship between total cholesterol, HDL, LDL, and triglyceride levels with HbA1c levels. All statistical analysis in this study was carried out using SPSS 28.0 version for Windows. All of these tests are considered significant if the p value was $p<0.05$.

3. Results and Discussion

3.1 Characteristics of Respondents

This research was conducted at Dr. M Yunus Hospital. Sampling is prospective. This study used 35 patients at RSUD Dr. M Yunus who were undergoing treatment at the internal medicine polyclinic at RSUD Dr. M Yunus and carried out lipid profile and HbA1c examinations. This study aims to determine the relationship between HbA1c and lipid profile in patients with type 2 diabetes mellitus. Based on the 2019 PERKENI guidelines one of the goals of controlling DM is to have HbA1c levels below 7% (HbA1c <7%) (Soelistijo, 2021). Thus, patients with HbA1c levels < 7% are classified as controlled glycemic control, while patients with HbA1c levels > 7% are classified as having uncontrolled glycemic control. In this study, out of 35 patients, there were 6 patients in the controlled glycemic control group and 29 patients in the uncontrolled glycemic control group **(Table 1)**.

Table 1. Characteristics of Respondents

Characteristics	HbA1c Levels		
	Controlled glycemic control (< 7%), n = 6	Uncontrolled glycemic control (≥ 7%), n = 29	p-value
Gender, n (%)			0.070
Male	4 (66.7)	8 (27.6)	
Female	2 (33.3)	21 (72.4)	
Average of Age (year)	60	58	0.0518
Average of HbA1c	4.8	10.7	0.000*

value			
Average of Suffered Time Period (year)	10	7	0.838
Average of BMI	19.4	24.3	0.838

**T-independent test p< 0.05*

Based on the characteristics of respondents with Type 2 diabetes mellitus from 35 study samples, it is known that out of 6 patients with controlled glycemic control, there were 4 people (66.7%) male and 2 (33.3%) female patients. While in the group of patients with uncontrolled glycemic control, the majority of patients were female as many as 21 people (72.4%), and the rest were male which is 8 people (27.6%). The results of the analysis with the independent T-test obtained a value of p= 0.070 which means there is no significant difference between the gender with the two groups. The results of this study are different with research conducted by Dharma Yudha *et al* (2022) which states that men are better able to control glycemic levels than female.In a study conducted by Alzahrani *et al* (2019) a total of 206 type 2 diabetes mellitus patients were selected for the study (141 females and 65 males). The participants basic characteristics were analyzed and compared according to gender. The females had significantly higher values for BMI *(p=0.002)* and HbA1c *(p=0.009)* compared to the males.

In age characteristics, it is seen that the average age of patients with controlled and uncontrolled glycemic control is 60 years old and 58 years old. The results of the analysis with independent T-test, obtained a value of p=0.518 which showed no difference between the age characteristics of the two groups of patients. The results of this study are different with research conducted by Mukti (2020) which showed that the average age of patients with diabetes mellitus was in the age range of 46-59 years. In a study Dharma Yudha *et al* (2022) it was found that the average age of patients with controlled glycemic control was 62.7 years and uncontrolled glycemic control was 60.7 years and there was no difference in age characteristics between two groups.

Patients with controlled glycemic control had an average HbA1c level of 4.8 and patients with uncontrolled glycemic control category had an average HbA1c level of 10.7. Independent T-test is used to determine the relationship between HbA1c levels in the two groups of patients, obtaining p value=0.000, so it can be interpreted that there is a difference between HbA1c levels between the two groups of patients. In line with research conducted by Dharma Yudha *et al* (2022)that the average HbA1c level in patients with controlled glycemic control group was 6.3 and in patients with uncontrolled glycemic control group was 9.6.

In the characteristics of long-suffering diabetes mellitus, it is seen that the average patient with controlled glycemic control has had diabetes mellitus for 10 years, and the group of patients with uncontrolled glycemic control has had diabetes mellitus for 7 years.

Analysis with independent T-test, obtained a value of p=0.838 which showed no difference between the length of diabetes mellitus in the two groups of patients.

BMI in patients with diabetes mellitus with controlled glycemic control the average is in the normal range of 19.4 while the average BMI in the group of patients with uncontrolled glycemic control is in the overweight range of 24.3. Overweight and obese are the most dominant risk factors for diabetes mellitus. Increased blood glucose levels can be caused due to reduced physical activity, while it can contribute to the body's energy balance, weight control, and prevent obesity (Erciyas *et al.,* 2004). Therefore, BMI in patients with diabetes mellitus must be controlled.

3.2 Differences in Lipid Profile Levels Based on Glycemic Control

Comparative analysis of lipid profiles in patients with Type 2 diabetes between controlled glycemic control and uncontrolled glycemic control was performed using an independent T-test. Differences in HbA1c levels and lipid profiles based on glycemic control are presented in Table 2 **(Table 2).**

Table 2. Differences In Lipid Profile Levels Based on Glycemic Control

Variable	Hba1c Average Levels		p Value
	Controlled glycemic control (< 7%), n = 6	Uncontrolled glycemic control (≥ 7%), n = 29	
Total Cholesterol	158.83 ± 23.96	201.51 ± 44.95	0.032*
HDL	43.50 ± 13.75	34.24 ± 7.62	0.026*
LDL	80.83 ± 22.69	121.96 ± 42.82	0.030*
Triglycerides	111.16 ± 48.06	156.89 ± 76.07	0.169

**T-independent test p< 0.05*

Improved glycemic control in diabetes mellitus generally has a beneficial effect on lipoprotein levels, with reduced cholesterol and triglyceride levels through decreased circulating very low-density lipoprotein (VLDL) and with increased LDL catabolism through decreased glucose and increased regulation of LDL receptors (Schofield *et al*., 2016). In this study, it was found that patients with Type 2 diabetes mellitus with controlled glycemic control (HbA1c < 7%), obtained significantly lower levels of total cholesterol, LDL, and triglycerides than patients with Type 2 diabetes mellitus with uncontrolled glycemic control (HbA1c > 7%). This research is in line with that conducted Dharma Yudha *et al* (2022), on this study showed that type 2 diabetes patients with controlled glycemic control had lower levels of total cholesterol, LDL, and triglycerides than patients with uncontrolled glycemic control.

The results showed that type 2 diabetes patients with controlled glycemic control had significantly lower total cholesterol levels, which amounted to 158.83-23.96 when compared

with Type 2 diabetes patients with uncontrolled glycemic control of 201.51-44. 95. Correlation test results between total cholesterol levels with HbA1c levels obtained a correlation coefficient of 0.364 (p=0.032) (Table 3). This shows a positive correlation with a weak correlation strength, meaning that the higher the HbA1c levels, the higher the total cholesterol levels.

This is in line with previous research conducted by Susilo *et al* (2020), in his research, there was a significant correlation between HbA1c values and total cholesterol levels in patients with Type 2 diabetes mellitus (p=0.030; r= +0.314). Goldberg reported that the cause of dyslipidemia in Type 2 diabetes mellitus is caused because insulin does not work properly it affects the liver to produce apolipoprotein (Goldberg, 1996). Apolipoprotein regulates the activity of the enzyme lipoprotein lipase (LpL) and cholesterol transport proteins. Other research also reported a positive correlation between HbA1c levels with total cholesterol (Erciyas *et al.,* 2004).

3.3 Correlation Between HbA1c Levels and Lipid Profile

Based on the test results of the relationship between HbA1c levels with lipid profile using the Pearson correlation test, obtained a weak positive correlation between total cholesterol and HbA1c levels (p<0.05) and a negative correlation with the strength of the weak correlation between HDL levels with hba1 levels. In theory, an increase in total cholesterol, LDL, and triglycerides in patients with Type 2 diabetes mellitus will be followed by an increase in HbA1c levels and vice versa. While in the analysis of the relationship between triglyceride levels with HbA1c levels obtained p value>0.05. Based on the results of this test proved that there is no significant relationship between triglyceride levels with HbA1c levels in patients with Type 2 DM. this is caused to high blood glucose levels due to uncontrolled glycemic control so that it is stored in the form of fat, especially triglycerides. So that if the glycemic control is not controlled it will cause an increase in blood glucose. The correlation test results between HbA1c levels and lipid profiles are presented in **(Table 3).**

Table 2. Correlation Test Results Between HbA1c Levels with Lipid Profile

Variable	Correlation Coefficient	p Value
Total Cholesterol	0.364	0.032*
HDL	-0.377	0.026*
LDL	0.367	0.030*
Triglycerides	0.238	0.169

**Spearman test p< 0.05*

In the examination of HDL levels between groups of patients with Type 2 diabetes in controlled glycemic control, there were significant differences when compared with groups of patients with Type 2 diabetes with uncontrolled glycemic control, which is 43.50-13.75

and 34.24-7. 62 (p=0.026; r =-0.377). The correlation test shows a negative correlation with weak correlation strength. This shows that all parts of lipids, namely total cholesterol, LDL, and triglycerides will increase significantly in patients with diabetes mellitus so in patients with uncontrolled glycemic control total cholesterol and LDL levels will increase significantly while HDL levels will decrease. The same results were obtained from the study, where there was a moderate negative relationship between HbA1c and HDL levels in patients with Type 2 diabetes mellitus (Nnakenyi *et al.,* 2022). This study is in line with that conducted by Samdani *et al* (2017) who said that there is a negative correlation between HbA1c levels with HDL levels.

LDL is an appropriate predictor of cardiovascular disease, LDL reduction in the use of statins can reduce the prevalence of cardiovascular disease in patients with diabetes mellitus significantly. In this study, there was a significant difference between LDL levels in the group of patients with controlled glycemic control and with an uncontrolled glycemic control group of patients, which respectively were 80.83-22.69 and 121.96-42.82. The correlation test showed a negative correlation with weak correlation strength (p=0.030; r=0.367). This shows that there is a significant difference between HbA1c and LDL levels, meaning that the higher the HbA1c level, the higher the LDL level. This study is in line with the research of Samdani *et al* (2017) which states that there is a significant positive correlation between HbA1c and LDL (p=0.024). Regulation of lipoprotein lipase enzyme activity and cholesterol ester transfer protein (CETP) that causes dyslipidemia in diabetes mellitus will affect insulin to apolipoprotein production in the liver (Meenu *et al*., 2013).

In patients with diabetes mellitus, the secretion of VLDL by the liver increases, especially VLDL1, which contains a lot of triglycerides. Overproduction of VLDL1 is associated with an increase in small dense LDL metabolically, with more atherogenic properties when compared to large buyout LDL because the arterial wall is well penetrated (Hidaka *et al.,* 2003). Patients with Type 2 diabetes mellitus will significantly decrease LDL catabolism so that it will cause a longer duration of LDL in plasma as a result of increased lipid deposition into the artery wall (Vergès, 2015).

Hypertriglyceridemia is a serum lipid disorder that is most commonly found in patients with diabetes mellitus. In the study, obtained significantly lower triglyceride levels in the group of patients with controlled glycemic control than in the group of patients with uncontrolled glycemic control, ie respectively 111.16-48.06 and 156.89-76. 07. Correlation test results obtained a correlation coefficient of 0.238 (p=0.169). It can be concluded that there is no significant difference between triglyceride levels in both groups of patients with a weak correlation. This is in line with research conducted by Alzahrani (2019) that state the same result.

The theory states that controlled glycemic control will get controlled triglyceride levels, while uncontrolled glycemic control will increase triglyceride levels. The effect of HbA1c value on HbA1c in patients with Type 2 diabetes occurs through the glycosylation process. Increased glucose will activate the enzyme lipoprotein lipase in adipose tissue as a result

there is an increase in triglyceride lipolysis in adipose tissue, this condition will produce excessive free fatty acids. These free fatty acids will enter the bloodstream, part of which is used as an energy source and part of which will be taken to the liver as a raw material for forming triglycerides

Lipid profiles such as total cholesterol, HDL, LDL, and triglycerides were significantly improved in patients with diabetes mellitus. HbA1c is not only used as a long-term biomarker of glycemic control, but also a precise predictor of lipid profile. Therefore, monitoring glycemic control using HbA1c is useful to identify the status of patients with diabetes mellitus to the risk of cardiovascular complications (Zulfian *et al.*, 2020).

4. Conclusion

Type 2 DM patients with controlled glycemic control had significantly lower levels of total cholesterol, LDL, and triglycerides when compared to type 2 DM patients with uncontrolled glycemic control. This means that the more controllable of glycemic control, the lower the lipid profile will also be controlled. In addition, there is a significant relationship between total cholesterol, HDL, and LDL levels to HbA1c in patients with Type 2 diabetes mellitus.

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Conflict of Interest

All Authors declare no conflict of interest and agree with the content of the manuscript.

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