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The Relationship Between Glycemic Control And Lipid Profile In Patients With Type 2 Diabetes Mellitus In Bangli General Hospital

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ABSTRACT
Type 2 Diabetes Mellitus (DM) is prone to diabetic dyslipidemia, which is a factor in increasing the risk of cardiovascular disease complications. This study aims to determine the relationship between glycemic control and lipid profiles in patients with type 2 DM. A cross-sectional study was conducted at the Internal Medicine Clinic of Bangli General hospital from January 2023 to December 2023, involving 60 type 2 DM patients who met the inclusion criteria. Patients were grouped into those with good glycemic control (HbA1c < 7%) and poor glycemic control (HbA1c ≥ 7%). Lower levels of total cholesterol (160.444 ± 30.608 mg/dl vs. 203.476 ± 45.471 mg/dl; p = 0.001), triglycerides (125.500 ± 56.019 vs. 202.047 ± 91.568; p = 0.002), and low-density lipoprotein (LDL-C) (93.072 ± 28.443 vs. 131.571 ± 44.590; p = 0.001) were observed in type 2 DM patients with good glycemic control. Higher levels of high-density lipoprotein (HDL-C) (50.022 ± 14.050 vs. 41.152 ± 12.619; p = 0.019) were observed in type 2 DM patients with good glycemic control. Statistical analysis revealed a positive correlation between total cholesterol levels (r = 0.277; p = 0.032), triglycerides (r = 0.386; p = 0.002), and LDL-C (r = 0.357; p = 0.005) with HbA1c levels. There was a negative correlation between HDL-C (r = -0.366; p = 0.004) and HbA1c levels. The significant correlation between HbA1c and lipid profiles highlights the importance of glycemic control in patients with type 2 DM. This can be explained by the pathogenesis of advanced-stage type 2 DM. There is a positive correlation between glycemic control (HbA1c) and total cholesterol, triglycerides, and LDL-C. There is a negative correlation between glycemic control (HbA1c) and HDL-C.

Keywords: Diabetes Mellitus, Cholesterol, HDL-C, LDL-C, Triglycerides

Introduction

Diabetes mellitus (DM) is a group of metabolic diseases characterized by hyperglycemia due to defects in insulin secretion, insulin action, or both (PERKENI, 2021). Currently, DM is one of the most prevalent chronic diseases worldwide (Sapra A BP, 2023). According to epidemiological studies, there are currently 387 million people with DM globally, and this number is expected to increase to 592 million by 2035 and 642 million by 2040 (Zheng et al., 2018).

HbA1c (glycated hemoglobin) is a type of hemoglobin that reflects the average plasma

glucose concentration over three months and has been recommended by PERKENI as a long-term glucose evaluation for patients with type 2 DM (PERKENI, 2021) (Goyal et al., 2021) (WHO, 2011) (Alzahrani et al., 2019). Elevated HbA1c levels are independently associated with an increased risk of both macrovascular and microvascular complications and are linked to metabolic syndrome (WHO, 2011) (PB PERKENI, 2021). HbA1c is not only an indicator of glycemic control but also a predictor of dyslipidemia (Goyal et al., 2021) (Setiati et al., 2014) (Kumar et al., 2022).

Type 2 DM patients are prone to diabetic dyslipidemia, a lipid metabolism disorder that contributes to the increased risk of cardiovascular disease complications. Diabetic dyslipidemia includes both quantitative and qualitative lipoprotein abnormalities, resulting in a shift towards an atherogenic lipid profile (Huang et al., 2021) (Reza et al., 2023). Hyperglycemia, insulin resistance, and relative insulin deficiency observed in type 2 DM patients likely contribute to lipid changes, as insulin plays a crucial role in regulating lipid metabolism (Huang et al., 2021).

Given the various empirical evidence presented, the relationship between glycemic control and lipid profiles needs further investigation. The evidence regarding the relationship between glycemic control and lipid profiles in type 2 DM patients is still conflicting. Therefore, this study aims to determine the relationship between glycemic control and lipid profiles in type 2 DM patients at Bangli General hospital.

Reseach Method

This study is an analytical correlational study using a cross-sectional approach to examine the relationship between glycemic control (HbA1c) and lipid profiles in type 2 DM patients. The study was conducted at the Internal Medicine Clinic of Bangli General hospital from January 2023 to December 2023. Data were collected from patient medical records. Ethical approval was obtained from the Health Research Ethics Committee of Bangli General hospital (No.400.7.22.2/1024/RSUD) to ensure that the study was conducted according to proper procedures. Consent was obtained from the subjects after explaining the details of the study in Indonesian and/or the local language (Balinese). Confidentiality was maintained in this study.

The target population consists of all outpatients diagnosed with type 2 DM, while the accessible population includes type 2 DM patients at Bangli General hospital, particularly those at the Internal Medicine Clinic who meet the inclusion and exclusion criteria. Inclusion criteria: patients diagnosed with type 2 DM with medical record data including HbA1c and lipid profiles (total cholesterol, HDL-C, LDL-C, triglycerides); Exclusion criteria: type 2 DM patients without medical record data of HbA1c and lipid profiles (total cholesterol, HDL-C, LDL-C, triglycerides), type 2 DM patients receiving previous dyslipidemia therapy (statins, fibrates, niacin), pregnant patients, patients with thyroid disease, chronic liver disease, chronic kidney disease, and other endocrine disorders. The minimum sample size required is 51 people (Dahlan., 2016).

The sampling technique used in this study is non-probability sampling, specifically purposive sampling based on the inclusion and exclusion criteria. The purposive sampling

yielded a sample size of 60 people, which met the study's requirements.

Dependent variable: the dependent variable in this study is the lipid profile, including total cholesterol, triglycerides, LDL-C, and HDL-C, measured on a numerical scale. Independent variable: the independent variable in this study is glycemic control measured through HbA1c levels. HbA1c levels will be categorized into two groups. Patients with HbA1c <7% are categorized as having good glycemic control, while patients with HbA1c ≥7% are categorized as having poor glycemic control. The measurement scale used is numerical.

Operationally, type 2 DM patients are defined as patients diagnosed with type 2 DM at the Internal Medicine Clinic of Bangli General hospital between January 2023 and December 2023. The assessment of patients is based on their medical records at the Internal Medicine Clinic of Bangli General hospital. Glycemic control is assessed using HbA1c laboratory results, which reflect the average plasma glucose levels. The lipid profile is assessed by measuring total cholesterol, triglycerides, LDL-C, and HDL-C levels.

Statistical analysis was performed with data homogeneity tests followed by comparative and correlation tests. Comparative tests of total cholesterol, triglycerides, LDL-C, and HDL-C levels were conducted between the good glycemic control and poor glycemic control groups. Comparative tests were conducted using the independent T-test. Correlation tests assessed the relationship between glycemic control (HbA1c) and total cholesterol, triglycerides, LDL-C, and HDL-C levels. The correlation test used is Pearson's correlation if the data distribution is normal; otherwise, the alternative test, Spearman's correlation, is used. All tests are considered significant if the p-value < 0.05. Data analysis was performed using SPSS software version 26.

Results and Discussion

In this study, out of 60 type 2 DM patients, 18 were in the good glycemic control and 42 were in the poor glycemic control. Among the 18 patients with good glycemic control, 7 (38.9%) were male, and 11 (61.1%) were female. In the poor glycemic control 42 patients, 24 (57.1%) were male, and 18 (42.9%) were female. Regarding age characteristics, the average age of patients with good glycemic control and poor glycemic control groups was 66.277 years and 60.170 years, respectively. Patients with good glycemic control had an average HbA1c level of 5.991, while the average HbA1c level in the poor glycemic control group was 9.471. The characteristics of the respondents are shown in Table 1.

Table 1. Respondent Characteristics

Characteristics	HbA1c		
	Good glycemic control (<7%) n = 18	Poor glycemic control (≥7%) n = 42	p-*value*
Gender, n (%)			0.201
Male	7 (38.9)	24 (57.1)	
Female	11 (61.1)	18 (42.9)	
Average Age	66.277	60.170	0.043
Average HbA1c	5.991	9.4710	0.000

A comparative analysis of the lipid profiles of type 2 DM patients between good glycemic control and poor glycemic control groups was conducted using an independent T-test. The results of this study showed that patients in the good glycemic control had lower levels of total cholesterol, triglycerides, and LDL-C, while good glycemic control had higher HDL-C levels. The differences in lipid profiles based on glycemic control are presented in Table 2.

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

Variable	HbA1c		
	Good glycemic control (<7%) n = 18	Poor glycemic control (≥7%) n = 42	p-*value*
Total Cholesterol	160.444 ± 30.608	203.476 ± 45.471	0.001
Triglycerides	125.500 ± 56.019	202.047 ± 91.568	0.002
K-LDL	93.072 ± 28.443	131.571 ± 44.590	0.001
K-HDL	50.022 ± 14.050	41.152 ± 12.619	0.019

Before conducting the correlation test between glycemic control (HbA1c) and lipid profiles, a normality test was performed using the Kolmogorov-Smirnov test, as the sample size in the study was >50. In the Kolmogorov-Smirnov test, HbA1c (p=0.200), total cholesterol (p=0.200), and LDL-C (p=0.200) data were normally distributed, whereas triglycerides (p=0.000) and HDL-C (p=0.040) data were not normally distributed, as shown in Table 3.

Table 3. Results of Normality Test for Glycemic Control (HbA1c) and Lipid Profile

Variable	Sig.	Description
HbA1c	0.200	Normal
Total Cholesterol	0.200	Normal
Triglycerides	0.000	Not Normal
K-LDL	0.200	Normal
K-HDL	0.040	Not Normal

The correlation test between glycemic control (HbA1c) and lipid profiles was conducted using Pearson's correlation for normally distributed data and Spearman's correlation for non-normally distributed data. A weak positive correlation was found between HbA1c and total cholesterol, triglycerides, and LDL-C. A positive correlation indicates a direct relationship; thus, it can be concluded that the higher the HbA1c level, the higher the total cholesterol, triglycerides, and LDL-C levels. A weak negative correlation was found between glycemic control (HbA1c) and HDL-C. A negative correlation indicates an inverse relationship; thus, it can be concluded that the higher the HbA1c level, the lower the HDL-C level. The results of the correlation test between glycemic control (HbA1c) and lipid profiles are presented in Table 4.

Table 4. Results of Correlation Test between Glycemic Control (HbA1c) and Lipid Profile

Relationship	Sig.	Correlation Coefficient
HbA1c with Total Cholesterol	0.032	0.277
HbA1c dengan K-LDL	0.005	0.357
HbA1c with Triglycerides	0.002	0.386
HbA1c dengan K-HDL	0.004	-0.366

Discussion

Patients with type 2 diabetes mellitus (DM) are vulnerable to diabetic dyslipidemia, a lipid metabolism disorder that encompasses not only quantitative but also qualitative lipoprotein abnormalities, leading to a shift towards an atherogenic lipid profile. The lipid abnormalities in type 2 DM are likely due to hyperglycemia, insulin resistance, and relative insulin deficiency observed in these patients. Dyslipidemia is a predictor of cardiovascular disease (Huang et al., 2021) (Reza et al., 2023).

In this study, it was found that patients with type 2 DM with good glycemic control (HbA1c < 7%) had lower levels of total cholesterol, triglycerides, and LDL-C compared to those with poor glycemic control (HbA1c ≥ 7%). This finding is consistent with a study by Handayani et al. (2023), which showed that total cholesterol, triglycerides, and LDL-C levels were lower in the good glycemic control group (Reza et al., 2023). This result is also in line with studies by Yudha et al., (2021) and (Artha et al., 2019).

Based on the correlation test results, a significant positive correlation was found between glycemic control (HbA1c) and total cholesterol (r = 0.277; p = 0.032), triglycerides (r = 0.386; p = 0.002), and LDL-C (r = 0.357; p = 0.005). The strength of the correlations is relatively low. This relationship pattern can be explained by the consistency of the results with previous studies or by using a pathophysiological approach to explain the relationship between glycemic control and lipid profile.

The results of this study are consistent with a study by Susilo et al. (2020), which found a significant relationship between HbA1c levels and total cholesterol levels in type 2 DM patients (p=0.030; r= +0.314) (Susilo et al., 2020). A similar study by Nnakenyi et al., (2022) also found a positive relationship between HbA1c and total cholesterol (r = 0.406, p <0.05), triglycerides (r = 0.273, p <0.05), and LDL-C (r = 0.409, p < 0.05). A study by Artha et al. (2019) involving 140 type 2 DM patients also showed a similar relationship, with positive correlations between HbA1c and total cholesterol, triglycerides, and LDL-C (r=0.472; r=0.276;r=0.679) (Artha et al., 2019).

Patients with type 2 DM experience a decrease in plasma campesterol levels (a marker of cholesterol absorption) and an increase in plasma lathosterol levels (a marker of cholesterol synthesis). This mechanism underlies the changes in cholesterol homeostasis. The expression of SREBP2 (which codes for sterol regulation, a factor regulating uptake and synthesis) is increased in patients with type 2 DM (Vergès, 2015).

Hypertriglyceridemia is the most common serum lipid disorder found in DM patients. The increase in plasma triglyceride levels in type 2 DM patients is largely due to an increase in the number of VLDL, particularly large VLDL1 particles, and the delayed catabolism of VLDL

leads to an increase in the VLDL pool. Decreased VLDL catabolism due to insulin resistance can lead to decreased lipoprotein lipase (LPL) activity, resulting in reduced catabolism of chylomicrons and VLDL, leading to more severe hypertriglyceridemia. Other mechanisms, such as de novo lipogenesis, also contribute to the increase in plasma triglycerides in type 2 DM (Vergès, 2015) (Huang et al., 2021).

In type 2 DM patients, LDL-C also increases. This is due to a significant decrease in LDL-C catabolism, resulting in a longer duration of LDL-C in the plasma, which can increase lipid deposition in the arterial walls. Another mechanism is a significant reduction in the number of cell surface LDL B/E receptors and decreased affinity of LDL-C to its receptors due to glycation of ApoB. Type 2 DM patients also experience an increase in oxidized LDL-C in the plasma. Oxidized LDL-C is formed from triglycerides that are abundant in VLDL, which exchange with cholesterol esters (CE) from LDL-C in the circulation. This results in triglyceride-rich but cholesterol ester-poor LDL, producing small dense LDL, known as small dense LDL particles, which are highly atherogenic (Susilo et al., 2020) (Artha et al., 2019).

The correlation test results showed a significant negative correlation between glycemic control (HbA1c) and HDL-C (r=-0.366; p = 0.004). The strength of the correlation is relatively low. Similar results were obtained in a study by Huang et al. (2021), which involved 3171 type 2 DM patients and found a negative relationship between HbA1c and HDL-C (p= 0.044) (Huang et al., 2021). A study by Handayani et al. (2023) also found a significant negative correlation between HbA1c and HDL-C (r=-0.377; p=0.026). The strength of the correlation is relatively low, as other factors such as lifestyle and diet can also affect HDL-C levels (Gordon, 1998).

The decrease in HDL-C in type 2 DM patients is also associated with hypertriglyceridemia and obesity. The hypertriglyceridemia condition activates CETP (cholesteryl ester transfer protein), which facilitates the transfer of cholesterol esters (CE) from HDL-C to triglyceride-rich lipoproteins (TGR-LPs), resulting in HDL-C that is poor in cholesterol esters but rich in triglycerides. This form of HDL-C is more easily catabolized, leading to a decrease in serum HDL-C levels (Vergès, 2015) (Susilo et al., 2020) (Kostapanos & Elisaf, 2014) (Barter, 2011).

The consequences of decreased HDL-C in type 2 DM patients are associated with a reduction in cardiovascular protection (Barter, 2011). One consequence is arterial stiffness, which leads to atherogenic effects (Vergès, 2015). Recent studies suggest that HDL-C has the ability to enhance glucose uptake by skeletal muscle and stimulate insulin secretion from pancreatic beta cells, so low HDL-C levels in type 2 DM may also contribute to worsening diabetes control. Studies have shown that for every 1 mg/dL decrease in HDL-C, the risk of coronary heart disease increases by 2% in men and 3% in women (Kostapanos & Elisaf, 2014) (Barter, 2011).

Glycemic control indirectly affects the lipid profile. Lipid profiles such as total cholesterol, triglycerides, and LDL-C will significantly increase in type 2 DM patients with poor glycemic control. HbA1c is not only used as a long-term biomarker for glycemic control but also as a predictor of lipid profile. Therefore, monitoring glycemic control using HbA1c is useful for identifying the status of diabetic patients regarding cardiovascular complications risk (Susilo et al., 2020).

Conclusion

The conclusion of this study is that there is a positive correlation between glycemic control (HbA1c) and total cholesterol, triglycerides, and LDL-C. There is a negative correlation between glycemic control (HbA1c) and HDL-C. Significantly lower levels of total cholesterol, triglycerides, and LDL-C were found in type 2 DM patients with good glycemic control. Significantly higher levels of HDL-C were found in type 2 DM patients with good glycemic control.

Based on this research, several recommendations are provided by the researchers for future studies. In this study, not all confounding variables were well-controlled, so the researchers recommend stricter control over other confounding variables. Future studies could use cohort study methods to explain the causal relationships between variables. The researchers also suggest increasing the sample size so that the study sample is sufficiently representative of the general population.

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