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

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ABSTRACT
Diabetes Mellitus (DM) tipe 2 rentan terhadap dislipidemia diabetik, yang meningkatkan risiko komplikasi penyakit kardiovaskular. Penelitian ini bertujuan untuk menentukan hubungan antara pengendalian glikemik dan profil lipid pada pasien DM tipe 2. Studi cross-sectional dilakukan di Poliklinik Penyakit Dalam RSUD Bangli dari Januari hingga Desember 2023, melibatkan 60 pasien DM tipe 2 yang memenuhi kriteria inklusi. Pasien dikelompokkan menjadi dua, yaitu dengan kontrol glikemik baik (HbA1c < 7%) dan kontrol glikemik buruk (HbA1c ≥ 7%). Pada pasien dengan kontrol glikemik baik, kadar kolesterol total lebih rendah (160,444 ± 30,608 mg/dl vs 203,476 ± 45,471 mg/dl; p= 0.001), trigliserida (125,500 ± 56,019 vs 202,047 ± 91,568; p= 0.002), dan low-density lipoprotein (K-LDL) (93,072 ± 28,443 vs 131,571 ± 44,590; p= 0.001). Kadar high-density lipoprotein (K-HDL) juga lebih tinggi (50,022 ± 14,050 vs 41,152 ± 12,619; p = 0.019) pada pasien dengan kontrol glikemik baik. Uji statistik menunjukkan korelasi positif antara kadar kolesterol total (r = 0.277; p = 0.032), trigliserida (r = 0.386; p = 0.002), dan K-LDL (r = 0.357; p = 0.005) dengan kadar HbA1c, serta korelasi negatif antara K-HDL (r=-0.366; p = 0.004) dan HbA1c. Korelasi signifikan ini menegaskan pentingnya pengendalian glikemik pada pasien DM tipe 2.
Keywords: Diabetes Mellitus, Cholesterol, K-HDL, K-LDL, Triglycerides

INTRODUCTION

Diabetes mellitus (DM) is a group of metabolic diseases characterized by hyperglycemia that occurs due to abnormalities in insulin secretion, insulin action, or both (Salsabila & Sjaaf, 2022). DM is currently one of the chronic diseases with the highest prevalence rate throughout the world (Voeltz, Tönnies, Brinks, & Hoyer, 2022). According to research Epidemiologically, currently there are 387 million people suffering from DM worldwide, which is expected to increase to 592 million people in 2035 to 642 million people in 2040 (Zheng, Ley, & Hu, 2018).

HbA1c (glycated hemoglobin) is a type of hemoglobin that shows the average concentration of plasma glucose in 3 months which has been recommended by PERKENI as a long-term glucose evaluation in type 2 DM sufferers (Goyal, Singhal, & Jialal, 2023). High HbA1c is independently associated with increased risk of macrovascular or microvascular complications and is associated with metabolic syndrome (Committee,

2011)(Indonesia, 2021). HbA1c is not only a sign of glycemic control but can also be used as a predictor of dyslipidemia (Saepudin, Ball, & Morrissey, 2016).

Type 2 DM patients are susceptible to diabetic dyslipidemia, namely abnormalities in lipid metabolism which is one of the factors that contributes to an increased risk of complications from cardiovascular disease. Diabetic dyslipidemia includes not only quantitative but also qualitative lipoprotein abnormalities resulting in a shift towards an atherogenic lipid profile (Kumar et al., 2022)(Devhy & Widana, 2019). The hyperglycemia, insulin resistance and relative insulin deficiency observed in Type 2 DM patients most likely contribute to lipid changes, because insulin plays an important role in regulating lipid metabolism (Reza, Dwi, Jihan, Kurnia, & Afra, 2023).

From the various empirical evidence presented above, the relationship between glycemic control and lipid profile needs to be studied further. Evidence regarding the relationship between glycemic control and lipid profile in patients with type 2 diabetes is currently conflicting. Because there is still conflicting evidence regarding the relationship between glycemic control and lipid profile, this research was carried out with the aim of determining the relationship between glycemic control and lipid profile in type 2 DM patients at Bangli Regional Hospital.

RESEARCH METHODS

This research is a correlational analytical study with a cross sectional approach to determine the relationship between glycemic control (HbA1c) with lipid profiles in type 2 DM patients. The research was carried out at the Internal Medicine Polyclinic at Bangli Regional Hospital periodJanuary 2023 – December 2023. Data was taken from the patient's medical record.

Ethical approval was obtained from the Health Research Ethics Committee of Bangli Regional Hospital (No.400.7.22.2/1024/RSUD) to ensure that the research was carried out in accordance with procedures. Consent was obtained from the subjects after explaining the details of the research in Indonesian and/or regional languages (Balinese). Confidentiality is guaranteed in this research.

The target population isall outpatients who have been diagnosed with type 2 DM, while the accessible population is type 2 DM sufferers at Bangli Regional Hospital, especially patientsInternal Medicine Polyclinic ywho meet the inclusion and exclusion criteria. Inclusion criteria: patients diagnosed with type 2 DM andthere is data in the medical record in the form of HbA1c and lipid profile (total cholesterol, K-HDL, K-LDL, triglycerides); Exclusion criteria: Type 2 DM patients who do not havedata in medical records in the form of HbA1c and lipid profile (total cholesterol, K-HDL, K-LDL, triglycerides), type 2 DM patients with previous dyslipidemia therapy (statins, fibrates, niacin), pregnant patients, patients who have thyroid disease, chronic liver disease, chronic kidney disease and other endocrine disorders. The minimum sample size required is 51 people.

The sampling technique in this research is non-probability sampling, namely purposive sampling by determining inclusion and exclusion criteria. From purposive sampling it was obtainedThe sample size of 60 people is what is required in this research.

Dependent variable: the dependent variable examined in this research islipid profile in the form oftotal cholesterol, triglycerides, K-LDL and K-HDL. The scale used is

numerical. Independent variable: the independent variable examined in this study is glycemic control through HbA1c examination.HbA1C levels will be grouped into 2 groups. Patients with HbA1c levels <7% were categorized as a controlled glycemic control group, while patients with HbA1c levelsHbA1c≥7%categorized as uncontrolled glycemic control group. The scale used is numerical.

By operational definition, type 2 DM patients are patients who have been diagnosed with type 2 DM at the Internal Medicine Polyclinic of Bangli Regional Hospital for the period January 2023 to December 2023. Patient assessments were obtained from the patient's medical records at the Internal Medicine Polyclinic of Bangli Regional Hospital. Glycemic control assessment is obtained from laboratory results of HbA1c, which is the average plasma glucose level. Assessment of the lipid profile is assessed by total cholesterol levels, triglycerides, K-LDL and K-HDL levels.

Statistical analysis was carried out by testing data homogeneity followed by comparative tests and correlation tests. Comparative tests between total cholesterol, triglyceride, K-LDL and K-HDL levels were carried out in the controlled glycemic control group and the uncontrolled glycemic control group. Comparative tests were carried out using the independent T test. The correlation test assesses the relationship between glycemic control (HbA1c) and total cholesterol, triglyceride, K-LDL and K-HDL levels. The correlation test used is the Pearson correlation test, if the patience data is normal, if the data patience data is not normal then an alternative test is used, namely the Spearman correlation test. All tests were considered significant if the p value < 0.05. Data analysis was carried out with the help of SPSS version 26 software.

RESULTS AND DISCUSSION

In this study, of 60 type 2 DM patients, there were 18 patients in the controlled glycemic control group and 42 patients in the uncontrolled glycemic control group. There were 18 patients with controlled glycemic control, 7 people (38.9%) were male and 11 people (61.1%) were female patients. In the uncontrolled glycemic control group there were 42 people, 24 people (57.1%) were men and 18 people (42.9%) were women. Judging from age characteristics, it was found that the mean age of patients with controlled and uncontrolled glycemic control was 66,277 years and 60,170 years respectively. Patients with controlled glycemic control had an average HbA1c level of 5,991 and the average HbA1c in the group of patients with uncontrolled glycemic control was 9,471. The characteristics of the respondents can be seen in Table 1.

Table 1. Characteristics of Respondents

Characteristics	HbA1c		p-value
	Controlled Glycemic Control (<7%) n = 18	Uncontrolled Glycemic Control (≥7%) n = 42	
Gender, n (%)			
Man	7 (38.9)	24 (57.1)	0.201
Woman	11 (61.1)	18 (42.9)	
Average Age	66,277	60,170	0.043

Average HbA1c	5,991	9.4710	0,000

Comparative analysis of the lipid profile of type 2 DM patients between controlled glycemic control and uncontrolled glycemic control was carried out using the independent T test. The results of this study showed that the group of patients with controlled glycemic control had lower levels of total cholesterol, triglycerides and K-LDL, while the group of patients with controlled glycemic control had higher K-HDL. 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		
	Controlled Glycemic Control (<7%) n = 18	**Uncontrolled Glycemic Control (≥7%) n = 42**	**p-value**
Total cholesterol	160,444 ± 30,608	203,476 ± 45,471	0.001
Ttriglycerides	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 carrying out a correlation test between glycemic control (HbA1c) and lipid profile, first carry out a normality test. The normality test used was the Kolmogorov-Smirnov test because the number of samples in the study was > 50. In the Kolmogorov-Smirnov test, data on HbA1c (p=0.200), total cholesterol (p=0.200), K-LDL (p=0.200) were normally distributed, while data on triglycerides (p=0.000) and K-HDL (p= 0.040) are not normally distributed and are presented in Table 3.

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

Variable	Sig.	Information
HbA1c	0.200	Normal
Total cholesterol	0.200	Normal
Triglycerides	0,000	Abnormal
K-LDL	0.200	Normal
K-HDL	0.040	Abnormal

Correlation test between glycemic control (HbA1c) and lipid profile using the Pearson correlation test for normally distributed data and the Spearman correlation test for abnormally distributed data, obtained a weak positive correlation between HbA1c and total cholesterol, triglycerides and K-LDL. A positive correlation indicates a unidirectional relationship, so it can be concluded that the higher the HbA1c level, the higher the total cholesterol, triglycerides and K-LDL will also be. There is a weak negative correlation between glycemic control (HbA1c) and K-HDL. Negative correlation indicates an opposite relationship, so it can be concluded that the higher the HbA1c level, the

lower the K-HDL. The results of the correlation test between glycemic control (HbA1c) and lipid profile are presented in Table 4.

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

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

Discussion

Type 2 DM patients are susceptible to diabetic dyslipidemia, namely abnormalities in lipid metabolism that not only include quantitative but also qualitative lipoprotein abnormalities that result in a shift towards an atherogenic lipid profile. Lipid abnormalities in type 2 DM are most likely the result of hyperglycemia, insulin resistance and relative insulin deficiency observed in type 2 DM patients. Dyslipidemia is a predictor of cardiovascular disease (Reza et al., 2023).

In this study it was found that type 2 DM patients with controlled glycemic control (HbA1c < 7%), had lower levels of total cholesterol, triglycerides and K-LDL than type 2 DM patients with uncontrolled glycemic control (HbA1c≥7%). This research is in line with that conducted by Handayani et al (2023) which showed that total cholesterol, triglyceride and K-LDL levels were lower in the controlled glycemic group. The results of this study are also in line with the results of research by Reza (2023) and Made Junior et al (2019) with similar findings.

Based on the results of the correlation test, 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 K-LDL (r = 0.357; p = 0.005). The strength of the correlation is low. This pattern of relationship can be explained based on the consistency of results with previous studies or an explanation using a pathophysiological theoretical approach regarding the relationship between glycemic control and lipid profile.

The results of this study are consistent with research conducted by Susilo et al (2020), in their research there was a significant relationship between the HbA1c value and total cholesterol levels in Type 2 DM sufferers (p=0.030; r= +0.314). (16) Similar research results also shown by Nnakenyi (2022), in his research showed that there was a positive relationship between HbA1c and total cholesterol (r = 0.406, p <0.05), triglycerides (r = 0.273, p <0.05), K-LDL (r= 0.409, p < 0.05). Research conducted by Made Junior et al (2019) using 140 type 2 DM patients also showed a similar thing, namely that there was a positive relationship between HbA1c and total cholesterol, triglyceria, K-LDL (r=0.472; r=0.276;r=0.679) .

Patients with Type 2 DM experience decreased plasma campesterol levels (a marker of cholesterol absorption) and increased plasma latosterol levels (a marker of cholesterol synthesis). This mechanism underlies changes in cholesterol homeostasis. The expression of SREBP2 (which codes for sterol regulation, a factor that regulates uptake and synthesis) is increased in type 2 DM patients (Vergès, 2015).

Hypertriglyceridemia is the most common serum lipid abnormality found in DM patients. The increase in plasma triglyceride levels in Type 2 DM patients is largely caused by an increase in the amount of VLDL, especially large VLDL1 (very low-density lipoprotein subfraction 1) particles and delays in VLDL catabolism causing an increase in the VLDL pool. Decreased VLDL catabolism due to insulin resistance can cause a decrease in lipoprotein lipase (LPL) activity, which results in decreased chylomicron and VLDL catabolism, resulting in more severe hypertriglyceridemia. Other mechanisms such as de novo lipogenesis also contribute to increasing plasma triglycerides in type 2 DM (Vergès, 2015).

In type 2 DM patients, K-LDL also increases. This is due to a significant reduction in K-LDL catabolism which causes a longer duration of K-LDL in plasma which can increase lipid deposition into the arterial wall. Another mechanism is the result of a significant reduction in the number of K-LDL B/E cell surface receptors and a decrease in the affinity of K-LDL to its receptor due to ApoB glycation (K, Kunikullaya, & Goturu, 2014). Patients with type 2 DM experience an increase in oxidized K-LDL in plasma. Oxidized K-LDL is formed from triglycerides which are abundant in VLDL and exchange with cholesterol esters (CE) from K-LDL in the circulation. This will produce LDL that is rich in triglycerides but lacking cholesterol esters, resulting in small dense LDL, known as small dense LDL. These small, dense LDL particles are highly atherogenic (Artha et al., 2019).

Then, based on the results of the correlation test between glycemic control (HbA1c) and K-HDL (r=-0.366; p = 0.004), a significant negative correlation was found. The strength of the correlation is low. Similar results were also obtained from research by Huang et al (2021) using 3171 type 2 DM patients showing that there was a negative relationship between HbA1c and K-HDL (p= 0.044). Research by Handayani et al (2023) also obtained similar results, namely significant relationship between HbA1c and K-HDL and negatively correlated (r=-0.377; p=0.026). The strength of the correlation is low because there are still other factors that influence K-HDL such as lifestyle and diet.

Decreased K-HDL in type 2 DM patients is also associated with hypertriglyceridemia and obesity. Hypertriglyceride conditions activate CETP (cholesteryl ester transfer protein) encouraging the transfer of cholesterol ester (CE) from K-HDL to triglyceride-rich lipoproteins (TGR-LPs) which results in K-HDL being poor in cholesterol ester but rich in triglycerides. Then K-HDL in this form is more easily catabolized so that the amount of serum HDL decreases (Kostapanos & Elisaf, 2014).

The consequences of decreasing K-HDL in type 2 DM patients are related to reduced cardiovascular protective effects (Barter, 2011). One of the consequences is arterial stiffness which causes atherogenic effects (Vergès, 2015). Recent studies show that K-HDL has the ability to increase glucose absorption by skeletal muscle and stimulate insulin secretion from pancreatic beta cells so that K-HDL concentrations are low in type 2 DM as well. may contribute to worsening diabetes control. Studies show that for every 1 mg/dL reduction in K-HDL levels, the risk of CHD increases by 2% in men and 3% in women (Barter, 2011).

Glycemic control indirectly influences the lipid profile. Lipid profiles such as total cholesterol, triglycerides, K-LDL will increase significantly in type 2 DM patients with uncontrolled glycemic control. HbA1c is not only used as a long-term biomarker for

glycemic control, but also as an appropriate predictor of lipid profile. Therefore, monitoring glycemic control using HbA1c is useful for identifying the status of diabetes mellitus patients regarding the risk of cardiovascular complications (Sulolipu, Handoyo, & Roziqin, 2019).

CONCLUSION

The conclusion of this study is that there is a positive correlation between glycemic control (HbA1c) and total cholesterol, triglycerides and K-LDL. There is a negative correlation between glycemic control (HbA1c) and K-HDL. Total cholesterol, triglyceride and K-LDL levels were significantly lower in Type 2 DM patients with good glycemic control. K-HDL levels were significantly higher in Type 2 DM patients with good glycemic control. Based on this research, there are several suggestions given by the researcher for further research, such as in this study not all confounding variables can be controlled properly, so the researcher suggests tighter control of other confounding variables. Future research can use research methods such as cohorts so that they can explain the causal relationship between variables.PResearchers also suggest increasing the sample size so that the research sample is adequate to represent the general population.

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