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Original research Articles

There is No Relationship Between HbA1C and HDL in Type 2 Diabetes Mellitus Patients

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Abstract:- Backgrounds: Diabetes mellitus is a metabolic disease characterized by hyperglycemia due to impaired insulin secretion. Hyperglycemia control is evaluated from the results of blood glucose control using HbA1C. Insulin resistance and hyperglycemia cause HDL function and the amount of HDL catabolized to increase, resulting in decreased HDL levels in the blood and increased HbA1C. The World Health Organization (WHO) claims that there are around 422 million individuals with diabetes worldwide, and the majority of sufferers live in low- and middle-income countries. In Indonesia, there are 19,465,100 diabetes sufferers aged between 20 and 79 years. Meanwhile, the adult population aged 20 to 79 years is 179,720,500 people, so the prevalence of diabetes in the age group of 20 to 79 years is 10.6%.

Objective: This study aims to examine the relationship between HbA1C and HDL in patients with type 2 diabetes mellitus.

Methods: This study is an observational analytical study with a cross-sectional design with consecutive non-random sampling. The subjects of this study were patients with Diabetes Mellitus aged 26 - 46 years who were treated as outpatients at the polyclinic of IZZA Hospital Cikampek. The research data were obtained from medical record data on HbA1C and HDL levels of outpatients. Data analysis was performed using SPSS 25.0 Software using the Spearman Correlation test (95% confidence level and 5% p-value).

Results: This study involved 61 subjects. High HbA1C levels were 44.26%, while normal HbA1C was 27%. Low HDL levels were 42.62%, while normal and high HDL were 57.38%. The results of the calculation of the relationship test between HbA1C and HDL in Type 2 Diabetes Mellitus Patients ($p = 0.507$; $r = -0.086$).

Conclusion: The results of the study showed that there was no significant relationship between HbA1C and HDL in Type 2 Diabetes Mellitus Patients

Keywords: HbA1C, HDL, Type 2 Diabetes Mellitus.

Supplementary information: The online version of this article(https://doi.org/xx.xxx/xxx.xx) contains supplementary material, which is available to autho-rized users.

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Introduction:

Diabetes mellitus is a group of metabolic diseases characterized by high blood sugar levels due to impaired secretion or function of insulin. This disease can cause damage to various organs such as the eyes, kidneys, nerves, heart, and blood vessels if uncontrolled, and can cause macro vascular and micro vascular complications.[1],[2] According to the World Health Organization (WHO), around 422 million people worldwide suffer from diabetes, with the majority of sufferers living in low- and middle-income countries.[3] The International Diabetes Federation (IDF) reports that the number of people with diabetes continues to increase, with an estimated 783 million people will have diabetes by 2045.[4] In Indonesia, the prevalence of diabetes in the 20-79 age group reaches 10.6%.[5] This disease can be evaluated by looking at the results of blood glucose control using the HbA1C examination.[6]

The HbA1c parameter describes blood sugar levels during 1-3 months, because the lifespan of erythrocytes is around 120 days, so HbA1C is used as the main indicator to control DM. [7] HbA1C is not only a biomarker that functions in controlling long-term glycemic but also predicts well for lipid profiles. [8] HbA1C examination is recommended every 3 months or 4 times a year to determine the quality of blood glucose control. [9] The Framingham study showed that patients with type 2 diabetes mellitus often experience increased triglyceride and VLDL levels and decreased HDL levels. [10] HDL cholesterol plays a role in transporting good cholesterol because it can remove cholesterol from the walls of blood vessels. HDL carries cholesterol to the liver to be processed and then converted into bile salts. Normal HDL levels protect against atherosclerosis, but levels are lower in DM patients. HDL affects the performance and differentiation of endothelial cells, one of which is the production of nitric oxide, and functions as a cyto protective and heals wounds. This function is thought to be particularly important for people with diabetes, who are known to have impaired endothelial function, micro- and macrovascular disease, and poor wound healing.[11] Some studies have shown a significant association between HbA1C and HDL levels, while others have not. This debate has motivated researchers to further explore the relationship between HbA1C and HDL in people with type 2 diabetes.

Materials and Methods

This study was conducted using an observational analytical design through a cross-sectional approach to assess the relationship between HbA1C and HDL in patients or sufferers of Type 2 Diabetes Mellitus through the collection and monitoring of medical record data. This study was attended by 61 respondents and was conducted from February 2024 to March 2024. The location of the study was at a Private Hospital, namely the Cikampek area, Karawang. The population in this study were people aged 26-46 years in the Cikampek area, Karawang. The target population in this study was type 2 Diabetes Mellitus patients at a Private Hospital. The research sample had inclusion criteria; Type 2 Diabetes Mellitus sufferers, and adult patients (26-46 years). Sample exclusion criteria included; Patients with a history of complications (stroke, heart failure, hypertension, cancer,), patients taking anti-cholesterol drugs, pneumonia infection, diabetes + HIV, long-term steroid users, autoimmune, chronic diseases.

Statistical Analysis

This study analyzed data from outpatient medical records at a Private Hospital, focusing on HbA1C and HDL levels. The data were analyzed using the SPSS program through uni-variate analysis to describe the characteristics of the HbA1C (independent) and HDL (dependent) variables, which were displayed in frequency and percentage. To determine the relationship between the two variables, bi-variate analysis was performed using the Spearman or Pearson correlation method. The Spearman method is used if the data is

not normally distributed, while Pearson is used if the data is normally distributed.

Results

This study was attended by 61 respondents, with the following characteristics.

Table 1. Respondent Characteristics

Characteristics	Frequency	%
Gender		
Man	30	49.18
Woman	31	50.82
Age		
<40	7	11.48
>40	54	88.52
HbA1C		
Good	34	55.74
Bad	27	44.26
HDL		
Low	26	42.62
High	35	57.38

Table 1 shows that out of 61 research subjects, 30 (49.18%) were men and 31 (50.82%) were women. Bad HbA1C was found in 27 people (44.26%), 34 people (55.74%) had good HbA1C, and low HDL was found in 26 people (42.62%), 35 people (57.38%) were high. 7 people (11.48%) were found with age 40 years 54 people (88.52%).

Table 2. Normality Test with Kolmogorov Smirnov

Data Normality Test Kolmogorov-Smirnov	
Variable	**P**
HbA1C	0.018
HDL	0.075

The results of the Kolmogorov Smirnov normality test in table 2 show that the HbA1C variable data shows an abnormal data distribution ($p = 0.018$; $p < 0.05$), but the distribution of the HDL variable data shows that the data is normally distributed ($p = 0.075$; $p < 0.05$). The correlation test between HbA1C and HDL was carried out using the Spearman correlation test in table 3.

Table 3. Spearman Correlation Test

Spearman Correlation Test			
Measurement	**r**	**N**	**P**
HbA1C and HDL	-0.086	61	0.507

Based on the results of the Spearman correlation test in Table 7, it can be seen that the significance result is p = 0.507 and the correlation r is -0.086. These results indicate an insignificant relationship (p = 0.507; p> 0.05). The correlation between the two variables shows a weak negative correlation (r: -0.086), meaning that an increase in HbA1C will be followed by a decrease in HDL values in type 2 DM patients.

Discussion

Based on the data in Table 1, it can be seen that the highest number of ages in this study were patients over 40 years old. According to a survey, the prevalence of diabetes and prediabetes in the 40-49 age group was 11.1% and 40.3%, while in the 60-69 age group, the prevalence increased to 23.9% and 47.6% respectively. Advanced age is one of the crucial factors in diabetes and prediabetes. Age differences cause changes in socio-demographic and clinical characteristics; therefore, age may be an important variable influencing the potential role of diabetes and prediabetes. Thus, clarifying the interaction between age and factors influencing abnormal glucose metabolism is essential for healthcare organizations to develop appropriate diabetes prevention and control programs.[12] In childhood, it may be too young to develop Type 2 Diabetes Mellitus. Fasting plasma glucose, but not insulin or parental (or maternal) diabetes, along with black race and obesity in early adolescence were predictors of early-onset diabetes at follow-up ages of 30-39 years. In addition, environmental exposures have been increasingly implicated in the risk of developing diabetes currently observed in the obesity epidemic, and all conventional cardiometabolic risk factors that begin at an early age are predictors of later (40-50 years) age of onset of diabetes.[13],[14]

Based on the results of the study, it shows that the highest gender in the study is female with a percentage of 50.92%. The study conducted by Sharahili et al. in 2023 also showed that 53.3% of respondents in this study were female. [15] According to health research data based on gender, women are generally less active but have a healthier diet by eating lots of fruits and vegetables and minimizing meat consumption. In a prospective cohort study with separate analyses for men and women, only women showed an increased risk of developing type 2 diabetes over 10 years, with a twofold risk in women who consumed soft drinks daily compared to non-alcoholic drinks. [16] Discrimination based on gender categories exacerbates environmental mental stress and stress reactions, especially in women. According to certain studies, women are more likely to experience negative cardio-metabolic effects due to psychological stress, job stress, and sleep disturbances.[17]

Type 2 DM is related to estrogen hormones, especially 17Beta-estradiol, which plays a role in protecting pancreatic beta cells from apoptosis and preventing insulin deficiency, thus explaining the lower prevalence of diabetes in women compared to men. Estradiol, a steroid hormone produced by the ovaries, is the most potent form of estrogen. In the blood, estradiol is bound to carrier proteins such as albumin and globulin. Although estradiol has a protective role in type 2 DM, the relationship between this hormone and type 2 diabetes in this study was relatively weak.[18]

Table 2 shows the results of the Pearson correlation normality test in this study, obtaining a p-value of 0.507 and R2 of -0.086. The p-value in this study shows that HbA1C and HDL have a statistically insignificant correlation (p-value <-1. Based on the test results, it can be concluded that HbA1C and HDL in type II DM patients have a weak and opposite (negative) relationship, but are not significant. Previous studies have also shown similar results, with no significant correlation between HbA1C and HDL levels in type 2 DM patients.[19] However, several studies, such as research by Khan et al. [20] involving 90 participants with a case-control studies method, showed that there was a significant relationship between diabetes mellitus conditions and HDL levels with p = 0.014. This is also supported by research by Handayani et al. [21] on 35 respondents at the Internal Medicine Clinic of M. Yunus Hospital, Medan, Indonesia in 2023, which reported that HbA1C levels and HDL levels had a strong opposite (negative) and significant relationship with R2 of -

0.377 and a p-value of 0.026.

Lipid abnormalities are common in diabetic patients and are seen in patients with Type 2 Diabetes Mellitus. The abnormal lipid profile observed in Type 2 Diabetes Mellitus is related to insulin resistance as reported in previous studies, causing increased release of free fatty acids from adipose tissue, impaired uptake of free fatty acids by insulin-dependent muscles, and increased fatty acid release into liver tissue. This is closely related to diabetic dyslipidemia, hypertension, and a high risk of cardiovascular disease. Chronic hyperglycemia causes apolipoprotein glycation and disrupts the normal pathway of lipoprotein metabolism.[22] The pathogenesis of diabetic dyslipidemia shows that insulin resistance plays a central role in the development of diabetic dyslipidemia. Diabetic dyslipidemia is mainly caused by the increased release of free fatty acids from insulin-resistant fat cells. Increased flow of free fatty acids to the liver, coupled with sufficient glycogen stores, increases triglyceride production, in turn stimulating the secretion of apolipoprotein B and VLDL cholesterol. In addition, hyperinsulinemia is also associated with low HDL levels.[23] Thus, people with diabetes often have high LDL and triacylglycerol levels and low HDL.[24]

Glycated hemoglobin (HbA1C) is an important indicator of long-term glycemic control and is closely related to mortality and cardiovascular morbidity in diabetic patients. HbA1C measures the average blood glucose over 2-3 months and is important in monitoring diabetes mellitus.[25] In type 2 diabetes (T2DM), fat metabolism is disturbed, leading to increased blood lipid levels and decreased HDL levels. Decreased HDL in T2DM patients may be associated with lower serum thiamine levels and low HDL production. A study by Huang et al. in 2021 showed that the relationship between HDL and HbA1C was closely related to the race and age of the respondents. A U-shaped relationship was detected between HDL and glycosylated hemoglobin for people of other races/ethnicities or aged 60 years and over, and the HDL change point was 60 mg/dL. In addition, this study also showed that an inverted U-shaped distribution between HDL and glycosylated hemoglobin in people under 40 years of age was detected, and the HDL inflection point was also located at 60 mg/dL.13 The U-shaped relationship pattern showed that high HbA1C levels were found at very low and very high HDL levels. Conversely, lower HbA1C levels were seen at moderate HDL levels.

The study showed that people with very low or very high HDL levels tended to have poorer glycemic control, as indicated by higher HbA1C levels. On the other hand, people with moderate HDL levels tended to have better glycemic control. HDL serves to protect blood vessels and has anti-diabetic effects, so increasing HDL can reduce the risk of diabetes and cardiovascular disease.[25] A study by Alzahrani et al. showed differences in HbA1C levels between genders, with women having higher HbA1C and higher HDL than men, but no significant correlation was found between the two.[26]

Limitations of the study

The limitations of this study are that the number of respondents involved is still small or less than 100 respondents and there are still many factors that influence HbA1C and HDL levels that have not been studied.

Conclusion

This study found that there was no significant relationship between HbA1C and HDL levels in patients with type 2 diabetes mellitus, with a weak negative correlation ($r = -0.086$) and p-value = 0.507. Although several previous studies have shown a significant relationship between the two variables, the results of this study do not support these findings. This may be influenced by variations in population characteristics or the methodology used. Therefore, further research is needed with a larger sample and more in-depth analysis methods to understand the relationship between HbA1C and HDL and its implications in the management of type 2 diabetes.

Ethical Declarations

Acknowledgments

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Ethics Approval and Consent to Participate

This research has received ethical approval from the Research Ethics Committee of the Faculty of Medicine, Universitas Trisakti. Number 28//KER-FK//II/2024. All respondents filled out informed consent and had the right to resign whenever the respondent wanted. The interviews' results were kept confidential and strictly protected by removing all personal identifiers from the form to protect the respondents' privacy.

Consent for Publication

Not applicable (no individual personal data included).

Availability of Data and Material

The data sets generated during and/or analyzed during the current study are available from the corresponding author upon reasonable request.

Competing Interests

The authors declare that there is no conflict of interest.

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Authors' Contributions

All authors listed have made a substantial, direct, and intellectual contribution to the work, and approved it for publication.

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