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## RESEARCH ARTICLE

## Serum High-Density Lipoprotein-Cholesterol Concentration as Determinant of Poor Glycemic Control in Type 2 Diabetes Mellitus Patients at a Public Health Center in Jakarta, Indonesia

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### Abstract

The risk factors for glycemic control in type 2 diabetes mellitus (T2DM) are poorly understood. This study assessed the prevalence of poor glycemic control and the predictive factors of poor glycemic control among T2DM outpatients in the community. This 30-day community-based cross-sectional study was conducted among ambulatory T2DM patients in Jakarta from May to June 2023. Data on age, sex, and level of education were collected by questionnaire, whereas data on body mass index, lipid profile, and HbA1c were obtained by measurement. Glycemic control was good if HbA1c < 7 % and poor if HbA1c ≥ 7%. The relationships between age, sex, level of education, body mass index, lipid profile, and glycemic control were determined using simple logistic regression. Multivariable logistic regression was used to determine the most influential risk factors of glycemic control. Poor glycemic control was found in 68.4% respondents, and obesity in 57.9% of respondents. After adjustment for age, level of education, and triglyceride concentration, the most influential factor for glycemic control was HDL concentration (aOR=4.43, 95% CI=1.19–16.5, p=0.027). Patients with T2DM with HDL < 40 mg/dl had a 4.63 times significantly higher odds of poor glycemic control than those with HDL ≥ 40 mg/dl. This study found a high prevalence of poor glycemic control in the community setting among individuals with T2DM, with HDL concentration as the most significant predictor. Meanwhile, a triglyceride concentration of ≥ 150 mg/dl independently provided 58% greater protection against glycemic control (p=0.035), but the effect was not significant after adjustment (p>0.05). The high prevalence of poor glycemic control, dyslipidemia, and obesity in T2DM patients requires routine screening and monitoring accompanied by health education on lifestyle modification for risk factor control, thus minimizing the risk of complications.

**Keywords:** Indonesia; risk factors; serum high-density lipoprotein-cholesterol; type 2 diabetes; urban population

### Introduction

Type 2 diabetes mellitus (T2DM) continues to rise globally, with a prevalence of 6,138.6 per 100,000 population in 2021 and a projected 59.7% increase by 2050.<sup>1</sup> Indonesia faces a similar trend, ranking fifth worldwide with 19.5 million T2DM cases in 2021, expected to reach 28.6 million by 2045.<sup>2,3</sup> Poor glycemic control contributes substantially to cardiovascular complications in T2DM, as endothelial dysfunction and coronary artery disease are exacerbated by elevated glycated hemoglobin (HbA1c).<sup>4</sup> The American Diabetes Association (ADA) recommends maintaining

HbA1c levels below 7% to reduce cardiovascular risk, with each 1% increase associated with a 13% rise in risk.<sup>5,6</sup> Despite its importance, the prevalence of poor glycemic control remains high across many settings, including Saudi Arabia (49.1%),<sup>7</sup> Malaysia (59.2%),<sup>8</sup> Ethiopia (61.1%),<sup>9</sup> Uganda (84.3%),<sup>10</sup> and Egypt (93%).<sup>11</sup>

Multiple studies have explored various predictors of glycemic control, including age,<sup>9,10,12</sup> sex,<sup>13,14</sup> education,<sup>9,15</sup> BMI,<sup>13,16</sup> and comorbidities, but the findings remain inconsistent. These inconsistencies also extend to research on lipid profiles, where their connection to glycemic control remains far from settled. Some studies report

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significant associations between dyslipidemia and poor glycemic control, particularly involving HDL cholesterol. Haghighatpanah et al.<sup>16</sup> and Wang et al.<sup>17</sup> found that abnormal HDL levels increased the odds of poor glycemic control (1.72- and 2.17-fold, respectively). Abd-Elraouf et al.<sup>11</sup> also identified elevated LDL and total cholesterol as predictors of higher HbA1c. In contrast, Awadalla et al.<sup>18</sup> reported no significant differences in HDL, LDL, triglycerides, or total cholesterol between patients with controlled and uncontrolled glycemia.

These inconsistencies underscore that we still have unanswered questions about the role of serum HDL cholesterol in determining glycemic control among people with T2DM. Although several studies suggest HDL abnormalities may contribute to poor glycemic regulation, their findings are not uniform. Moreover, there is limited local evidence from Indonesia, a country with rapidly increasing T2DM prevalence and unique demographic, dietary, and health-system characteristics. Local data are therefore essential to determine whether HDL is an important predictor of glycemic control in Indonesian patients, particularly in the early years following diagnosis, a critical period for preventing long-term complications.<sup>19</sup>

This study aimed to measure the prevalence of poor glycemic control among T2DM cases newly diagnosed in the last 5 years and to identify its influencing factors, as measured by glycosylated hemoglobin.

## Methods

This analytical, observational, cross-sectional study was conducted on ambulatory T2DM patients at a public health center in Jakarta from May to June 2023. A total of 114 patients with T2DM were collected by consecutive non-random sampling. The inclusion criteria for prospective subjects were: patients with T2DM if meeting one of the following ADA criteria:<sup>20</sup> HbA1c  $\geq 6.5\%$  or fasting blood glucose  $\geq 126$  mg/dl (7.0 mmol/l) or 2-hour post prandial blood glucose  $\geq 200$  mg/dl (11.1 mmol/l) during the oral glucose tolerance test (OGTT), or random plasma glucose  $\geq 200$  mg/dl (11.1 mmol/l); capable of good verbal communication, and agreeing to become study subjects by giving written informed consent. The exclusion criteria were ever receiving or currently

receiving insulin therapy and hypolipidemic drugs, having cardiovascular disease, or abnormal liver or renal function.

The sample size was computed using (1) the formula for an infinite (unknown) population and (2) the formula for a finite (known) population:

$$n_0 = \frac{(Z\alpha^2) \times p \times q}{d} \dots\dots(1)$$

description:  $n_0$ : required optimal sample size,  $Z\alpha$ : 1.96,  $p$ : prevalence of poor glycemic control in diabetes mellitus =  $59.2\% = 0.592$ ,<sup>8</sup>  $q$ :  $(1-p) = 0.408$ , determined degree of confidence or accuracy of measurement = 0.05, resulting in  $n_0 = 371$ .

$$n = n_0 / (1 + (n_0/N)) \dots\dots(2)$$

The sample size was calculated using the Dobson formula for a cross-sectional study and adjusted for the finite population. Based on a 59.2% prevalence of poor glycemic control,<sup>8</sup> 95% confidence, and 5% margin of error, the initial sample size was 371. Given that the total number of persons with T2DM at the study site was 228, the finite population correction yielded a final sample size of 114.

The data collected in this study comprised the characteristics of age, sex, and level of education, followed by the determination of body mass index and drawing of venous blood for the determination of blood lipid concentrations (TC, TG, HDL cholesterol, LDL cholesterol) and of HbA1c for evaluation of the glycemic control of the respondents. Age was categorized into elderly ( $\geq 60$  years) and non-elderly ( $< 60$  years), sex into male and female, and level of education into low (no formal schooling–junior high school) and high (senior high school–tertiary education). Height and weight were determined by means of a portable microtoise and Sage portable scales in accordance with the WHO procedures.<sup>21</sup>

Subjects were asked to remove their footwear, hat, hair accessories, or any high hairdos, take off belts, and empty their pockets to remove cell phones, wallets, or coins. In measuring height, the subject was asked to stand with the feet together, heels against the wall, knees straight, and eyes on the same level as the ears. The measuring arm was gently slid down onto the head, and the subject was asked to breathe in, with the results

recorded to an accuracy of 0.1 cm. To determine body weight, the portable scale was placed on a firm, flat surface. The scale was then switched on until the 0.0 digits appeared. The subject was then asked to step onto the scale, face forward, arms at the sides, and stand still. The weight was recorded to an accuracy of 0.1 cm.

Body mass index (BMI) was calculated by dividing the weight in kg by the square of the height in meters, and was classified into non-obese (BMI < 25 kg/m<sup>2</sup>) and obese (≥ 25 kg/m<sup>2</sup>) in accordance with the WHO Asia-Pacific BMI categories.<sup>22</sup>

After an overnight fast of 10 to 12 hours, a total of 10 ml of venous blood was collected in vacutainers with and without EDTA. For HbA1c determination, EDTA-treated blood was directly examined. In contrast, for the determination of blood lipid levels (TC, TG, HDL cholesterol, and LDL cholesterol), venous blood samples without EDTA were centrifuged at 2000 RPM for 10 minutes. The obtained serum was frozen at -70°C before use for laboratory examinations, performed simultaneously on samples from all subjects and assessed by enzymatic colorimetry using the Roche Cobas c111 instrument (Germany). Blood lipids were categorized by means of the criteria of the Third Report of the Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III, or ATP III).<sup>22</sup> Total cholesterol was categorized into <200 and ≥200 mg/dl, triglycerides into <150 mg and ≥150 mg/dl, HDL cholesterol into ≥40 and <40 mg/dl, and LDL cholesterol into <100 and ≥100 mg/dl. Glycemic control was based on hemoglobin A1c (HbA1c) concentration and categorized in line with the ADA criteria into good (HbA1c < 7%) and poor (HbA1c ≥ 7%).<sup>5</sup>

Data cleaning was performed before data analysis, using consistency, range, and logical checks. We recheck the laboratory value involved by verifying the original laboratory reports, confirming unit consistency, and screening for any data-entry errors. Values represent actual biological variation and not measurement artifacts; we did not apply additional outlier-handling or transformation procedures.

We used the Kolmogorov-Smirnov test to determine the normality of the distribution of all numerical variables. Normally distributed numerical data were presented as mean ± SD,

whereas non-normally distributed numerical data were presented as median (min–max). Categorical data were presented as the number of respondents (n), percentages (%), odds ratios (OR), and 95% confidence intervals (95% CI). The relationships of socio-demographic characteristics (age, sex, educational level), BMI, and blood lipids with glycemic control were evaluated using simple logistic regression; variables with p-values ≤ 0.25 were then tested in multivariate logistic regression to identify the most influential factors on glycemic control and to control for confounding factors. A two-tailed p < 0.05 was considered statistically significant. Statistical analyses were performed using SPSS version 25.0 (IBM Corp., NY, USA). Our study received ethical clearance from the Research Ethics Commission, Faculty of Medicine, Universitas Trisakti, under number 001/KER/FK/1/2022.

## Results

The median age of respondents was 56 (35–80) years; the majority were females (72.8%), with the most frequent level of education being senior high school (33.3%). The majority of the subjects (77.2%) had malnutrition, with 1.8% undernutrition, 17.5% overweight, and 57.9% obese. Dyslipidemia was also apparent in the majority of the respondents, with high levels of cholesterol, LDL, and triglycerides. However, the majority of respondents (73.7%) had HDL concentrations ≥ 40 mg/dl. The prevalence of respondents with poor glycemic control was 78 (68.4%). Still, there was no significant difference in age, BMI, or blood lipids between those with poor and good glycemic control (Table 1).

Four variables met the requirements for a multivariable logistic regression (p < 0.25): age (p = 0.091), level of education (p = 0.210), triglyceride concentration (p = 0.035), and high-density lipoprotein concentration (p = 0.007, Table 2).

The results of multivariate analysis, after adjustment for age, level of education, and triglyceride concentration, showed that the most influential factor of glycemic control in patients with T2DM was HDL cholesterol concentration. Patients with T2DM who had an HDL concentration of < 40 mg/dl had 4.43 times higher odds of poor glycemic control compared



**Table 1 Subject Characteristics**

Variables	All Subjects	Glycemic Control		p-value
		Good (n=36)	Poor (n=78)	
Age (years) <sup>a</sup>	56 (35–80)	60 (39–79)	53.50 (35–80)	0.441 <sup>§</sup>
Body mass index (kg/m <sup>2</sup> ) <sup>b</sup>	26.29±4.57	26.8±5.03	26.04±4.36	0.395 <sup>§</sup>
Blood lipids (mg/dl)				
Total cholesterol <sup>b</sup>	209.47±44.09	201.97±33.17	212.94±48.10	0.161 <sup>§</sup>
Triglycerides <sup>a</sup>	154 (52–1593)	125.5 (61–322)	168.5 (52–1593)	0.060 <sup>§</sup>
HDL cholesterol <sup>b</sup>	45.86±9.65	47 (30–83)	43.5 (24–78)	0.064 <sup>§</sup>
LDL cholesterol <sup>a</sup>	135 (43–324)	135.36±29.5	144.41±43.37	0.259 <sup>§</sup>
Glycemic control, n (%)				
Good	36 (31.6)			
Poor	78 (68.4)			

Note: values presented as amedian (min–max), bmean±SD. Data analysis: <sup>§</sup>independent t-test, <sup>§</sup>Mann-Whitney test. Classification of categorical data: glycemic control categorized into good (HBA1c <7%) and poor (HBA1c ≥7%)<sup>§</sup>

**Table 2 Relationship of Several Risk Factors with Glycemic Control in Study Subjects**

Variables	Glycemic Control <sup>a</sup>		OR	95% CI	p-value <sup>b</sup>
	Good n=36 (%)	Poor n=78 (%)			
Age (years)					
Non-elderly	17 (25.4)	50 (74.6)	1	0.90–4.45	0.091 <sup>§</sup>
Elderly	19 (40.4)	28 (59.6)	1.99		
Sex					
Female	27 (32.5)	56 (62.5)	1	0.34–2.10	0.721
Male	9 (29.0)	22 (71.0)	0.85		
Level of education					
Low	23 (36.5)	40 (63.5)	1	0.26–1.34	0.210
High	13 (25.5)	38 (74.5)	0.59		
Body mass index (kg/m <sup>2</sup> )					
Non-obese	13 (27.1)	35 (72.9)	1	0.64–3.25	0.386
Obese	23 (34.8)	43 (65.2)	1.44		
Blood lipids (mg/dl)					
Cholesterol concentration					
<200	17 (32.7)	35 (67.3)	0.91	0.41–2.01	0.815
≥200	19 (30.6)	43 (69.4)	1		
Triglyceride concentration					
<150	22 (41.5)	31 (58.5)	0.42	0.19–0.94	0.035 <sup>§</sup>
≥150	14 (23.0)	47 (77.0)	1		
HDL concentration					
<40	3 (10.0)	27 (90.0)	5.82	1.63–20.75	0.007 <sup>§</sup>
≥40	33 (39.3)	51 (60.7)	1		
LDL concentration					
<100	3 (30.0)	7 (70.0)	1.08	0.26–4.46	0.910
≥100	33 (31.7)	71 (68.3)	1		

Note: <sup>a</sup>classification of categorical data: level of education categorized into low (no formal schooling–junior high school) and high (senior high school–tertiary education); age categorized into elderly (≥60 years) and non-elderly (<60 years); BMI categorized into obese (BMI ≥25 mg/kg<sup>2</sup>) and non-obese (BMI <25 kg/m<sup>2</sup>); glycemic control categorized into good (HBA1c <7%) and poor (HBA1c ≥7%); OR: odds ratio; CI: confidence interval; <sup>b</sup>statistical analysis with simple logistic regression test; <sup>§</sup>p-value <0.25 meets requirements for performing analysis with the multivariable logistic regression test

**Table 3 Results of Multivariable Logistic Regression Analysis**

Variables	aOR	95% CI	p-value <sup>a</sup>
Age (years)			
Non-elderly	1	0.52–3.12	0.594
Elderly	1.28		
Level of education			
Low	1	0.28–1.77	0.458
High	0.71		
Triglyceride concentration (mg/dl)			
<150	0.49	0.20–1.16	0.105
≥150	1		
Glycemic control, n (%)			
<40	4.43	1.19–16.5	0.027*
≥40	1		

Note: aOR: adjusted odds ratio, CI: confidence interval, <sup>a</sup>statistical analysis with multiple logistic regression test, \*statistical significance at p-value <0.05

to those with an HDL concentration of ≥40 mg/dl (Table 3).

## Discussion

In our study, poor glycemic control was found in around two-third of the patients or 68.4%, which is higher than in some developing countries, such as Saudi Arabia (49.1%),<sup>7</sup> and Malaysia (59.2%),<sup>8</sup> but lower than in others, such as Uganda (84.3%)<sup>10</sup> and Egypt (93%).<sup>11</sup> The cause of the different prevalences of poor glycemic control in T2DM may be controlled by various factors, such as socio-demographic characteristics, life style, lack of regular follow up,<sup>19</sup> lack of political will to encourage the communities to improve health issues, and lack of knowledge of T2DM patients about glycemic control.<sup>23</sup> The varying prevalence of glycemic control may also be caused by the different tests used to measure this variable. Moreover, the differing HbA1c cut-off points used to measure blood glucose concentration may also result in the varying prevalences of poor glycemic control. For example, some use HbA1c ≥7% as a cut-off point, while others use HbA1c >7%.<sup>24</sup>

Based on our study results, most T2DM patients were unable to achieve good glycemic control. This finding should motivate the government and related stakeholders to more actively find solutions for this problem. Knowledge of the predisposing factors of poor glycemic control can be effectively applied to control T2DM and prevent its long-term complications. In this

connection, more efforts should be made to achieve good glycemic control, which requires cooperation between T2DM patients and their health care providers. The latter should not only implement pharmacotherapeutic management but should also actively take promotive and preventive steps by instituting T2DM educational programs, T2DM screening, increasing primary health service capacity and capability, such as strengthening the role of health cadres, standardization of health services, and home visits, where these services agree with the Indonesian MoH policy, namely the transformation of primary health care.<sup>25</sup>

Our study showed that age was not a risk factor for poor glycemic control in T2DM ( $p > 0.05$ ). The survey by Tegegne et al.<sup>9</sup> showed that older age had 2.12 times the odds of poor glycemic control (aOR=2.12, 95% CI=1.27–2.97). Patrick et al.<sup>10</sup> showed that age of the patients was identified to be an independent risk factor, where middle age and old age had 4.48 and 4.28 times higher odds, respectively, for poor glycemic control than did younger age (aOR=4.48, 95%CI=1.56–14.50,  $p=0.009$  and aOR=4.28, 95%CI= 1.18–15.58,  $p=0.03$ , respectively). Different results were shown by Shamshirgaran et al.<sup>12</sup> suggesting that middle age (50–59 years) and old age groups (60 years of age and older) had 0.48 and 0.44 times lower odds, respectively, to having poor glycemic control compared to age under 50 years (aOR=0.49, 95% CI=0.28–0.86 and aOR=0.44, 95% CI=0.24–0.80, respectively). Our study

results differ from those of the studies of Tegegne et al.,<sup>9</sup> Almalki et al.,<sup>7</sup> and Patrick et al.,<sup>10</sup> who showed that older age was more vulnerable to poor glycemic control than was younger age, and the study of Shamshirgaran et al.<sup>12</sup> showing that older age had a lower risk of poor glycemic control.

The differences between our study and other studies may have been caused by differences in respondent characteristics, with the median age of 56 (35–80) years showing a lower percentage in the elderly age group (41.3%) than in the non-elderly age group (see Table 1). Lifestyle factors (dietary patterns, physical activity, etc.) may also contribute to individual variation and influence glycemic control. Additionally, the consensus is that aging is often associated with poorer glycemic control in people with diabetes due to physiological changes related to age. In contrast, with advancing age, some persons progressively lose the ability to regulate glucose levels as they did when they were younger, making it difficult for them to maintain stable blood sugar levels.<sup>26</sup> However, it has been known that the aging process is not identical between individuals and that other factors may affect glycemic control, such as having diabetes for a longer duration, having comorbidities, and poor adherence to diabetes management,<sup>9,13</sup> which are significantly associated with higher odds of poor glycemic control.

Our study found that educational level was not a risk factor for poor glycemic control in T2DM. The results of the present study agree with those of Athar et al.,<sup>15</sup> who showed that the level of education is not associated with glycemic control. However, differing results were reported by Bereda et al.,<sup>14</sup> Tegegne et al.,<sup>9</sup> and Traore et al.,<sup>27</sup> indicating that education is negatively associated with glycemic control. This may have resulted from different cutoff points for educational levels, comparing the uneducated with the educated, or comparing the educated with the ignorant. In contrast, in our study, we compared lower education (up to junior high school) with higher education (at least senior high school). The cutoff for glycemic control in our study was A1c level, whereas Bereda et al.<sup>14</sup> used fasting glucose >130 mg/dl.

People with a low level of health literacy have poorer health outcomes, such as a higher risk of complications, hospitalization, higher

treatment costs, and higher mortality risk.<sup>28,29</sup> The influence of health literacy on glycemic control was shown by the study of Butayeva et al.<sup>28</sup> Health literacy depends on several factors, such as individual competence, environmental factors, resources, and community context.<sup>30</sup> Therefore the authorities should not rely solely on routine formal education, but should also improve community health literacy. In T2DM, better health literacy is associated with better self-management of diabetes-related skills, better understanding of disease-related knowledge, better treatment adherence, and higher glycemic control.<sup>28,31</sup>

After controlling for other variables using multivariate analysis, our study showed that low HDL concentrations are risk factors for glycemic control in patients with T2DM (see Table 3). Our results agree with those of Wang et al.<sup>17</sup> and Haghighatpanah et al.,<sup>16</sup> showing that HDL concentrations were significantly associated with poor glycemic control. Abdelraouf et al.<sup>11</sup> reported that increased LDL and TC concentrations were significant predictors of increased HbA1c. Artha et al.<sup>32</sup> found that the LDL cholesterol-to-HDL cholesterol ratio is the most influential risk factor for poor glycemic control. Different results were reported by Awadalla et al.,<sup>18</sup> who found no significant differences in TG, TC, LDL, and HDL between the glycemic control group and the uncontrolled group. There are noteworthy inconsistencies between studies. The differences in the study population may lead to contradictory results. These findings reveal that glycemic control prevalence can vary even within the same country, depending on the study region. Overall, it can be hypothesized that inadequate glycemic control is associated with dyslipidemia components in T2DM. These inconsistent results may be partly due to the relative stability of HbA1c over time,<sup>17</sup> while blood lipids are dynamically changing.<sup>33</sup> In addition, studies on the relationship between HbA1c and blood lipids at different time points over a period of time may present different results.<sup>17</sup> Because of the association between glycemic control and blood lipids, it is necessary to take both variables into account to prevent T2DM-associated micro- and macrovascular complications. In T2DM, the high prevalence of metabolic dyslipidemia (elevated triglycerides) and low HDL cholesterol levels may be due to increased free fatty acid flux secondary

to insulin resistance.<sup>34</sup>

The Action for Health in Diabetes (AHEAD) study on 4,199 overweight/obese adults with T2DM but free of CVD shows that participants with metabolic dyslipidemia had a 1.30 higher risk of the composite CVD outcome and a 1.48 higher risk of coronary artery disease events.<sup>35</sup> Increasing HDL cholesterol in patients with atherogenic metabolic dyslipidemia may help reduce CVD risk associated with high T2DM prevalence, because each 1-mg/dl increase in HDL cholesterol results in a 2–3% lower CVD risk.<sup>36</sup> HDL has antidiabetic effects by inhibiting ER stress-induced beta cell apoptosis<sup>37</sup> and by improving insulin sensitivity.<sup>38</sup> In T2DM, HDL maintains blood glucose concentrations by also removing excess glucose from the circulation. HDL is also cardioprotective through the mechanism of reverse cholesterol transport, which carries cholesterol and macrophages from atherosclerotic plaques into the liver for excretion from the body<sup>39,40</sup> and protects against ischemia-induced damage, particularly in the heart, through mediation of tissue glucose for energy production.<sup>38</sup>

Increasing HDL cholesterol in patients with atherogenic metabolic dyslipidemia may help reduce CVD risk, as each 1-mg/dL increase in HDL is associated with a 2–3% lower risk of CVD.<sup>36</sup> HDL also contributes to glucose regulation and insulin sensitivity, providing metabolic benefits relevant to T2DM.<sup>37,38</sup> Its cardioprotective effects, including its role in reverse cholesterol transport, further support its role in reducing atherosclerotic burden.<sup>39,40</sup> These established functions offer biological plausibility for the associations observed in our study, and the mechanistic details have been condensed to maintain focus on the study's findings.

Apart from the inconsistencies in blood lipid parameters related to risk factors for poor glycemic control in T2DM patients, the American College of Cardiology/American Heart Association has classified T2DM patients with a higher atherosclerotic CVD risk and has suggested lower intakes of low-density lipoprotein cholesterol.<sup>41</sup> The known controllable cardiovascular risk factors in T2DM include the high prevalence of poor glycemic control, the prominence of high LDL-low HDL dyslipidemia, and the presence of obesity in most respondents. Strategies are needed not

only for glycemic control by administration of anti-glycemic and hypolipidemic medications, but also for improving weight management, including support for lifestyle modification, with adjunctive pharmacotherapy to reduce the risk of cardiovascular disease.

The program of the Indonesian MoH, in the form of the integrated development post (*pos binaan terpadu*), remains the MoH's strategy as a community-based health initiative and actively provides education and early and curative detection of non-communicable diseases, as exemplified by T2DM blood glucose testing.<sup>42</sup> Therefore, as a rule, the individuals in question compensate for their poor general education by more focused attendance at clinical education sessions on their illness. Attention is needed when formulating future policies related to health literacy among respondents with a higher level of education. Healthcare professionals can encourage T2DM patients to learn about and acquire knowledge related to diabetes. Interventions such as using social media to access and share reliable sources of diabetes knowledge could be instituted to raise patient health literacy, thereby improving their glycemic control.<sup>43</sup>

Our study has some limitation. This study did not account for potential confounders, such as dietary intake, physical activity, comorbidities, and medication adherence, which may introduce statistical bias. Serum glucose and lipid metabolism are affected by lifestyle, such as consumption of high-fat and processed foods, which was proven to increase the risk of poor glucose tolerance among overweight or obese adults.<sup>44</sup> There were also instrument-related methodological limitations, because HbA1c level can be measured by several methods, including cation-exchange chromatography, electrophoresis, immunoassays, and affinity chromatography, each with its own limitations. In addition, the HbA1c content of blood samples depends on erythrocyte lifespan and globin chain properties, not exclusively on blood glucose levels.<sup>45</sup>

Other limitation of our study, as it is well known, the cross-sectional study design does not allow causal inference, so a prospective study is required. The width of the 95% CI for the TG value in our study. It is hoped that future studies will use this study's data as a basis for increasing the number of study samples. We used

consecutive sampling in this study because it was the most practical way to recruit all eligible participants during the study period and to ensure that no cases were intentionally skipped. However, as a non-probability sampling method, consecutive sampling may introduce selection bias, as the sample depends on who presents during the recruitment period. We acknowledge this limitation and have applied consistent eligibility criteria across the entire study period to help reduce potential bias. In this study, oral antihyperglycemic use was recorded, but the small number of users precluded meaningful analysis; therefore, these medications were not included in the main results. Subsequent studies can look into the cause of this phenomenon. Further studies that account for the above-mentioned confounding factors should be conducted to reduce bias. The other factors that should be considered in future studies are low adherence to diabetes management, low family support for diabetes mellitus management, presence of abdominal obesity, and presence of a history of hospitalization, which might be associated with prolonged poor control of T2DM.<sup>27</sup>

## Conclusions

HDL concentrations are potential markers for predicting glycemic control in patients with T2DM. Routine HDL examinations and maintenance of HDL at high concentrations may minimize the risk of complications in T2DM subjects through adjunctive pharmacotherapy, particularly in the population of the present study.

## Conflict of Interest

The authors have no conflicts of interest to declare.

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# Serum High-Density Lipoprotein-Cholesterol Concentration as Determinant of Poor Glycemic Control in Type 2 Diabetes Mellitus Patients at a Public Health Center in Jakarta, Indonesia

*By Yenny Yenny*

## RESEARCH ARTICLE

## Serum High-Density Lipoprotein-Cholesterol Concentration as Determinant of Poor Glycemic Control in Type 2 Diabetes Mellitus Patients at a Public Health Center in Jakarta, Indonesia

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### Abstract

The risk factors for glycemic control in type 2 diabetes mellitus (T2DM) are poorly understood. This study assessed the prevalence of poor glycemic control and the predictive factors of poor glycemic control among T2DM outpatients in the community. This 30-day community-based cross-sectional study was conducted among ambulatory T2DM patients in Jakarta from May to June 2023. Data on age, sex, and level of education were collected by questionnaire, whereas data on body mass index, lipid profile, and HbA1c were obtained by measurement. Glycemic control was good if HbA1c <7% and poor if HbA1c ≥7%. The relationships between age, sex, level of education, body mass index, lipid profile, and glycemic control were determined using simple logistic regression. Multivariable logistic regression was used to determine the most influential risk factors of glycemic control. Poor glycemic control was found in 68.4% respondents, and obesity in 57.9% of respondents. After adjustment for age, level of education, and triglyceride concentration, the most influential factor for glycemic control was HDL concentration (aOR=4.43, 95% CI=1.19–16.5, p=0.027). Patients with T2DM with HDL <40 mg/dl had a 4.63 times significantly higher odds of poor glycemic control than those with HDL ≥40 mg/dl. This study found a high prevalence of poor glycemic control in the community setting among individuals with T2DM, with HDL concentration as the most significant predictor. Meanwhile, a triglyceride concentration of ≥150 mg/dl independently provided 58% greater protection against glycemic control (p=0.035), but the effect was not significant after adjustment (p>0.05). The high prevalence of poor glycemic control, dyslipidemia, and obesity in T2DM patients requires routine screening and monitoring accompanied by health education on lifestyle modification for risk factor control, thus minimizing the risk of complications.

**Keywords:** Indonesia; risk factors; serum high-density lipoprotein-cholesterol; type 2 diabetes; urban population

### Introduction

Type 2 diabetes mellitus (T2DM) continues to rise globally, with a prevalence of 6,138.6 per 100,000 population in 2021 and a projected 59.7% increase by 2050.<sup>1</sup> Indonesia faces a similar trend, ranking fifth worldwide with 19.5 million T2DM cases in 2021, expected to reach 28.6 million by 2045.<sup>2,3</sup> Poor glycemic control contributes substantially to cardiovascular complications in T2DM, as endothelial dysfunction and coronary artery disease are exacerbated by elevated glycated hemoglobin (HbA1c).<sup>4</sup> The American Diabetes Association (ADA) recommends maintaining

HbA1c levels below 7% to reduce cardiovascular risk, with each 1% increase associated with a 13% rise in risk.<sup>5,6</sup> Despite its importance, the prevalence of poor glycemic control remains high across many settings, including Saudi Arabia (49.1%),<sup>7</sup> Malaysia (59.2%),<sup>8</sup> Ethiopia (61.1%),<sup>9</sup> Uganda (84.3%),<sup>10</sup> and Egypt (93%).<sup>11</sup>

Multiple studies have explored various predictors of glycemic control, including age,<sup>9,10,12</sup> sex,<sup>13,14</sup> education,<sup>9,15</sup> BMI,<sup>13,16</sup> and comorbidities, but the findings remain inconsistent. These inconsistencies also extend to research on lipid profiles, where their connection to glycemic control remains far from settled. Some studies report

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significant associations between dyslipidemia and poor glycemic control, particularly involving HDL cholesterol. Haghighatpanah et al.<sup>16</sup> and Wang et al.<sup>17</sup> found that abnormal HDL levels increased the odds of poor glycemic control (1.72- and 2.17-fold, respectively). Abd-Elraouf et al.<sup>14</sup> also identified elevated LDL and total cholesterol as predictors of higher HbA1c. In contrast, Awadalla et al.<sup>18</sup> reported no significant differences in HDL, LDL, triglycerides, or total cholesterol between patients with controlled and uncontrolled glycemia.

These inconsistencies underscore that we still have unanswered questions about the role of serum HDL cholesterol in determining glycemic control among people with T2DM. Although several studies suggest HDL abnormalities may contribute to poor glycemic regulation, their findings are not uniform. Moreover, there is limited local evidence from Indonesia, a country with rapidly increasing T2DM prevalence and unique demographic, dietary, and health-system characteristics. Local data are therefore essential to determine whether HDL is an important predictor of glycemic control in Indonesian patients, particularly in the early years following diagnosis, a critical period for preventing long-term complications.<sup>19</sup>

This study aimed to measure the prevalence of poor glycemic control among T2DM cases newly diagnosed in the last 5 years and to identify its influencing factors, as measured by glycosylated hemoglobin.

## Methods

This analytical, observational, cross-sectional study was conducted on ambulatory T2DM patients at a public health center in Jakarta from May to June 2023. A total of 114 patients with T2DM were collected by consecutive non-random sampling. The inclusion criteria for prospective subjects were: patients with T2DM if meeting one of the following ADA criteria:<sup>20</sup> HbA1c  $\geq 6.5\%$  or fasting blood glucose  $\geq 126$  mg/dl (7.0 mmol/l) or 2-hour post prandial blood glucose  $\geq 200$  mg/dl (11.1 mmol/l) during the oral glucose tolerance test (OGTT), or random plasma glucose  $\geq 200$  mg/dl (11.1 mmol/l); capable of good verbal communication, and agreeing to become study subjects by giving written informed consent. The exclusion criteria were ever receiving or currently

receiving insulin therapy and hypolipidemic drugs, having cardiovascular disease, or abnormal liver renal function.

The sample size was computed using (1) the formula for an infinite (unknown) population and (2) the formula for a finite (known) population:

$$n_0 = \frac{(Z\alpha^2) \times p \times q}{d} \dots\dots(1)$$

description:  $n_0$ : required optimal sample size,  $Z\alpha$ : 1.96,  $p$ : prevalence of poor glycemic control in diabetes mellitus =  $59.2\% = 0.592$ ,<sup>8</sup>  $q$ :  $(1-p) = 0.408$ , determined degree of confidence or accuracy of measurement = 0.05, resulting in  $n_0 = 371$ .

$$n = n_0 / (1 + (n_0/N)) \dots\dots(2)$$

The sample size was calculated using the Dobson formula for a cross-sectional study and adjusted for the finite population. Based on a 59.2% prevalence of poor glycemic control,<sup>8</sup> 95% confidence, and 5% margin of error, the initial sample size was 371. Given that the total number of persons with T2DM at the study site was 228, the finite population correction yielded a final sample size of 114.

The data collected in this study comprised the characteristics of age, sex, and level of education, followed by the determination of body mass index and drawing of venous blood for the determination of blood lipid concentrations (TC, TG, HDL cholesterol, LDL cholesterol) and of HbA1c for evaluation of the glycemic control of the respondents. Age was categorized into elderly ( $\geq 60$  years) and non-elderly ( $< 60$  years), sex into male and female, and level of education into low (no formal schooling–junior high school) and high (senior high school–tertiary education). Height and weight were determined by means of a portable microtoise and Sage portable scales in accordance with the WHO procedures.<sup>21</sup>

Subjects were asked to remove their footwear, hat, hair accessories, or any high hairdos, take off belts, and empty their pockets to remove cell phones, wallets, or coins. In measuring height, the subject was asked to stand with the feet together, heels against the wall, knees straight, and eyes on the same level as the ears. The measuring arm was gently slid down onto the head, and the subject was asked to breathe in, with the results



recorded to an accuracy of 0.1 cm. To determine body weight, the portable scale was placed on a firm, flat surface. The scale was then switched on until the 0.0 digits appeared. The subject was then asked to step onto the scale, face forward, arms at the sides, and stand still. The weight was recorded to an accuracy of 0.1 cm.

Body mass index (BMI) was calculated by dividing the weight in kg by the square of the height in meters, and was classified into non-obese ( $\text{BMI} < 25 \text{ kg/m}^2$ ) and obese ( $\geq 25 \text{ kg/m}^2$ ) in accordance with the WHO Asia-Pacific BMI categories.<sup>22</sup>

After an overnight fast of 10 to 12 hours, a total of 10 ml of venous blood was collected in vacutainers with and without EDTA. For HbA1c determination, EDTA-treated blood was directly examined. In contrast, for the determination of blood lipid levels (TC, TG, HDL cholesterol, and LDL cholesterol), venous blood samples without EDTA were centrifuged at 2000 RPM for 10 minutes. The obtained serum was frozen at  $-70^\circ\text{C}$  before use for laboratory examinations, performed simultaneously on samples from all subjects and assessed by enzymatic colorimetry using the Roche Cobas c111 instrument (Germany). Blood lipids were categorized by means of the criteria of the Third Report of the Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III, or ATP III).<sup>22</sup> Total cholesterol was categorized into  $< 200$  and  $\geq 240$  mg/dl, triglycerides into  $< 150$  mg and  $\geq 150$  mg/dl, HDL cholesterol into  $\geq 40$  and  $< 40$  mg/dl, and LDL cholesterol into  $< 100$  and  $\geq 100$  mg/dl. Glycemic control was based on hemoglobin A1c (HbA1c) concentration and categorized in line with the ADA criteria into good (HbA1c  $< 7\%$ ) and poor (HbA1c  $\geq 7\%$ ).<sup>5</sup>

Data cleaning was performed before data analysis, using consistency, range, and logical checks. We recheck the laboratory value involved by verifying the original laboratory reports, confirming unit consistency, and screening for any data-entry errors. Values represent actual biological variation and not measurement artifacts; we did not apply additional outlier-handling or transformation procedures.

We used the Kolmogorov-Smirnov test to determine the normality of the distribution of all numerical variables. Normally distributed numerical data were presented as mean  $\pm$  SD,

whereas non-normally distributed numerical data were presented as median (min–max). Categorical data were presented as the number of respondents (n), percentages (%), odds ratios (OR), and 95% confidence intervals (95% CI). The relationships of socio-demographic characteristics (age, sex, educational level), BMI, and blood lipids with glycemic control were evaluated using simple logistic regression; variables with p-values  $\leq 0.25$  were then tested in multivariate logistic regression to identify the most influential factors on glycemic control and to control for confounding factors. A two-tailed  $p < 0.05$  was considered statistically significant. Statistical analyses were performed using SPSS version 25.0 (IBM Corp., NJ, USA). Our study received ethical clearance from the Research Ethics Commission, Faculty of Medicine, Universitas Trisakti, under number 001/KER/FK/1/2022.

## Results

The median age of respondents was 56 (35–80) years; the majority were females (72.8%), with the most frequent level of education being senior high school (33.3%). The majority of the subjects (77.2%) had malnutrition, with 1.8% undernutrition, 17.5% overweight, and 39.9% obese. Dyslipidemia was also apparent in the majority of the respondents, with high levels of cholesterol, LDL, and triglycerides. However, the majority of respondents (73.7%) had HDL concentrations  $\geq 40$  mg/dl. The prevalence of respondents with poor glycemic control was 78 (68.4%). Still, there was no significant difference in age, BMI, or blood lipids between those with poor and good glycemic control (Table 1).

Four variables met the requirements for a multivariable logistic regression ( $p < 0.25$ ): age ( $p = 0.091$ ), level of education ( $p = 0.210$ ), triglyceride concentration ( $p = 0.035$ ), and high-density lipoprotein concentration ( $p = 0.007$ , Table 2).

The results of multivariate analysis, after adjustment for age, level of education, and triglyceride concentration, showed that the most influential factor of glycemic control in patients with T2DM was HDL cholesterol concentration. Patients with T2DM who had an HDL concentration of  $< 40$  mg/dl had 4.43 times higher odds of poor glycemic control compared

**Table 1 Subject Characteristics**

Variables	All Subjects	Glycemic Control		p-value
		Good (n=36)	Poor (n=78)	
Age (years) <sup>a</sup>	56 (35–80)	60 (39–79)	53.50 (35–80)	0.441 <sup>s</sup>
Body mass index (kg/m <sup>2</sup> ) <sup>b</sup>	26.29±4.57	26.8±5.03	26.04±4.36	0.395 <sup>s</sup>
Blood lipids (mg/dl)				
Total cholesterol <sup>b</sup>	209.47±44.09	201.97±33.17	212.94±48.10	0.161 <sup>s</sup>
Triglycerides <sup>a</sup>	154 (52–1593)	125.5 (61–322)	168.5 (52–1593)	0.060 <sup>s</sup>
HDL cholesterol <sup>b</sup>	45.86±9.65	47 (30–83)	43.5 (24–78)	0.064 <sup>s</sup>
LDL cholesterol <sup>a</sup>	135 (43–324)	135.36±29.5	144.41±43.37	0.259 <sup>s</sup>
Glycemic control, n (%)				
Good	36 (31.6)			
Poor	78 (68.4)			

Note: values presented as a median (min–max), b mean±SD. Data analysis: <sup>a</sup>independent t-test, <sup>s</sup>Mann-Whitney test. Classification of categorical data: glycemic control categorized into good (HbA1c <7%) and poor (HbA1c ≥7%)<sup>5</sup>

**Table 2 Relationship of Several Risk Factors with Glycemic Control in Study Subjects**

Variables	Glycemic Control <sup>a</sup>		OR	95% CI	p-value <sup>b</sup>
	Good n=36 (%)	Poor n=78 (%)			
Age (years)					
Non-elderly	17 (25.4)	50 (74.6)	1	0.90–4.45	0.091 <sup>s</sup>
Elderly	19 (40.4)	28 (59.6)	1.99		
Sex					
Female	27 (32.5)	56 (62.5)	1	0.34–2.10	0.721
Male	9 (29.0)	22 (71.0)	0.85		
Level of education					
Low	23 (36.5)	40 (63.5)	1	0.26–1.34	0.210
High	13 (25.5)	38 (74.5)	0.59		
Body mass index (kg/m <sup>2</sup> )					
Non-obese	13 (27.1)	35 (72.9)	1	0.64–3.25	0.386
Obese	23 (34.8)	43 (65.2)	1.44		
Blood lipids (mg/dl)					
Cholesterol concentration					
<200	17 (32.7)	35 (67.3)	0.91	0.41–2.01	0.815
≥200	19 (30.6)	43 (69.4)	1		
Triglyceride concentration					
<150	22 (41.5)	31 (58.5)	0.42	0.19–0.94	0.035 <sup>s</sup>
≥150	14 (23.0)	47 (77.0)	1		
HDL concentration					
<40	3 (10.0)	27 (90.0)	5.82	1.63–20.75	0.007 <sup>s</sup>
≥40	33 (39.3)	51 (60.7)	1		
LDL concentration					
<100	3 (30.0)	7 (70.0)	1.08	0.26–4.46	0.910
≥100	33 (31.7)	71 (68.3)	1		

Note: <sup>a</sup>classification of categorical data: level of education categorized into low (no formal schooling–junior high school) and high (senior high school–tertiary education); age categorized into elderly (≥60 years) and non-elderly (<60 years); BMI categorized into obese (BMI ≥25 mg/kg<sup>2</sup>) and non-obese (BMI <25 kg/m<sup>2</sup>); glycemic control categorized into good (HbA1c <7%) and poor (HbA1c ≥7%); OR: odds ratio; CI: confidence interval; <sup>b</sup>statistical analysis with simple logistic regression test; <sup>s</sup>p-value <0.25 meets requirements for performing analysis with the multivariable logistic regression test

**Table 3 Results of Multivariable Logistic Regression Analysis**

Variables	aOR	95% CI	p-value <sup>a</sup>
Age (years)			
Non-elderly	1	0.52–3.12	0.594
Elderly	1.28		
Level of education			
Low	1	0.28–1.77	0.458
High	0.71		
Triglyceride concentration (mg/dl)			
<150	0.49	0.20–1.16	0.105
≥150	1		
Glycemic control, n (%)			
<40	4.43	1.19–16.5	0.027*
≥40	1		

Note: aOR: adjusted odds ratio, CI: confidence interval, \*statistical analysis with multiple logistic regression test, \*statistical significance at p-value <0.05

to those with an HDL concentration of ≥40 mg/dl (Table 3).

## Discussion

In our study, poor glycemic control was found in around two-third of the patients or 68.4%, which is higher than in some developing countries, such as Saudi Arabia (49.1%),<sup>7</sup> and Malaysia (59.2%),<sup>8</sup> but lower than in others, such as Uganda (84.3%)<sup>10</sup> and Egypt (93%).<sup>11</sup> The cause of the different prevalences of poor glycemic control in T2DM may be controlled by various factors, such as socio-demographic characteristics, life style, lack of regular follow up,<sup>19</sup> lack of political will to encourage the communities to improve health issues, and lack of knowledge of T2DM patients about glycemic control.<sup>23</sup> The varying prevalence of glycemic control may also be caused by the different tests used to measure this variable. Moreover, the differing HbA1c cut-off points used to measure blood glucose concentration may also result in the varying prevalences of poor glycemic control. For example, some use HbA1c ≥7% as a cut-off point, while others use HbA1c >7%.<sup>24</sup>

Based on our study results, most T2DM patients were unable to achieve good glycemic control. This finding should motivate the government and related stakeholders to more actively find solutions for this problem. Knowledge of the predisposing factors of poor glycemic control can be effectively applied to control T2DM and prevent its long-term complications. In this

connection, more efforts should be made to achieve good glycemic control, which requires cooperation between T2DM patients and their health care providers. The latter should not only implement pharmacotherapeutic management but should also actively take promotive and preventive steps by instituting T2DM educational programs, T2DM screening, increasing primary health service capacity and capability, such as strengthening the role of health cadres, standardization of health services, and home visits, where these services agree with the Indonesian MoH policy, namely the transformation of primary health care.<sup>25</sup>

Our study showed that age was not a risk factor for poor glycemic control in T2DM ( $p > 0.05$ ). The survey by Tegegne et al.<sup>9</sup> showed that older age had 2.12 times the odds of poor glycemic control (aOR=2.12, 95% CI=1.27–2.97). Patrick et al.<sup>10</sup> showed that age of the patients was identified to be an independent risk factor, where middle age and old age had 4.48 and 4.28 times higher odds, respectively, for poor glycemic control than younger age (aOR=4.48, 95%CI=1.56–14.50,  $p=0.009$  and aOR=4.28, 95%CI= 1.18–15.58,  $p=0.03$ , respectively). Different results were shown by Shamshirgaran et al.<sup>12</sup> suggesting that middle age (50–59 years) and old age groups (60 years of age and older) had 0.48 and 0.44 times lower odds, respectively, to having poor glycemic control compared to age under 50 years (aOR=0.49, 95% CI=0.28–0.86 and aOR=0.44, 95% CI=0.24–0.80, respectively). Our study



results differ from those of the studies of Tegegne et al.,<sup>9</sup> Almalki et al.,<sup>7</sup> and Patrick et al.,<sup>10</sup> who showed that older age was more vulnerable to poor glycemic control than was younger age, and the study of Shamshirgaran et al.<sup>12</sup> showing that older age had a lower risk of poor glycemic control.

The differences between our study and other studies may have been caused by differences in respondent characteristics, with the median age 37.56 (35–80) years showing a lower percentage in the elderly age group (41.3%) than in the non-elderly age group (see Table 1). Lifestyle factors (dietary patterns, physical activity, etc.) may also contribute to individual variation and influence glycemic control. Additionally, the consensus is that aging is often associated with poorer glycemic control in people with diabetes due to physiological changes related to age. In contrast, with advancing age, some persons progressively lose the ability to regulate glucose levels as they did when they were younger, making it difficult for them to maintain stable blood sugar levels.<sup>26</sup> However, it has been known that the aging process is not identical between individuals and that other factors may affect glycemic control, such as having diabetes for a longer duration, having comorbidities, and poor adherence to diabetes management,<sup>9,13</sup> which are significantly associated with higher odds of poor glycemic control.

Our study found that educational level was not a risk factor for poor glycemic control in T2DM. The results of the present study agree with those of Athar et al.,<sup>15</sup> who showed that the level of education is not associated with glycemic control. However, differing results were reported by Bereda et al.,<sup>14</sup> Tegegne et al.,<sup>9</sup> and Traore et al.,<sup>27</sup> indicating that education is negatively associated with glycemic control. This may have resulted from different cutoff points for educational levels, comparing the uneducated with the educated, or comparing the educated with the ignorant. In contrast, in our study, we compared lower education (up to junior high school) with higher education (at least senior high school). The cutoff for glycemic control in our study was A1c level, whereas Bereda et al.<sup>14</sup> used fasting glucose >130 mg/dl.

People with a low level of health literacy have poorer health outcomes, such as a higher risk of complications, hospitalization, higher

treatment costs, and higher mortality risk.<sup>28,29</sup> The influence of health literacy on glycemic control was shown in the study of Butayeva et al.<sup>28</sup> Health literacy depends on several factors, such as individual competence, environmental factors, resources, and community context.<sup>30</sup> Therefore the authorities should not rely solely on routine formal education, but should also improve community health literacy. In T2DM, better health literacy is associated with better self-management of diabetes-related skills, better understanding of disease-related knowledge, better treatment adherence, and higher glycemic control.<sup>28,31</sup>

After controlling for other variables using multivariate analysis, our study showed that low HDL concentrations are risk factors for glycemic control in patients with T2DM (see Table 3). Our results agree with those of Wang et al.<sup>17</sup> and Haghighatpanah et al.,<sup>16</sup> showing that HDL concentrations were significantly associated with poor glycemic control. Abdelraouf et al.<sup>11</sup> reported that increased LDL and TC concentrations were significant predictors of increased HbA1c. Artha et al.<sup>32</sup> found that the LDL cholesterol-to-HDL cholesterol ratio is the most influential risk factor for poor glycemic control. Different results were reported by Awadalla et al.,<sup>18</sup> who found no significant differences in TG, TC, LDL, and HDL between the glycemic control group and the uncontrolled group. There are noteworthy inconsistencies between studies. The differences in the study population may lead to contradictory results. These findings reveal that glycemic control prevalence can vary even within the same country, depending on the study region. Overall, it can be hypothesized that inadequate glycemic control is associated with dyslipidemia components in T2DM. These inconsistent results may be partly due to the relative stability of HbA1c over time,<sup>17</sup> while blood lipids are dynamically changing.<sup>33</sup> In addition, studies on the relationship between HbA1c and blood lipids at different time points over a period of time may present different results.<sup>17</sup> Because of the association between glycemic control and blood lipids, it is necessary to take both variables into account to prevent T2DM-associated micro- and macrovascular complications. In T2DM, the high prevalence of metabolic dyslipidemia (elevated triglycerides) and low HDL cholesterol levels may be due to increased free fatty acid flux secondary

to insulin resistance.<sup>34</sup>

The Action for Health in Diabetes (AHEAD) study on 4,199 overweight/obese adults with T2DM but free of CVD shows that participants with metabolic dyslipidemia had a 1.30 higher risk of the composite CVD outcome and a 1.48 higher risk of coronary artery disease events.<sup>35</sup> Increasing HDL cholesterol in patients with atherogenic metabolic dyslipidemia may help reduce CVD risk associated with high T2DM prevalence, because each 1-mg/dL increase in HDL cholesterol results in a 2–3% lower CVD risk.<sup>36</sup> HDL has antidiabetic effects by inhibiting ER stress-induced beta cell apoptosis<sup>37</sup> and by improving insulin sensitivity.<sup>38</sup> In T2DM, HDL maintains blood glucose concentrations by also removing excess glucose from the circulation. HDL is also cardioprotective through the mechanism of reverse cholesterol transport, which carries cholesterol and macrophages from atherosclerotic plaques into the liver for excretion from the body<sup>39,40</sup> and protects against ischemia-induced damage, particularly in the heart, through mediation of tissue glucose for energy production.<sup>38</sup>

Increasing HDL cholesterol in patients with atherogenic metabolic dyslipidemia may help reduce CVD risk, as each 1-mg/dL increase in HDL is associated with a 2–3% lower risk of CVD.<sup>36</sup> HDL also contributes to glucose regulation and insulin sensitivity, providing metabolic benefits relevant to T2DM.<sup>37,38</sup> Its cardioprotective effects, including its role in reverse cholesterol transport, further support its role in reducing atherosclerotic burden.<sup>39,40</sup> These established functions offer biological plausibility for the associations observed in our study, and the mechanistic details have been condensed to maintain focus on the study's findings.

Apart from the inconsistencies in blood lipid parameters related to risk factors for poor glycemic control in T2DM patients, the American College of Cardiology/American Heart Association has classified T2DM patients with a higher atherosclerotic CVD risk and has suggested lower intakes of low-density lipoprotein cholesterol.<sup>41</sup> The known controllable cardiovascular risk factors in T2DM include the high prevalence of poor glycemic control, the prominence of high LDL-low HDL dyslipidemia, and the presence of obesity in most respondents. Strategies are needed not

only for glycemic control by administration of anti-glycemic and hypolipidemic medications, but also for improving weight management, including support for lifestyle modification, with adjunctive pharmacotherapy to reduce the risk of cardiovascular disease.

The program of the Indonesian MoH, in the form of the integrated development post (pos binaan terpadu), remains the MoH's strategy as a community-based health initiative and actively provides education and early and curative detection of non-communicable diseases, as exemplified by T2DM blood glucose testing.<sup>42</sup> Therefore, as a rule, the individuals in question compensate for their poor general education by more focused attendance at clinical education sessions on their illness. Attention is needed when formulating future policies related to health literacy among respondents with a higher level of education. Healthcare professionals can encourage T2DM patients to learn about and acquire knowledge related to diabetes. Interventions such as using social media to access and share reliable sources of diabetes knowledge could be instituted to raise patient health literacy, thereby improving their glycemic control.<sup>43</sup>

Our study has some limitation. This study did not account for potential confounders, such as dietary intake, physical activity, comorbidities, and medication adherence, which may introduce statistical bias. Serum glucose and lipid metabolism are affected by lifestyle, such as consumption of high-fat and processed foods, which was proven to increase the risk of poor glucose tolerance among overweight or obese adults.<sup>44</sup> There were also instrument-related methodological limitations, because HbA1c level can be measured by several methods, including cation-exchange chromatography, electrophoresis, immunoassays, and affinity chromatography, each with its own limitations. In addition, the HbA1c content of blood samples depends on erythrocyte lifespan and globin chain properties, not exclusively on blood glucose levels.<sup>45</sup>

Other limitation of our study, as it is well known, the cross-sectional study design does not allow causal inference, so a prospective study is required. The width of the 95% CI for the TG value in our study. It is hoped that future studies will use this study's data as a basis for increasing the number of study samples. We used



consecutive sampling in this study because it was the most practical way to recruit all eligible participants during the study period and to ensure that no cases were intentionally skipped. However, as a non-probability sampling method, consecutive sampling may introduce selection bias, as the sample depends on who presents during the recruitment period. We acknowledge this limitation and have applied consistent eligibility criteria across the entire study period to help reduce potential bias. In this study, oral antihyperglycemic use was recorded, but the small number of users precluded meaningful analysis; therefore, these medications were not included in the main results. Subsequent studies can look into the cause of this phenomenon. Further studies that account for the above-mentioned confounding factors should be conducted to reduce bias. The other factors that should be considered in future studies are low adherence to diabetes management, low family support for diabetes mellitus management, presence of abdominal obesity, and presence of a history of hospitalization, which might be associated with prolonged poor control of T2DM.<sup>27</sup>

## Conclusions

HDL concentrations are potential markers for predicting glycemic control in patients with T2DM. Routine HDL examinations and maintenance of HDL at high concentrations may minimize the risk of complications in T2DM subjects through adjunctive pharmacotherapy, particularly in the population of the present study.

## Conflict of Interest

The authors have no conflicts of interest to declare.

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# Serum High-Density Lipoprotein-Cholesterol Concentration as Determinant of Poor Glycemic Control in Type 2 Diabetes Mellitus Patients at a Public Health Center in Jakarta, Indonesia

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