

Correlation of HbA1c, Non-HDL Cholesterol, and Remnant Cholesterol in Type 2 Diabetes Mellitus Patients on Statin Therapy

Khoirun Mukhsinin Putra^{1*}, Yulianto Kusnadi¹, Ratna Maila Dewi¹, Alwi Shahab¹

¹Division of Endocrinology, Metabolism and Diabetes, Internal Medicine Department, Faculty of Medicine, Universitas Sriwijaya/ Dr. Mohammad Hoesin General Hospital, Palembang, Indonesia

*E-mail: mukhsinin@unsri.ac.id

Abstract

Type 2 diabetes mellitus (T2DM) is commonly associated with the characteristic lipid derangements of atherogenic dyslipidaemia and a significantly increased risk of cardiovascular disease. Remnant cholesterol (RC) and non-high-density lipoprotein (non-HDL) cholesterol are established markers of the overall burden of circulating atherogenic lipoproteins. However, the correlation between these lipid markers and glycemic control remains unclear. This study aimed to determine the correlation between RC and non-HDL cholesterol and to evaluate the correlation of each marker with glycemic control in patients with T2DM. This cross-sectional study employed the anonymized secondary clinical data obtained from the medical records of patients who visited the Integrated Diabetes Clinic of Dr Mohammad Hoesin General Hospital, Palembang, Indonesia, during November-December 2025. All participants were on statin therapy at the time of data collection. RC was calculated as total cholesterol minus LDL cholesterol minus HDL cholesterol. Non-HDL cholesterol was calculated as total cholesterol minus HDL cholesterol. The variables were not normally distributed; hence, Spearman's rank correlation test was performed. A total of 100 eligible participants were included in the analysis. RC was positively correlated with non-HDL cholesterol ($r = 0.618$; $p < 0.001$). No statistically significant correlation was found between HbA1c and non-HDL cholesterol ($r = -0.180$; $p = 0.074$). In this population, RC was positively correlated with non-HDL cholesterol but not with HbA1c. These findings should be interpreted in the context of universal statin use and the inherent mathematical relationship between the calculated lipid variables.

Keywords: Remnant Cholesterol, Non-HDL Cholesterol, HbA1c, Type 2 Diabetes Mellitus, Atherogenic Dyslipidemia

1. Introduction

The worldwide incidence of type 2 diabetes mellitus (T2DM) is rapidly increasing and is now considered a major public health problem due to its increasing incidence and its significant effect on morbidity and mortality. According to the latest IDF Diabetes Atlas (2025), the prevalence of diabetes is continuously increasing in almost all regions, including South-East Asia. Indonesia is one of the countries with the highest number of people suffering from diabetes, which causes a considerable problem to the health care system of the country. Cardiovascular disease remains the leading cause of death in type 2 diabetes mellitus patients.¹⁻⁵

Atherogenic dyslipidemia is a lipid profile characterized by increased triglyceride-rich lipoproteins, decreased HDL cholesterol levels, and increased small-dense LDL particles. The pathophysiology of T2DM is

strongly associated with insulin resistance, which is the main cause of lipid problems. Previous studies in Indonesia have reported that approximately 60% of patients with T2DM have dyslipidemia. In a population-based study in Bali, more than 85% of people with diabetes had high non-HDL cholesterol. Together, these data highlight the important role of lipid abnormalities in the cardiovascular risk associated with T2DM.⁶⁻⁸

Remnant cholesterol (RC) is the cholesterol present in the remnants of triglyceride-rich lipoproteins, principally very low-density lipoprotein (VLDL) and intermediate-density lipoprotein (IDL) particles. Remnants of lipoproteins are highly atherogenic because they infiltrate the arterial wall and cause vascular inflammation and promote development of atherosclerotic plaques. Varbo et al demonstrated a causal association between increased RC levels and

the onset of ischemic heart disease.³ RC has been linked to insulin resistance and postprandial lipid metabolism abnormalities, indicating its pathophysiological role in T2DM.^{6,9–11}

Non-HDL cholesterol is a measure of all atherogenic lipoproteins circulating in the blood, including LDL, VLDL, IDL, lipoprotein(a) and remnant lipoproteins. It is calculated as total cholesterol minus HDL cholesterol and is a better measure of total atherogenic lipid burden than LDL cholesterol alone, especially in patients with hypertriglyceridemia or insulin resistance. Non-HDL cholesterol has been identified as an important secondary therapeutic target in dyslipidaemia management in current worldwide guidelines.^{12–14} In routine clinical practice, RC is usually calculated by subtracting the LDL and HDL cholesterol values from the total cholesterol.¹⁵ Consequently, RC should be regarded as a constituent of non-HDL cholesterol rather than an entirely independent lipid marker, and any observed relationship between these variables should be interpreted with consideration of their shared calculation.¹⁵

Although RC and non-HDL cholesterol are inherently linked from both biological and mathematical perspectives, evidence describing their relationship among statin-treated individuals with T2DM remains limited, particularly in Indonesia. In routine clinical practice, metabolic assessment predominantly depends on glycemic indices, particularly HbA1c, despite growing evidence that disruptions in glucose and lipid metabolism do not necessarily advance simultaneously. This study attempted to ascertain the correlation between RC and non-HDL cholesterol and to examine whether either parameter was linked to glycemic control in patients with T2DM.

2. Method

This cross-sectional observational analytic study used secondary data from medical records of adult patients with T2DM at the Integrated Diabetes Clinic of Dr. Mohammad Hoesin General Hospital, Palembang, Indonesia, during November and December 2025. The study was conducted in accordance with the recommendations from the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) (Figure 1).

Eligible participants were patients with a diagnosis of T2DM and complete records of fasting total cholesterol, HDL cholesterol, LDL cholesterol, HbA1c, body mass index (BMI), and other relevant clinical indicators (≥ 18 years). All participants were provided with atorvastatin 20 mg daily during the data collection period. Patients with incomplete medical records, pregnancy, acute infections, acute diseases, advanced chronic kidney disease, chronic liver disease, systemic corticosteroid medication, or other diseases that can significantly affect lipid metabolism were excluded from the study.

Blood samples were obtained after fasting and were subsequently analyzed in the clinical laboratory of the hospital. HDL cholesterol (HDL-C) was measured by the precipitation method, LDL cholesterol (LDL-C) was measured by an enzymatic colorimetric test, and HbA1c was measured by high-performance liquid chromatography (HPLC). Total cholesterol (TC) was measured by the cholesterol oxidase–phenol aminophenazone (CHOD-PAP) method. RC was calculated by subtracting TC from LDL-C and HDL-C. Non-HDL cholesterol was calculated by subtracting TC from HDL-C. Body mass index (BMI) was calculated as $\text{weight (kg)} / \text{height (m)}^2$.

Statistical analysis was carried out using IBM SPSS Statistics version 26.0. Normality of the distribution of variables was tested using the Shapiro-Wilk normality test. The data were expressed as mean $\pm$ standard deviation

or median (interquartile range) for continuous variables. Pearson correlation analysis was used for normally distributed variables, and Spearman's rank correlation was used for variables where the normality assumption was not met. Two-sided p values <0.05 were considered statistically significant. The study protocol was approved by the Health Research Ethics Committee of Dr. Mohammad Hoesin General Hospital (Approval No. DP.04.03/D.XVII.9.4/ETIK/177/2026). For this study, informed consent was waived by the Ethics Committee as this was a study on

anonymized secondary data from medical records.

3. Result

The medical data were used to select 245 patients with Type 2 Diabetes Mellitus at the outset. Of these, 145 patients were excluded due to chronic kidney disease (CKD) (n = 55), acute diseases (n = 40), or incomplete data (n = 50). Consequently, the final analysis comprised 100 patients who satisfied the eligibility criteria (Figure 1).

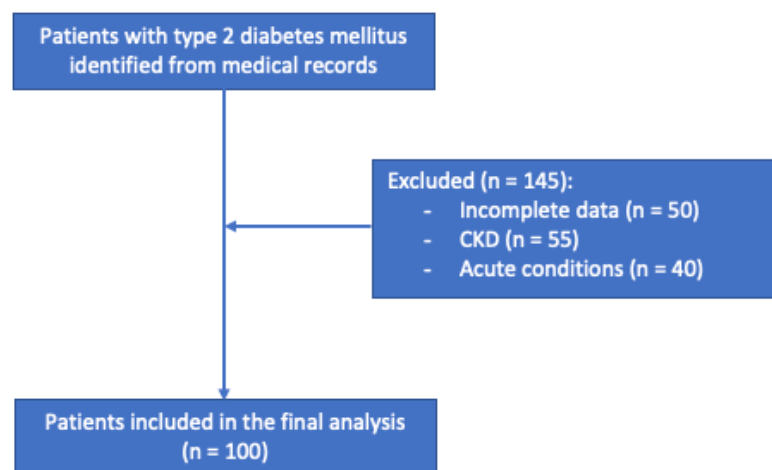


Figure 1. Flow diagram of participant selection

Table 1. Baseline Demographic and Clinical Data of the Study Population (n = 100)

Variable	Overall
Age, years	50.46 ± 3.63
21–40 years, n (%)	5 (5.0)
41–60 years, n (%)	95 (95.0)
Body mass index, kg/m ²	24.24 ± 2.01
Normal, n (%)	20 (20.0)
Overweight, n (%)	33 (33.0)
Obese, n (%)	47 (47.0)
HbA1c, %	8.69 ± 2.10
<7%, n (%)	26 (26.0)
≥7%, n (%)	74 (74.0)
Total cholesterol, mg/dL	227.84 ± 27.38
LDL cholesterol, mg/dL	129.03 ± 21.49
HDL cholesterol, mg/dL	38.64 ± 10.95
Remnant cholesterol, mg/dL	60.17 ± 21.89
Non-HDL cholesterol, mg/dL	189.20 ± 33.96
<130 mg/dL, n (%)	14 (14.0)
≥130 mg/dL, n (%)	86 (86.0)
Statin therapy, n (%)	-
Atorvastatin 20 mg/day, n (%)	100 (100.0)

Table 1 presents the baseline demographic and clinical data of the study population. The mean body mass index (BMI) of the subjects was $24.24 \pm 2.01 \text{ kg/m}^2$, and the mean age was 50.46 ± 3.63 years. Mean HbA1c was $8.69 \pm 2.10\%$ and mean total cholesterol, LDL cholesterol, HDL cholesterol, remnant cholesterol and non-HDL cholesterol were $227.84 \pm 27.38 \text{ mg/dL}$, $129.03 \pm 21.49 \text{ mg/dL}$, $38.64 \pm 10.95 \text{ mg/dL}$, $60.17 \pm 21.89 \text{ mg/dL}$ and $189.20 \pm 33.96 \text{ mg/dL}$, respectively. The majority of the patients (95.0%) were overweight or obese (80.0%), had HbA1c levels of $\geq 7\%$ (74.0%) and had non-HDL cholesterol levels of $\geq 130 \text{ mg/dL}$ (86.0%). All patients were treated with atorvastatin 20 mg daily.

The Shapiro–Wilk test demonstrated that all variables had a non-normal distribution, and Spearman's rank correlation analysis was conducted. Table 2 illustrates a

moderate positive correlation between non-HDL cholesterol and remnant cholesterol ($r = 0.618$, $p < 0.001$). Conversely, HbA1c was associated with non-HDL cholesterol in a faint negative manner that was not statistically significant ($r = -0.180$, $p = 0.074$).

The scatter plot of the correlation between non-HDL cholesterol and remnant cholesterol is shown in Figure 2. A positive correlation between non-HDL cholesterol and remnant cholesterol was observed, indicating a positive correlation between the two parameters. The correlation analysis' findings are corroborated by the regression line.

In contrast, the scatter diagram of Figure 3 demonstrates that there is no linear correlation between HbA1c and non-HDL cholesterol. The data points are dispersed over a broad area, further confirming the absence of statistically significant correlation between the two variables.

Table 2 Correlation Analysis of Study Variables

Variables	Correlation coefficient (r)*	p-value
RC vs Non-HDL	0.618	<0.001
HbA1c vs Non-HDL	-0.180	0.074

*Note: Correlation analyses were performed using Spearman's rank correlation because all variables showed non-normal distributions according to the Shapiro–Wilk test.

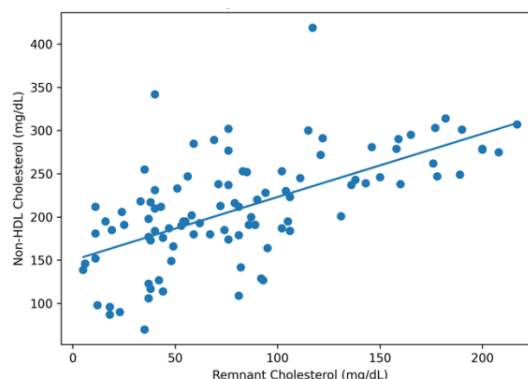


Figure 2. Scatter Plot of the Correlation Between Remnant Cholesterol and Non-HDL Cholesterol

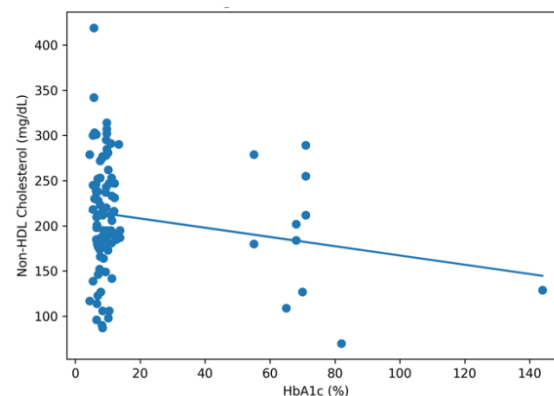


Figure 3. Scatter Plot of the Correlation Between HbA1c and Non-HDL Cholesterol

4. Discussion

In this study, remnant cholesterol showed a moderate positive correlation with non-HDL cholesterol among patients with T2DM ($r = 0.618$, $p < 0.001$). This observation is biologically plausible because remnant cholesterol constitutes one component of the non-HDL cholesterol fraction, making a positive relationship between the two parameters expected. Nevertheless, interpretation of this correlation should acknowledge that both indices are derived from overlapping lipid components. Consequently, part of the observed correlation may result from mathematical dependence rather than representing a completely independent biological phenomenon. RC quantifies the cholesterol carried by the remnants of triglyceride-rich lipoproteins, particularly VLDL and IDL particles.^{3,9} These remnant lipoproteins readily penetrate the arterial wall, initiate inflammatory signalling, and promote the development of atherosclerotic lesions. In contrast, non-HDL cholesterol represents the cumulative concentration of circulating atherogenic lipoproteins rather than a single lipoprotein fraction.^{16,17} Therefore, despite the inherent mathematical overlap between these measures, the observed relationship is also supported by established biological

mechanisms and previous experimental and clinical evidence.¹⁵

Insulin resistance, a hallmark of T2DM, provides a common metabolic basis for elevations in both remnant cholesterol and non-HDL cholesterol. Reduced insulin sensitivity enhances lipolysis within adipose tissue, increasing the delivery of free fatty acids to the liver. The increased hepatic free fatty acid flux stimulates hepatic VLDL synthesis and secretion. As a consequence, circulating triglyceride-rich lipoproteins and their remnant particles accumulate, contributing to higher concentrations of both RC and non-HDL cholesterol.^{10,11} The clinical profile of our participants supports this mechanism, as most individuals were overweight or obese and exhibited elevated non-HDL cholesterol concentrations, findings compatible with insulin resistance-associated atherogenic dyslipidemia. Together, these observations reinforce the close metabolic relationship between insulin resistance and atherogenic lipid abnormalities in T2DM.

In contrast to the findings for RC, HbA1c was not significantly associated with non-HDL cholesterol in this study. These results suggest that long-term glycaemic status did not parallel non-HDL cholesterol concentrations in this study population. Persistent hyperglycaemia is known to promote advanced glycation end-product formation,

increase hepatic lipogenesis, and enhance the production of atherogenic lipoproteins.^{8,18} Despite these biological mechanisms, previous clinical studies have reported inconsistent associations between glycaemic control and lipid abnormalities. Such variability is likely explained by differences in medication use, diabetes duration, metabolic heterogeneity, and patient characteristics across study populations. Accordingly, the lack of a statistically significant correlation in this study should not be interpreted as evidence that HbA1c lacks clinical relevance for cardiovascular risk assessment. HbA1c continues to be an established indicator of long-term glycaemic exposure and is strongly associated with the development of diabetic microvascular complications and cardiovascular outcomes.

Our findings differ from those reported in several previous investigations evaluating the relationship between HbA1c and lipid parameters. For example, Putri et al observed a significant positive association between HbA1c and non-HDL cholesterol.⁸ Differences in participant characteristics, treatment status, and study methodology may explain these inconsistent findings. Notably, every participant in this study was receiving atorvastatin therapy, which may have lowered lipid concentrations independently of glycaemic control and thereby weakened the observed correlation. Furthermore, information regarding diabetes duration and antidiabetic treatment was unavailable, and these unmeasured variables may also have influenced the study results.

From a clinical perspective, these findings support the combined assessment of glycaemic and lipid parameters when evaluating patients with T2DM. Since HbA1c and non-HDL cholesterol reflected different metabolic domains in this cohort, simultaneous evaluation of both parameters may provide a more comprehensive

metabolic assessment. Nevertheless, this study was not designed to assess cardiovascular outcomes, atherosclerotic burden, or major adverse cardiovascular events. Consequently, these findings should not be interpreted as evidence that RC is superior to HbA1c for cardiovascular risk prediction. Future studies incorporating additional lipid biomarkers and cardiovascular endpoints are needed to determine the incremental clinical value of RC beyond conventional metabolic markers.

Several limitations should be considered when interpreting this study. First, the cross-sectional nature of the study does not permit conclusions regarding causal relationships. Second, reliance on secondary medical records limited adjustment for potentially important confounding variables. Third, the mathematical dependence between calculated RC and non-HDL cholesterol may have contributed to the strength of the observed correlation. Fourth, universal atorvastatin treatment may have modified lipid profiles independently of glycemic control. In addition, apolipoprotein B and direct triglyceride levels were not available, which limited a more complete characterization of atherogenic dyslipidemia. Finally, since the study was performed in one center and the age distribution was relatively homogeneous, the extrapolation of these findings to broader populations should be performed with caution. Accordingly, confirmation in larger, multicenter prospective studies is warranted before these observations can be generalized.

5. Conclusion

In statin-treated individuals with type 2 diabetes mellitus, we identified a moderate positive correlation between remnant cholesterol and non-HDL cholesterol, but no significant correlation between HbA1c and non-HDL cholesterol. These findings suggest

that glycaemic control and atherogenic lipid burden may be complementary rather than interchangeable metabolic areas. The cross-sectional design, mathematical overlap among lipid measures, and widespread statin use highlight the need for prospective studies to determine the independent clinical importance of remnant cholesterol in the assessment of cardiovascular risk.

References

1. Duncan BB, Magliano DJ, Boyko EJ. [IDF Diabetes Atlas 11th edition 2025: global prevalence and projections for 2050](#). Nephrol Dial Transplant. 2025 Jan 1;41(1):7–9. doi:10.1093/NDT/GFAF177 PubMed PMID: 40874767.
2. Ko YS, Hsu LA, Wu S, Liao MS, Teng MS, Chou HH, et al. [Causal Associations Between Remnant Cholesterol Levels and Atherosclerosis-Related Cardiometabolic Risk Factors: A Bidirectional Mendelian Randomization Analysis](#). Genes (Basel). 2025 Feb 1;16(2):157. doi:10.3390/GENES16020157/S1 PubMed PMID: 40004488.
3. Varbo A, Benn M, Tybjaerg-Hansen A, Jørgensen AB, Frikke-Schmidt R, Nordestgaard BG. [Remnant cholesterol as a causal risk factor for ischemic heart disease](#). J Am Coll Cardiol. 2013 Jan 29;61(4):427–36. doi:10.1016/J.JACC.2012.08.1026 PubMed PMID: 23265341.
4. Chen X, Du X, Lu F, Zhang J, Xu C, Liang M, et al. [The Association Between the Triglyceride–Glucose Index, Its Combination with the Body Roundness Index, and Chronic Kidney Disease in Patients with Type 2 Diabetes in Eastern China: A Preliminary Study](#). Nutrients 2025, Vol 17, Page 492. 2025 Jan 29;17(3):492. doi:10.3390/NU17030492 PubMed PMID: 39940350.
5. Jalgaonkar MP, Parmar UM, Kulkarni YA, Oza MJ. [SIRT1-FOXOs activity regulates diabetic complications](#). Pharmacol Res. 2022 Jan 1;175. doi:10.1016/J.PHRS.2021.106014 PubMed PMID: 34856334.
6. Soewondo P, Soegondo S, Suastika K, Pranoto A, Soeatmadji DW, Tjokroprawiro A. [The DiabCare Asia 2008 study – Outcomes on control and complications of type 2 diabetic patients in Indonesia](#). Medical Journal of Indonesia. 2010 Nov 1;19(4):235–44. doi:10.13181/MJI.V19I4.412
7. Suastika K, Semadi IMS, Dwipayana IMP, Saraswati MR, Gotera W, Budhiarta AAG, et al. [Dyslipidemia in diabetes: a population-based study in Bali](#). Int J Gen Med. 2019 Sep 1;12:313–21. doi:10.2147/IJGM.S215548 PubMed PMID: 31564954.
8. Putri KW, Soelistijo SA, Prabowo GI, Widya Putri K, Soelistijo SA, Prabowo GI. [Association between HbA1c and Non-HDL-Cholesterol in Type 2 Diabetes Mellitus at a Tertiary Hospital in Indonesia](#). Cardiovascular and Cardiometabolic Journal (CCJ). 2025 Sep 30;6(2):73–82. doi:10.20473/CCJ.V6I2.2025.73-82
9. Nordestgaard BG. [Triglyceride-Rich Lipoproteins and Atherosclerotic Cardiovascular Disease: New Insights from Epidemiology, Genetics, and Biology](#). Circ Res. 2016 Feb 19;118(4):547–63. doi:10.1161/CIRCRESAHA.115.306249/ASSET/34006DC8-DOA1-4798-BAC6-730978FEADF1/ASSETS/GRAPHIC/547FI G07.JPEG PubMed PMID: 26892957.
10. Vargas-Vázquez A, Fermín-Martínez CA, Antonio-Villa NE, Fernández-Chirino L, Ramírez-García D, Dávila-López G, et al. [Insulin resistance potentiates the effect of remnant cholesterol on](#)

- [cardiovascular mortality in individuals without diabetes.](#) Atherosclerosis. 2024 Aug 1;395:117508. doi:10.1016/J.ATHEROSCLEROSIS.2024.117508 PubMed PMID: 38570208.
11. Li B, Liu Y, Zhou X, Chen L, Yan L, Tang X, et al. [Remnant cholesterol is more positively related to diabetes, prediabetes, and insulin resistance than conventional lipid parameters and lipid ratios: A multicenter, large sample survey.](#) J Diabetes. 2024 Aug 1;16(8):e13592. doi:10.1111/1753-0407.13592 PubMed PMID: 39136535.
12. Bergmann K. Non-HDL [Cholesterol and Evaluation of Cardiovascular Disease Risk.](#) EJIFCC. 2010 Oct;21(3):64. PubMed PMID: 27683375.
13. Blumenthal RS, Morris PB, Gaudino M, Johnson HM, Anderson TS, Bittner VA, et al. 2026 [ACC/AHA/AACVPR/ABC/ACPM/ADA/AGS/APhA/ASPC/NLA/PCNA Guideline on the Management of Dyslipidemia: A Report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines.](#) Circulation. 2026 Apr 28;153(17). doi:10.1161/CIR.0000000000001423
14. Lu W, Resnick HE, Jablonski KA, Jones KL, Jain AK, Howard WMJ, et al. [Non-HDL Cholesterol as a Predictor of Cardiovascular Disease in Type 2 Diabetes: The Strong Heart Study.](#) Diabetes Care. 2003 Jan 1;26(1):16–23. doi:10.2337/DIACARE.26.1.16 PubMed PMID: 12502653.
15. Ferrer R, Mansilla A, Tondo M, Blanco-Vaca F. [Remnant cholesterol: new outcomes highlight its potential as a clinically useful cardiovascular risk factor.](#) J Lab Precis Med. 2023 Apr 30;8(0). doi:10.21037/JLPM-22-70/COIF
16. Barbalho SM, Tofano RJ, de Oliveira MB, Quesada KR, Barion MR, Akuri MC, et al. [HDL-C and non-HDL-C levels are associated with anthropometric and biochemical parameters.](#) J Vasc Bras. 2019;18:e20180109. doi:10.1590/1677-5449.180109 PubMed PMID: 31312214.
17. Alkouri O, Al-Bashaireh AM, Alobaidly A, Alharbi G, Alabkal RM, Hasan A, et al. [Non-HDL Cholesterol and Residual Cardiometabolic Risk in Middle Eastern Patients with Atherosclerotic Cardiovascular Disease.](#) Healthcare. 2026 Feb 25;14(5):565. doi:10.3390/HEALTHCARE14050565 PubMed PMID: 41827519.
18. Poznyak A V., Sukhorukov VN, Surkova R, Orekhov NA, Orekhov AN. [Glycation of LDL: AGEs, impact on lipoprotein function, and involvement in atherosclerosis.](#) Front Cardiovasc Med. 2023 Jan 24;10:1094188. doi:10.3389/FCVM.2023.1094188 PubMed PMID: 36760567.