Research in Molecular Medicine

Research Paper

Uric Acid-to-HDL Ratio Is Not Associated With Coronary Artery Disease in Type 2 Diabetesy

Abbas Abdulhussein Dahash AL-Shiblawi[1], Fatemeh Sadat Hoseini[1], Farimah Sadat Mousavi Kiasari[2], Sahar Eskandari Ghadi[2], Abbas Khonakdar-Tarsi[1, 3*], Hadis Musavi[1, 3, 4]

1. Department of Clinical Biochemistry and Genetics, Faculty of Medicine, Mazandaran University of Medical Sciences, Sari, Iran.
2. Department of Cardiology, Cardiovascular Research Center, Faculty of Medicine, Mazandaran University of Medical Sciences, Sari, Iran.
3. Immunogenetics Research Center, Mazandaran University of Medical Sciences, Sari, Iran.
4. Thalassemia Research Center, Hemoglobinophaty Institute, Mazandaran University of Medical Sciences, Sari, Iran.

Use your device to scan and read the article online

Citation AL-Shiblawi AAD, Hoseini FS, Mousavi Kiasari FS, Eskandari Ghadi S, Khonakdar-Tarsi A, Musavi H. Uric Acid-to-HDL Ratio Is Not Associated With Coronary Artery Disease in Type 2 Diabetesy. Research in Molecular Medicine. 2026; 14(3):127-138. http://dx.doi.org/10.22034/rmm.14.3.256.2

http://dx.doi.org/10.22034/rmm.14.3.256.2

Article Type:
Research Paper

Article info:
Received: 23 Feb 2026
Revised: 10 Jun 2026
Accepted: 05 Jul 2026

Keywords:
Type 2 diabetes mellitus, Uric acid-to-HDL ratio, Coronary artery disease (CAD), Glycemic control, Lipid profile, Cardiometabolic risk

ABSTRACT

Background: The uric acid-to-high-density lipoprotein cholesterol ratio (UHR) has recently emerged as a potential cardiometabolic biomarker. This study evaluated the association between UHR and coronary artery disease (CAD), glycemic control, and lipid-related parameters in patients with type 2 diabetes mellitus (T2DM).

Materials and Methods: In this cross-sectional comparative study, 120 patients with T2DM were enrolled and categorized into those with angiographically documented CAD (DM_CD, n=60) and those without CAD (DM, n=60). Fasting blood glucose levels, HbA1c levels, lipid profile, serum uric acid levels, creatinine levels, complete blood count parameters, inflammatory indices, and the triglyceride-glucose (TyG) index were measured. UHR was calculated as serum uric acid divided by high-density lipoprotein cholesterol (HDL-C). Group comparisons, correlation analyses, and multivariable logistic regression were performed.

Results: UHR did not differ significantly between patients with and without CAD (0.139±0.06 vs 0.126±0.045, P=0.123) and was not associated with fasting blood glucose levels, HbA1c levels, or the TyG index. Patients with CAD had significantly higher neutrophil-to-lymphocyte ratio (NLR), neutrophil count, and hematocrit, and lower lymphocyte and platelet counts (all P<0.05). In multivariable logistic regression, only NLR remained independently associated with CAD (adjusted OR=3.99; 95% CI, 1.52%, 10.52%; P=0.005), whereas UHR, the TyG index, and HbA1c levels were not.

Conclusion: UHR was not associated with CAD or glycemic control and was not an independent predictor of CAD in patients with T2DM. These findings do not support the use of UHR for discriminating established CAD in this study population. Larger prospective studies with adjustment for potential confounding factors are warranted.

*** Corresponding Author:**
Abbas Khonakdar-Tarsi, MD.
Address: *Department of Medical Biochemistry and Genetics, Faculty of Medicine, Mazandaran University of Medical Sciences, Sari, Iran.*
Phone: *+98 (911) 2235164*
E-mail: *khonakdarab@gmail.com*

Copyright © 2026 The Author(s);
This is an open access article distributed under the terms of the Creative Commons Attribution License (CC-By-NC 4.0: https://creativecommons.org/licenses/by-nc/4.0/legalcode.en), which permits use, distribution, and reproduction in any medium, provided the original work is properly cited and is not used for commercial purposes.

Introduction

Type 2 diabetes mellitus (T2DM) is one of the most prevalent chronic metabolic disorders worldwide and represents a major public health concern. The global burden of T2DM continues to increase, affecting millions of individuals and imposing substantial healthcare costs. The disease is characterized by insulin resistance, progressive β-cell dysfunction, and chronic hyperglycemia, all of which contribute to the development of microvascular and macrovascular complications. Among these complications, coronary artery disease (CAD) remains the leading cause of morbidity and mortality in patients with T2DM and is responsible for a significant proportion of diabetes-related deaths worldwide [1]. The increased cardiovascular risk observed in patients with T2DM is multifactorial and involves a complex interplay of metabolic abnormalities, endothelial dysfunction, oxidative stress, chronic inflammation, and dyslipidemia. Persistent hyperglycemia promotes vascular injury through the formation of advanced glycation end-products, activation of inflammatory pathways, and increased oxidative stress, thereby accelerating atherosclerotic processes [1]. Consequently, identifying simple, inexpensive, and readily available biomarkers that reflect both metabolic status and cardiovascular risk has become an important clinical and research objective. Uric acid, the final product of purine metabolism in humans, has attracted considerable attention as a potential marker of metabolic and cardiovascular dysfunction. Although uric acid exhibits antioxidant properties under physiological conditions, elevated serum uric acid concentrations have been associated with oxidative stress, endothelial dysfunction, inflammation, insulin resistance, and atherosclerosis [2, 3]. Previous studies have demonstrated significant associations between hyperuricemia and several cardiometabolic disorders, including obesity, hypertension, metabolic syndrome, T2DM, and cardiovascular disease [3, 4].

Furthermore, elevated serum uric acid levels have been linked to adverse cardiovascular outcomes and increased cardiometabolic risk in both diabetic and non-diabetic populations [2-4]. HDL-C, on the other hand, is widely recognized as a protective lipid fraction because of its anti-inflammatory, antioxidant, anti-thrombotic, and anti-atherogenic properties. HDL-C plays an important role in reverse cholesterol transport and contributes to the maintenance of endothelial function. Reduced HDL-C levels are frequently observed in patients with T2DM and are associated with poor metabolic health and increased cardiovascular risk [5]. Since serum uric acid and HDL-C represent two biologically distinct but closely related aspects of cardiometabolic health, combining these parameters into a single index may provide a more comprehensive assessment of metabolic risk. In recent years, the UHR has emerged as a novel biomarker that integrates information from both serum uric acid and HDL-C levels. Several studies have suggested that UHR may be associated with insulin resistance, metabolic syndrome, prediabetes, and T2DM [6-8]. Kocak et al. reported that UHR was a strong predictor of metabolic syndrome among patients with T2DM [6]. Similarly, other investigators have demonstrated associations between UHR and glycemic control parameters, suggesting that this ratio may reflect underlying metabolic dysfunction [7, 8]. These findings have generated growing interest in the potential clinical utility of UHR as an easily obtainable cardiometabolic marker. More recently, population-based studies have expanded the potential significance of UHR beyond metabolic disorders. Elevated UHR has been associated with incident diabetes, cardiovascular disease, and increased cardiovascular mortality in individuals with diabetes [9, 10]. Despite these observations, the available evidence remains inconsistent. Some studies have reported strong associations between UHR and markers of glycemic control, whereas others have found weaker or non-significant relationships. Moreover, relatively few studies have specifically evaluated the association between UHR and CAD among patients with established T2DM. In addition to metabolic abnormalities, inflammation is increasingly recognized as a key contributor to the development and progression of both diabetes and cardiovascular disease. Hematological inflammatory markers, including the NLR , have been associated with adverse cardiovascular outcomes and may provide additional insight into cardiometabolic risk stratification. Therefore, simultaneous assessment of metabolic, biochemical, and inflammatory parameters may improve our understanding of the factors associated with cardiovascular complications in patients with T2DM.

We hypothesized that patients with T2DM and angiographically confirmed CAD would have higher UHR values than diabetic patients without CAD, and that UHR would be associated with metabolic and inflammatory parameters. Therefore, this exploratory cross-sectional comparative study aimed to compare UHR between T2DM patients with and without CAD and to investigate the association between UHR and glycemic, lipid, inflammatory, and hematological markers. Given the limited and inconsistent evidence, the study also sought to evaluate whether UHR provides additional value as a potential marker of CAD in this population.

Research in Molecular Medicine

Materials and Methods

Study design and participants

This exploratory cross-sectional comparative study was conducted at the Diabetes Center of Imam Hospital, Mazandaran University of Medical Sciences, Sari, Iran. A total of 120 adult patients with established T2DM were consecutively recruited during the study period according to predefined eligibility criteria. Participants were categorized into two groups based on the presence of CAD: Patients with angiographically documented or clinically confirmed CAD (DM_CD group, n=60) and patients without evidence of CAD (DM group, n=60). The diagnosis of T2DM was established according to the American Diabetes Association diagnostic criteria. CAD was confirmed from documented medical records, including coronary angiography demonstrating significant coronary stenosis, previous myocardial infarction, prior coronary revascularization (percutaneous coronary intervention or coronary artery bypass grafting), or a documented diagnosis by a cardiologist.

Eligible participants were between 40 and 75 years of age and had a confirmed diagnosis of T2DM for at least two years before enrollment. All participants provided written informed consent before inclusion in the study. Patients were excluded if they had chronic kidney disease, advanced liver disease, acute or chronic inflammatory disorders, active infection, autoimmune disease, malignancy, or hematologic disorders, were pregnant, or were under current treatment with medications known to substantially influence serum uric acid concentrations, including urate-lowering agents (e.g. allopurinol or febuxostat) or uricosuric drugs. Demographic information, including age, sex, and smoking status was collected for all participants. However, detailed information regarding body mass index (BMI), duration of diabetes beyond the eligibility criterion, and medication use—including antidiabetic agents, statins, antihypertensive medications, diuretics, sodium-glucose cotransporter-2 (SGLT2) inhibitors, antiplatelet agents, and other uric acid-modifying therapies—was not consistently available in the study database and therefore could not be incorporated into the statistical analyses. These variables were considered potential sources of residual confounding.

Sample size

An a priori sample size calculation was not performed before participant recruitment. Instead, all consecutive eligible patients who fulfilled the predefined inclusion and exclusion criteria during the study period were enrolled. Consequently, the present investigation should be considered an exploratory study, and its findings should be interpreted cautiously until confirmed by larger prospective studies with adequate statistical power.

Blood collection and laboratory measurements

Following an overnight fast of 10–12 hours, approximately 10 mL of venous blood was collected from each participant. Five milliliters were transferred into EDTA-containing tubes for complete blood count (CBC) and glycated hemoglobin (HbA1c) analyses, while the remaining blood was collected into plain tubes for serum preparation. Samples were centrifuged at 3000 rpm for 15 minutes, and serum aliquots were stored at −80°C until biochemical analyses were performed. Serum levels of fasting blood glucose (FBS), triglycerides (TG), total cholesterol (TC), HDL-C, low-density lipoprotein cholesterol (LDL-C), uric acid, creatinine, aspartate aminotransferase (AST), alanine aminotransferase (ALT), calcium, and phosphorus were measured using enzymatic colorimetric methods (Pars Azmoon Co., Tehran, Iran) on an automated chemistry analyzer (BT-3000 Plus, Biotecnica Instruments, Italy). HbA1c levels were directly measured using high-performance liquid chromatography (HPLC) with a Bio-Rad D-10 HbA1c Analyzer (Bio-Rad Laboratories, Hercules, CA, USA). Complete blood count parameters, including white blood cell count (WBC), red blood cell count (RBC), hemoglobin (HGB), hematocrit (HCT), mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH), mean corpuscular hemoglobin concentration (MCHC), red cell distribution width (RDW), platelet count (PLT), and mean platelet volume (MPV), were determined using a Sysmex XN-1000 automated hematology analyzer (Sysmex Corporation, Kobe, Japan).

Calculated indices

The following indices were calculated using standard formulas:

- UHR = Serum Uric acid (mg/dL) / HDL-C (mg/dL)
- Uric acid-to-creatinine ratio (UCR) = Serum uric acid (mg/dL) / Serum creatinine (mg/dL)
- TyG index = ln [Fasting triglycerides (mg/dL) × Fasting blood glucose (mg/dL) / 2]
- NLR = Absolute neutrophil count / Absolute lymphocyte count

- Platelet-to-lymphocyte ratio (PLR) = Platelet count / absolute lymphocyte count

- Hemoglobin-to-platelet ratio (HPR) = Hemoglobin / platelet count

- Total cholesterol-to-HDL cholesterol ratio (TC/HDL)

- LDL cholesterol-to-HDL cholesterol ratio (LDL/HDL)

- Triglyceride-to-HDL cholesterol ratio (TG/HDL)

- Non-HDL cholesterol = Total cholesterol − HDL cholesterol

- Cholesterol atherogenic ratio (ChAR) = Total cholesterol / HDL cholesterol

Statistical analysis

Statistical analyses were performed using SPSS 26 software, version (IBM Corp., Armonk, NY, USA). Continuous variables were assessed for normality using the Kolmogorov–Smirnov test and are presented as Mean±SD or median (interquartile range), as appropriate. Categorical variables are expressed as frequencies and percentages. Comparisons between the DM_CD and DM groups were performed using the independent-samples t-test for normally distributed variables or the Mann–Whitney U test for non-normally distributed variables. Categorical variables were compared using the chi-square test or Fisher's exact test, when appropriate. Associations between UHR and clinical or laboratory variables were evaluated using Pearson's or Spearman's correlation coefficients according to data distribution. Because HDL-C is mathematically incorporated into the UHR formula, correlations between UHR and HDL-C were interpreted with caution and were not considered evidence of an independent biological association. To identify factors associated with CAD, univariate logistic regression analyses were initially performed for selected variables, including UHR, HbA1c, TyG index, and NLR. Variables demonstrating clinical relevance or statistical significance in univariate analyses were subsequently entered into a multivariable logistic regression model. Odds ratios (ORs) with corresponding 95% confidence intervals (95% CIs) were reported. Adjustment for BMI, detailed medication use, and duration of diabetes was not possible because these data were unavailable. Accordingly, the possibility of residual confounding cannot be excluded, and the findings should be interpreted as exploratory. All statistical tests were two-sided, and $P<0.05$ was considered statistically significant.

Results

Comparison of glycemic, metabolic, inflammatory, and biochemical parameters between the study groups

A total of 120 patients were included in the study, comprising 60 patients in the DM-CD group and 60 patients in the DM group. The mean age was 66.4±7.1 years in the DM group and 68.4±7.4 years in the DM-CD group, with no statistically significant difference between the groups (P=0.2). Male participants accounted for 54.2% of the DM group and 58.3% of the DM_CD group (P=0.42). All participants had been diagnosed with T2DM within the previous five years. BMI was not available in the study database and therefore could not be included in the baseline comparisons.

Comparison of glycemic parameters and UHR between the DM_CD and DM groups

As shown in Table 1, there were no statistically significant differences between the DM_CD and DM groups regarding the primary outcome, UHR (0.139±0.06 vs 0.126±0.045, P=0.123). Similarly, glycemic parameters, including fasting blood sugar levels (166.38±82.45 vs 161.91±59.98 mg/dL, P=0.657), HbA1c levels (7.42±2.87 vs 7.27±2.09%, P=0.652), and the TyG index (9.48±0.87 vs 9.44±0.63, P=0.671), were comparable between the two groups. These findings indicate that neither glycemic control nor insulin resistance, as assessed by the TyG index, differed significantly between patients with diabetes and celiac disease and those with diabetes alone.

Comparison of metabolic syndrome components and atherogenic indices between the DM_CD and DM groups

Table 2 presents the comparison of metabolic syndrome components and atherogenic indices between the two study groups. No statistically significant differences were observed in serum levels of triglycerides (211.1±179.68 vs 181.42±99.56 mg/dL, P=0.141), HDL cholesterol (42.1±13.56 vs 40.21±8.49 mg/dL, P=0.234), LDL cholesterol (80.31±29.83 vs 84.82±35.75 mg/dL, P=0.521), or total cholesterol (150.71±43.9 vs 151.3±43.30 mg/dL, P=0.951) between the DM_CD and DM groups. Likewise, all evaluated atherogenic indices, including the TG/HDL ratio (P=0.104), total cholesterol/HDL ratio (P=0.483), LDL/HDL ratio (P=0.727), and non-HDL cholesterol (P=0.951), were comparable between the groups.

Table 1. Comparison of glycemic parameters and UHR between the DM_CD and DM groups

Variables		Mean±SD		P
		DM_CD Group (n=60)	DM Group (n=60)	
Primary outcome	UHR	0.139±0.06	0.126±0.045	0.123
Glycemic control & Insulin resistance	FBS (mg/dL)	166.38±82.45	161.91±59.98	0.657
	HbA1c (%)	7.42±2.87	7.27±2.09	0.652
	TyG index	9.48±0.87	9.44±0.63	0.671

Abbreviations: DM_CD: Diabetes mellitus with celiac disease; DM: Diabetes mellitus; UHR: Uric acid-to-high-density lipoprotein cholesterol ratio; FBS: Fasting blood sugar; HbA1c: Glycated hemoglobin; TyG: Triglyceride-glucose index.

Comparison of inflammatory, hematological, uric acid-related, renal, and hepatic markers between the DM_CD and DM groups

As shown in Table 3, patients in the DM_CD group exhibited significantly higher inflammatory activity than those in the DM group, as reflected by an increased NLR (2.57±1.19 vs 1.52±0.62, P<0.001). This finding was accompanied by significantly higher neutrophil counts (4967.64±2285.01 vs 3794.47±1162.63 cells/µL, P<0.001) and lower lymphocyte counts (2.09±0.57 vs 2.75±0.79 $\times 10^3/\mu L$, P<0.001). Hematocrit levels were also significantly higher in the DM_CD group (40.86±5.19% vs 38.04±3.58%, P=0.003), whereas platelet counts were significantly lower (227.34±56.12 vs 256.42±83.03 $\times 10^3/\mu L$, P=0.045). Although the platelet-to-lymphocyte ratio (PLR), hemoglobin-to-platelet ratio (HPR), red blood cell count, and hemoglobin concentration tended to differ between groups, these differences did not reach statistical significance (P>0.05). Likewise, no significant differences were observed in WBC count, MCV, MCH, MCHC, RDW, or MPV.

Regarding uric acid-related parameters, serum uric acid concentrations and the uric acid-to-creatinine ratio (UCR) were comparable between the groups (P=0.112 and P=0.250, respectively). Renal function, assessed by serum creatinine levels, also did not differ significantly (P=0.433). In contrast, liver enzymes were modestly but significantly higher in the DM_CD group, with both AST and ALT levels showing statistically significant elevations (P<0.05 for both).

Table 2. Comparison of metabolic syndrome components and atherogenic indices between the DM_CD and DM groups

Variables		Mean±SD		P
		DM_CD Group (n=60)	DM Group (n=60)	
Metabolic syndrome components	TG (mg/dL)	211.1±179.68	181.42±99.56	0.141
	HDL (mg/dL)	42.1±13.56	40.21±8.49	0.234
	LDL (mg/dL)	80.31±29.83	84.82±35.75	0.521
	Chol (mg/dL)	150.71±43.9	151.3±43.3	0.951
Atherogenic indices	TG/HDL ratio	6.56±10.78	4.85±3.27	0.104
	Chol/HDL ratio	4.03±2.65	3.84±1.38	0.483
	LDL/HDL ratio	2.11±1.16	2.19±1.07	0.727
	Non-HDL (Chol - HDL)	108.93±47.46	109.15±43.57	0.951

Abbreviations: DM_CD: Diabetes mellitus with celiac disease; DM: Diabetes mellitus; TG: Triglycerides; HDL: High-density lipoprotein cholesterol; LDL: Low-density lipoprotein cholesterol; Chol (TC): Total cholesterol; TG/HDL: Triglyceride-to-HDL cholesterol ratio; Chol/HDL (TC/HDL): Total cholesterol-to-HDL cholesterol ratio; LDL/HDL: Low-density lipoprotein cholesterol-to-HDL cholesterol ratio; Non-HDL: Non-high-density lipoprotein cholesterol.

Table 3. Comparison of inflammatory, hematological, uric acid, renal, and hepatic markers between the DM_CD and DM groups

Variables		Mean±SD		P
		DM_CD Group (n=60)	DM Group (n=60)	
Inflammatory & hematological markers	NLR	2.57±1.19	1.52±0.62	<0.001
	PLR	116.39±40.61	99.14±39.35	0.07
	HPR	0.062±0.018	0.054±0.018	0.057
	WBC (×10³/µL)	7.89±2.50	7.25±1.51	0.156
	RBC (×10⁶/µL)	4.95±0.77	4.63±0.68	0.072
	HGB (g/dL)	13.25±2.52	12.41±1.32	0.059
	HCT (%)	40.86±5.19	38.04±3.58	0.003
	MCV (fL)	82.95±9.07	83.25±9.56	0.9
	MCH (pg)	26.9±4.01	27.18±3.64	0.684
	MCHC (g/dL)	32.31±2.15	32.58±1.39	0.372
	RDW (%)	13.6±2.8	13.71±1.78	0.921
	MPV (fL)	9.98±1.98	9.38±1.68	0.420
	PLT (×10³/µL)	227.34±56.12	256.42±83.03	0.045
	Neutrophil count (cells/µL)	4967.64±2285.01	3794.47±1162.63	<0.001
	Lymphocyte count (×10³/µL)	2.09±0.57	2.75±0.79	<0.001
Uric acid related parameters	Uric acid (mg/dL)	5.38±1.97	4.81±1.23	0.112
	UCR (uric acid/creatinine)	5.1±1.78	4.71±1.32	0.250
Renal function	Cr (mg/dL)	1.15±0.67	1.07±0.19	0.433
Liver function	AST (U/L)	27.28±16.14	24.55±4.51	<0.05
	ALT (U/L)	27.64±19.88	24.39±8.47	<0.05

Abbreviations: DM_CD: Diabetes mellitus with celiac disease; DM: Diabetes mellitus; NLR: Neutrophil-to-lymphocyte ratio; PLR: Platelet-to-lymphocyte ratio; HPR: Hemoglobin-to-platelet ratio; WBC: White blood cell count; RBC: Red blood cell count; HGB: Hemoglobin; HCT: Hematocrit; MCV: Mean corpuscular volume; MCH: Mean corpuscular hemoglobin; MCHC: Mean corpuscular hemoglobin concentration; RDW: Red cell distribution width; MPV: Mean platelet volume; PLT: Platelet count; UCR: Uric acid-to-creatinine ratio; Cr: Creatinine; AST: Aspartate aminotransferase; ALT: Alanine aminotransferase.

Correlation analyses

As shown in Table 4, UHR demonstrated a significant inverse correlation with HDL cholesterol (r=−0.540, P<0.001), indicating that higher UHR values were associated with lower HDL concentrations. UHR also showed weak but statistically significant positive correlations with the LDL/HDL ratio (r=0.238, P=0.047) and the total cholesterol-to-HDL ratio (r=0.267, P=0.025). Although a positive correlation was observed between UHR and the TG/HDL ratio (r=0.212), this association did not reach statistical significance (P=0.076). No significant correlations were identified between UHR and the TyG index and fasting blood sugar (FBS), HbA1c, triglyceride, LDL cholesterol, total cholesterol, or non-HDL cholesterol levels. Among patients without CAD (Table 5), UHR exhibited a moderate positive correlation with triglyceride levels (r=0.386, P=0.020), as well as a stronger positive correlation with the TG/HDL ratio (r=0.545, P=0.001). UHR was also positively associated with the total cholesterol-to-HDL ratio (r=0.342, P=0.041).

Table 4. Correlations between UHR and metabolic parameters in the overall study population

Variables	r	P (2-tailed)
UHR	1	—
TyG index	0.153	0.207
FBS	0.003	0.981
TG	0.151	0.209
Chol	-0.075	0.536
LDL	-0.034	0.780
HDL	-0.54	0.000
HbA1c	0.003	0.981
TG/HDL ratio	0.212	0.076
LDL/HDL ratio	0.238	0.047
Non-HDL-C	0.038	0.752
TC/HDL ratio	0.267	0.025

Abbreviations: UHR: Uric acid-to-high-density lipoprotein cholesterol ratio; TyG: Triglyceride-glucose index; FBS: Fasting blood sugar; TG: Triglycerides; Chol (TC): Total cholesterol; LDL: Low-density lipoprotein cholesterol; HDL: High-density lipoprotein cholesterol; HbA1c: Glycated hemoglobin; Non-HDL-C: Non-high-density lipoprotein cholesterol.

Table 5. Correlations between UHR and metabolic parameters in DM patients

Variables	r	P (2-tailed)
UHR	1	—
TyG index	0.17	0.320
FBS	-0.127	0.459
TG	0.386	0.020
Chol	-0.059	0.732
LDL	-0.087	0.617
HDL	-0.657	0.000
HbA1c	-0.127	0.459
TG/HDL ratio	0.545	0.001
LDL/HDL ratio	0.219	0.207
Non-HDL-C	0.071	0.683
TC/HDL ratio	0.342	0.041

Abbreviations: UHR: Uric acid-to-high-density lipoprotein cholesterol ratio; CAD: Coronary artery disease; TyG: Triglyceride-glucose index; FBS: Fasting blood sugar; TG: Triglycerides; Chol (TC): Total cholesterol; LDL: Low-density lipoprotein cholesterol; HDL: High-density lipoprotein cholesterol; HbA1c: Glycated hemoglobin; Non-HDL-C: Non-high-density lipoprotein cholesterol.

Table 6. Correlations between UHR and metabolic parameters in patients with DM_CD

Variables	r	P (2-tailed)
UHR	1	—
TyG index	0.139	0.434
FBS	0.07	0.696
TG	0.032	0.854
Chol	-0.08	0.648
LDL	0.042	0.810
HDL	-0.47	0.004
HbA1c	0.07	0.696
TG/HDL ratio	0.076	0.664
LDL/HDL ratio	0.303	0.077
Non-HDL-C	0.024	0.892
TC/HDL ratio	0.224	0.196

Abbreviations: UHR: Uric acid-to-high-density lipoprotein cholesterol ratio; CAD: Coronary artery disease; TyG: Triglyceride-glucose index; FBS: Fasting blood sugar; TG: Triglycerides; Chol (TC): Total cholesterol; LDL: Low-density lipoprotein cholesterol; HDL: High-density lipoprotein cholesterol; HbA1c: Glycated hemoglobin; Non-HDL-C: Non-high-density lipoprotein cholesterol.

In contrast, a strong inverse correlation was observed between UHR and HDL cholesterol levels (r=−0.657, P<0.001). No statistically significant associations were found between UHR and the TyG index, FBS levels, HbA1c levels, total cholesterol levels, LDL cholesterol levels, LDL/HDL ratio, or non-HDL cholesterol levels. As presented in Table 6, the only statistically significant association observed in patients with CAD was a moderate inverse correlation between UHR and HDL cholesterol levels (r=−0.470, P=0.004). Although the LDL/HDL ratio demonstrated a weak positive correlation with UHR (r=0.303), this relationship did not reach statistical significance (P=0.077). Likewise, no significant correlations were found between UHR and the TyG index, FBS levels, HbA1c levels, triglyceride levels, total cholesterol levels, LDL cholesterol levels, TG/HDL ratio, non-HDL cholesterol levels, or the total cholesterol-to-HDL ratio.

Logistic regression analysis

Table 7 summarizes the results of the univariate and multivariable logistic regression analyses for factors associated with the presence of CAD. In the univariate

Table 7. Univariate and multivariable logistic regression analyses

Variables	Unadjusted OR (95% CI)	P	Adjusted OR (95% CI)	P
UHR	1.02 (0.93–1.12)	0.658	1.07 (0.95–1.21)	0.276
NLR	4.63 (1.95–10.98)	<0.001	3.99 (1.52–10.52)	0.005
TyG index	1.07 (0.64–1.79)	0.787	0.37 (0.08–1.77)	0.212
HbA1c	1.02 (0.88–1.2)	0.760	1.18 (0.8–1.74)	0.414

Abbreviations: OR: Odds ratio; CI: Confidence interval; NLR: Neutrophil-to-lymphocyte ratio; TyG: Triglyceride-glucose index; UHR: Uric acid-to-HDL cholesterol ratio.

Note: Odds ratios are presented with their corresponding 95% confidence intervals.

analysis, NLR was the only variable significantly associated with CAD, with each unit increase in NLR corresponding to a 4.63-fold higher odds of CAD (OR=4.63; 95% CI, 1.95%, 10.98%; P<0.001). In contrast, UHR, the TyG index, and HbA1c levels were not significantly associated with CAD in the unadjusted model.

After adjustment for the other clinical variables, NLR remained an independent predictor of CAD (adjusted OR=3.99; 95% CI, 1.52%, 10.52%; P=0.005). Although the adjusted odds ratio for UHR increased substantially, its association with CAD did not reach statistical significance (adjusted OR=1.07; 95% CI, 0.95%, 1.21%; P=0.276), reflecting considerable uncertainty as indicated by the extremely wide confidence interval. Neither the TyG index (adjusted OR=0.37; 95% CI, 0.08%, 1.77%; P=0.212) nor HbA1c levels (adjusted OR=1.18; 95% CI, 0.85, 1.74%; P=0.414) showed an independent association with CAD. Overall, these findings identify NLR as the only independent clinical predictor of CAD among the variables evaluated in the regression model.

Discussion

The present cross-sectional comparative study investigated the association between UHR and glycemic control parameters and CAD in patients with T2DM. The principal finding was that UHR did not differ significantly between patients with and without CAD. Moreover, UHR was not significantly associated with FBS and HbA1c levels or the TyG index and was not an independent predictor of CAD in multivariable logistic regression analysis. These findings suggest that UHR has limited utility for discriminating established CAD in patients with T2DM.

UHR has recently attracted considerable attention as a novel cardiometabolic marker because it combines serum uric acid, which has been associated with oxidative stress, inflammation, endothelial dysfunction, and insulin resistance, with HDL-C, which has well-established anti-inflammatory and anti-atherogenic properties. Previous studies have reported associations between elevated UHR and poor glycemic control, metabolic syndrome, insulin resistance, and adverse cardiovascular outcomes [7, 10, 11]. Previous studies have reported that UHR is significantly higher in patients with poor glycemic control, and an association between UHR and diabetic control has also been observed in newly diagnosed diabetes [7].

In contrast, we did not observe significant associations between UHR and conventional glycemic indices, including FBS and HbA1c levels and the TyG index. These discrepant findings may be explained by differences in study populations. Previous investigations frequently included newly diagnosed diabetic patients or heterogeneous metabolic populations, whereas our study included patients with established T2DM. In addition, glycemic control was broadly comparable between the two study groups, reducing the likelihood of detecting differences in UHR. Collectively, these findings suggest that the relationship between UHR and glycemic control may depend on disease stage, patient characteristics, and metabolic heterogeneity.

Another important finding was the absence of a significant difference in UHR between diabetic patients with and without CAD. Previous epidemiological studies have suggested that elevated UHR is associated with cardiovascular disease, cardiovascular mortality, and all-cause mortality [10-12]. However, these studies primarily evaluated long-term cardiovascular risk rather than the presence of established CAD. Consistent with our logistic regression analysis, UHR was not independently associated with CAD after adjustment for the available covariates. Therefore, although UHR may be associated with future cardiovascular risk in some populations, our findings do not support its use as a discriminator of established CAD in patients with T2DM.

Recent studies have provided additional insight into the potential role of UHR across different cardiovascular settings. A large population-based study by Yi et al. demonstrated that elevated UHR was associated with a higher prevalence of cardiovascular disease and adverse lipid profiles, supporting its role as a marker of cardiometabolic dysfunction rather than a disease-specific biomarker [13]. Likewise, Sun et al., using NHANES data from diabetic individuals, reported that higher UHR was independently associated with myocardial infarction, suggesting that UHR may be more useful for identifying individuals at increased cardiovascular risk than for distinguishing the presence of established coronary artery disease in cross-sectional analyses [14]. Conversely, studies conducted in acute coronary syndrome populations have shown that UHR correlates with angiographic CAD severity, particularly among patients with non-ST-elevation myocardial infarction. These differences highlight that the clinical significance of UHR may vary according to the study population, disease stage, and cardiovascular endpoint evaluated. Therefore, the absence of a significant association between UHR and established CAD in our cohort does not necessarily contradict

its potential prognostic value in other clinical settings but rather suggests that its diagnostic performance may be context-dependent [13-15].

Correlation analyses should also be interpreted cautiously. The strong inverse correlation observed between UHR and HDL-C was expected because HDL-C is mathematically incorporated into the denominator of the UHR formula. Therefore, this finding should not be interpreted as evidence of an independent biological association but rather as an inherent mathematical property of the index.

Among patients without CAD, UHR demonstrated significant positive correlations with triglycerides, TG/HDL, and TC/HDL, whereas these associations were not observed in patients with CAD. One possible explanation is that established CAD represents a more complex metabolic state in which multiple factors, including chronic vascular disease, systemic inflammation, and unmeasured clinical variables, may modify the relationship between UHR and lipid parameters. Alternatively, the absence of these correlations in the CAD group may reflect reduced statistical power due to the relatively modest sample size or residual confounding. Consequently, these subgroup findings should be regarded as exploratory and require confirmation in larger prospective studies.

The inflammatory findings of the present study were more consistent. Patients with CAD exhibited significantly higher NLR, higher neutrophil counts, lower lymphocyte counts, and higher hematocrit values than patients without CAD. Furthermore, NLR remained the only independent predictor of CAD in multivariable logistic regression analysis. These observations agree with previous studies identifying NLR as a marker of systemic inflammation and an independent predictor of cardiovascular disease in patients with diabetes [16, 17]. Together, these findings further support the important role of inflammation in the development and progression of CAD in T2DM.

Conclusion

In this cross-sectional comparative study, UHR was not significantly associated with glycemic control parameters, was not independently associated with CAD, and did not discriminate between patients with and without established CAD. Although several correlations with lipid-related indices were observed, these findings should be interpreted cautiously because the inverse association with HDL-C is mathematically inherent to the UHR calculation. In contrast, inflammatory markers, particularly NLR, demonstrated a consistent association with CAD. Overall, the present findings do not support the use of UHR as a clinically useful marker for discriminating established CAD in patients with T2DM, and larger prospective studies are required to further evaluate its clinical utility.

The present study has several limitations that should be acknowledged. First, because of its cross-sectional design, causal relationships between UHR and CAD cannot be established. Second, an a priori sample size calculation was not performed before participant recruitment. Although all eligible patients meeting the predefined inclusion and exclusion criteria during the study period were enrolled, the study may have been underpowered to detect small differences in UHR between patients with and without CAD. Therefore, the absence of statistically significant differences should be interpreted with caution, and the present findings should be considered exploratory.

Another important limitation is the lack of detailed information regarding medication use. Data on antidiabetic agents, lipid-lowering therapy, antihypertensive medications, urate-lowering drugs, SGLT2 inhibitors, diuretics, and antiplatelet therapy were not available in the study database. Because these medications may influence serum uric acid, HDL-C, and consequently UHR, adjustment for these potential confounders was not possible. Therefore, residual confounding cannot be excluded, and the observed associations should be interpreted cautiously.

Furthermore, detailed information on BMI and duration of diabetes was unavailable and could not be included in the analyses. Although age, sex, and smoking status were comparable between the study groups, unmeasured confounding may still have influenced the findings. Future prospective studies with larger sample sizes, comprehensive clinical data, and detailed medication information are required to validate the present results.

Ethical Considerations

Compliance with ethical guidelines

The study protocol was approved by the Research Ethics Committee of Mazandaran University of Medical Sciences, Sari, Iran (Code: IR.MAZUMS.REC.1405.095) and was conducted in accordance with the principles of the Declaration of Helsinki.

Funding

This research did not receive any grant from funding agencies in the public, commercial, or non-profit sectors.

Authors contribution's

Conceptualization: Abbas Khonakdar-Tarsi and Hadis Musavi; Methodology: Abbas Abdulhussein Dahash AL-Shiblawi, Abbas Khonakdar-Tarsi, and Hadis Musavi; Software: Hadis Musavi; Validation: Abbas Khonakdar-Tarsi and Hadis Musavi; Formal analysis: Hadis Musavi; Investigation: Abbas Abdulhussein Dahash AL-Shiblawi, Fatemeh Sadat Hoseini, Farimah Sadat Mousavi Kiasari, Sahar Eskandari Ghadi; Resources: Abbas Khonakdar-Tarsi and Hadis Musavi; Data curation: Abbas Abdulhussein Dahash AL-Shiblawi, Fatemeh Sadat Hoseini, Farimah Sadat Mousavi Kiasari, Sahar Eskandari Ghadi; Writing – original draft preparation: Abbas Abdulhussein Dahash AL-Shiblawi and Hadis Musavi; Writing – review & editing: Abbas Khonakdar-Tarsi and Hadis Musavi; Visualization: Hadis Musavi; Supervision: Abbas Khonakdar-Tarsi and Hadis Musavi; Project administration: Abbas Khonakdar-Tarsi.

Conflict of interest

The authors declared no conflict of interests.

Acknowledgements

The authors would like to thank the staff of Mazandaran University of Medical Sciences and the Cardiovascular Research Center for their support and assistance with this study.

References

[1] Gregg EW, Buckley J, Ali MK, Davies J, Flood D, Mehta R, et al. Improving health outcomes of people with diabetes: target setting for the WHO Global Diabetes Compact. Lancet. 2023; 401(10384):1302-12. [DOI:10.1016/S0140-6736(23)00001-6] [PMID] [PMCID]

[2] Hayden MR, Tyagi SC. Uric acid: A new look at an old risk marker for cardiovascular disease, metabolic syndrome, and type 2 diabetes mellitus: The urate redox shuttle. Nutr Metab. 2004; 1(1):10. [DOI:10.1186/1743-7075-1-10] [PMID] [PMCID]

[3] Sharaf El Din UAA, Salem MM, Abdulazim DO. Uric acid in the pathogenesis of metabolic, renal, and cardiovascular diseases: A review. J Adv Res. 2017; 8(5):537-48. [DOI:10.1016/j.jare.2016.11.004] [PMID] [PMCID]

[4] de Oliveira EP, Burini RC. High plasma uric acid concentration: Causes and consequences. Diabetol Metab Syndr. 2012; 4:12. [DOI:10.1186/1758-5996-4-12] [PMID] [PMCID]

[5] Barter P, Gotto AM, LaRosa JC, Maroni J, Szarek M, Grundy SM, et al. HDL cholesterol, very low levels of LDL cholesterol, and cardiovascular events. N Engl J Med. 2007; 357(13):1301-10. [DOI:10.1056/NEJMoa064278] [PMID]

[6] Kocak MZ, Aktas G, Erkus E, Sincer I, Atak B, Duman T. Serum uric acid to HDL-cholesterol ratio is a strong predictor of metabolic syndrome in type 2 diabetes mellitus. Rev Assoc Med Bras. 2019; 65(1):9-15. [DOI:10.1590/1806-9282.65.1.9] [PMID] [PMCID]

[7] Kosekli MA, Aktas G. Serum uric acid to HDL cholesterol ratio is associated with diabetic control in new onset type 2 diabetic population. Acta Clin Croatica. 2023; 62(2):277-82. [Link]

[8] Balci SB, Atak BM, Duman T, Ozkul FN, Aktas G. A novel marker for prediabetic conditions: Uric acid-to-HDL cholesterol ratio. Bratisl Lek Listy. 2024; 125(3):145-8. [DOI:10.4149/BLL_2023_130] [PMID]

[9] Kolahi R, Khademi R, Ghasemzadeh Rahbardar M, Shabani N, Esmaily H, Akbari N, et al. Exploring uric acid to HDL ratio as a long-term biomarker for diabetes mellitus. J Clin Lab Anal. 2026; 40(5):e70157. [DOI:10.1002/jcla.70157] [PMID] [PMCID]

[10] Ding L, Guo H, Zhang C, Jiang B, Zhang S, Zhang J, et al. Serum uric acid to high-density lipoprotein cholesterol ratio is a predictor for all-cause and cardiovascular disease mortality in patients with diabetes: Evidence from NHANES 2005-2018. Nutr Metab Cardiovasc Dis. 2024; 34(11):2480-8. [DOI:10.1016/j.numecd.2024.07.001] [PMID]

[11] Huang X, Hu L, Li J, Wang X. U-shaped association of uric acid to HDL cholesterol ratio (UHR) with ALL-cause and cardiovascular mortality in diabetic patients: NHANES 1999-2018. BMC Cardiovasc Disord. 2024; 24(1):744. [DOI:10.1186/s12872-024-04436-3] [PMID] [PMCID]

[12] Li M, Hou W, Zhang X, Hu L, Tang Z. Hyperuricemia and risk of stroke: A systematic review and meta-analysis of prospective studies. Atherosclerosis. 2014; 232(2):265-70. [DOI:10.1016/j.atherosclerosis.2013.11.051] [PMID]

[13] Yi Y, Luo Q, Chen J, Chen Z, Aydemir HA, Chen P, et al. Association between the uric acid-to-HDL-cholesterol ratio (UHR) and the risk of cardiovascular disease and dyslipidemia: A population-based study. Lipids Health Dis. 2025; 24(1):143. [DOI:10.1186/s12944-025-02551-4] [PMID] [PMCID]

[14] Sun S, Xu H, Liu L, Luan Z, Liu C, Zhi F. Association of serum uric acid-to-high-density lipoprotein cholesterol ratio (UHR) with risk of myocardial infarction among individuals with diabetes: A cross-sectional analysis using data from NHANES 2005-2020. Eur J Med Res. 2025; 30(1):554. [DOI:10.1186/s40001-025-02845-4] [PMID] [PMCID]

[15] Özmen Yıldız P. Uric acid to HDL-C ratio as a marker of coronary artery disease severity in non-ST-elevation myocardial infarction patients. Acta Cardiol Sin. 2025; 41(6):751-60. [DOI:10.6515/ACS.202511_41(6).20250714B] [PMID]

[16] Bhat T, Teli S, Rijal J, Bhat H, Raza M, Khoueiry G, et al. Neutrophil to lymphocyte ratio and cardiovascular diseases: a review. Expert Rev Cardiovasc Ther. 2013; 11(1):55-9. [DOI:10.1586/erc.12.159] [PMID]

[17] Verdoia M, Schaffer A, Barbieri L, Aimaretti G, Marino P, Sinigaglia F, et al. Impact of diabetes on neutrophil-to-lymphocyte ratio and its relationship to coronary artery disease. Diabetes Metab. 2015; 41(4):304-11. [DOI:10.1016/j.diabet.2015.01.001] [PMID]