Research Article

Relationship Between Uric Acid/HDL Ratio, Biochemical, and Hematological Parameters in Type 2 Diabetic Patients with and Without Nephropathy

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ABSTRACT

Objectives: Diabetic nephropathy (DN) is a major complication of type 2 diabetes mellitus (T2DM). This study aims to evaluate the association of the uric acid-to-high-density lipoprotein cholesterol ratio (UHR) with biochemical parameters in patients with and without DN.

Methods: In this comparative cross-sectional study, 120 patients with T2DM (60 with DN and 60 without DN) were enrolled. Clinical, biochemical, lipid, renal, inflammatory, and hematological parameters were measured. Correlations between UHR and glycemic indices were analyzed, and receiver operating characteristic (ROC) analysis was performed.

Results: Patients with DN had higher triglyceride and creatinine levels, lower high-density lipoprotein cholesterol (HDL-C) levels, and borderline higher UHR (P=0.05) than those without DN. No significant differences were found for HbA1c, fasting blood glucose, postprandial glucose, mean plasma glucose, triglyceride-glucose index, or serum uric acid. UHR was not significantly correlated with any glycemic index (all P>0.05). ROC analysis showed poor discriminatory performance of UHR for DN (AUC=0.452, P=0.475).

Conclusion: Although UHR was borderline elevated in patients with DN, it was not associated with glycemic indices and showed poor diagnostic performance. These findings suggest that UHR has limited utility as an independent biomarker of diabetic nephropathy in T2DM.

Keywords: Type 2 Diabetes Mellitus, Diabetic Nephropathy, Uric Acid-to-HDL Ratio, HbA1c, Glycemic Control

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Introduction

Type 2 diabetes mellitus (T2DM) is one of the most prevalent chronic metabolic diseases worldwide and represents a major cause of morbidity and mortality due to its long-term vascular complications. The global prevalence of diabetes continues to rise, creating a substantial burden on healthcare systems and increasing the incidence of microvascular complications, including diabetic nephropathy (DN), retinopathy, and neuropathy (1).

Diabetic nephropathy is among the most serious complications of T2DM and remains a leading cause of chronic kidney disease (CKD) and end-stage renal disease worldwide (2, 3). The pathogenesis of DN is complex and involves persistent hyperglycemia, oxidative stress, endothelial dysfunction, chronic low-grade inflammation, and metabolic abnormalities (4). Although poor glycemic control is considered a major contributor to development of renal injury, clinical observations indicate that not all patients with elevated Hemoglobin A1c (HbA1c) levels develop nephropathy, whereas some patients with relatively similar glycemic status exhibit substantial differences in renal function. These findings suggest that factors beyond glucose control may influence the development and progression of diabetic kidney disease (5).

Dyslipidemia is a common metabolic abnormality in diabetes, characterized by elevated triglyceride concentrations, reduced HDL-C, and qualitative changes in low-density lipoproteins (6). These lipid disturbances drive endothelial dysfunction, oxidative stress, and inflammatory responses, all of which are recognized contributors to the progression of CKD (7, 8). Notably, reduced HDL-C levels may compromise antioxidant and anti-inflammatory protective mechanisms, thereby facilitating renal and vascular injury (7-10).

Serum uric acid has increasingly been recognized as a potential marker of metabolic and renal dysfunction. Elevated uric acid levels have been associated with oxidative stress, endothelial damage, inflammatory pathways activation, and the progression of CKD (11, 12). Recently, the uric acid-to-HDL ratio (UHR) has garnered significant attention as a novel biomarker that integrates two biologically opposing factors. Whereas uric acid signifies pro-inflammatory and pro-oxidative activities, HDL-C confers protective anti-inflammatory and antioxidant effects. Accordingly, the UHR may offer a more comprehensive evaluation of metabolic and inflammatory status than either parameter alone (13). In this regard, several studies have demonstrated significant associations between elevated UHR and insulin resistance, metabolic syndrome, cardiovascular disease, CKD, and diabetic kidney injury (14, 15). These observations suggest that UHR may be linked to DN and could potentially serve as a simple and cost-effective biomarker for risk stratification; however, the evidence remains inconsistent and requires further validation (14, 16).

In addition to metabolic disturbances, chronic low-grade inflammation has been increasingly recognized as a key contributor to DN. Biomarkers derived from routine laboratory parameters, including the monocyte-to-HDL cholesterol ratio (MHR), have recently been proposed as indicators of systemic inflammatory burden and may provide additional information regarding the progression of diabetic kidney disease (17).

Despite growing evidence implicating UHR in renal and metabolic disorders, its relationship with glycemic control remains controversial (15,16). While some studies have reported associations between UHR and HbA1c, others suggest that UHR may primarily reflect underlying inflammatory and renal mechanisms (17,18). Accordingly, further investigation is warranted to clarify whether UHR is associated with glycemic status or represents an independent marker of DN. In this context, the present study aimed to investigate the UHR and evaluate its relationship with HbA1c and other glycemic control parameters in diabetic patients with nephropathy compared with diabetic subjects without nephropathy. Additionally, lipid profile parameters, renal function markers, and inflammatory indices were assessed to further characterize the association of UHR with metabolic and inflammatory parameters in both patient groups (with and without DN).

Methods

Study Design and Participants

This comparative cross-sectional study was conducted at the Diabetes Center of Imam Hospital, Sari, Iran. Patient enrollment, clinical data collection, and blood sampling were performed from September 2025 to May 2026. A total of 120 patients with T2DM were enrolled and divided into two groups: 60 patients with DN and 60 patients without nephropathy. The inclusion criteria comprised age between 40 and 70 years, a confirmed diagnosis of T2DM according to the American Diabetes Association criteria, a duration of diabetes of at least 5 years, and willingness to participate in the study. Exclusion criteria included congestive heart failure, advanced liver disease, acute infection, pregnancy, malignancy, autoimmune diseases, and the use of medications known to directly affect serum uric acid concentrations, including allopurinol, febuxostat, and thiazide diuretics.

Demographic and clinical information, including age, sex, duration of diabetes, smoking status, and medication history, were obtained from medical records and participant interviews. Detailed information regarding the use of some medications that may influence HDL-C or serum uric acid levels, such as

statins and sodium-glucose cotransporter-2 (SGLT2) inhibitors, was not consistently available in the medical records and therefore could not be incorporated into the statistical analyses.

The study protocol was approved by the Ethics Committee of Mazandaran University of Medical Sciences (Ethics Code: IR.MAZUMS.REC.1405.099). The study was conducted in accordance with the principles of the Declaration of Helsinki. Written informed consent was obtained from all participants prior to enrollment. Confidentiality of participant information was maintained throughout the study, and participation was entirely voluntary. Participants were free to withdraw from the study at any time without affecting their medical care.

Definition of Diabetic Nephropathy

Patients were classified as having DN based on documented nephrology evaluations and clinical records from the Diabetes Center. The diagnosis was established according to standard clinical criteria, including persistent albuminuria (>300 mg/day) or urinary albumin-to-creatinine ratio (UACR >300 mg/g), and/or estimated glomerular filtration rate (eGFR) <60 mL/min/1.73 m². Group allocation was confirmed using documented clinical diagnoses and laboratory findings from the patients' medical files. However, although eGFR and UACR data contributed to the original diagnostic and classification process, the complete numerical values were not available for inclusion in the current statistical analyses.

Data Collection and Laboratory Measurements

Approximately 10 mL of venous blood was collected from each participant after an overnight fast of 10–12 hours. Five milliliters of blood were transferred into Ethylenediaminetetraacetic acid (EDTA)-containing tubes for HbA1c measurement, while the remaining 5 mL were collected into plain tubes for serum separation. Samples were centrifuged at 3000 rpm for 15 minutes at 4°C, and serum aliquots were stored at −80°C until analysis.

Fasting blood glucose (FBG) , total cholesterol (TC), triglycerides (TG), HDL-C , low-density lipoprotein cholesterol (LDL-C), uric acid, creatinine, urea, blood urea nitrogen (BUN), alkaline phosphatase (ALP), aspartate aminotransferase (AST), alanine aminotransferase (ALT), and C-reactive protein (CRP) were measured using commercially available enzymatic kits (Pars Azmoon Co., Tehran, Iran) on an automated biochemistry analyzer (BT 3000 Plus, Biotecnica Instruments, Italy). HbA1c was determined by high-performance liquid chromatography (HPLC) using a DS5 Glycomat analyzer (Drew Scientific, UK). 2hour postprandial glucose (2hpp) was measured two hours after a standard meal. Mean plasma glucose (PG) was estimated from HbA1c using the validated equation:

Mean PG (mg/dL) = 28.7 × HbA1c (%) − 46.7

Complete blood count parameters, including white blood cell count (WBC), red blood cell count (RBC), hemoglobin (Hb), hematocrit (HCT), platelet count, neutrophil count, lymphocyte count, and monocyte count, were measured using an automated hematology analyzer (Sysmex KX-21N, Sysmex Corporation, Kobe, Japan). All laboratory analyses were performed according to the manufacturers' instructions and under internal quality-control procedures.

Calculation of Biochemical and Inflammatory Indices

The UHR was calculated as the ratio of serum uric acid to HDLC. Lipid-derived indices included the total cholesterol-to-HDL cholesterol ratio (TC/HDL), triglyceride-to-HDL cholesterol ratio (TG/HDL), and LDL cholesterol-to-HDL cholesterol ratio (LDL/HDL). Non-HDL cholesterol was calculated by subtracting HDL-C from TC.

Inflammatory indices were calculated as follows:

Monocyte-to-HDL cholesterol ratio (MHR): monocyte count/HDL-C

Neutrophil-to-lymphocyte ratio (NLR): neutrophil count/lymphocyte count

Monocyte-to-lymphocyte ratio (MLR): monocyte count/ lymphocyte count

Platelet-to-lymphocyte ratio (PLR): platelet count/ lymphocyte count

Hemoglobin-to-platelet ratio (HPR): hemoglobin concentration/platelet count

Insulin resistance was estimated using the TyG index according to the following formula:

TyG = ln [fasting TG (mg/dL) × FBG (mg/dL) / 2]

Statistical Analysis

Statistical analyses were performed using SPSS version 22.0 (IBM Corp., Armonk, NY, USA). Continuous variables were expressed as mean ± standard deviation (SD), whereas categorical variables were presented as frequencies and percentages. Normality of data distribution was assessed using the Kolmogorov–Smirnov test. Between-group comparisons were performed using the independent-samples t test for normally distributed variables and the Mann–Whitney U test for non-normally distributed variables. Comparisons of categorical variables, including sex distribution, were performed using the chi-square test. Pearson correlation analysis was employed to examine the associations between UHR and HbA1c, FBG, 2hpp, PG, and TyG index. Receiver operating characteristic (ROC) curve analysis was performed to assess the ability of UHR to discriminate between patients with DN and those without nephropathy, and the area under the curve (AUC) was calculated. A twosided Pvalue < 0.05 was considered statistically significant.

Results

Participant Characteristics

A total of 120 patients were enrolled in the study, comprising 60 patients in the DN group and 60 in the nonnephropathy group. The mean age was 62.4 ± 8.1 years in the DM group and 64.1 ± 7.6 years the group of patients without nephropathy, with no statistically significant difference between the groups (P = 0.18). Male participants constituted 54.2% of the diabetic group without nephropathy and 58.3% of the DN group (P = 0.42). All participants had been diagnosed with T2DM within the preceding five years; accordingly, diabetes duration was generally comparable across the study population. Body mass index (BMI) data were unavailable in the study database and could not, therefore, be included in the baseline comparisons.

Uric Acid-Related and Glycemic Parameters

Table 1 presents a comparison of uric acid-related and glycemic parameters between the two groups. Serum uric acid levels were nearly identical in both groups (4.80 ± 1.22 vs. 4.80 ± 1.25 mg/dL, P = 0.112). The UHR was higher in the DN group than in the group of diabetic patients without nephropathy (0.141 ± 0.066 vs. 0.124 ± 0.046), reaching borderline statistical significance (P = 0.050). No significant differences were observed in glycemic control parameters between the two groups. HbA1c was 8.31 ± 1.70% in the diabetic patients without nephropathy and 8.05 ± 1.86% in the DN group (P = 0.652). FBG levels were 168.21 ± 60.67 mg/dL and 157.49 ± 84.48 mg/dL in patients without and with nephropathy, respectively (P = 0.657). Similarly, 2hpp values were comparable between two groups of patients (P = 0.941). Mean PG was slightly higher in the diabetic patients without nephropathy than in the DN group (187.19 ± 54.07 vs. 179.02 ± 56.88 mg/dL), although the difference was not statistically significant (P = 0.432). The TyG index was also similar between the two groups (10.18 ± 0.59 vs. 10.17 ± 0.82, P = 0.671).

Lipid Profile and Lipid-Derived Indices

Table 2 compares lipid profile parameters and lipid derived indices between the DN group (patients with diabetic nephropathy) and diabetic patients without nephropathy. Total cholesterol levels were lower in the DN group than in the group of patients without nephropathy (143.32 ± 40.72 vs. 156.69 ± 48.20 mg/dL), although the difference did not reach statistical significance (P = 0.107). TG levels were significantly higher in the DN group compared with the group of patients without nephropathy (207.50 ± 134.88 vs. 180.04 ± 94.65 mg/dL, P = 0.009). VLDL levels were comparable between the two groups. HDL-C levels were significantly lower in the DN group than in the group of patients without nephropathy (36.64

Table 1. Comparison of uric acid-related and glycemic parameters between diabetic patients with and without nephropathy

Variable	Patients without nephropathy(n=60)	Patients with nephropathy (n=60)	P-value
Uric Acid Related Parameters			
Uric Acid (mg/dL)	4.80 ± 1.22	4.80 ± 1.25	0.112
UHR (Uric Acid/HDL)	0.124 ± 0.046	0.141 ± 0.066	0.05
Glycemic control parameters			
HbA1c (%)	8.31 ± 1.70	8.05 ± 1.86	0.652
FBG (mg/dL)	168.21 ± 60.67	157.49 ± 84.48	0.657
2hpp (mg/dL)	271.35 ± 90.52	270.09 ± 89.78	0.941
Mean PG (mg/dL)	187.19 ± 54.07	179.02 ± 56.88	0.432
TyG index (Insulin Resistance)	10.18 ± 0.59	10.17 ± 0.82	0.671

Abbreviations: UHR, uric acid-to-high-density lipoprotein cholesterol ratio; HbA1c, glycated hemoglobin; FBG, fasting blood glucose; 2HPP, 2-hour postprandial plasma glucose; Mean PG, mean plasma glucose; TyG, triglyceride-glucose index. Data are presented as Mean ± SD.

Table 2. Comparison of lipid profile and lipid-derived indices between diabetic patients with and without nephropathy

Variable	Patients without nephropathy (n=60)	Patients with nephropathy (n=60)	P-value
Lipid Profile			
Chol (mg/dL)	156.69 ± 48.20	143.32 ± 40.72	0.107
TG (mg/dL)	180.04 ± 94.65	207.50 ± 134.88	0.009
VLDL (mg/dL)	34.15 ± 13.61	34.33 ± 17.44	0.951
HDL (mg/dL)	40.93 ± 8.75	36.64 ± 10.25	0.04
LDL (mg/dL)	91.23 ± 38.74	77.15 ± 27.58	0.05
Lipid Ratios			
Chol/HDL ratio	3.98 ± 1.42	4.27 ± 1.68	0.483
TG/HDL ratio	4.45 ± 2.98	5.92 ± 4.12	0.104
LDL/HDL ratio	2.26 ± 1.06	2.15 ± 0.93	0.727
Non-HDL (Chol - HDL)	115.76 ± 48.18	106.68 ± 41.15	0.951

Abbreviations: TG, triglycerides; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; VLDL-C, very-low-density lipoprotein cholesterol. Data are presented as Mean ± SD.

± 10.25 vs. 40.93 ± 8.75 mg/dL, P = 0.040). LDL levels were also lower in the DN group (77.15 ± 27.58 vs. 91.23 ± 38.74 mg/dL), with a borderline significant difference (P = 0.050). No significant differences were observed in lipid ratios between the two groups. The TG/HDL ratio was higher in the DN group, but the difference was not significant (P = 0.104). Similarly, the LDL/HDL ratio did not differ significantly between groups. Non-HDL levels were slightly lower in the DN group compared with the group of patients without nephropathy (106.68 ± 41.15 vs. 115.76 ± 48.18), with no significant difference observed (P = 0.951).

Renal and Liver Function Tests, Inflammatory Markers, and Hematological Parameters

Table 3 presents a comparison of renal function parameters, liver enzymes, inflammatory markers, and hematological indices between the DN group (patients with diabetic nephropathy) and the group of diabetic patients without nephropathy. Regarding renal function parameters, creatinine levels were significantly higher in the DN group than in the group of patients without nephropathy (1.24 ± 0.39 vs. 1.09 ± 0.23 mg/dL, P = 0.030). In contrast, urea and BUN levels did not differ significantly between the groups.

Regarding liver function parameters, ALP, SGOT, and SGPT levels were higher in the DN group compared with the group of patients without nephropathy; however, none of these differences reached statistical significance.

Among inflammatory markers, CRP levels were higher in the DN group compared with the group of patients without nephropathy (5.92 ± 3.77 vs. 4.46 ± 2.79 mg/L), although the difference was not statistically significant (P = 0.089). MHR was higher in the DN group and demonstrated borderline statistical significance (0.0151 ± 0.0081 vs. 0.0115 ± 0.0049, P = 0.050). No significant differences were observed for NLR, MLR, PLR and HPR parameters.

For hematological parameters, WBC counts were slightly higher in the DN group in comparison with the group of patients without nephropathy (7.64 ± 1.93 vs. 7.29 ± 1.49 $\times 10^3/\mu L$), but the difference was not significant (P = 0.156). Similarly, RBC count, Hb level, and HCT showed no significant differences between the two groups.

Correlation Between UHR and Glycemic Parameters

Table 4 presents the correlations between UHR

Table 3. Comparison of renal function, liver enzymes, inflammatory markers, and hematological parameters between diabetic patients with and without nephropathy

Variable	Patients without nephropathy (n=60)	Patients with nephropathy (n=60)	P-value
Renal Function			
Urea (mg/dL)	37.57 ± 12.04	40.45 ± 16.12	0.278
Creatinine (mg/dL)	1.09 ± 0.23	1.24 ± 0.39	0.03
BUN (mg/dL)	17.76 ± 6.68	17.94 ± 5.54	0.876
Liver Function			
ALP (U/L)	176.37 ± 56.75	219.92 ± 62.57	0.112
SGOT (U/L)	24.45 ± 4.49	36.17 ± 34.49	0.241
SGPT (U/L)	24.40 ± 8.30	33.39 ± 28.69	0.302
Inflammatory Markers			
CRP (mg/L)	4.46 ± 2.79	5.92 ± 3.77	0.089
MHR	0.0115 ± 0.0049	0.0151 ± 0.0081	0.05
NLR	1.51 ± 0.62	1.49 ± 0.58	0.856
MLR	0.179 ± 0.073	0.183 ± 0.066	0.758
PLR	99.34 ± 37.44	99.46 ± 39.37	0.986
HPR	0.0531 ± 0.0176	0.0508 ± 0.0187	0.513
Hematological Parameters			
WBC ($\times 10^3/\mu L$)	7.29 ± 1.49	7.64 ± 1.93	0.156
RBC ($\times 10^6/\mu L$)	4.64 ± 0.66	4.51 ± 0.65	0.072
HGB (g/dL)	12.43 ± 1.27	12.21 ± 2.34	0.059
HCT (%)	38.15 ± 3.44	38.47 ± 4.95	0.684

Abbreviations: BUN, blood urea nitrogen; *ALP*, alkaline phosphatase; SGOT, serum glutamic-oxaloacetic transaminase; SGPT, serum glutamic-pyruvic transaminase; CRP, C-reactive protein; MHR, monocyte-to-HDL ratio; NLR, neutrophil-to-lymphocyte ratio; MLR, monocyte-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. Data are presented as Mean ± SD.

Table 4. Correlations between UHR and glycemic parameters in patients with and without diabetic nephropathy.

Variable	Patients with nephropathy group r (P-value)	Patients without nephropathy group r (P-value)
FBG	-0.212 (0.183)	0.066 (0.710)
2HPP	-0.217 (0.174)	0.141 (0.501)
Mean PG	-0.218 (0.188)	0.054 (0.772)
TyG Index	0.065 (0.685)	0.266 (0.129)
HbA1c	-0.208 (0.197)	0.055 (0.768)

and glycemic parameters in the both groups. In the DN group, UHR showed weak negative correlations with FBG (r = -0.212, P = 0.183), 2hpp (r = -0.217, P = 0.174), mean PG (r = -0.218, P = 0.188), and HbA1c (r = -0.208, P = 0.197). No correlation was observed between UHR and the TyG index (r = 0.065, P = 0.685). In the group of diabetic patients without nephropathy, UHR demonstrated no significant correlations with FBG, 2hpp, mean PG, TyG index, and HbA1c.

Diagnostic Importance of UHR

The ROC analysis evaluating the ability of UHR to discriminate DN is presented in Figure 1. The AUC was 0.452, indicating poor discriminative performance. The ROC analysis was not statistically significant (P = 0.475).

Discussion

The present study investigated the association between the UHR and biochemical, inflammatory, and glycemic parameters in patients with T2DM, both with and without nephropathy. The principal findings revealed that patients with DN had significantly higher triglyceride, creatinine, and MHR levels, along with significantly lower HDLC levels, and borderline lower LDL levels, compared with the group of patients without nephropathy. Additionally, the UHR was elevated in the DN group; however, this difference reached only borderline statistical significance (P = 0.050). No significant differences were observed in HbA1c or other glycemic parameters, and no significant correlations were identified between UHR and HbA1c, FBG, 2hpp, PG, and the TyG index.

One of the notable findings of the present study was the tendency toward higher UHR values in patients with DN, despite comparable serum uric acid levels between groups. The UHR has recently garnered attention as a composite biomarker that reflects the balance between the potentially deleterious effects of uric acid and the protective properties of HDLC. Elevated uric acid has been linked to oxidative stress, endothelial dysfunction, inflammatory pathways activation, and progression of renal injury, whereas HDL-C exerts antioxidant, anti-inflammatory, and vasculoprotective effects. Consequently, an increased UHR may reflect a more unfavorable metabolic and inflammatory milieu associated with renal impairment (18-21). Several previous studies have reported positive associations between elevated UHR and diabetic kidney disease. For instance, Aktas et al. suggested that UHR may be associated with renal involvement in patients with T2DM, while Xuan et al. reported associations between higher UHR values and diabetic complications (14, 15). Nevertheless, the findings of the present study warrant cautious interpretation. Although UHR was higher in patients with DN, the observed difference was only of borderline statistical significance, thereby providing limited evidence for a clinically meaningful association. Therefore, our findings provide only limited support for a relationship between UHR and diabetic nephropathy and do not confirm UHR as an independent diagnostic marker.

An important observation was the poor diagnostic performance of UHR in the ROC analysis. The area under the curve (AUC) was 0.452 and the analysis did not reach statistical significance (P = 0.475). Although

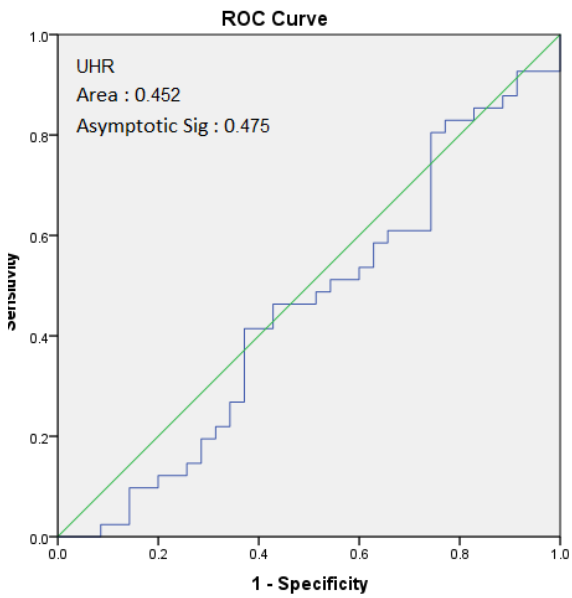


Figure 1. ROC curve showing the ability of the UHR to discriminate diabetic nephropathy among patients with type 2 diabetes mellitus.
Abbreviations: ROC, receiver operating characteristic; AUC, area under the curve; UHR, uric acid-to-high-density lipoprotein cholesterol ratio.

an AUC below 0.5 may suggest inverse discriminatory capacity, the lack of statistical significance indicates that this finding should be interpreted with caution, as it may reflect random variation rather than a true inverse association. Moreover, the non-significant ROC curve does not support a biologically meaningful inverse relationship between UHR and diabetic nephropathy. This result contrasts from several previously published studies and may be attributable to methodological and population related factors. The relatively modest sample size, the borderline difference in UHR between groups, differences in patient characteristics, and residual confounding may all have contributed to the observed findings. Furthermore, although nephropathy classification was based on documented clinical diagnoses incorporating UACR and eGFR assessments, complete numerical UACR and eGFR data were unavailable for inclusion in the statistical analyses. Therefore, larger studies with comprehensive renal phenotyping are warranted to clarify the diagnostic utility of UHR in diabetic nephropathy (22, 23).

Despite the study emphasis on glycemic control, no significant association was observed between UHR and HbA1c or other glycemic indices. Moreover, glycemic parameters were comparable between the two study groups. These findings suggest that the modest elevation of UHR observed in patients with nephropathy may be more closely related to inflammatory, lipid-related, or renal mechanisms than to glycemic status per se. Although chronic hyperglycemia remains a major contributor to diabetic microvascular complications, increasing evidence indicates that oxidative stress, inflammation, endothelial dysfunction, and lipid abnormalities also play critical roles in the development and progression of diabetic kidney disease (5, 18, 19, 24). The absence of significant correlations between UHR and glycemic indices in the present study supports the possibility that UHR reflects biological processes distinct from glycemic control.

The lipid profile findings further underscore the contribution of metabolic disturbances to diabetic nephropathy. Patients with DN demonstrated significantly higher triglyceride and lower HDL-C levels than diabetic patients without nephropathy. Diabetic dyslipidemia has been implicated in glomerular injury, mesangial expansion, endothelial dysfunction, and progression of CKD (7, 8). Reduced HDL-C may compromise antioxidant and anti-inflammatory defenses, whereas elevated TG may promote lipid accumulation and inflammatory activation within renal tissues. These mechanisms may contribute both to renal dysfunction and to elevated UHR values.

Assessment of renal function markers revealed significantly higher serum creatinine levels in patients with DN, consistent with impaired renal function. Although serum urea and BUN did not differ significantly between two groups, elevated creatinine supports the clinical classification of nephropathy. Previous studies have reported the associations between elevated UHR and impaired renal function; however, the poor discriminatory performance observed in the present study suggests that UHR should not be considered a reliable standalone marker for identifying diabetic nephropathy (14, 15).

Inflammatory markers were also evaluated in this study. MHR was higher in the DN group and demonstrated borderline statistical significance, whereas CRP, NLR, MLR, PLR, and HPR did not differ significantly between two groups. MHR has been proposed as a marker of chronic low-grade inflammation and has been associated with cardiovascular and renal disorders (25). The observed increase in MHR may indicate enhanced inflammatory activity among patients with nephropathy, although the borderline statistical significance warrants cautious interpretation and further investigation.

Liver function parameters and hematological indices were included to provide a broader evaluation of systemic biochemical and hematological status and to explore potential associations with diabetic nephropathy. No significant differences were observed between groups for these parameters, suggesting that they were unlikely to be major contributors to the observed differences in UHR or nephropathy status in the present study (26, 27).

Potential confounding factors merit consideration when interpreting these findings. Age and sex distribution were comparable between the study groups, and all participants had been diagnosed with T2DM within the preceding five years, suggesting broadly comparable diabetes duration across the study population. However, several factors known to influence serum uric acid and HDLC concentrations could not be comprehensively evaluated. In particular, detailed information on medications that could affect these parameters such as statins and sodium-glucose cotransporter-2 (SGLT2) inhibitors, was not consistently available. Consequently, residual confounding cannot be ruled out and may have influenced the observed associations.

The present study has several limitations. First, its cross-sectional design precludes causal inference regarding the observed associations. Second, the sample size was relatively modest and may have limited statistical power. Third, although diabetic nephropathy classification was based on documented clinical diagnoses incorporating UACR and eGFR assessments, complete numerical UACR and eGFR data were unavailable for inclusion in the present analyses. Fourth, although age, sex distribution, and the broad duration of diabetes were generally comparable between study groups, detailed information regarding medications that may influence HDL-C or serum uric acid levels, including statins and SGLT2 inhibitors, was not consistently available. Therefore, residual confounding cannot be excluded. Finally, this was a single-center study, which may limit

the generalizability of the findings. Future multicenter studies with larger sample sizes, comprehensive renal assessments, and adjustment for potential confounding variables are warranted to better define the clinical utility of UHR in diabetic nephropathy.

Conclusion

Patients with diabetic nephropathy demonstrated higher triglyceride, creatinine, MHR, and UHR values along with lower HDL-C concentrations compared with diabetic patients without nephropathy. However, the elevation in UHR attained only borderline statistical significance and showed no significant association with HbA1c or other glycemic control parameters. Furthermore, UHR exhibited limited discriminatory performance in ROC analysis and failed to reliably distinguish patients with nephropathy from those without nephropathy in the present study. These findings suggest that UHR may reflect metabolic, inflammatory, and renal alterations associated with diabetic nephropathy; however, the current evidence does not support its use as an independent diagnostic or predictive biomarker. Therefore, the present findings should be interpreted with caution and considered exploratory. Further studies with larger sample sizes, comprehensive assessment of renal function, and adjustment for potential confounding factors are required to elucidate the clinical significance and potential utility of UHR in diabetic kidney disease.

Conflict of Interest

The authors declare that they have no conflict of interest.

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