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Associations of hs-CRP and Interleukin-6 with Diabetic Nephropathy in Patients with Type 2 Diabetes Mellitus: A Cross-Sectional Study from Uzbekistan

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Abstract

Diabetic nephropathy is a major microvascular complication of type 2 diabetes mellitus (T2DM) and a leading cause of chronic kidney disease worldwide. Chronic low-grade inflammation may contribute to its development and progression; however, data from Central Asia are limited. This study evaluated the associations of high-sensitivity C-reactive protein (hs-CRP) and interleukin-6 (IL-6) with diabetic nephropathy among patients with T2DM in Uzbekistan.

Methods: A cross-sectional study included 227 patients with T2DM, comprising 95 patients without complications and 132 patients with diabetic nephropathy. Demographic, clinical, and laboratory data were collected. Group comparisons were performed using the Mann–Whitney U test for continuous variables and the Chi-square test for categorical variables. Multivariable logistic regression analyses, Spearman correlation, ROC curve analyses were conducted. Statistical significance was defined as $p < 0.05$.

Results: Patients with diabetic nephropathy were older, had a longer duration of diabetes, and more frequently had hypertension. Hs-CRP and IL-6 levels were significantly higher in patients with diabetic nephropathy than in those without complications (hs-CRP: 7.50 [5.40–8.60] vs. 4.54 [3.40–6.38] mg/L, $p < 0.001$; IL-6: 13.30 [11.28–16.20] vs. 8.40 [5.55–10.60] pg/mL, $p < 0.001$). In the fully adjusted Model 4, both hs-CRP (AOR 1.28, 95% CI 1.07–1.54) and IL-6 (AOR 1.50, 95% CI 1.31–1.72) remained independently associated with diabetic nephropathy.

Conclusion: Elevated hs-CRP and IL-6 levels were independently associated with diabetic nephropathy among patients with T2DM in Uzbekistan. Longer diabetes duration, hypertension, and higher fasting plasma glucose levels were also independently associated with diabetic nephropathy. These findings support a role for chronic low-grade inflammation in diabetic nephropathy and suggest that hs-CRP and IL-6 may be useful biomarkers for identifying patients at increased risk of diabetic kidney complications.

Background

Type 2 diabetes mellitus (T2DM) is a major global public health challenge. In 2020, 460–462 million individuals—around 6% of the world's population—were living with diabetes [1]. Projections from the Global Burden of Disease Study (GBD) indicate that this prevalence may rise to 10% by 2050 [2]. A key concern in T2DM is that inadequate glycaemic control and poorly managed risk factors contribute to the development of both microvascular and macrovascular complications [3].

Microvascular complications, including diabetic nephropathy, neuropathy, and retinopathy, often emerge early in the disease course [4]. Among these, diabetic nephropathy is one of the most serious, as it can progress to chronic kidney disease and substantially impair patients' quality of life while increasing treatment burden [5]. Although prevalence varies across regions, millions of individuals worldwide are affected [14]. In Central Asia, diabetic nephropathy develops in approximately 30–40% of patients with diabetes [6].

Both non-modifiable and modifiable risk factors influence the development of diabetic nephropathy. Non-modifiable factors include age and duration of diabetes, with higher risk observed in older individuals and those with long-standing disease [9–11]. Modifiable factors—such as hypertension, obesity, poor glycaemic control, physical inactivity, and unhealthy dietary patterns—also play a critical role in disease progression [12–18].

T2DM also represents a growing health burden in Uzbekistan, where approximately 6–7% of the adult population is affected [7]. Recent data indicate a marked increase in the incidence of chronic kidney disease and related mortality associated with diabetic nephropathy [8].

Emerging evidence suggests that chronic low-grade inflammation plays a significant role in the pathogenesis of diabetic nephropathy. High-sensitivity C-reactive protein (hs-CRP), a widely studied inflammatory biomarker, has been associated with an increased risk of diabetic complications, including diabetic nephropathy [19–21]. Moreover, increasing evidence indicates that elevated interleukin-6 (IL-6) levels are associated with the occurrence and progression of diabetic complications, particularly diabetic nephropathy [37].

Despite the growing burden of diabetes and its complications, evidence regarding the association of inflammatory biomarkers, particularly hs-CRP and IL-6, with diabetic nephropathy in the Uzbek population remains limited. Therefore, the present study aimed to investigate the associations of hs-CRP and IL-6 with diabetic nephropathy among patients with T2DM in Uzbekistan.

Materials and Methods

Study location and design

This cross-sectional study was conducted between the Institute of Immunology and Human Genomics of the Academy of Sciences of the Republic of Uzbekistan and Samarkand State Medical University.

Study population and data collection.

A total of 227 patients with (T2DM) were included in this cross-sectional study, comprising 95 patients without microvascular complications and 132 patients with diabetic nephropathy. Clinical, demographic, and risk factor data were collected between January 20, 2026, and March 1, 2026, at the Samarkand Branch of the Republican Specialised Scientific and Practical Medical Centre of Endocrinology.

Data on age, sex, hypertension, smoking status, body mass index (BMI), HbA1c, fasting plasma glucose (FPG), duration of diabetes, estimated glomerular filtration rate (eGFR), and urinary albumin-to-creatinine ratio (UACR) were obtained from medical records. Blood samples were collected for the measurement of high-sensitivity C-reactive protein (hs-CRP) and interleukin-6 (IL-6) for research purposes.

All study participants were diagnosed with T2DM in accordance with national clinical standards, developed on the World Health Organisation and American Diabetes Association recommendations [23].

T2DM was defined by the presence of at least one of the following criteria: fasting plasma glucose (FPG) ≥ 7.0 mmol/L, 2-hour plasma glucose ≥ 11.1 mmol/L during an oral glucose tolerance test (OGTT), glycated haemoglobin (HbA1c) ≥ 6.5%, or random plasma glucose ≥ 11.1 mmol/L in the presence of classic symptoms (polydipsia, polyuria, and unexplained weight loss) [22]. Patients with diabetic nephropathy were identified based on a documented clinical diagnosis in their medical records. They were confirmed using indicators of renal function and albuminuria, including eGFR and UACR, according to the National Clinical Protocols for the Diagnosis and Management of Diabetic Nephropathy issued by the Ministry of Health of the Republic of Uzbekistan [24]. Serum creatinine was used to calculate eGFR, while UACR was used to assess albuminuria and support the diagnosis and staging of diabetic nephropathy. The staging of chronic kidney disease based on glomerular filtration rate and the categorisation of CKD according to albuminuria levels were performed in accordance with the National Clinical Protocols for the Diagnosis and Management of Diabetic Nephropathy and the KDIGO 2022 Clinical Practice Guideline for Diabetes Management in Chronic Kidney Disease [38].

Inclusion criteria for study participants are set as:

- -Adults aged ≥ 18 years
- -Patients, both sexes
- -Diagnosed with T2DM according to national clinical standards.
- -T2DM without complications or only with nephropathy

Exclusion criteria:

- -Age under 18 years
- -Type 1 diabetes mellitus or gestational diabetes
- -Severe or advanced-stage diabetic complications.
- -T2DM with other microvascular complications (neuropathy, retinopathy)
- - Acute infectious, inflammatory, or systemic illnesses at the time of study participation.

Study groups

Participants were divided into two groups:

- **-T2DM without complications**: patients with T2DM who had no documented microvascular complications, including diabetic nephropathy, retinopathy, or neuropathy.
- **-T2DM with diabetic nephropathy**: patients with T2DM who had a documented clinical diagnosis of diabetic nephropathy in their medical records. For this group, diabetic nephropathy was further supported by available renal assessment data, including UACR and eGFR. Patients with other documented microvascular complications were excluded from this group to ensure that the analysis focused solely on diabetic nephropathy.

Laboratory tests

Interleukin-6

Venous blood samples were collected after an overnight fast. Serum interleukin-6 (IL-6) concentrations were measured using a commercially available enzyme-linked immunosorbent assay (ELISA) kit (Interleukin-6-IFA-BEST, Vector-Best, Russia; analytical sensitivity 0.5 pg/mL, measurement range 0–300 pg/mL) according to the manufacturer's instructions.

High-sensitivity C-reactive protein

Serum high-sensitivity C-reactive protein (hs-CRP) concentrations were measured using a high-sensitivity ELISA kit (CRP-IFA-BEST High-Sensitivity, Vector-Best, Russia; analytical sensitivity: 0.05 mg/L; measurement range: 0–10 mg/L) according to the manufacturer's instructions.

Data analysis

Descriptive statistical analyses were calculated using Microsoft Excel, while inferential statistical analyses were performed using JASP (version 0.19.3.0) and JAMOVI (version 2.6.44).

Initially, all continuous variables were checked for data distribution by the Shapiro-Wilk test. If the data were normally distributed, data were presented as mean ± standard deviation (SD), and comparisons were analysed by an independent Student t test. Non-normally distributed variables, such as median (interquartile range, IQR) and compared by the Mann–Whitney U test. All categorical variables were analysed by using the chi-squared test and are shown as absolute numbers with percentages.

Next, logistic regression analysis was performed to evaluate the independent association between C-reactive protein and IL-6 with diabetic nephropathy. Four models were established: Model 1 was adjusted for age, sex, smoking status, hypertension, duration of diabetes, BMI, FPG, and HbA1c. Model 2 was additionally adjusted for hs-CRP, whereas Model 3 was additionally adjusted for IL-6. Model 4 was adjusted for all clinical, glycaemic, and inflammatory factors, including both hs-CRP and IL-6. Spearman correlation analysis was performed to evaluate the associations of hs-CRP and IL-6 with clinical and renal parameters among patients with T2DM. Correlation analysis was conducted for descriptive purposes and to explore the relationships between inflammatory biomarkers and markers of renal function.

The discriminatory ability of the four models was assessed using ROC curve analysis. AUCs with 95% confidence intervals were calculated, and pairwise comparisons between models were performed using DeLong's test and presented in supplementary table S1. Statistical significance was defined as a p-value < 0.05.

Results

Descriptive and comparison analysis

A total of 227 patients with T2DM were included, comprising 95 patients without complications and 132 patients with diabetic nephropathy, as shown in Table 1.

Table 1
Baseline characteristics of study participants

Variable	T2DM without complications (n = 95)	T2DM with diabetic nephropathy (n = 132)	p-value
Age, years	52 [42–62]	61 [52–67]	< 0.001
Sex, male, n (%)	48 (50.5%)	64 (48.5%)	0.762
Diabetes duration, years	10 [8–12]	14 [10–17]	< 0.001
Smoking, n (%)	20 (21.0%)	27 (20.5%)	0.913
Hypertension, n (%)	51 (54.2%)	104 (78.8%)	< 0.001
BMI, kg/m²	28.4 [26.4–30.0]	27.3 [24.3–30.9]	0.071
HbA1c, %	9.7 [8.9–10.2]	10.0 [8.04–10.83]	0.817
FPG, mmol/L	12.1 [10.3–13.5]	12.9 [10.5–16.0]	0.037
Hs-CRP, mg/L	4.54 [3.40–6.38]	7.50 [5.40–8.60]	< 0.001
Interleukin-6	8.40 [5.55–10.60]	13.30 [11.28–16.20]	< 0.01
Creatinine, μmol/L	85.6 [76.7–96.7]	147.5 [132.7–176.7]	< 0.001
UACR, mg/g	17.8 [14.6–25.1]	70.6 [45.6–143.0]	< 0.001
UACR category, n (%)			
A1 (< 30 mg/g)	95 (100.0%)	1 (0.8%)	
A2 (30–300 mg/g)	0 (0.0%)	126 (95.5%)	
A3 (> 300 mg/g)	0 (0.0%)	5 (3.8%)	
eGFR, mL/min/1.73 m²	86.9 [78.9–95.6]	45.6 [36.5–56.5]	< 0.001
eGFR category, n (%)			
G1 (≥ 90)	38 (40.0%)	2 (1.5%)	
G2 (60–89)	57 (60.0%)	16 (12.1%)	
G3a (45–59)	0 (0.0%)	59 (44.7%)	
G3b (30–44)	0 (0.0%)	45 (34.1%)	
G4 (15–29)	0 (0.0%)	10 (7.6%)	

Note: Continuous variables are presented as median [interquartile range] and categorical variables as n (%). P-values were calculated using the Mann–Whitney U test for continuous variables and the Chi-square test for categorical variables. Statistical significance was defined as $p < 0.05$.

Patients with diabetic nephropathy were significantly older than those without complications: 61 [52–67] years versus 52 [42–62] years, respectively ($p < 0.001$). Diabetes duration was also significantly longer in the nephropathy group: 14 [10–17] years versus 10 [8–12] years ($p < 0.001$) (Table 1, Fig. 1). The proportion of hypertension was higher among patients with diabetic nephropathy than among those without complications: 104 (78.8%) versus 51 (54.2%) ($p < 0.001$). Sex distribution, smoking status, BMI, and HbA1c did not differ significantly between the groups (Table 1).

Serum IL-6 concentrations were significantly elevated in patients with diabetic nephropathy compared with those without complications (13.30 [11.28–16.20] vs. 8.40 [5.55–10.60], $p < 0.001$) (Fig. 2B). Hs-CRP levels were also significantly higher in the nephropathy group: 7.50 [5.40–8.60] mg/L versus 4.54 [3.40–6.38] mg/L ($p < 0.001$) (Table 1, Fig. 2A).

As expected, renal markers differed significantly between groups, with higher creatinine and UACR levels and lower eGFR values among patients with diabetic nephropathy.

Association between risk factors, hs-CRP and diabetic nephropathy.

Multivariable logistic regression analyses were performed to evaluate factors associated with diabetic nephropathy among patients with T2DM.

In Model 1, after adjustment for age, sex, diabetes duration, smoking status, BMI, hypertension, HbA1c, and FPG, age (AOR = 1.035, 95% CI: 1.007–1.06, $p = 0.015$), diabetes duration (AOR = 1.27, 95% CI: 1.17–1.38, $p < 0.001$), hypertension (AOR = 2.57, 95% CI: 1.24–5.33, $p = 0.011$), and FPG (AOR = 1.16, 95% CI: 1.04–1.28, $p = 0.008$) were independently associated with increased odds of diabetic nephropathy. In contrast, sex, smoking status, BMI, and HbA1c were not significantly associated with diabetic nephropathy after adjustment for potential confounders. Among the significant predictors, diabetes duration showed the strongest association with diabetic nephropathy, indicating that each additional year of diabetes duration was associated with a 27% increase in the odds of developing nephropathy (Table 2).

Table 2
Multivariable logistic regression analysis of clinical, glycaemic, and inflammatory factors associated with diabetic nephropathy.

Variable	Model 1	Model 2	Model 3	Model 4
	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)
Age (per year)	1.035 (1.007–1.06) *	1.03 (0.998–1.06)	1.04 (1.00–1.07) *	1.03 (0.997–1.07)
Sex (male)	1.16 (0.60–2.21)	1.22 (0.60–2.46)	0.87 (0.38–1.98)	0.92 (0.39–2.15)
Duration (per year)	1.27 (1.17–1.38) ***	1.30 (1.17–1.43) ***	1.3 (1.16–1.45) ***	1.30 (1.16–1.46) ***
Smoking (yes)	1.18 (0.53–2.62)	1.43 (0.61–3.35)	1.22 (0.44–3.37)	1.45 (0.51–4.10)
BMI (kg/m²)	0.97 (0.90–1.03)	0.95 (0.89–1.02)	0.98 (0.90–1.07)	0.97 (0.89–1.06)
Hypertension (yes)	2.57 (1.24–5.33) *	2.81 (1.27–6.22) *	3.24 (1.26–8.34) *	3.17 (1.19–8.35) *
HbA1c (%)	0.98 (0.82–1.17)	1.01 (0.83–1.22)	0.88 (0.70–1.10)	0.90 (0.71–1.14)
FPG	1.16 (1.04–1.28) **	1.19 (1.06–1.33) **	1.20 (1.04–1.38) *	1.21 (1.06–1.39) **
Hs-CRP	—	1.48 (1.27–1.73) ***	—	1.28 (1.07–1.54) **
IL-6	—	—	1.56 (1.37–1.78) ***	1.50 (1.31–1.72) ***

Note: OR, odds ratio; CI, confidence interval; BMI, body mass index; hs-CRP, high-sensitivity C-reactive protein; IL-6, interleukin-6. Model 1 included age, sex, diabetes duration, smoking, BMI, hypertension, HbA1c, and FPG. Model 2 = Model 1 + hs-CRP. Model 3 = Model 1 + IL-6. Model 4 = Model 1 + hs-CRP + IL-6. *p < 0.05; **p < 0.01; ***p < 0.001.

In Model 2, after additional adjustment for hs-CRP, diabetes duration (AOR = 1.30, 95% CI: 1.17–1.43, p < 0.001), hypertension (AOR = 2.81, 95% CI: 1.27–6.22, p = 0.011), and FPG (AOR = 1.19, 95% CI: 1.06–1.33, p = 0.004) remained independently associated with increased odds of diabetic nephropathy. Furthermore, hs-CRP was independently associated with diabetic nephropathy (AOR = 1.48; 95% CI, 1.27–1.73; p < 0.001). Age, sex, smoking status, BMI, and HbA1c were not significantly associated with diabetic nephropathy after adjustment (Table 2).

In Model 3, after additional adjustment for IL-6, age (AOR = 1.04, 95% CI: 1.00–1.07, p = 0.032), diabetes duration (AOR = 1.30, 95% CI: 1.16–1.45, p < 0.001), hypertension (AOR = 3.24, 95% CI: 1.26–8.34, p = 0.015), and FPG (AOR = 1.20, 95% CI: 1.04–1.38, p = 0.010) remained independently associated with diabetic nephropathy. Moreover, IL-6 was independently associated with diabetic nephropathy (AOR =

1.56, 95% CI: 1.37–1.78, p < 0.001). Sex, smoking status, BMI, and HbA1c were not significantly associated with diabetic nephropathy in this model (Table 2).

In Model 4, as presented in Fig. 3, after simultaneous adjustment for clinical and demographic factors (age, sex, diabetes duration, smoking status, BMI, hypertension, HbA1c, and FPG) and inflammatory biomarkers (hs-CRP and IL-6), diabetes duration (AOR = 1.30, 95% CI: 1.16–1.46, p < 0.001), hypertension (AOR = 3.17, 95% CI: 1.19–8.35, p = 0.021), FPG (AOR = 1.21, 95% CI: 1.06–1.39, p = 0.007), hs-CRP (AOR = 1.28, 95% CI: 1.07–1.54, p = 0.008), and IL-6 (AOR = 1.50, 95% CI: 1.31–1.72, p < 0.001) remained independently associated with diabetic nephropathy. Age was no longer statistically significant after the inclusion of both inflammatory biomarkers (AOR = 1.03, 95% CI: 0.997–1.07, p = 0.071). Similarly, sex, smoking status, BMI, and HbA1c were not significantly associated with diabetic nephropathy. These findings suggest that both hs-CRP and IL-6 are independent inflammatory predictors of diabetic nephropathy beyond established clinical and glycaemic risk factors (Table 2, Fig. 3).

Correlation of hs-CRP and IL-6 with Clinical and Renal Parameters Among Patients with T2DM

Spearman correlation analysis demonstrated that both hs-CRP and IL-6 were significantly associated with markers of renal impairment (Supplementary Table S2). hs-CRP was positively correlated with age (ρ = 0.185, p = 0.005) and UACR (ρ = 0.287, p < 0.001), and negatively correlated with eGFR (ρ = −0.314, p < 0.001). IL-6 showed a strong positive correlation with UACR (ρ = 0.574, p < 0.001) and a strong negative correlation with eGFR (ρ = −0.516, p < 0.001) (Supplementary Table S1). Neither biomarker was significantly associated with BMI, FPG, or HbA1c. These findings suggest that inflammatory biomarkers are more strongly related to renal dysfunction than to glycaemic control, with IL-6 demonstrating stronger associations than hs-CRP

ROC Analysis of Logistic Regression Models for Predicting Diabetic Nephropathy.

ROC curve analysis demonstrated progressive improvement in model discrimination with the addition of inflammatory biomarkers. The clinical model (Model 1) showed good discriminative ability, with an AUC of 0.814 (95% CI, 0.759–0.869; p < 0.001). Incorporation of hs-CRP in Model 2 significantly improved predictive performance, increasing the AUC to 0.863 (95% CI 0.816–0.911, p < 0.001). The addition of IL-6 in Model 3 resulted in a further increase in discrimination, yielding an AUC of 0.926 (95% CI 0.890–0.961, p < 0.001). The combined model including both hs-CRP and IL-6 (Model 4) demonstrated the highest predictive accuracy, with an AUC of 0.933 (95% CI 0.900–0.966, p < 0.001) (Fig. 4).

Pairwise comparisons using DeLong's test demonstrated that Model 2 significantly outperformed Model 1 (p = 0.012), while Model 3 exhibited significantly greater discriminatory performance than both Model 1 (p < 0.001) and Model 2 (p = 0.003). Similarly, Model 4 showed significantly improved discrimination compared with Model 1 and Model 2 (both p < 0.001). However, the difference between Model 3 and Model 4 was not statistically significant (AUC difference = 0.007, p = 0.208), indicating that IL-6

contributed the majority of the incremental predictive value, whereas the additional contribution of hs-CRP beyond IL-6 was limited. Detailed pairwise ROC comparisons are presented in Supplementary Table S2.

These findings indicate that the addition of inflammatory biomarkers, particularly IL-6, substantially enhanced the ability of the model to discriminate between patients with and without diabetic nephropathy.

Discussion

In this cross-sectional study of 227 patients with T2DM in Uzbekistan, hs-CRP levels were significantly higher in patients with diabetic nephropathy than in those without microvascular complications. In addition, elevated hs-CRP was independently associated with diabetic nephropathy after adjustment for potential confounders. These findings are consistent with previous studies that have suggested a link between systemic inflammation and diabetic kidney disease [25, 26]. In addition, hs-CRP has been linked to albuminuria, a key marker of diabetic nephropathy [27]. The association between hs-CRP and diabetic nephropathy may also reflect the role of chronic low-grade inflammation in disease pathogenesis. This inflammatory state may contribute to endothelial dysfunction, oxidative stress, and renal injury, thereby promoting the development and progression of diabetic nephropathy. [28].

In our cohort, age and duration of diabetes were also associated with diabetic nephropathy. These are well-established, non-modifiable risk factors for T2DM-related complications, which highlight the importance of early diagnosis, regular screening, and timely prevention strategies [29, 30]. Likewise, hypertension showed a higher adjusted odds ratio in our study, confirming its role as a major risk factor for diabetic nephropathy [31, 32, 33]. This may be explained by elevated blood pressure increasing intraglomerular pressure, which promotes glomerular hyperfiltration, endothelial injury, and progressive albuminuria [32, 33].

Among glycaemic control parameters, FPG was significantly associated with diabetic nephropathy in our study, suggesting that higher FPG levels may contribute to renal injury in patients with T2DM [34]. In contrast to fasting plasma glucose, HbA1c was not independently associated with diabetic nephropathy in any of the multivariable models. Although HbA1c is a well-established marker of long-term glycaemic control, its predictive value may be attenuated in patients with established diabetic nephropathy. One possible explanation is treatment intensification, whereby patients with more advanced disease are more likely to receive insulin therapy and closer metabolic monitoring, resulting in improved HbA1c levels despite ongoing renal impairment [35, 36].

In our study, IL-6 was moderately positively correlated with UACR ($\rho = 0.574$, $p < 0.001$) and moderately negatively correlated with eGFR ($\rho = -0.516$, $p < 0.001$). These findings are consistent with previous studies that reported significant associations between elevated IL-6 levels

(r = 0.651, p < 0.001), increased albuminuria and reduced renal function among patients with diabetic kidney disease, further supporting the role of inflammation in disease progression [42].

In addition, IL-6 was independently associated with diabetic nephropathy after adjustment for clinical and glycaemic factors. This finding is consistent with previous studies that have identified IL-6 as a key inflammatory mediator in the development and progression of diabetic kidney disease [39, 40].

Furthermore, previous studies have reported that IL-6 remained an independent predictor of diabetic kidney disease even after adjustment for renal function parameters, including eGFR. ROC analyses in these studies demonstrated good discriminatory performance, with AUC values of approximately 0.88 and an optimal IL-6 cut-off of around 4.7 pg/mL [41]. Consistent with these findings, IL-6 was independently associated with diabetic nephropathy in our study and demonstrated substantial discriminatory ability when incorporated into predictive models. Notably, the addition of IL-6 resulted in a greater improvement in model discrimination than hs-CRP alone, while the combined model achieved the highest AUC. These findings suggest that IL-6 may provide important incremental predictive value beyond conventional clinical risk factors and support its potential utility as a biomarker associated with diabetic nephropathy among patients with T2DM in Uzbekistan.

To our knowledge, this is among the first studies to evaluate the independent and combined associations of hs-CRP and IL-6 with diabetic nephropathy in a Central Asian population, providing novel evidence from Uzbekistan

Limitation

This study has several limitations. First, the cross-sectional design precludes the establishment of causal relationships between inflammatory biomarkers and diabetic nephropathy. Second, the study was conducted at a single specialised centre, which may limit the generalisability of the findings to patients with T2DM in other regions of Uzbekistan. Third, although both hs-CRP and IL-6 were evaluated, other important inflammatory mediators were not assessed. Therefore, the inflammatory profile of diabetic nephropathy may not have been fully characterised. Future studies should investigate additional biomarkers, including tumour necrosis factor-alpha (TNF-α) and other inflammatory cytokines, to provide a more comprehensive understanding of the role of inflammation in diabetic nephropathy. In addition, information on insulin use and other antidiabetic medications was not incorporated into the multivariable models and may have influenced glycaemic parameters, particularly HbA1c.

Conclusion

In this cohort, we found that the inflammatory biomarkers IL-6 and hs-CRP were independently associated with diabetic nephropathy among patients with T2DM after adjustment for clinical, glycaemic, and other established risk factors. In addition, longer diabetes duration, hypertension, and higher FPG levels were independently associated with diabetic nephropathy. Correlation analyses further demonstrated significant associations between inflammatory biomarkers and renal function parameters,

while ROC analysis showed that the inclusion of hs-CRP and IL-6 improved the predictive performance of the models. These findings support the role of chronic low-grade inflammation in the development and progression of diabetic nephropathy and suggest that hs-CRP and IL-6 may serve as useful biomarkers for identifying patients at increased risk of diabetic kidney complications in Uzbekistan. Further prospective studies are needed to validate these findings and assess their clinical utility in risk stratification and early detection of diabetic nephropathy.

Abbreviations

BMI
Body Mass Index
CKD
Chronic Kidney Disease
Hs
CRP–High–sensitivity C–Reactive Protein
IL
6–Interleukin–6
eGFR
Estimated Glomerular Filtration Rate
FPG
Fasting Plasma Glucose
HbA1c
Glycated Haemoglobin
KDIGO
Kidney Disease Improving Global Outcomes
OGTT
Oral Glucose Tolerance Test
T2DM
Type 2 Diabetes Mellitus
U0ACR
Urinary Albumin–to–Creatinine Ratio
WHO
World Health Organisation

Declarations

Ethics approval and consent to participate

The study protocol was reviewed and approved by the Institutional Review Board of the Institute of Immunology and Human Genomics, Academy of Sciences of the Republic of Uzbekistan, in accordance with the Bioethics and Safety Act (IRB No: 2026-0001). The study was conducted in accordance with the

Declaration of Helsinki. Written informed consent was obtained from all participants before inclusion in the study.

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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Author Contribution

ON, NR, and ShZ conceptualized and designed the study. AK, JK, AQ, and US collected the data. DT, ON, and KE performed the statistical analyses. ON, MN, and NA drafted the manuscript. NR, JK, HI, and MN critically reviewed the manuscript. ON supervised the study. All authors read and approved the final manuscript.

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Data Availability

The datasets generated and/or analysed during the current study are available from the corresponding author on reasonable request.

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Figures

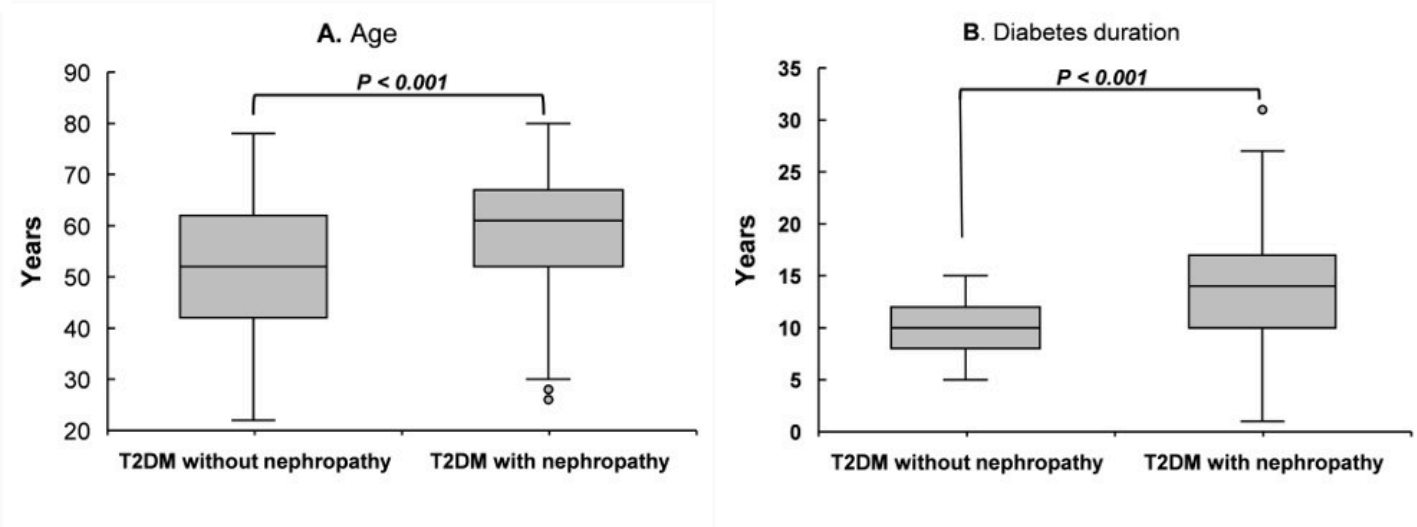


Figure 1

Boxplot comparison of (A) age and (B) diabetes duration between patients with T2DM with and without diabetic nephropathy. P-values were calculated using the Mann–Whitney U test

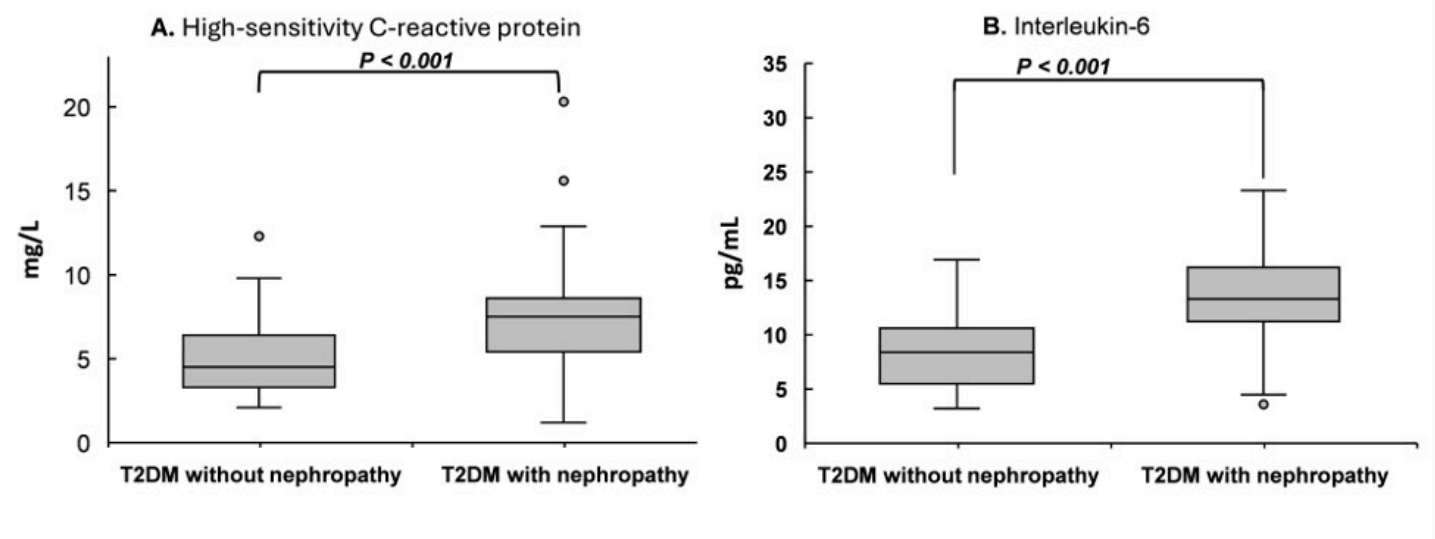


Figure 2

Boxplot comparison of high-sensitivity hs-C-reactive protein (A) and interleukin-6 (B) between patients with T2DM with and without diabetic nephropathy. P-values were calculated using the Mann–Whitney U test.

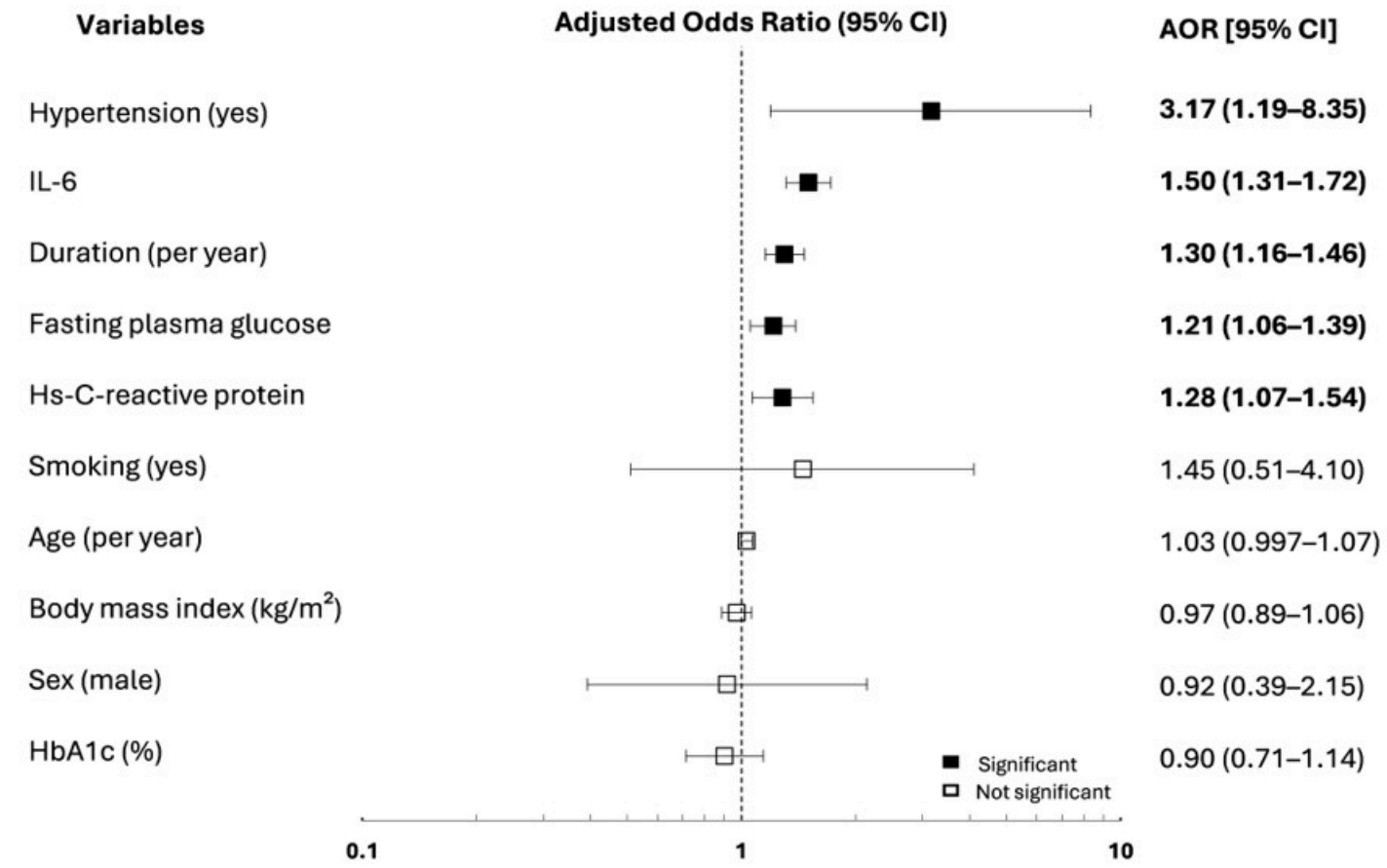


Figure 3

Forest plot of independent clinical, glycaemic, and inflammatory predictors of diabetic nephropathy among patients with T2DM (Model 4).

Note: Squares represent adjusted odds ratios (AORs), and horizontal lines indicate 95% confidence intervals (CIs). Bold AOR values indicate statistically significant predictors ($p < 0.05$). Results are derived from the fully adjusted multivariable logistic regression model (Model 4).

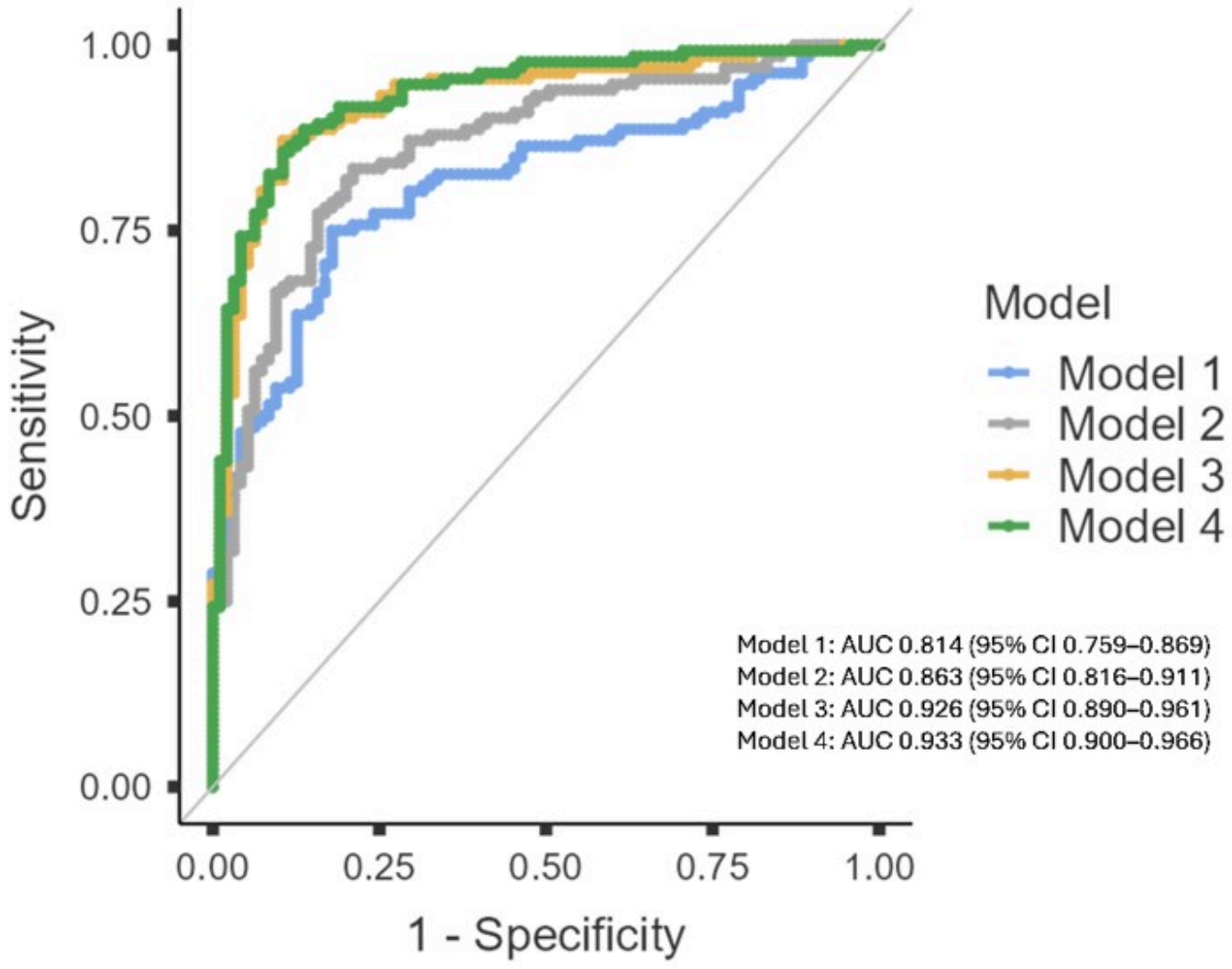


Figure 4

ROC curves comparing the predictive performance of four logistic regression models for diabetic nephropathy among patients with T2DM.

Note: Model 1 included age, sex, diabetes duration, smoking status, hypertension, BMI, HbA1c, and FPG. Model 2 included Model 1 plus hs-CRP. Model 3 included Model 1 plus IL-6. Model 4 included Model 1 plus both hs-CRP and IL-6.

Supplementary Files

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- SupplementaryMaterial.docx