International Journal of Medicine
pISSN 1468-3814 | eISSN 2667-7008
https://theinternationalmedicine.com/

Original Researcher Article *DOI: 10.61336/im/26-3-100*

Association of High-Sensitivity C-Reactive Protein with Diabetic Nephropathy in Type 2 Diabetes Mellitus: A Hospital-Based Study

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Received: 22-02-2026
Revised: 08-03-2026
Accepted: 19-03-2026
Published: 30-03-2026

Abstract

Background: : Diabetic nephropathy is a major microvascular complication of Type 2 Diabetes Mellitus (T2DM) and is increasingly recognized as an inflammatory-mediated disorder. High-sensitivity C-reactive protein (hs-CRP) is a marker of systemic inflammation and may play a role in renal injury. Aim of the study was to evaluate the correlation between serum hs-CRP levels and diabetic nephropathy in T2DM patients and to assess its utility as a predictive biomarker. ***Material and Methods:*** A hospital-based cross-sectional study was conducted among 100 subjects divided into non-diabetic controls and T2DM patients with nephropathy. Clinical evaluation, biochemical investigations, renal function tests, UACR, hs-CRP measurement, and renal ultrasound were performed. Statistical analysis included Pearson correlation, logistic regression, and multivariate regression. ***Results:*** T2DM patients with nephropathy had significantly elevated hs-CRP levels compared to controls ($p < 0.001$). hs-CRP showed strong positive correlation with albuminuria ($r = 0.71$), HbA1c ($r = 0.62$), serum creatinine ($r = 0.67$), duration of diabetes ($r = 0.54$), BMI ($r = 0.48$), and triglycerides ($r = 0.45$). Logistic regression demonstrated significantly increased odds of nephropathy with rising hs-CRP levels. Multivariate analysis confirmed hs-CRP as an independent predictor of albuminuria ($\beta = 0.42$, $p < 0.001$). ***Conclusion:*** Elevated serum hs-CRP is strongly associated with diabetic nephropathy and independently predicts renal involvement. hs-CRP may serve as a useful adjunct biomarker for early detection and risk stratification in T2DM patients.

Keywords: Type 2 Diabetes Mellitus, Diabetic Nephropathy, hs-CRP, Inflammation, Albuminuria, Renal Function.

INTRODUCTION

Type 2 Diabetes Mellitus (T2DM) is a rapidly growing global health concern characterized by chronic hyperglycemia resulting from insulin resistance and impaired insulin secretion. The International Diabetes Federation estimates that over 537 million adults were affected worldwide in 2021, with projections rising sharply in the coming decades, particularly in India, which bears a significant proportion of this burden (1). One of the most serious complications of T2DM is diabetic nephropathy, affecting approximately 20–40% of patients and representing a leading cause of end-stage renal disease globally (2,3). Clinically, diabetic nephropathy is characterized by persistent albuminuria, progressive decline in glomerular filtration rate (GFR), and increased cardiovascular risk (4). While chronic hyperglycemia has traditionally been considered the primary driver of nephropathy through mechanisms such as advanced glycation end product formation and oxidative stress, emerging evidence highlights the pivotal role of chronic low-grade inflammation in its pathogenesis (5). Inflammatory pathways involving cytokine activation, endothelial dysfunction, and renal fibrosis contribute significantly to disease progression, suggesting that biomarkers of inflammation may provide additional insights into early detection and risk stratification.

High-sensitivity C-reactive protein (hs-CRP), an acute-phase reactant produced by hepatocytes in response to interleukin-6, has gained attention as a sensitive marker of subclinical inflammation (6). Unlike conventional CRP, hs-CRP can detect low-grade inflammatory states and has been widely studied in cardiovascular diseases. Recent studies suggest that elevated hs-CRP levels are also associated with diabetic microvascular complications, including nephropathy (7). Several observational studies have demonstrated a positive correlation between hs-CRP levels and albuminuria, with higher levels observed in patients with microalbuminuria and macroalbuminuria compared to normoalbuminuric individuals (8). Furthermore, prospective cohort studies have shown that elevated hs-CRP independently predicts decline in renal function, even after adjusting for traditional risk factors such as glycemic control and blood pressure (9). Mechanistic studies also

suggest that CRP may directly contribute to renal injury by promoting endothelial dysfunction, monocyte recruitment, and fibrotic signaling pathways (10).

Despite these findings, significant research gaps remain. Most existing studies have been conducted in Western populations, and data from Indian settings are limited, despite differences in genetic susceptibility, earlier onset of diabetes, and higher prevalence of insulin resistance (11). Additionally, variability in hs-CRP cut-off values and the predominance of cross-sectional study designs limit the generalizability and causal interpretation of existing evidence. Current clinical guidelines primarily rely on albuminuria and eGFR for diagnosis and monitoring of diabetic nephropathy, and hs-CRP is not yet incorporated into routine clinical practice (12). Moreover, there is a lack of comprehensive studies evaluating the relationship between hs-CRP and multiple clinical parameters such as glycemic control, duration of diabetes, obesity, and lipid abnormalities within the Indian population.

In this context, the present study aims to evaluate serum hs-CRP levels in patients with T2DM and to assess its association with diabetic nephropathy. The study further seeks to compare hs-CRP levels between diabetic and non-diabetic individuals, examine its correlation with established risk factors, and determine its potential utility as an early biomarker for nephropathy. By generating region-specific data, this study intends to bridge existing knowledge gaps and contribute to improved understanding of the role of inflammation in diabetic kidney disease.

MATERIALS AND METHODS

Study Design and Setting

This hospital-based cross-sectional analytical study was conducted in the Department of General Medicine at Mamata General Hospital, Khammam, over a period of two years from April 2024 to February 2026. A total of 100 participants were included and selected using a simple random sampling method from both outpatient and inpatient departments. The study population was divided into two groups: Group A included patients without Type 2 Diabetes Mellitus (T2DM) and nephropathy, while Group B included patients with T2DM and nephropathy. The study aimed to compare serum high-sensitivity C-reactive protein (hs-CRP) levels between the two groups and evaluate its association with diabetic nephropathy. All laboratory investigations were performed in the central laboratory under standardized conditions.

Inclusion Criteria

- Patients aged ≥40 years
- Patients with or without Type 2 Diabetes Mellitus with nephropathy
- Patients willing to provide written informed consent

Exclusion Criteria

- Type 1 Diabetes Mellitus
- Hypertension
- Chronic alcohol consumption (>120 g/day)
- Liver or gastrointestinal diseases
- Elevated liver enzymes (>3 times normal)
- Use of hepatotoxic drugs (corticosteroids, methotrexate, amiodarone, tamoxifen)
- Chronic infections (tuberculosis, sarcoidosis)
- Hemolytic anemia or hemoglobinopathies
- Patients unwilling to participate

Study Tool

The primary study tool was biochemical assessment of serum hs-CRP levels using a high-sensitivity immunoassay method. hs-CRP values were recorded in mg/L and categorized based on standard reference ranges. Microalbuminuria estimation from spot urine samples was used to define diabetic nephropathy, along with serum creatinine levels.

Data Collection

- **Demographic details:** Age and sex
- **Clinical history:** Duration of diabetes, treatment history, risk factors
- **Anthropometry:** Height, weight, BMI, waist circumference, hip circumference, waist–hip ratio
- **Clinical examination:** Blood pressure measurement, systemic examination, fundus evaluation for diabetic retinopathy

- **Laboratory investigations:**
  - Complete blood count and ESR
  - Fasting and postprandial blood glucose

- HbA1c
- Blood urea and serum creatinine
- Lipid profile
- Serum hs-CRP
- Urine microalbumin

Statistical Analysis

Data were entered into Microsoft Excel and analyzed using SPSS software. Quantitative variables were expressed as mean ± standard deviation, while qualitative variables were presented as frequencies and percentages. Comparative analysis between groups and correlation between hs-CRP and diabetic nephropathy were assessed using appropriate statistical tests. A p-value <0.05 was considered statistically significant.

RESULTS

Table 1: Comparison of Baseline Characteristics and Risk Factors between Non-Diabetic Controls and T2DM Patients with Nephropathy

Variable	Non-Diabetic (n=50)	T2DM with Nephropathy (n=50)	p-value
Age (years)	52.4 ± 6.8	58.9 ± 7.4	**<0.001***
Male (%)	28 (56%)	32 (64%)	0.41
Female (%)	22 (44%)	18 (36%)	—
BMI (kg/m²)	24.1 ± 2.3	28.3 ± 3.1	**<0.001***
HbA1c (%)	5.2 ± 0.6	6.6 ± 1.2	**<0.001***
Hypertension (%)	10 (20%)	34 (68%)	**<0.001***
Dyslipidemia (%)	12 (24%)	30 (60%)	**0.002***
Smoking (%)	8 (16%)	18 (36%)	**0.03***
Family History (%)	14 (28%)	26 (52%)	**0.01***

The comparison of baseline characteristics revealed that patients with T2DM and nephropathy were significantly older than non-diabetic controls (58.9 ± 7.4 vs 52.4 ± 6.8 years, p<0.001). BMI and HbA1c levels were also significantly higher in the nephropathy group, indicating greater obesity and poorer glycemic control (p<0.001). A significantly higher proportion of patients with nephropathy had hypertension, dyslipidemia, smoking history, and positive family history (p<0.05), highlighting the increased burden of cardiovascular and metabolic risk factors. However, no significant difference was observed in gender distribution between the two groups (p=0.41).

Table 2: Comparison of Hematological and Inflammatory Parameters between Non-Diabetic Controls and T2DM Patients with Nephropathy

Parameter	Non-Diabetic	T2DM Nephropathy	p-value
Hemoglobin (g/dL)	13.6 ± 1.2	11.8 ± 1.4	**<0.001***
TLC (/mm³)	7200 ± 850	8940 ± 1120	**<0.001***
Platelets (lakhs/mm³)	2.6 ± 0.4	3.1 ± 0.5	**0.002***
ESR (mm/hr)	14.2 ± 4.1	32.6 ± 8.5	**<0.001***
hs-CRP (mg/L)	1.4 ± 0.6	6.8 ± 2.4	**<0.001***

Patients with T2DM and nephropathy demonstrated significant hematological and inflammatory alterations compared to non-diabetic controls. Hemoglobin levels were significantly lower (11.8 ± 1.4 vs 13.6 ± 1.2 g/dL, p<0.001), indicating anemia. In contrast, total leukocyte count and platelet count were significantly higher in the nephropathy group (p<0.001 and p=0.002 respectively), reflecting an underlying inflammatory state. ESR and hs-CRP levels were markedly elevated (p<0.001), further confirming the presence of systemic inflammation in patients with diabetic nephropathy. Overall, these findings highlight a strong association between inflammation and renal involvement in T2DM.

Table 3: Comparison of Glycemic Status and Lipid Profile between Non-Diabetic Controls and T2DM Patients with Nephropathy

Parameter	Non-Diabetic	T2DM Nephropathy	p-value
FBS (mg/dL)	92.4 ± 8.6	168.7 ± 34.5	**<0.001***
PPBS (mg/dL)	118.3 ± 12.5	242.6 ± 48.2	**<0.001***
Total Cholesterol (mg/dL)	176.4 ± 28.5	224.7 ± 36.2	**<0.001***
LDL (mg/dL)	102.3 ± 22.1	142.6 ± 30.4	**<0.001***
HDL (mg/dL)	48.5 ± 6.3	38.4 ± 5.8	**<0.001***
Triglycerides (mg/dL)	138.2 ± 24.7	210.8 ± 42.3	**<0.001***

Patients with T2DM and nephropathy exhibited significantly higher fasting and postprandial blood glucose levels compared to non-diabetic controls ($p<0.001$), indicating poor glycemic control. Lipid profile analysis revealed significantly elevated total cholesterol, LDL, and triglycerides, along with significantly reduced HDL levels in the nephropathy group ($p<0.001$). These findings indicate the presence of marked dyslipidemia and metabolic derangement in patients with diabetic nephropathy, contributing to disease progression and increased cardiovascular risk.

Table 4: Comparison of Renal Function, Urinary Findings, and Electrolyte Parameters between Non-Diabetic Controls and T2DM Patients with Nephropathy

Parameter	Non-Diabetic	T2DM Nephropathy	p-value
Blood Urea (mg/dL)	28.6 ± 6.4	52.3 ± 14.2	**<0.001***
Serum Creatinine (mg/dL)	0.9 ± 0.2	2.1 ± 0.8	**<0.001***
eGFR (mL/min/1.73m²)	98.6 ± 12.4	37.8 ± 14.6	**<0.001***
UACR (mg/g)	12.6 ± 5.8	286.4 ± 112.3	**<0.001***
Proteinuria (%)	2 (4%)	42 (84%)	**<0.001***
RBCs (%)	1 (2%)	10 (20%)	**0.01***
Casts (%)	0 (0%)	12 (24%)	**0.002***
Sodium (mEq/L)	139.2 ± 3.4	134.8 ± 5.2	**<0.001***
Potassium (mEq/L)	4.2 ± 0.4	5.1 ± 0.6	**<0.001***
Bicarbonate (mEq/L)	24.8 ± 2.1	19.6 ± 3.4	**<0.001***
Reduced Kidney Size (%)	0	18 (36%)	**<0.001***
Increased Echogenicity (%)	0	22 (44%)	**<0.001***

Patients with T2DM and nephropathy showed significantly impaired renal function compared to non-diabetic controls, with higher blood urea and serum creatinine levels and markedly reduced eGFR ($p<0.001$). Urinary parameters revealed significantly elevated UACR, higher prevalence of proteinuria, and increased presence of RBCs and casts ($p<0.05$), indicating significant renal damage. Electrolyte imbalance was also evident, with lower sodium and bicarbonate levels and higher potassium levels in the nephropathy group ($p<0.001$). Additionally, ultrasonographic findings such as reduced kidney size and increased echogenicity were significantly more common in these patients. Overall, these findings confirm advanced renal dysfunction and structural abnormalities in T2DM with nephropathy.

Table 5: Association of Serum hs-CRP with Disease Severity and Clinical Parameters in T2DM Patients with Nephropathy

Variable	Value	p-value
Normoalbuminuria	3.2 ± 1.1	—
Microalbuminuria	5.9 ± 1.8	**<0.001***
Macroalbuminuria	8.7 ± 2.5	**<0.001***
Albuminuria (r)	0.71	**<0.001***
HbA1c (r)	0.62	**<0.001***
Creatinine (r)	0.67	**<0.001***
Duration (r)	0.54	**0.002***
BMI (r)	0.48	**0.006***
Triglycerides (r)	0.45	**0.01***

Serum hs-CRP levels showed a significant progressive increase with worsening stages of albuminuria, from normoalbuminuria to macroalbuminuria ($p<0.001$), indicating a strong association with disease severity. hs-CRP also demonstrated significant positive correlations with albuminuria ($r=0.71$), HbA1c ($r=0.62$), serum creatinine ($r=0.67$), duration of diabetes ($r=0.54$), BMI ($r=0.48$), and triglycerides ($r=0.45$) ($p<0.05$). These findings suggest that elevated hs-CRP is closely linked with both metabolic derangement and progressive renal dysfunction in diabetic nephropathy.

Table 6: Multivariate Regression Analysis of Factors Associated with Diabetic Nephropathy

Variable	Effect Size	95% CI	p-value
hs-CRP (OR)	12.91	3.23 – 51.53	**<0.001***
hs-CRP (β)	0.42	—	**<0.001***
HbA1c (β)	0.31	—	**0.01***
Duration (β)	0.26	—	**0.02***
Creatinine (β)	0.35	—	**0.004***
BMI (β)	0.18	—	0.08

Regression analysis demonstrated that hs-CRP was a strong independent predictor of diabetic nephropathy, with a high odds ratio (OR 12.91, $p<0.001$). hs-CRP also showed a significant positive regression coefficient ($\beta=0.42$), indicating its

strong influence on disease severity. Other significant predictors included HbA1c (β=0.31, p=0.01), duration of diabetes (β=0.26, p=0.02), and serum creatinine (β=0.35, p=0.004). Although BMI showed a positive association (β=0.18), it was not statistically significant (p=0.08). These findings highlight inflammation, glycemic control, disease duration, and renal function as key determinants of diabetic nephropathy.

DISCUSSION

The present hospital-based cross-sectional analytical study demonstrated a strong association between systemic inflammation, assessed by serum hs-CRP, and diabetic nephropathy in patients with Type 2 Diabetes Mellitus. Patients with nephropathy exhibited higher BMI, poorer glycemic control, and greater prevalence of comorbidities. Mean hs-CRP levels were significantly elevated (6.8 ± 2.4 mg/L vs 1.4 ± 0.6 mg/L, p<0.001), with strong positive correlations with albuminuria, HbA1c, serum creatinine, duration of diabetes, BMI, and triglycerides. hs-CRP also emerged as an independent predictor of nephropathy (OR 12.91), indicating a key role of inflammation in diabetic renal injury.

Chronic hyperglycemia induces oxidative stress, endothelial dysfunction, and inflammatory cytokine release (IL-6, TNF-α), leading to increased CRP synthesis [5,10]. This inflammatory state contributes to glomerular damage and fibrosis. The strong correlation between hs-CRP and albuminuria highlights its association with early nephropathy and endothelial dysfunction.

Poor glycemic control was significantly associated with elevated hs-CRP, suggesting that hyperglycemia and inflammation act synergistically in accelerating renal damage. Similar observations have been reported in earlier studies linking HbA1c and duration of diabetes with nephropathy progression.

The study also demonstrated a significant association between hs-CRP and metabolic factors such as BMI and triglycerides, supporting the role of obesity and insulin resistance in promoting inflammation. Adipose tissue-derived cytokines further enhance CRP production, aligning with previous findings in Indian populations.

Renal parameters showed significant deterioration in the nephropathy group, including higher creatinine, UACR, and reduced eGFR. The positive correlation between hs-CRP and creatinine indicates that inflammatory burden increases with worsening renal function. The progressive rise in hs-CRP across stages of albuminuria suggests a dose-response relationship.

The findings are consistent with earlier studies. Brantsma et al. reported an association between CRP and albuminuria [13], while Takebayashi et al. linked hs-CRP with diabetic microangiopathy [14]. Mahajan et al. demonstrated elevated hs-CRP in T2DM with correlations to obesity and glycemic control [15]. Zakkerkish et al. showed that albuminuria correlates with duration of diabetes and renal dysfunction [16].

Further studies by Bashir et al. [17] and Shaheer et al. [18] confirmed significant associations between hs-CRP and microalbuminuria, along with metabolic parameters, closely resembling the present findings. Longitudinal evidence from Sinha et al. [19] demonstrated that elevated hs-CRP predicts incident nephropathy, while Tang et al. [20] showed that higher hs-CRP levels independently increase the risk of diabetic kidney disease.

Although some studies have shown variability in early stages, hs-CRP has not yet been incorporated into routine nephropathy screening [12]. However, the strong associations observed in the present study support its role as an adjunct biomarker for early risk stratification.

The study's strengths include comprehensive evaluation of inflammatory, metabolic, and renal parameters and contribution of region-specific data. However, its cross-sectional design limits causal inference, and findings may not be generalizable.

CONCLUSION

The present study demonstrates that serum hs-CRP levels are significantly elevated in patients with Type 2 Diabetes Mellitus and diabetic nephropathy and show strong associations with albuminuria, poor glycemic control, renal dysfunction, duration of diabetes, obesity, and hypertriglyceridemia. These findings highlight the role of chronic low-grade inflammation in the pathogenesis and progression of diabetic nephropathy. hs-CRP was identified as an independent predictor, suggesting its potential as an adjunct biomarker for early risk stratification and assessment of disease severity. Although current diagnosis relies on albuminuria and eGFR, hs-CRP may provide additional clinical value. Further large-scale prospective studies are required to validate its predictive role and clinical utility.

REFERENCES

1. International Diabetes Federation. IDF Diabetes Atlas. 2021.
2. Alicic RZ, Rooney MT, Tuttle KR. Diabetic kidney disease: challenges and opportunities. Kidney Int. 2017;92(3):515–27.
3. Afkarian M, et al. Clinical manifestations of diabetic kidney disease. J Am Soc Nephrol. 2016;27(2):344–52.
4. Thomas MC, et al. Diabetic kidney disease. Lancet. 2015;385(9980):2252–63.

5. Navarro-González JF, Mora-Fernández C. Inflammatory pathways in diabetic nephropathy. Nat Rev Nephrol. 2008;4(6):327–36.
6. Pepys MB, Hirschfield GM. C-reactive protein: a critical update. J Clin Invest. 2003;111(12):1805–12.
7. Pradhan AD, et al. Inflammatory biomarkers and risk of diabetes complications. JAMA. 2001;286(3):327–34.
8. Stehouwer CD, et al. Increased urinary albumin excretion and inflammatory markers. Diabetes. 2002;51(4):1157–61.
9. de Boer IH, et al. hs-CRP and risk of kidney disease progression. Clin J Am Soc Nephrol. 2011;6(3):529–36.
10. Verma S, et al. CRP promotes endothelial dysfunction. Circulation. 2002;106(8):913–9.
11. Anjana RM, et al. Diabetes epidemiology in India. Lancet Diabetes Endocrinol. 2017;5(8):585–96.
12. American Diabetes Association. Standards of medical care in diabetes. Diabetes Care. 2023;46(Suppl 1):S191–202.
13. Brantsma AH, Bakker SJ, Hillege HL, de Zeeuw D, de Jong PE, Gansevoort RT; PREVEND Study Group. Urinary albumin excretion and its relation with C-reactive protein and the metabolic syndrome in the prediction of type 2 diabetes. Diabetes Care. 2005;28(10):2525-30.
14. Takebayashi K, Suetsugu M, Matsutomo R, Wakabayashi S, Aso Y, Inukai T. Correlation of high-sensitivity C-reactive protein and plasma fibrinogen with individual complications in patients with type 2 diabetes. South Med J. 2006;99(1):23-7.
15. Mahajan A, Tabassum R, Chavali S, Dwivedi OP, Bharadwaj M, Tandon N, Bharadwaj D. High-sensitivity C-reactive protein levels and type 2 diabetes in urban North Indians. J Clin Endocrinol Metab. 2009;94(6):2123-7.
16. Zakkerkish M, Shahbazian HB, Shahbazian H, Latifi SM, Aleali AM. Albuminuria and its correlates in type 2 diabetic patients. Iran J Kidney Dis. 2013;7(4):268-76.
17. Bashir S, Shabbir I, Khan MI, Aasim M. Role of C-reactive protein as a marker for microalbuminuria in type 2 diabetics. J Ayub Med Coll Abbottabad. 2014;26(1):32-4.
18. Shaheer AK, Tharayil AK, Krishna PW, Kumar BS. A Comparative Study of High Sensitivity C-Reactive Protein and Metabolic Variables in Type 2 Diabetes Mellitus with and without Nephropathy. J Clin Diagn Res. 2017;11(9):BC01-BC04.
19. Sinha SK, Nicholas SB, Sung JH, Correa A, Rajavashisth TB, Norris KC, Lee JE. hs-CRP Is Associated With Incident Diabetic Nephropathy: Findings From the Jackson Heart Study. Diabetes Care. 2019;42(11):2083-2089.
20. Tang M, Cao H, Wei XH, Zhen Q, Liu F, Wang YF, Fan NG, Peng YD. Association Between High-Sensitivity C-Reactive Protein and Diabetic Kidney Disease in Patients With Type 2 Diabetes Mellitus. Front Endocrinol (Lausanne). 2022;13:885516.