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ORIGINAL ARTICLE

Pathological Changes in Renal Tissue in Response to Diabetes: A Prospective Study

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ABSTRACT:

Aim: The aim of this prospective study was to investigate the pathological changes in renal tissue associated with diabetes mellitus and correlate these histopathological findings with clinical and biochemical parameters to better understand the progression and severity of diabetic nephropathy. **Materials and Methods:** A total of 80 patients diagnosed with either type 1 or type 2 diabetes mellitus and suspected of having diabetic nephropathy were enrolled from a tertiary care hospital. Clinical suspicion was based on elevated urinary albumin excretion, declining eGFR, or persistent hypertension. Exclusion criteria included known non-diabetic kidney diseases, acute kidney injury, or immunosuppressive therapy. Each patient underwent clinical and laboratory evaluation, including assessment of fasting blood glucose, HbA1c, serum creatinine, lipid profile, and urine protein parameters. Renal biopsies were obtained under ultrasound guidance and analyzed via light microscopy, immunofluorescence, and electron microscopy. Histopathological grading followed the Renal Pathology Society (RPS) classification. **Results:** The study cohort had a mean age of 55.6 ± 9.8 years, with a male predominance (60%) and an average diabetes duration of 10.3 ± 5.1 years. Type 2 diabetes was predominant (82.5%), and hypertension was prevalent in 77.5% of patients. Laboratory evaluations showed poor glycemic control (mean HbA1c 8.4 ± 1.2%), elevated serum creatinine (2.1 ± 0.9 mg/dL), and reduced eGFR (54.3 ± 18.7 mL/min/1.73 m²). Renal biopsies revealed GBM thickening in 90%, mesangial expansion in 81.3%, nodular glomerulosclerosis in 60%, arteriolar hyalinosis in 66.3%, and interstitial fibrosis in 62.5%. According to the RPS classification, 35% of patients were in Class III and 10% in Class IV, indicating advanced disease. Multiple regression analysis identified age, duration of diabetes, HbA1c, systolic blood pressure, proteinuria, and mesangial expansion as significant predictors of reduced eGFR ($R^2 = 0.62$, $p < 0.001$). **Conclusion:** This study demonstrates a high burden of histopathological damage among diabetic patients with suspected nephropathy, with most presenting in advanced stages. Key clinical parameters such as poor glycemic control, longer disease duration, and hypertension strongly correlated with worsening renal pathology and declining eGFR. These findings reinforce the necessity for early detection, tight glycemic control, and aggressive management of hypertension. Renal biopsy remains crucial for accurate diagnosis and prognosis in diabetic kidney disease.

Keywords: Diabetic nephropathy, Renal biopsy, Mesangial expansion, Glomerulosclerosis, eGFR

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INTRODUCTION

Diabetes mellitus, a chronic metabolic disorder marked by persistent hyperglycemia, has emerged as one of the most significant global health challenges of the 21st century. Among its many complications, diabetic nephropathy stands as a major cause of morbidity and mortality, as well as the leading cause of end-stage renal disease (ESRD) worldwide. The kidneys, vital organs responsible for maintaining fluid and electrolyte balance, filtering metabolic waste, and regulating blood pressure, are especially vulnerable to the long-term effects of elevated blood glucose. Chronic exposure to hyperglycemia induces a cascade of biochemical and structural alterations within renal tissues, culminating in progressive kidney dysfunction.[1,2]

Diabetic nephropathy does not manifest suddenly; rather, it develops gradually over years, moving through a series of pathological changes. The initial stages are often clinically silent, characterized by subtle histological and molecular transformations that precede functional impairment. With time, these early changes give rise to more pronounced structural damage and clinical symptoms, including microalbuminuria, reduced glomerular filtration rate (GFR), and ultimately, renal failure. Understanding the progression of these pathological alterations is critical not only for early diagnosis but also for the development of effective interventions aimed at halting or reversing kidney damage.[3]

The hallmark features of diabetic renal pathology involve both the glomerular and tubular compartments of the nephron, along with the interstitial and vascular components. At the glomerular level, thickening of the basement membrane, mesangial expansion, and podocyte injury are among the earliest observable changes. These alterations disrupt the filtration barrier, allowing proteins to leak into the urine—a clinical indicator of declining renal function. In parallel, the tubulointerstitial compartment undergoes its own set of changes, including tubular atrophy, interstitial fibrosis, and inflammatory cell infiltration.

These combined pathologies contribute to the progressive loss of nephron units and worsening renal function over time.[4]

One of the defining features of diabetic renal pathology is the excessive accumulation of extracellular matrix proteins, leading to glomerulosclerosis and interstitial fibrosis. Hyperglycemia induces oxidative stress, activates the renin-angiotensin-aldosterone system (RAAS), and upregulates various profibrotic cytokines, all of which contribute to tissue remodeling and scarring. Moreover, chronic inflammation—marked by the activation of immune cells and release of pro-inflammatory mediators—plays a central role in driving kidney injury and fibrosis. The interplay between metabolic disturbances, hemodynamic stress, and inflammatory signaling defines the complex pathophysiological landscape of diabetic kidney disease.[5,6]

Despite significant advances in our understanding of diabetic nephropathy, many aspects of its pathogenesis remain unclear. While much of the existing knowledge is derived from cross-sectional studies and animal models, there is a growing need for longitudinal investigations that track pathological changes in human renal tissue over time. Prospective studies provide a unique opportunity to observe the temporal evolution of diabetic kidney disease, identify early biomarkers of injury, and evaluate the impact of therapeutic interventions in real time. Such studies are essential for developing predictive models of disease progression and tailoring personalized treatment strategies.[7,8]

MATERIALS AND METHODS

This prospective study was conducted on a cohort of 80 patients diagnosed with diabetes mellitus at tertiary care hospital. Inclusion criteria comprised adult patients aged 18 years or older, with either type 1 or type 2 diabetes mellitus, and clinical suspicion of diabetic nephropathy based on elevated urinary albumin excretion, declining estimated glomerular filtration rate (eGFR), or persistent hypertension. Patients with known non-diabetic kidney disease, acute kidney injury, or those on immunosuppressive therapy were excluded.

All enrolled patients underwent comprehensive clinical evaluation, including detailed medical history, physical examination, and laboratory investigations. Blood samples were collected for analysis of fasting blood glucose, HbA1c, serum creatinine, blood urea nitrogen, lipid profile, and electrolyte levels. Urine samples were analyzed for albumin-to-creatinine ratio (ACR), proteinuria, and urinary sediment examination. Renal function was assessed using eGFR, calculated by the CKD-EPI formula.

Renal tissue samples were obtained via ultrasound-guided percutaneous kidney biopsy under local anesthesia, after obtaining informed consent from all participants. Biopsy specimens were processed for light microscopy, immunofluorescence, and electron microscopy. Histological examination focused on identifying characteristic diabetic nephropathy changes, including glomerular basement membrane thickening, mesangial expansion, nodular glomerulosclerosis (Kimmelstiel–Wilson nodules), arteriolar hyalinosis, and interstitial fibrosis. The severity of pathological changes was graded using established classification systems such as the Renal Pathology Society's classification of diabetic nephropathy.

All data were recorded and statistically analyzed using SPSS version 21.0. Continuous variables were expressed as mean ± standard deviation, and categorical variables as frequencies and percentages. Associations between clinical parameters and histopathological findings were assessed using appropriate statistical tests, including t-tests, chi-square tests, and correlation analysis, with a p-value of <0.05 considered statistically significant. Ethical approval for the study was obtained from the institutional review board, and all procedures were conducted in accordance with the Declaration of Helsinki.

RESULTS

Table 1: Baseline Demographic and Clinical Characteristics

The study included 80 diabetic patients, with a mean age of 55.6 ± 9.8 years, indicating a middle-aged population. There was a slight male predominance, with 60% males (48 patients) and 40% females (32 patients). The average duration of diabetes was 10.3 ± 5.1 years, suggesting long-standing disease in most patients. A majority, 82.5%, had Type 2 diabetes mellitus, while only 17.5% had Type 1 diabetes, reflecting the higher prevalence of Type 2 in the general population. Hypertension was highly prevalent, seen in 77.5% of the cohort, which is consistent with its frequent co-existence with diabetic nephropathy. The mean BMI was 27.4 ± 3.5 kg/m², indicating that most patients were overweight. Smoking history was reported by 22.5% of the participants, a known risk factor for accelerated microvascular damage, including renal complications.

Table 2: Laboratory Parameters of Study Participants

The laboratory analysis showed poor glycemic control among the participants, with a mean fasting blood glucose of 162.5 ± 38.6 mg/dL and an average HbA1c of 8.4 ± 1.2%, both exceeding optimal target values. This persistent hyperglycemia likely contributed to progressive renal injury. The mean serum creatinine level was 2.1 ± 0.9 mg/dL, and the mean eGFR was 54.3 ± 18.7 mL/min/1.73 m², indicating varying degrees of renal impairment, with many patients likely in CKD stages 3–4. Blood urea nitrogen averaged 32.7 ± 10.4 mg/dL, further supporting the presence of renal dysfunction. A significant majority,

82.5%, had albumin-to-creatinine ratios (ACR) >300 mg/g, indicating macroalbuminuria, and 73.8% had proteinuria exceeding 1g/day, reinforcing the clinical suspicion of advanced diabetic nephropathy.

Table 3: Histopathological Findings in Renal Biopsy

Histological analysis of renal biopsy specimens revealed that GBM thickening was the most common finding, observed in 90% of patients, a hallmark of early diabetic nephropathy. Mesangial expansion was found in 81.3%, while nodular glomerulosclerosis (Kimmelstiel–Wilson nodules)—a classic lesion of diabetic kidney disease—was present in 60%. Arteriolar hyalinosis, reflecting vascular injury, was seen in 66.3% of cases. Additionally, interstitial fibrosis and tubular atrophy (IFTA) were noted in 62.5%, suggesting chronicity and irreversible damage. Global glomerulosclerosis, indicative of complete glomerular loss, was present in 42.5% of patients, reflecting significant disease burden.

Table 4: Classification of Diabetic Nephropathy Based on RPS System

Using the Renal Pathology Society classification, patients were stratified by severity of histopathological changes. Only 10% were classified as Class I (GBM thickening only), while 18.8% had Class IIa and 26.3% had Class IIb, denoting progressive mesangial expansion. A large proportion, 35%, fell into Class III, characterized by nodular glomerulosclerosis, and 10% reached Class IV, indicating advanced global glomerulosclerosis. These findings suggest that most patients presented at a relatively advanced histological stage of diabetic nephropathy, consistent with the high levels of proteinuria and reduced eGFR observed clinically.

Table 5: Multiple Linear Regression Analysis for Predictors of eGFR

The multiple regression analysis identified several significant predictors of reduced eGFR. Age was inversely associated with eGFR ($\beta = -0.42$, $p = 0.016$), indicating that older patients had poorer renal function. Duration of diabetes also showed a negative correlation ($\beta = -0.38$, $p = 0.008$), underscoring the cumulative renal damage over time. Poor glycemic control, as reflected by HbA1c ($\beta = -0.45$, $p = 0.021$), was another significant predictor of declining eGFR. Systolic blood pressure was negatively associated with eGFR ($\beta = -0.33$, $p = 0.007$), suggesting that hypertension contributes to renal deterioration. The presence of proteinuria ($\beta = -0.51$, $p = 0.023$) and mesangial expansion on biopsy ($\beta = -0.47$, $p = 0.020$) were also significantly associated with lower eGFR, highlighting their role in renal function decline. The model had an R^2 value of 0.62, indicating that these variables explained 62% of the variability in eGFR, with the model being statistically significant ($p< 0.001$).

Table 1: Baseline Demographic and Clinical Characteristics (n = 80)

Parameter	Value
Age (mean ± SD, years)	55.6 ± 9.8
Gender (Male/Female)	48 (60%) / 32 (40%)
Duration of Diabetes (years)	10.3 ± 5.1
Type of Diabetes	Type 1: 14 (17.5%), Type 2: 66 (82.5%)
Hypertension	62 (77.5%)
BMI (kg/m²)	27.4 ± 3.5
Smoking History	18 (22.5%)

Table 2: Laboratory Parameters of Study Participants

Laboratory Parameter	Mean ± SD / n (%)
Fasting Blood Glucose (mg/dL)	162.5 ± 38.6
HbA1c (%)	8.4 ± 1.2
Serum Creatinine (mg/dL)	2.1 ± 0.9
eGFR (mL/min/1.73 m²)	54.3 ± 18.7
Blood Urea Nitrogen (mg/dL)	32.7 ± 10.4
ACR > 300 mg/g	66 (82.5%)
Proteinuria (>1g/day)	59 (73.8%)

Table 3: Histopathological Findings in Renal Biopsy (n = 80)

Histopathological Feature	Frequency (%)
GBM Thickening	72 (90%)
Mesangial Expansion	65 (81.3%)
Nodular Glomerulosclerosis (K-W Nodules)	48 (60%)
Arteriolar Hyalinosis	53 (66.3%)
Interstitial Fibrosis and Tubular Atrophy (IFTA)	50 (62.5%)
Global Glomerulosclerosis	34 (42.5%)

Table 4: Classification of Diabetic Nephropathy Based on Renal Pathology Society (RPS) System

Class (RPS Classification)	Frequency (%)
Class I (GBM thickening only)	8 (10%)
Class IIa (Mild mesangial expansion)	15 (18.8%)
Class IIb (Severe mesangial expansion)	21 (26.3%)
Class III (Nodular sclerosis)	28 (35%)
Class IV (Advanced glomerulosclerosis)	8 (10%)

Table 5: Multiple Linear Regression Analysis for Predictors of eGFR

Independent Variable	β Coefficient	Standard Error	t-value	p-value
Age (years)	-0.42	0.17	-2.47	0.016*
Duration of Diabetes (years)	-0.38	0.14	-2.71	0.008*
HbA1c (%)	-0.45	0.19	-2.37	0.021*
Systolic BP (mmHg)	-0.33	0.12	-2.75	0.007*
Presence of Proteinuria (Yes=1)	-0.51	0.22	-2.32	0.023*
Mesangial Expansion (Yes=1)	-0.47	0.20	-2.35	0.020*

DISCUSSION

In the present study, the mean age of participants was 55.6 ± 9.8 years, with a predominance of Type 2 diabetes (82.5%) and hypertension (77.5%), which aligns with the typical demographic of diabetic nephropathy (DN). Similar demographic trends were reported by *Parving et al.* (2006), who observed that DN predominantly affected middle-aged individuals with long-standing Type 2 diabetes and comorbid hypertension. Our findings also showed a male predominance (60%), supporting the gender trend seen in that study. The high prevalence of hypertension among participants emphasizes its role as a co-factor in renal damage progression.[9]

The laboratory parameters revealed poor glycemic control (mean HbA1c = 8.4 ± 1.2%) and significant renal impairment (mean eGFR = 54.3 ± 18.7 mL/min/1.73 m²). These values are consistent with those reported by *Mogensen et al.* (2003), who found that patients with HbA1c >8% were more likely to exhibit rapid decline in renal function and higher albuminuria levels. In our study, 82.5% had ACR >300 mg/g and 73.8% had proteinuria >1g/day, further confirming the association between hyperglycemia and nephropathy severity. This parallels findings from the referenced study, underscoring the need for tight glycemic control to prevent or slow DN progression.[10]

Histopathological examination revealed glomerular basement membrane (GBM) thickening in 90% of patients and mesangial expansion in 81.3%, both of which are classic pathological features of DN. Notably, nodular glomerulosclerosis was present in 60% of cases. These observations are in concordance with findings by *Fioretto et al.* (1995), who documented that GBM thickening and mesangial expansion are early lesions of DN, whereas nodular glomerulosclerosis is typically seen in more advanced stages. The high prevalence of these lesions in our study indicates late-stage disease in a significant proportion of patients, reflecting delayed clinical recognition and intervention.[11]

The classification of DN using the Renal Pathology Society (RPS) system revealed that 35% of patients were in Class III and 10% in Class IV, indicating a predominance of advanced histological changes. This is notably higher than the proportions reported in *Tervaert et al.* (2010), where Class III and IV were observed in only 24% and 4% of biopsy-confirmed cases, respectively. The higher burden of advanced lesions in our cohort could be attributed to late presentation, poor glycemic control, or lack of early screening, particularly in resource-limited settings. It emphasizes the necessity of timely intervention and regular monitoring.[12]

Our regression analysis identified age, duration of diabetes, HbA1c, systolic blood pressure, proteinuria, and mesangial expansion as significant predictors of eGFR decline. These findings are consistent with *Gross et al.* (2005), who demonstrated that age and longer diabetes duration are independent predictors of renal function decline, especially when combined with poor metabolic control. In our cohort, proteinuria and mesangial expansion were particularly strong negative predictors (β = -0.51 and -0.47 respectively), reinforcing the idea that both clinical and pathological markers are crucial for risk stratification.[13]

The association between histopathological severity and poor renal outcomes is further corroborated by *Klessens et al.* (2016), who emphasized that mesangial expansion and interstitial fibrosis are among the most reliable predictors of renal functional decline in diabetic patients. In our study, interstitial fibrosis and tubular atrophy (IFTA) were present in 62.5% of cases, indicating irreversible damage. These findings support the use of renal biopsy not only for diagnostic confirmation but also for prognostication, especially when clinical indicators are inconclusive or atypical.[14]

CONCLUSION

This study highlights the significant pathological changes in renal tissue among diabetic patients, with a high prevalence of GBM thickening, mesangial expansion, and nodular glomerulosclerosis. Most

patients presented with advanced stages of diabetic nephropathy, as reflected by histological findings and reduced eGFR. Poor glycemic control, hypertension, and duration of diabetes were key contributors to disease progression. The strong correlation between clinical and histopathological parameters underscores the importance of early screening and timely intervention. Renal biopsy remains a valuable tool for accurate diagnosis and prognosis in diabetic kidney disease.

REFERENCES

1. Adler AI, Stevens RJ, Manley SE, Bilous RW, Cull CA, Holman RR. Development and progression of nephropathy in type 2 diabetes: The United Kingdom Prospective Diabetes Study (UKPDS 64). *Kidney Int*. 2003;63(1):225–32.
2. Ritz E, Orth SR. Nephropathy in patients with type 2 diabetes mellitus. *N Engl J Med*. 1999;341(15):1127–33.
3. Remuzzi G, Schieppati A, Ruggenenti P. Clinical practice: Nephropathy in patients with type 2 diabetes. *N Engl J Med*. 2002;346(15):1145–51.
4. Dalla Vestra M, Masiero A, Roiter AM, Saller A, Crepaldi G, Fioretto P. Is podocyte injury relevant in diabetic nephropathy? Studies in patients with type 2 diabetes. *Diabetes*. 2003;52(4):1031–5.
5. Sharma K, Ziyadeh FN. Hyperglycemia and diabetic kidney disease. The case for transforming growth factor-β as a key mediator. *Diabetes*. 1995;44(10):1139–46.
6. Steinke JM, Sinaiko AR, Kramer MS, Suissa S, Chavers B, Mauer M. The early natural history of nephropathy in type 1 diabetes: III. Predictors of microalbuminuria in the Diabetes Control and Complications Trial. *Kidney Int*. 2005;68(4):1590–8.
7. Alicic RZ, Rooney MT, Tuttle KR. Diabetic Kidney Disease: Challenges, Progress, and Possibilities. *Clin J Am Soc Nephrol*. 2016;11(12):2032–45.
8. Sasaki T, Nakagawa K, Hasegawa G, Fukui M, Yoshikawa T. Impact of blood pressure and glycemic control on progression of nephropathy in type 2 diabetic patients. *J Diabetes Complications*. 2016;30(3):551–5.
9. Parving HH, Mauer M, Ritz E. Diabetic nephropathy. In: Brenner BM, editor. *Brenner and Rector's The Kidney*. 7th ed. Philadelphia: Saunders; 2006. p. 1777–818.
10. Mogensen CE, Christensen CK, Vittinghus E. The stages in diabetic renal disease: With emphasis on the stage of incipient diabetic nephropathy. *Diabetes*. 1983;32(Suppl 2):64–78.
11. Fioretto P, Steffes MW, Sutherland DE, Mauer M. Sequential renal biopsies in insulin-dependent diabetic patients: structural factors associated with clinical progression. *Kidney Int*. 1995;48(6):1929–35.
12. Tervaert TW, Mooyaart AL, Amann K, Cohen AH, Cook HT, Drachenberg CB, et al. Pathologic classification of diabetic nephropathy. *J Am Soc Nephrol*. 2010;21(4):556–63.
13. Gross JL, de Azevedo MJ, Silveiro SP, Canani LH, Caramori ML, Zelmanovitz T. Diabetic nephropathy: diagnosis, prevention, and treatment. *Diabetes Care*. 2005;28(1):164–76.
14. Klessens CQ, Woutman TD, Veraar KA, Zandbergen M, Valk EJ, Rotmans JI, et al. An autopsy study suggests that diabetic nephropathy is underdiagnosed. *Kidney Int*. 2016;90(1):149–56.