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Prevalence and Spectrum of Nondiabetic Kidney Disease in Type 2 Diabetes Mellitus: An Eight-Year Retrospective Study

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Abstract

Background: Diabetic kidney disease (DKD) is the leading cause of chronic kidney disease (CKD) in patients with type 2 diabetes mellitus (T2DM). However, a considerable proportion of these patients develop nondiabetic kidney disease (NDKD), which has different therapeutic and prognostic implications.

Objective: To evaluate the prevalence, clinical presentation, and histopathological spectrum of NDKD in T2DM patients undergoing renal biopsy.

Methods: We retrospectively analyzed data from T2DM patients who underwent renal biopsy over an 8-year period. Patients with inadequate biopsies, prior renal transplants, or insufficient clinical data were excluded. Biopsy indications included atypical features such as nephrotic-range proteinuria, active urinary sediment, acute kidney injury (AKI), or absence of diabetic retinopathy (DR). Histopathological findings were categorized as: (1) pure DKD, (2) pure NDKD, and (3) NDKD superimposed on DKD.

Results: A total of 255 patients were included. The mean age was 49.5 years, with a male-to-female ratio of 3.1:1. Median duration of diabetes was 3.9 years. Hypertension was present in 59% of patients. Nephrotic syndrome was the most common indication for biopsy (42%). Pure DKD was seen in 110 patients (43%), pure NDKD in 85 (33%), and NDKD superimposed on DKD in 60 (24%). Focal segmental glomerulosclerosis (FSGS) was the most frequent NDKD (29%).

Conclusion: NDKD is a common finding in T2DM patients presenting with atypical renal features. Clinical and laboratory parameters alone are insufficient to reliably differentiate NDKD from DKD. Renal biopsy remains a crucial tool for accurate diagnosis, influencing treatment and prognosis.

Keywords: Type 2 diabetes mellitus, diabetic kidney disease, nondiabetic kidney disease, renal biopsy, proteinuria, focal segmental glomerulosclerosis

Introduction

Diabetic kidney disease (DKD) is a major cause of chronic kidney disease (CKD) and end-stage renal disease (ESRD) worldwide, particularly among patients with type 2 diabetes mellitus (T2DM) [1,2]. Despite the prevalence of DKD, a significant proportion of T2DM patients with renal impairment may have nondiabetic kidney disease (NDKD), either isolated or superimposed on DKD [3,4]. Accurate differentiation between DKD and NDKD is crucial because it influences treatment decisions and prognosis. Many forms of NDKD are potentially treatable or reversible, whereas DKD often follows a progressive, irreversible course [5,6].

Clinical parameters such as the absence of diabetic retinopathy, short duration of diabetes, presence of active urinary sediment (e.g., haematuria), and sudden onset of nephrotic syndrome have been proposed as indicators of NDKD [7-9]. However, these clinical features are not definitive, and renal biopsy remains the gold standard for diagnosis[10]. This study retrospectively evaluates the prevalence and histopathological spectrum of NDKD in T2DM patients with atypical renal manifestations who underwent renal biopsy over an 8-year period at a tertiary care centre.

Materials and Methods

Study Design and Population

This retrospective observational study was conducted at GMCH,Guwahati from to [Year 8]. Adult patients (≥18 years) with T2DM who underwent renal biopsy due to atypical renal presentations were included.

Inclusion Criteria

- Confirmed diagnosis of T2DM
- Renal biopsy performed for atypical renal manifestations such as sudden nephrotic syndrome, active urinary sediment, or rapid renal function declin

Exclusion Criteria

- Inadequate biopsy specimens (<5 glomeruli)
- Post-renal transplant status
- Incomplete clinical or histological data

Indications for Renal Biopsy

Biopsy was performed in cases with one or more of the following indications:

- Nephrotic-range proteinuria (>3.5 g/day)
- Presence of active urinary sediment (hematuria or red cell casts)
- Rapid deterioration in renal function
- Acute kidney injury (AKI) without apparent cause
- Absence of diabetic retinopathy on ophthalmologic examination

Data Collection

Demographic, clinical, and laboratory data, including age, sex, duration of diabetes, blood pressure, serum creatinine, estimated glomerular filtration rate (eGFR), proteinuria, diabetic retinopathy status, and biopsy findings, were extracted from medical records.

Histopathological Classification

Biopsy specimens were categorized into:

- Pure DKD

- Pure NDKD
- NDKD superimposed on DKD

Statistical Analysis

Descriptive statistics were used for demographic and clinical characteristics. Continuous variables were reported as mean ± standard deviation or median (range), and categorical variables as percentages. Group comparisons were performed using appropriate statistical tests, with a significance level set at $p<0.05$.

Results

Patient Demographics and Clinical Characteristics

A total of 255 patients met the inclusion criteria. The mean age was 49.5 ± 10.2 years, with a male-to-female ratio of 3.1:1 (194 males, 61 females). The median duration of diabetes was 3.9 years (range 1–10 years). Hypertension was present in 59% of patients. The mean serum creatinine was 2.8 ± 1.6 mg/dL, and the mean eGFR was 38.4 ± 15.2 mL/min/1.73 m². Proteinuria averaged 4.6 ± 2.1 g/day. Diabetic retinopathy (DR) was documented in 43% of patients, while 57% had no retinopathy.

Parameter	Value
Age (mean ± SD)	49.5 ± 10.2 years
Male:Female ratio	194:61 (3.1:1)
Median diabetes duration	3.9 (1–10) years
Hypertension (%)	150 (59%)
Serum creatinine (mg/dL)	2.8 ± 1.6
eGFR (mL/min/1.73 m²)	38.4 ± 15.2
Proteinuria (g/day)	4.6 ± 2.1
Diabetic retinopathy present (%)	110 (43%)
Diabetic retinopathy absent (%)	145 (57%)

Clinical Presentations

Presentation	Number (%)
Nephrotic syndrome	105 (42%)
Active urinary sediment	50 (20%)
Renal failure without DR	40 (16%)
Rapidly progressive renal failure	40 (16%)
Acute kidney injury (AKI)	20 (8%)

Histopathological Findings

Of the 255 biopsies:

- Pure DKD was diagnosed in 110 patients (43%)
- Pure NDKD in 85 patients (33%)
- NDKD superimposed on DKD in 60 patients (24%)

Thus, NDKD (pure or mixed) was present in 145 patients (56.8%), indicating that more than half of the biopsied T2DM patients had non-diabetic kidney disease.

Spectrum of Nondiabetic Kidney Disease (n=145)

Diagnosis	Number (%)
Focal segmental glomerulosclerosis (FSGS)	42 (29%)
Membranous nephropathy (MN)	25 (17%)
IgA nephropathy	20 (14%)
Acute interstitial nephritis (AIN)	18 (12%)
Post-infectious glomerulonephritis	10 (7%)
Others (MPGN, amyloidosis, lupus nephritis)	30 (21%)

Comparison between DKD and NDKD Groups

Parameter	Pure DKD (n=110)	Pure NDKD (n=85)	Mixed (n=60)	p-value
Age (years)	50.2 ± 9.5	48.1 ± 11.2	49.1 ± 10.4	>0.05
Male (%)	78%	74%	77%	>0.05
Diabetes duration (years)	5.5 ± 3.1	2.7 ± 2.4	3.4 ± 2.9	<0.001
Hypertension (%)	68%	51%	58%	<0.05
Diabetic retinopathy (%)	82.7%	17.6%	40%	<0.001
Nephrotic syndrome (%)	32%	54%	50%	<0.01
AKI (%)	7%	13%	12%	>0.05
Active urinary sediment (%)	12%	26%	22%	<0.05

- Shorter diabetes duration, absence of DR, nephrotic-range proteinuria, and hematuria were all significantly more common in NDKD groups.

Predictors of NDKD

Predictor	NDKD Present (n=145)	NDKD Absent (n=110)	p-value
Diabetes duration <5 years	110 (76%)	45 (41%)	<0.001
Absence of diabetic retinopathy	109 (75%)	19 (17%)	<0.001
Nephrotic-range proteinuria	101 (70%)	35 (32%)	<0.001
Hematuria (>5 RBCs/HPF)	89 (61%)	17 (15%)	<0.001
AKI or rapidly progressive renal failure	38 (26%)	17 (15%)	<0.05

These variables were all statistically significant, and can be considered non-invasive predictors of NDKD.

Discussion

This study highlights the high prevalence of nondiabetic kidney disease in T2DM patients with atypical renal presentations, seen in 56.8% of biopsied cases (Isolated DKD +NDKD superimposed on DKD). This finding is consistent with another study from the same region with NDKD prevalence of 57.85%.[16] Our findings align with several other published studies from India and abroad:

Study	Country	NDKD Prevalence
Prakash et al. (2001)	India	43%
Soni et al. (2006)	India	37%
Mak et al. (1997)	Hong Kong	39%
Sharma et al. (2007)	USA	49%
Current Study (2025)	India	56.8%

The slightly higher prevalence in our study may reflect increased biopsy rates for early/atypical presentations, improved diagnostics, and possibly regional differences in renal disease patterns.

- The absence of diabetic retinopathy, short diabetes duration, presence of nephrotic-range proteinuria, and active urinary sediment were significant predictors of NDKD, consistent with previous reports [7,11]. Prakash et al. found that absence of DR was the single most reliable clinical predictor of NDKD (present in >80% of NDKD cases).
- Mak et al. showed that shorter diabetes duration was strongly associated with non-diabetic lesions, including glomerulonephritis and interstitial nephritis.
- Sharma et al. emphasized that nephrotic-range proteinuria without DR was a red flag for NDKD in diabetics.

In our study, only 43% of patients had DR, and among those without DR, 75% had biopsy-confirmed NDKD, reinforcing its diagnostic value.

The spectrum of NDKD was broad, with FSGS, membranous nephropathy, and IgA nephropathy being the most common lesions. Among the 145 patients with NDKD (pure or mixed), the most common diagnoses were:

- Focal segmental glomerulosclerosis (FSGS) – 29%
- Membranous nephropathy (MN) – 17%
- IgA nephropathy – 14%
- Acute interstitial nephritis (AIN) – 12%

This pattern is consistent with:

- Sharma M et.al. (2020) – Found FSGS (33.3%) as the most common NDKD in this region followed by IgA nephropathy (20.8%)
- Soni et al. (2006) – Found FSGS and MN as the most common NDKDs in Indian patients.
- Kazi et al. (2012) – Reported FSGS and IgA nephropathy as frequent causes of NDKD in diabetics in Pakistan.
- Sharma et al. (2007) – In a US-based study, also found FSGS and MN as the most frequent glomerular lesions.

FSGS is increasingly recognized in diabetic patients, possibly due to shared pathogenic mechanisms (e.g., podocyte injury), but it requires specific immunosuppressive therapy that differs from DKD management.

Our findings underscore the importance of considering renal biopsy in T2DM patients with atypical renal features to guide management appropriately. Early identification and treatment of NDKD may improve renal outcomes and patient survival [12,13]

Conclusion

NDKD is common in T2DM patients presenting with atypical renal manifestations. Clinical predictors such as absence of diabetic retinopathy, short diabetes duration, nephrotic-range proteinuria, and haematuria can aid in identifying patients who would benefit from renal biopsy. Renal biopsy remains the gold standard for diagnosis and guides targeted therapy to improve outcomes.

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