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Unmasking non-albuminuric diabetic kidney diseasea clinical evaluation in type 2 diabetes mellitus

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Abstract
Background: Diabetic kidney disease (DKD) is a major cause of chronic kidney disease and end-stage kidney disease worldwide. Traditionally, albuminuria has been considered the earliest clinical marker of DKD. However, a significant proportion of patients with type 2 diabetes mellitus (T2DM) demonstrate declining renal function in the absence of albuminuria, referred to as non-albuminuric diabetic kidney disease (NA-DKD), which may remain undetected with conventional screening strategies.
Objectives: To determine the prevalence of NA-DKD in patients with T2DM, compare clinical and biochemical characteristics between albuminuric and non-albuminuric DKD, identify associated risk factors, and emphasize the importance of eGFR-based screening.
Methods: This cross-sectional observational study included 80 adult patients with T2DM attending a tertiary care center. Clinical evaluation, blood pressure measurement, and BMI assessment were performed. Laboratory investigations included serum creatinine, estimated glomerular filtration rate (eGFR) calculated using the CKD-EPI equation, urinary albumin-creatinine ratio (ACR), HbA1c, and lipid profile. Patients were categorized into albuminuric DKD and NA-DKD based on eGFR and ACR values. Statistical analysis was performed to compare clinical and biochemical parameters between groups.
Results: Among the study population, albuminuric DKD was present in 40%, NA-DKD in 22.5%, and no DKD in 37.5% of patients. NA-DKD patients were significantly older, had lower BMI, higher systolic blood pressure, and better glycemic control compared to albuminuric DKD patients, despite similar reduction in eGFR. NA-DKD was associated with higher LDL cholesterol levels and a greater prevalence of hypertension and cardiovascular disease, while diabetic retinopathy was less common compared to albuminuric DKD. Reliance on albuminuria alone would have missed 22.5% of patients with significant renal impairment.
Conclusion: NA-DKD represents a substantial and distinct phenotype of DKD in patients with T2DM. Screening strategies based solely on albuminuria are insufficient, and routine assessment of eGFR is essential for early identification of this high-risk group.

Keywords: Type 2 diabetes mellitus, diabetic kidney disease, non-albuminuric diabetic kidney disease, albuminuria, estimated glomerular filtration rate, chronic kidney disease, cardiovascular risk, egfr-based screening

Introduction

- Diabetic kidney disease (DKD) is the leading cause of chronic kidney disease (CKD) and end-stage kidney disease (ESKD) worldwide.
- For this reason, early diagnosis and treatment are relevant to prevent the
- progression of this disease.
- Currently, the urinary albumin excretion rate and the estimated glomerular filtration rate (eGFR) are widely accepted as diagnosis criteria, and the presence of micro albuminuria has been recommended as the first clinical sign of DKD.
- Beyond this classical clinical course, some studies report a non-classical clinical course of DKD, where kidney function declines but albuminuria levels are normal. This group of patients is recognized as having the 'non-albuminuric DKD' (NA- DKD) phenotype.
- Recent evidence has shown that around 20–40% of patients with type 2 diabetes mellitus (T2DM) have declining kidney function without the presence of albuminuria.
- **Significance:** Often missed by standard ACR-based screening, yet carries significant cardiovascular risk.

Objectives

- To determine prevalence of NADKD in T2DM
- To compare albuminuric DKD and NADKD
- To assess associated clinical risk factors
- To highlight importance of eGFR-based screening

Study Design

- **Study type:** Cross-sectional observational study
- **Setting:** General Medicine OPD & nephro unit
- **Sample size:** 80 patients

Study Population

- Adult patients with Type 2 Diabetes Mellitus Attending OPD / nephro unit

Inclusion Criteria

- Age ≥18 years
- Diagnosed Type 2 Diabetes Mellitus
- Willing to give informed consent-

Exclusion Criteria

- Type 1 DM
- Known primary renal disease
- Acute kidney injury

Methodology

- Detailed clinical history and physical examination performed
- Blood pressure and BMI recorded

Laboratory investigations included

- Serum creatinine
- Estimated GFR calculated using CKD-EPI equation
- Urinary albumin-creatinine ratio (ACR)
- HbA1cLipid profile
- Patients were categorized into albuminuric DKD and non-albuminuric DKD based on eGFR and ACR values
- Data were analyzed using appropriate statistical methods

Definitions

- **DKD:** eGFR <60 ml/min/1.73 m² and/or ACR ≥30 mg/g
- **Albuminuric DKD:** ACR ≥30 mg/g
- **NADKD:** eGFR <60 ml/min/1.73 m² ACR <30 mg/g

Results: Prevalence of phenotype

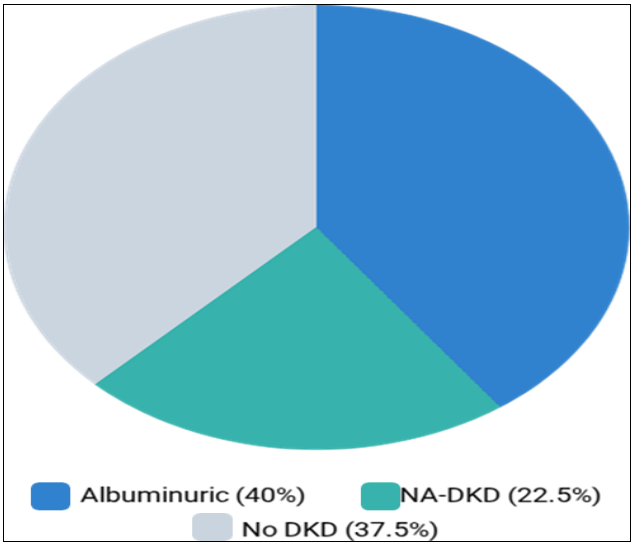
Key Findings (N=80):

Albuminuric DKD: 32 patients (40%) - The most common presentation.

- **Non-Albuminuric DKD:** 18 patients (22.5%) - Represents nearly 1 in 4 patients

No DKD: 30 patients (37.5%) - Preserved renal function

Interpretation: Relying on Albuminuria alone would miss 22.5% of patients with significant renal impairment.

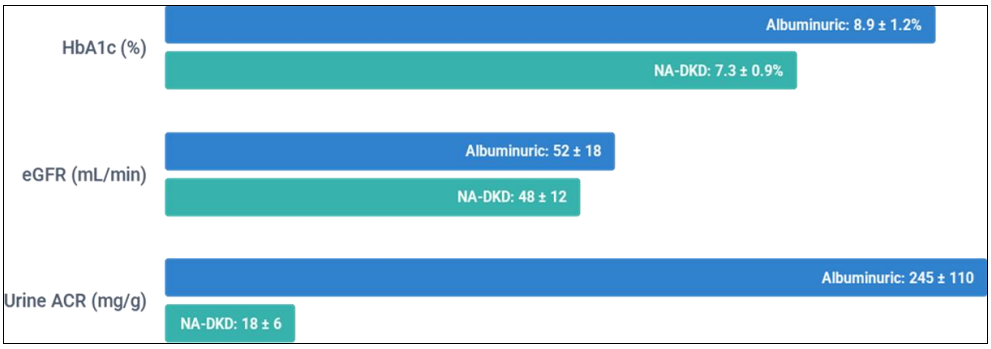


Results: Baseline Demographics

Parameter (Mean ± SD)	Albuminuric DKD (n=32)	NA-DKD (n=18)	P-Value
Age (years)	58.4 ± 7.2	66.1 ± 6.5	< 0.01
Gender (Male %)	56.2%	55.5%	0.82
Duration of Diabetes (years)	11.5 ± 4.2	12.8 ± 5.1	0.34
BMI (kg/m²)	29.5 ± 4.1	25.8 ± 3.2	0.02
Systolic BP (mmHg)	135 ± 12	148 ± 14	0.03
Smokers (%)	28.1%	33.3%	0.65

*NA-DKD patients were significantly older, had lower BMI, and higher Systolic BP compared to the classic Albuminuric group.

Comparison: Glycemic & Renal Profile



Insight: NA-DKD patients have better glycemic control (lower HbA1c) yet similar decline in eGFR compared to classic DKD.

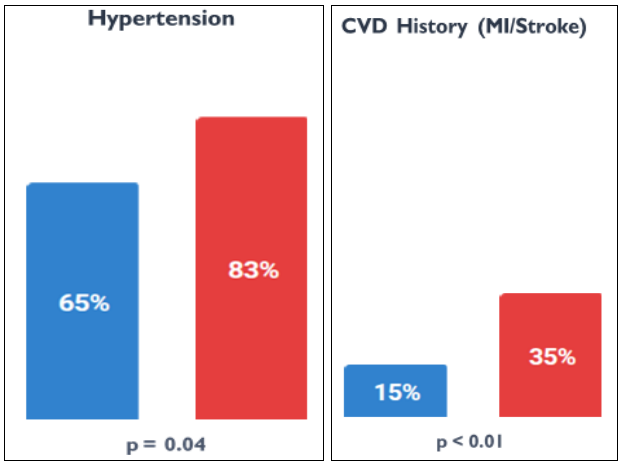
Comparison: Lipid Profile

Lipid Parameter (mg/dL)	Albuminuric DKD	NA-DKD	P-Value
Total Cholesterol	195 ± 35	210 ± 40	0.12
Triglycerides	185 ± 45	142 ± 30	< 0.01
HDL Cholesterol	42 ± 8	45 ± 9	0.24
LDL Cholesterol	115 ± 25	132 ± 28	0.04

- Classic Albuminuric DKD is associated with high Triglycerides (Dyslipidemia of Insulin Resistance

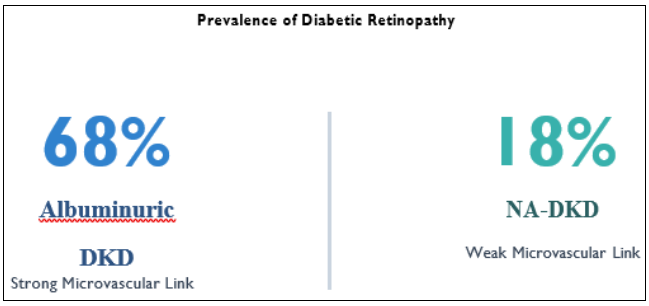
NA-DKD presents with higher LDL Cholesterol, fitting the macrovascular atherosclerosis phenotype.

Results: Comorbidities Profile



- Albuminuric DKD
- NA- DKD

Distinct Phenotype: Retinopathy



Clinical Pearl: The absence of Retinopathy in a patient with low GFR is a strong predictor of the Non-Albuminuric phenotype.

Discussion: Pathophysiology

Classic Albuminuric DKD

- **Primary Driver:** Hyperglycemia
- Glomerular Hyperfiltration
- Glomerulosclerosis
- Microvascular Damage
- Strong association with Retinopathy

Non-Albuminuric DKD

- **Primary Driver:** Aging & Hypertension
- Intrarenal Arteriosclerosis
- Tubulointerstitial Fibrosis
- Macrovascular Damage
- Strong association with CVD

Conclusion

1. Significant Burden

NA-DKD constitutes a substantial proportion (22.5%) of diabetic kidney disease in our tertiary care setting.

2. Distinct Clinical Profile

Compared to classic DKD, NA-DKD patients are older, have better glycemic control, lower triglycerides, but a significantly higher burden of Hypertension and CVD.

3. Screening Implication

Screening with UACR alone is insufficient. Mandatory inclusion of eGFR calculation is essential to unmask this "silent" high-risk group.

Discussion

- Non-albuminuric DKD (NA-DKD) emerged as a significant and under-recognized phenotype of DKD in type 2 diabetes mellitus.
- A considerable number of patients had reduced eGFR despite normal ACR, indicating that
- albuminuria alone is inadequate for DKD screening.
- Compared to albuminuric DKD, NA-DKD patients demonstrated:
- Better glycemic control and lower BMI, suggesting mechanisms beyond classical hyperglycemia- induced microvascular damage.
- Higher prevalence of hypertension, dyslipidemia, and cardiovascular disease, pointing toward a
- vascular and hemodynamic basis of renal injury.
- Greater use of ACEI/ARB therapy, which may mask albuminuria and contribute to the non- albuminuric presentation.
- Decline in eGFR correlated more strongly with age and duration of hypertension than with glycemic indices, reinforcing the role of macrovascular and ischemic mechanisms.
- These findings support NA-DKD as a distinct clinical entity, rather than a transitional stage of
- classical albuminuric DKD

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