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SPECTRUM OF KIDNEY DISEASE IN DIABETIC POPULATION- A 3 YEAR STUDY

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INTRODUCTION

Diabetic kidney disease (DKD) is characterized by persistent proteinuria, hypertension, and a progressive decline in renal function and is the leading cause of end-stage kidney disease worldwide. About 30%-40% of patients with diabetes usually present with frank diabetic nephropathy characterized histologically by nodular or diffuse mesangial sclerosis, arteriolar hyalinosis, microaneurysms, and exudative lesions. In patients with Type 2 diabetes mellitus (T2 DM), NON -Diabetic Kidney Diseases(NDKD) can occur either in isolation or superimposed on DKD.[2] The timely diagnosis of NDKD in this group is of paramount importance as many NDKD can be successfully treated and improve the overall renal prognosis. Short of biomarkers, as of now, kidney biopsy is the gold standard in diagnosing NDKD in T2 DM patients.[1] Published literature has shown varying prevalence of NDKD that could be attributed to the differences in the various criteria adopted by the clinicians to subject a patient to kidney biopsy. The diagnosis of presumed DKD is mainly clinically based on the presence of long-standing diabetes with the presence of retinopathy. Several clinical parameters have been used by physicians to suspect NDKD in T2 DM, including rapid-onset proteinuria, massive proteinuria, lack of retinopathy, presence of hematuria, active urine sediments, rapid decline of renal function, and features suggestive of systemic disease. However, no consensus exists, and the decision to proceed for the kidney biopsy depends on treating physician's clinical judgment.[2] In this study, we retrospectively reviewed kidney biopsies from patients with T2 Diabetes Mellitus and reported the prevalence and factors predicting the presence of NDKD in T2 DM.

AIM

To study the prevalence of NDKD in T2 Diabetes Mellitus patients

OBJECTIVES: To assess the prevalence of NDKD in Type 2 diabetes mellitus patients presenting to a tertiary care hospital from south India and also to analyze clinical clues to establish a diagnosis of NDKD.

PATIENTS AND METHODS

Patient and methods: It is a retrospective observational study of analyzing patient characteristics and renal biopsies. All Diabetic patients with a clinical suspicion of non-diabetic kidney disease who underwent renal biopsy during the study period between January 2022 and January 2025 were included. Based on the biopsy findings, the patients were classified into three groups (isolated diabetic nephropathy, isolated NDKD, and NDKD with underlying diabetic nephropathy) and patients' characteristics were compared between the groups for analysis.

Study Design

It is a retrospective observational study of analyzing patient characteristics and renal biopsies. All Diabetic patients with a clinical suspicion of non-diabetic kidney disease who underwent renal biopsy during the study period between January 2022 and January 2025 were included.

Sample Size

A total of 376 Type 2 Diabetic Mellitus patients who underwent biopsy Gandhi Hospital between January 2022 and January 2025 for this study.

Inclusion Criteria

All diabetic patients with indications for renal biopsy.

RESULTS

- A total of 376, diabetic pts in whom renal biopsies were done for atypical features were analyzed for the study. Among these, 182 biopsies showed features of DKD, 85 had features of NDKD overlapped with DKD and 109 biopsies had features of isolated NDKD.

- The patient characteristics were analyzed between the groups to identify the clinical clues that could possibly suggest Non-Diabetic Kidney Disease. Table details these characteristics. Age, sex, mean blood pressure, and glycemic control were comparable between the groups. 72% of the patients were hypertensive while the rest were non-hypertensive. The years of diabetes and hypertension were notably higher in the class with DKD, with a median of six years and two years, respectively. Unexplained renal failure was more frequent in the non-diabetic group with an incidence of 56.8%. Interestingly the incidences of azotemia, hypoalbuminemia, hypertriglyceridemia, anemia, and active urinary sediments were not significantly different between the groups. It may account for the observation that microscopic hematuria is seen in up to 30% of patients with diabetic kidney disease. Surprisingly, the occurrence of diabetic retinopathy was near between the groups, and mean blood pressure was not meaningfully distinct between diabetic and non-diabetic groups (Table).

Table: Patient characteristics between the groups.

Patient Characterstics	Diabetic Nephropathy (N= 182)	Diabetic Nephropathy With Non Diabetic Kidney Disease (N=85)	Non Diabetic Kidney Disease (N= 109)	P Value
Mean Age in Years	54.36	54.24	52.16	0.614
Mean Duration of Diabetes in Years	10.3	6.8	4.6	0.002
Mean Duration of Hypertension in Years	2.8	2.2	4.8	0.036
Unexplained Renal Failure	21.7%	37.2%	56.4%	<0.0001
Mean Blood Pressure (mmHg)	142	138	144	0.557
Mean Serum Creatinine-(mg/dl)	3.4	1.9	4.2	0.820
Mean Blood Urea mg/dl)	37.2	39.7	59.6	0.059
Haematuria	10.25%	14.76%	18.29%	0.090
Mean Haemoglobin(g/dl)	10.8	10.7	10.3	0.866
Mean Serum Albumin(g/dl)	3.5	3	3	0.455
Mean Total Cholestrol (mg/dl)	171	132	114	0.559
Mean Triglyceride (mg/dl)	150	158	248	0.457
Mean Hba1c%	8.5	8.4	8.1	0.739
Number of Diabetic Retinopathy	60%	75%	7.6%	<0.0001

Diagnosis	NDKD (n = 109; 28.9%), (n%)	DKD+ NDKD (n = 85, 22.6%), (n%)
Acute Tubulo- Interstitial Nephritis	40 (36.6%)	24 (28.2%)
Chronic Tubulo-Interstitial Nephritis	17(15.5%)	12 (14.1%)
Membranous Nephropathy	14 (12.8%)	7 (8.2%)
Infection Related Glomerulonephritis	11 (10.0%)	18(21.1%)
Hypertensio Related Kidney Disease	6 (5.5%)	17 (20%)
Iga Nephropathy	6 (5.0%)	4 (4.7%)
Amyloid	5 (4.5%)	1 (1.7%)
Lupus Nephritis	4 (3.6%)	1 (1.7%)
C3 Glomerulopathy	1 (0.9%)	0
Thrombotic Microangiopathy	2 (1.8%)	0
Podocytopathies (Mcd And Fsgs)	3 (2.7%)	1 (1.7%)

DISCUSSION

In our study, the frequency of NDKD in diabetic cases was 28.9%. In various studies, NDKDs also isolated or overlapped on an underlying DKD, have been described to be 8% to 85% which reflects the wide array of clinical grounds for renal biopsy. Kittrawee et al. had taken similar inclusion criteria as our study and found NDKD to be 49% of their cases - 20% had isolated NDKD and another 29% had NDKD superimposed on DKD.[4] Our study showed a prevalence 28.9 % of cases are isolated NDKD. 22.6% of NDKD cases have an underlying or overlapping DKD. Considering the wide range and paucity of data from the region, it is difficult to draw any reasonable conclusion. However, this wide variation is the reason why more studies are required to establish the

clinical grounds for biopsy and further evaluation in Diabetic patients presenting with renal failure.

Regarding the role of Diabetic Retinopathy as an indicator of diabetic nephropathy, the vast majority of studies support its role in predicting DKD vs NDKD. DR was less frequent among the NDKD group (7.6 vs 60 vs 75 %, $p < 0.001$)

We found that patients with a longer duration of diabetes (>5 years) and hypertension (two years) were more likely to have DKD even though they have atypical features. Similar findings were found in the study by Yenigun et al, those with a duration of DM of >8+/-2 years were most likely associated with DKD. However, rather surprisingly mean blood pressure readings were not meaningfully distinguished between all the three groups.[5]

Similarly, unexplained renal failure which was 37.2%, and rapid worsening of renal function in diabetic patients were most likely associated with NDKD. This finding is similar to the results from Jin Kim, who reported that the presence of NDKD was substantially higher in patients presenting with an unexplained decline in the renal function being 20%.[6]

Interestingly none of the other parameters including, 24-hour proteinuria levels, presence of hypertension, and degree of hypoalbuminemia found any statistical significance in our study. A similar finding was reported by Mak et al.[7] in their study who reported no noteworthy variance in serum creatinine, albumin, glycosylated hemoglobin, and absence of retinopathy between DKD and NDKD groups. Thus it is reasonable to derive that the indicators for biopsy in diabetic patients need to be reviewed further.

Among the NDKD, Acute Interstitial Nephritis was 47.2%, the commonest cause.In a retrospective analysis of community-acquired acute kidney injury (AKI), reported from an tertiary care center in south India, Acute Interstitial Nephritis was found to be the usual routine cause of AKI in patients who underwent renal biopsy. Proton pump inhibitors, commonly available in our population as an over-the-counter drug have also been speculated as a causative agent of AIN.

Limitations of the study being small study population and comprised regional population. Studies with large numbers and different population groups will be helpful in authenticating the results.

CONCLUSIONS

The clinical dilemma in differentiating DKD from NDKD still exists. The current clinical criteria do not effectively differentiate the two as the natural course of DKD in a population with type 2 DM is not well documented.

From the current study, prolonged DM and hypertension of more than five years and two years, respectively, predict DKD. While unexplained renal failure was most likely with NDKD. Hence, there is a need to further refine the clinical criteria to suspect non-diabetic renal disease in diabetic patients.

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