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Original Research Paper

Nephrology

CLINICAL AND LABORATORY PROFILE OF NON PROTEINURIC DIABETIC KIDNEY DISEASE – OBSERVATIONAL STUDY AT A TERTIARY CARE CENTRE

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ABSTRACT Renal derangement in diabetes mellitus type 2 (T2DM) encompasses a spectrum of etiologies such as, resulting from diabetes predominantly (diabetic kidney disease or DKD), or from etiologies other than diabetes (non-diabetic kidney disease or NDKD) or combined.[1] Proteinuria has been thought to be the first sign of renal dysfunction and the defining feature of diabetic kidney disease. Nonetheless, latest research suggests that a significant percentage of patients with diabetes have non-proteinuric diabetic kidney disease, which is characterised by renal derangement without proteinuria. [2] DKD may be classified into proteinuric DKD or P-DKD, and non-proteinuric DKD or NP-DKD. An e-GFR of 60 mL/min/1.73 m2 or lesser and albuminuria of 300 mg/d or lesser, is an indicator of NP-DKD [2] The exact causes of this DKD phenotype are unknown, but they could include a rise in the percentage of elderly individuals, persons with diabetes mellitus, patients of hypertension, dyslipidaemia, obesity, hyperuricemia, microangiopathy, or patients undergoing more rigorous treatment, such as renoprotective medication. [3] This study was undertaken to study the clinical and laboratory characteristics of NP-DKD in Type 2 Diabetes Mellitus patients at a tertiary care center.

KEYWORDS : DKD - Diabetic Kidney Disease; P-DKD – Proteinuric-Diabetic Kidney Disease; NP-DKD – Non-Proteinuric Diabetic Kidney Disease; e-GFR – estimated Glomerular filtration rate.

INTRODUCTION

Chronic kidney disease (CKD) is one of the leading disorders resulting in premature morbidity and mortality worldwide. The most prevalent cause of CKD worldwide is diabetes associated renal derangement (DKD). The onset of microalbuminuria, the first indication of DKD, foretells a steady decline in glomerular filtration rate (e-GFR). Recent data, however, indicates that a sizable fraction of type 2 diabetes patients also have CKD without proteinuria.[3]

Renal derangement in long-term diabetic patients typically starts with glomerular hyperfiltration, or an elevated glomerular filtration rate, followed by microalbuminuria (UACR 30–300 mg/g creatinine) and macroalbuminuria (UACR greater than 300 mg/g creatinine), and these changes were once thought to be a unidirectional process eventually resulting in end-stage renal disease (ESRD). Thus, it was also believed that the development of macroalbuminuria would be followed by renal derangement with e-GFR < 60 mL/min/1.73 m2. [2]

Initially used as a pathological term, "diabetic nephropathy" denoted a particular glomerulopathy that included mesangial enlargement, nodular glomerular sclerosis, and thickening of the glomerular basement membrane. [4]

The phrase "diabetic kidney disease" was later adopted by the National Kidney Foundation in 2007 in its "clinical practice recommendations and guidelines for the diagnosis and treatment of individuals with CKD and diabetes." [5]

The incidence of NP-DKD averages 20% in type 1 diabetes and 40% in type 2 diabetes, according to recent findings. This suggests that DKD is now increasingly recognised to be clinically diverse. [6]

Interstitial fibrosis, tubular atrophy and arteriosclerosis are the main pathological features of NP-DKD, along with varying degrees of glomerular sclerosis, that are comparable to changes seen in biopsies of hypertensive nephrosclerosis. Another explanation is that the majority of patients with NP-DKD are those who reacted effectively to blockades of the renin-angiotensin system, which prevents proteinuria by protecting the glomerulus. [7]

According to recent data, people with NP-DKD had a lesser frequency of diabetic retinopathy than in P-DKD, which might indicate micro-angiopathy, may not be the primary driving pathophysiologic mechanism. Also, individuals with non-proteinuric diabetic kidney disease are less likely to have a rapid deterioration in renal parameters than those with proteinuric diabetic kidney disease. Interstitial fibrosis along with tubular atrophy were more severe in those who advanced to advanced CKD or ESKD than in those who did not, indicating that tubular damage may be a significant factor in the natural evolution of CKD in the absence of proteinuria. [2,8]

Aims And Objective Of The Study

- To identify the clinical and laboratory characteristics of patients with NP-DKD

Methodology

An observational study conducted on 200 patients of NP- DKD admitted at RRMCH, Bangalore.

Inclusion Criteria

- Patients with age more than 18 years.
- Patients willing to give informed consent.
- DKD patients, regardless of duration, hemodialysis or biopsy.
- Absence of albuminuria on urine analysis, defined as UACR < 300mg/g of creatinine.

Exclusion Criteria

- Patients with age less than 18 years.
- Patients not willing to give informed consent.
- Type 1 diabetes individuals.
- CKD due to other causes, such as cystic kidney disease, malignancy, vasculopathies.

Duration Of The Study: 18 months.

The study was undertaken after obtaining approval from the Institutional Ethics Committee and informed written consent from patients. Detailed history was taken, clinical examination; investigations (electrocardiography, laboratory and echocardiography) were done. Data was collected and analyzed using SPSS statistical software version 22.

RESULTS

Age Distribution: the average age was 53.61 ± 10.17 years.

The highest proportion of patients belonged to the 51-60 years' age group (38%), closely followed by the 61-70 years' age group (25%).

Sex Distribution: 56 patients (28%) were females and 144 patients (72%) were males.

Duration Of Diabetes: Majority of the patients belonged to the category of duration beyond 10 years: 98 patients (49%), 63 patients (31.5%) with duration of CKD between 5-10 years and 39 patients (19.5%) with duration of CKD less than 5 years.

Treatment: 79% of patients were on oral hypoglycemic agents (OHA), while 21% were on insulin therapy.

Glycemic Indices: Glycemic indices revealed poor glycemic control among the study population, with a mean fasting blood sugar (FBS) of 150.11 ± 40.59 mg/dL, postprandial blood sugar (PPBS) of 208.54 ± 51.40 mg/dL, and an HbA1c level of 9.03 ± 1.86%.

Stage Of eGFR: 15 patients (7.5%) had stage 3A CKD, 27 patients (13.5%) had stage 3B CKD, 61 patients (30.5%) had stage 4 CKD and 97 patients (48.5%) had stage 5 CKD.

Presence Of Comorbidities: 148 patients (74%) had hypertension, 92 patients (46%) had dyslipidemia, 23 patients (11.5%) had Ischemic heart disease, 7 patients (3.5%) had peripheral arterial disease and 18 patients (9%) had cerebrovascular accident.

Presence Of Retinopathy: Of the 200 patients, some form of diabetic retinopathy was found in 114 patients, with majority belonging to stage of mild NPDR (35%) and least prevalence of maculopathy (1.5%).

Laboratory Parameters: The mean serum urea was 94.52 mg/dl ± 28.44, mean serum creatinine was 4.78mg/dl ± 4.20, and mean creatinine clearance was 19.23 ml/min ± 10.01. The mean UACR was 232.87 ± 50. 2 mg/g of creatinine.

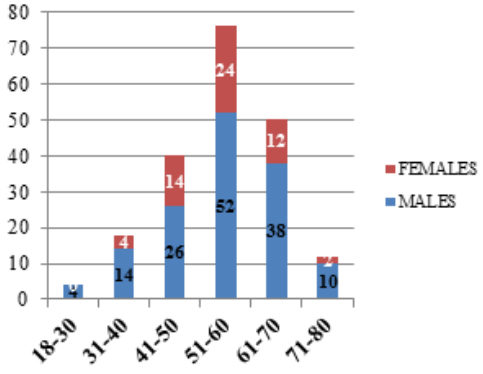


Fig 1: Age And Sex Distribution Of Study Population

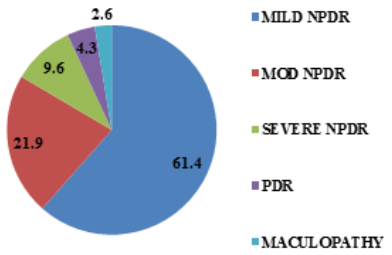
Table 1: Prevalence Of Dr.

PREVALENCE OF RETINOPATHY	PATIENTS	PERCENTAGE
NO RETINOPATHY	86	43%
RETINOPATHY	114	57%

Table 2: Stage Of Dr.

STAGE OF RETINOPATHY	PATIENTS	PERCENTAGE
NO RETINOPATHY	86	43%
MILD NPDR	70	35%
MODERATE NPDR	25	12.5%
SEVERE NPDR	11	5.5%
PDR	5	2.5%
MACULOPATHY	3	1.5%

FIG 2: SPECTRUM OF RETINOPATHY



DISCUSSION

From the above data, we can infer that most patients of NP-DKD are elderly, predominantly male, with long standing diabetes of more than 10 years, and most had poor glycemic control despite treatment, suggesting possibly inadequacy of treatment and non-compliance to treatment. Hypertension was the most prevalent comorbidity and most patients had some form of diabetic retinopathy on funduscopic examination.

CONCLUSION:

As of 2024, an estimated 589 million persons between 20 and 79 years' are suffering with diabetes across the globe. Additionally, it was projected that more than 3.4 million deaths in 2024 among those aged 20 to 79 were attributable to diabetes. [9] In India, estimates range from 101 million people with diabetes to 136 million people with prediabetes. [10] An e-GFR of 60 mL/min/1.73 m2 or lesser and albuminuria of 300 mg/d or lesser, is an indicator of NP-DKD. [2] This possible variant or phenotype of DKD indicates that renal function and albuminuria levels in diabetic individuals are dissociated, underscoring the need for a more comprehensive knowledge of renal dysfunction beyond those associated with elevated albuminuria. [2]

Given that it does not appear to represent the underlying renal lesion in the majority of DKD patients, the high number of patients with modest excretion of urinary protein indicates that the conventional clinical understanding of diabetic nephropathy is evolving. [11] Such a shift could also be a result of medication modifications, specifically to help diabetes patients achieve better glycaemic control, lower blood pressure (BP), and lower cholesterol levels. This opinion is in line with the UKPDS findings, which indicate that red blood cell-glycated haemoglobin (HbA1c) is a well-known risk factor for elevated proteinuria but not for impaired e-GFR. [12]

Estimation of GFR is obviously associated with the higher diagnosis of chronic renal disease in diabetic subjects, as there is no proteinuria in these patients. In fact, it has been proposed that people with diabetes who have normo-albuminuria may be an artificial population, resulting from over diagnosis of CKD since the MDRD equation underestimates high GFR. [13]

Nevertheless, more studies are required to identify the exact risk factors, pathogenic mechanisms and the risk of progression to proteinuric DKD.

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