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Frequency of Diabetic Nephropathy among Patients of Type 2 Diabetes Mellitus

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ABSTRACT

Diabetic Nephropathy (DN) is a predominant consequence of Type 2 Diabetes Mellitus (T2DM), contributing to chronic renal disease. **Objective:** To determine the frequency of diabetic nephropathy and its correlation with glycemic control. **Methods:** A cross-sectional study was conducted at the Nephrology and Diabetic OPD of Lahore General Hospital from July to November 2024.A total of 282 type 2 diabetic patients were enrolled.Clinical evaluation, fundoscopy, neurological examination, and laboratory tests were performed.Diabetic nephropathy was diagnosed based on albuminuria and eGFR. Statistical significance was set at $p < 0.05$. **Results:** Out of 282 patients, 150 (53.2%) were males and 132 (46.8%) females.The majority (43.3%) were aged 50–59 years. Microalbuminuria and macroalbuminuria were present in 20.9% and 32.3%, respectively. Mean serum creatinine and eGFR were 1.16 ± 0.53 mg/dL and 68.15 ± 24.58 mL/min/1.73m^2. Mean HbA1c and FBS levels were 8.40 ± 1.84% and 137.03 ± 19.19 mg/dL. Hypertension was noted in 41.5%. Diabetic nephropathy was significantly more prevalent in those with FBS >140 mg/dL (29.1%) and HbA1c >7.5% (32.6%) compared to those with lower values ($p < 0.05$). Declining eGFR was also significantly associated with nephropathy, with most cases found in those with eGFR <60 mL/min/1.73m^2 ($p < 0.001$). **Conclusion:** The study revealed a high frequency of diabetic nephropathy in type 2 diabetes, linked to poor glycemic control, declining eGFR and complications.

INTRODUCTION

Diabetic Nephropathy (DN) is the most common sequela of type 2 diabetes mellitus and a predominant cause of chronic renal disease and end-stage renal disease worldwide [1]. DN is defined by a rise in albumin excretion, a decrease in GFR or both.It impairs kidney function and changes the normal process of eliminating waste and extra fluid from the body (Neild, 2004).The global burden of DN continues to rise due to the increasing prevalence of T2DM, with approximately 30–40% of diabetic patients developing renal impairment over time [2].T2DM patients are more prone to develop DN (40%) compared to Type I Diabetes Mellitus (T1DM) (30%) [3].The pathophysiology of DN is multifactorial, involving hyperglycemia-induced glomerular injury, oxidative stress, inflammation and endothelial dysfunction, leading to progressive albuminuria and dropping Glomerular Filtration Rate (GFR) [4]. Ali *et al.*, in (2023) documented that hypertension, dyslipidemia and prolonged diabetes were strong determinants of DN, with smoking and obesity further worsening renal dysfunction [5]. Microalbuminuria, an early indicator of renal dysfunction, presents before nephropathy becomes evident and serves as a predictive factor for CKD progression. Consequently, early detection of albuminuria and estimation of GFR are essential for risk stratification and timely intervention to prevent renal deterioration [6, 7]. Alongside the global prevalence of DM,

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the incidence of DN has been on the rise. According to risk assessment management program in China, the prevalence of CKD in 15856 diabetic patients was 38.8% [8]. Sana *et al.*, in (2020) documented a DN prevalence of 30.1%, with 25.6% of T2DM patients demonstrating microalbuminuria and 4.5% progressing macroalbuminuria [9]. Similarly, Ullah *et al.*, in (2024) noted that 54% of T2DM patients had DN, with 31% presenting microalbuminuria and 19% having macroalbuminuria [10]. According to the analysis of third national health and nutrition assessment survey, prevalence of DN in United States (US) population was observed to be 2.2% [11].Diabetic kidney disease increases the mortality risk by 31.1% in Diabetic patients [12].The American Diabetes Association (ADA) endorses once-a-year screening for albuminuria and eGFR assessments in diabetic patients to facilitate early detection and intervention [13].Despite these guidelines, DN remains underdiagnosed in many regions, specifically in low- and middle-income areas, where resources are limited.This research aims to evaluate frequency of DN among patients with T2DM and assess its association with key clinical and biochemical parameters.

These findings will contribute in the making of national health policies, counselling and treatment planning.

METHODS

A cross-sectional study was executed at Lahore General Hospital, Lahore, in the Nephrology Department and the Diabetic Outpatient Department (OPD) from July to November 2024. Ethical approval for the study was obtained from the Institutional Review Board of Postgraduate Medical Institute/Ameer-ud-Din Medical College, Lahore General Hospital, Lahore (Approval Reference No. 00/168/2023), and informed consent was taken from all patients before enrollment. A non-probability consecutive sampling technique was utilized for participant enrollment. A sample size of 282 patients was calculated using the following formula, based on an expected prevalence of diabetic nephropathy of 24.2%, with a 95% confidence level (Z = 1.96), 5% margin of error (d = 0.05), population size of 1,000,000, and design effect (DEFF)=1[14].

$$n=\frac{\text{DEFF X N X}p(1-p)}{[\frac{d^2}{Z^2}\text{ X }(N-1)+p(1-p)]}$$

All patients diagnosed with T2DM aged over 18 years and willing to participate were recruited in study after taking consent. Patients who had T1DM, obstructive uropathy, congestive heart failure, liver diseases, autoimmune diseases, neoplasm, UTI or taking medications that could affect insulin sensitivity such as corticosteroids and hormone replacement therapy were not enrolled in the study. Patients who were taking medications that affect kidney function or had experienced an acute kidney injury in the last 6 months were also excluded. A proforma was utilized to gather demographic, clinical and laboratory data, including age, sex, body mass index, duration of DM, history of HTN, ischemic heart disease and medication use such as oral hypoglycemic drugs, insulin, antihypertensives, and lipid-lowering agents. All the patients were examined for other microvascular complication of diabetes e.g., diabetic retinopathy and neuropathy with fundoscopy and nervous system examination respectively. BP was quantified by standardized sphygmomanometer after five minutes of rest, with two readings 3-4 min apart taken and averaged. After an overnight fasting of at least eight to ten hours blood samples were gathered to evaluate fasting blood sugar using an automated chemistry analyzer, glycosylated haemoglobin (HbA1c) by high-performance liquid chromatography, a gold-standard method approved by the National Glycohemoglobin Standardization Program (NGSP) and serum creatinine was measured using the Jaffe kinetic method, a widely accepted, cost-effective, and reproducible photometric technique based on creatinine's reaction with alkaline picrate [15, 16]. A mid-stream urine sample was obtained to evaluate urinary albumin-to-creatinine ratio using an automated immunoturbidimetric assay, with albuminuria grouped as normal (<30 mg/g), microalbuminuria (30–299 mg/g) or macroalbuminuria (≥300 mg/g). Immediately, urine samples were stored at 2-4°C. To stop bacterial overgrowth, sodium azide (0.02%) was added to the urine sample [17]. All samples before the assay were mixed well. Estimated glomerular filtration rate (eGFR) was measured using the CKD-EPI formula and patients were categorized into CKD stages ranging from stage 1 to stage 5 [18]. Diabetic nephropathy was characterized as a decline in eGFR <60 mL/min/1.73 m2, prolonged macroalbuminuria confirmed on at least two occasions three to six months apart, provided that other causes of CKD are ruled out. Secondary outcomes included associations between diabetic nephropathy and glycemic control (HbA1c levels), blood pressure status and diabetes duration. Statistical analysis was performed using IBM SPSS Statistics, Version 26.0 (IBM Corp., Armonk, NY, USA). Categorical variables were demonstrated in the form of frequency and percentages and descriptive variables were mentioned as mean and standard deviation. The Chi-Square test was employed to examine associations between categorical variables such as age group, gender, glycemic control (HbA1c and FBS levels), eGFR categories, and albuminuria stages. A confidence level of 95% was used for all statistical analyses. Results were considered statistically significant at a p-value ≤ 0.05.

RESULTS

The study included 282 patients diagnosed with T2DM. The average age of study participants was 56.39 ± 9.89 years. The mean body mass index and duration of DM were 29.59 ± 5.20 kg/m^2 and 8.02 ± 4.57 years respectively. The mean Fasting Blood Sugar (FBS) level was 137.03 ± 19.19 mg/dL. The average serum creatinine level was 1.16 ± 0.53 mg/dL

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and the mean eGFR was 68.15 ± 24.58 mL/min/1.73m^2. The mean glycated hemoglobin (HbA1c) level was 8.40 ± 1.84%. The most of patients was categorized under 50-59 years age group (43.26%), followed by the 40-49 years group (21.99%), with a male predominance of 53.19%. Overweight and obesity (BMI ≥25 kg/m^2) were prevalent, with 32.62% overweight and 44.68% obese. Renal function assessment revealed that 53.19% of patients had albuminuria, with 20.92% having microalbuminuria and 32.27% having macroalbuminuria. A drop in renal function was noted, with 43.61% of patients having an eGFR<60. Glycemic control was suboptimal, with 66.31% of patients having HbA1c >7.5%. The prevalence of diabetic complications was notable, with 51.06% having retinopathy and 62.77% having neuropathy. Poor fasting glucose control (>140 mg/dL) was observed in 40.07%, and 41.49% of patients had hypertension. For further details see Table 1.

Table 1: Baseline Characteristics of Study Patients

Variables	Mean ± SD
Age Groups (Years)	
30-39	10 (3.55)
40-49	62 (21.99)
50-59	122 (43.26)
60-69	45 (15.96)
≥70	43 (15.25)
BMI (kg/m^2)	
18-24	64 (22.70)
25-30	92 (32.62)
31-35	84 (29.79)
≥36	42 (14.89)
Gender	
Male	150 (53.19)
Female	132 (46.81)
Urinary Albumin to Creatinine Ratio (UACR)	
<30 mg/g	132 (46.81)
30-299 mg/g	59 (20.92)
≥300 mg/g	91 (32.27)
Estimated Glomerular Filtration Rate (eGFR) (mL/min/1.73m^2)	
G1 (≥90)	94 (33.33)
G2 (60-89)	65 (23.05)
G3a (45-59)	52 (18.44)
G3b (30-44)	55 (19.50)
G4 (15-29)	16 (5.67)
Glycated Hemoglobin (HbA1c)	
≤7.5 %	95 (33.69)
>7.5 %	187 (66.31)
Retinopathy	
Yes	144 (51.06)
No	138 (48.94)
Neuropathy	
Yes	177 (62.77)
No	105 (37.23)
Fasting Blood Sugar (FBS, mg/dL)	
≤140	169 (59.93)
>140	113 (40.07)
Hypertension (HTN, mmHg)	
Yes	117 (41.49)
No	165 (58.51)

Nephropathy was diagnosed in 42.60% of patients (Figure 1).

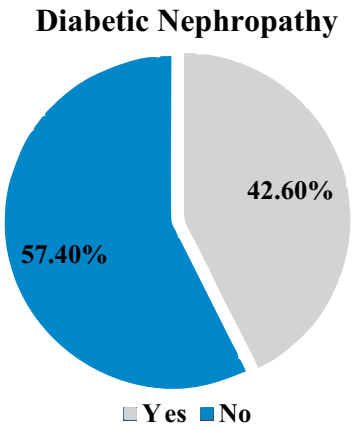

Figure 1: Frequency of Diabetic nephropathy in studied Cohort (n=282)

A statistically significant association was found between eGFR stages and albuminuria levels ($\chi^2 = 276.48$, p *< 0.001), with worsening eGFR showing higher proportions of macroalbuminuria. Among patients with eGFR ≥90 (G1), 71.21% had normal UACR, while no cases of microalbuminuria or macroalbuminuria were found. In contrast, in eGFR 60-89 (G2), 44.38% had albuminuria and in eGFR 45-59 (G3a), 72.23% had albuminuria. UACR abnormalities became more pronounced in eGFR 30-44 (G3b), where 65.80% had macroalbuminuria and in eGFR 15-29 (G4), where all patients had macroalbuminuria (Table 2). The Pearson Chi-Square test was used to assess the association between eGFR categories and UACR levels. The p-value obtained was ≤ 0.05, indicating a statistically significant relationship (p ≤ 0.05). The percentages within each cell represent the proportion within each UACR classification. Nephropathy was significantly associated with age (*p =0.018), with the highest prevalence in 50-59 years group (52.50%), while gender showed no significant correlation (p = 0.967). Poor glycemic control was strongly linked to nephropathy, with HbA1c >7.5% (76.70%, *p = 0.002) and fasting blood sugar >140 mg/dL (68.30%, *p < 0.001) being major risk factors. Diabetic complications were significantly associated, as 72.50% of nephropathy cases had retinopathy (*p < 0.001) and 75.01% had neuropathy (*p < 0.001).

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Table 2: Association Between eGFR Categories and Urinary Albumin-to-Creatinine Ratio (UACR) Levels (n=282)

CKD Stages		Albuminuria			Total Frequency (%)	p-Value
		< 30 Frequency (%)	30-299 Frequency (%)	30-299 Frequency (%)		
eGFR (mL/min/1.73m^2)	Stage 1	94 (71.21)	0 (0.00)	0 (0.00)	94 (33.33)	< 0.001*
	Stage 2	36 (27.27)	21 (35.59)	8 (8.79)	65 (23.05)	
	Stage 3a	2 (1.52)	29 (49.15)	21 (23.08)	52 (18.44)	
	Stage 3b	0 (0.00)	9 (15.25)	46 (50.55)	55 (19.50)	
	Stage 4	0 (0.00)	0 (0.00)	16 (17.58)	16 (5.67)	

DISCUSSION

This study assessed the frequency and baseline characteristics of diabetic nephropathy in type 2 DM patients.The mean age of participants in present researchs was 56.39 ± 9.89 years, which is parallel with studies conducted by Jeerasuwannakul *et al.*, in (2021) (56.36 ± 13.88 years) and Wan *et al.*, in (2024)(mean age 61.4 years) [19, 20].Age was significantly associated with nephropathy (p = 0.018), with highest prevalence seen in the 50-59 years age group (52.5%).This observation is parallel with studies by Merid *et al.*, in (2024) and Farah *et al.*, in (2021) which reported a significant correlation between older age and nephropathy progression [21, 22]. The mean BMI in this study was 29.59 ± 5.20 kg/m^2, with overweight and obesity present in 32.6% and 44.7% of patients, respectively. This consistent with the findings of Farah *et al.*, in (2021), where 66% of patients had BMI >30 kg/m^2, and Ali *et al.*, in (2023), who reported obesity in 51.4% of nephropathy patients [5, 22].Obesity is a well-established risk factor for nephropathy, contributing to glomerular hyperfiltration and renal injury.HTN was noted in 41.5% of patients, comparable to Elhefnawy and Elsayed., in (2019) (28.5%) and Aboelnasr *et al.*, in (2020)(48.4%)[23, 24]. The significant correlation between systolic blood pressure and nephropathy progression has been observed in many studies, including Hussain *et al.*, in (2021), which recorded an odds ratio of 1.67 for nephropathy in hypertensive patients and Merid *et al.*, in (2024), where hypertension significantly decreased survival in nephropathy patients (p < 0.001)[21, 25].The correlation between eGFR decline and albuminuria was significant (p < 0.001), validating previous findings from Kebede *et al.*, in (2021), where progressive eGFR decline was a measure of nephropathy [26]. Glycemic control was an important predictor of nephropathy in this study, with HbA1c >7.5% noted in 66.3% of patients and significantly correlated with nephropathy (p= 0.002). This finding is parallel with Jeerasuwannakul *et al.*, in (2021), which observed a mean HbA1c of 8.57 ± 2.31% in proteinuric patients and Wan *et al.*, in (2024), where HbA1c >8% was correlated with high risk of CKD (OR 1.29, 95% CI 1.24–1.34) [19, 20]. Analogously, Ali *et al.*, in (2023) noted that 100% of nephropathy patients had HbA1c >7%, compared to 40.5% in non-nephropathy patients (p< 0.05) [5].Renal function assessment showed that 42.6% of patients had nephropathy, with microalbuminuria in 20.9% and macroalbuminuria in 32.3%.These results match those reported by Ullah *et al.*, in (2024), where nephropathy was noted in 54% of patients (31% microalbuminuria and 19% macroalbuminuria) and Elhefnawy and Elsayed, in (2019), which recorded microalbuminuria in 31.8% and macroalbuminuria in 7.9% of patients [10, 23].Prevalence of albuminuria was similar to that documented by Wan *et al.*, (2024), where 48.1% of T2DM patients had albuminuria and Farah *et al.*, in (2021), where 44.7% of patients had albuminuria, indicating significant renal involvement [20, 22].The mean eGFR in this research was 68.15 ± 24.58 mL/min/1.73m^2, with 43.6% of patients having eGFR <60, reflecting dropping renal function. This matches well with Wan *et al.*, in (2024), where 22.4% of T2DM patients had eGFR <60 and Farah *et al.*, in (2021), where 19.17% had CKD with eGFR <60 [20, 22].Similarly, Ali *et al.*, in (2023) documented that nephropathy patients had lower eGFR than those without nephropathy [5].This study showed a clear trend of increasing albuminuria with declining eGFR, with all patients in the G4 eGFR category demonstrating macroalbuminuria(>300 mg/g)[15].This trend corresponds with findings from Fenta *et al.*, in (2023), which observed albuminuria as a strong predictor of CKD and Hussain et al., in(2021), which highlighted albuminuria as early indicator of diabetic nephropathy [25, 27].These results emphasize the need for routine renal function assessment, particularly albuminuria and eGFR monitoring, to detect nephropathy early and slow CKD progression.Diabetic complications such as retinopathy and neuropathy were associated with nephropathy (p < 0.001). Retinopathy was noted in 51.1% of patients, in consistent with Farah *et al.*, in (2021), which documented retinopathy in 34.12% of diabetic nephropathy patients and Wan *et al.*, in (2024), which reorted an OR of 1.19 (95% CI 1.13–1.26) for retinopathy forecasting CKD [20, 22].Similarly, neuropathy was found in 62.8% of patients, with a significant correlation with nephropathy, consistent with findings from Merid *et al.*, in (2024), where diabetic neuropathy significantly reduced survival probability (p = 0.0397) [21].Fasting blood sugar was significantly correlated with nephropathy (p < 0.001), with 68.3% of patients having FBS >140 mg/dL.This is supported by Jeerasuwannakul *et al.*, in (2021), which found an independent association between fasting plasma glucose and proteinuria (aOR 1.009, p < 0.05) [19].Similarly,

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Ali *et al.*, in (2023) reported that 64.8% of nephropathy patients had fasting blood sugar >200 mg/dL, compared to 29.7% in non-nephropathy patients [5].This research provides valuable insights into the frequency of diabetic nephropathy among T2DM patients, utilizing a comprehensive analysis of renal function parameters, glycemic control, and associated microvascular complications.The strengths include a well-defined study population, standardized diagnostic criteria and robust statistical analysis.However, limitations include its cross-sectional design, which limits causality assessment and single-center data, reducing generalizability.

CONCLUSIONS

This study demonstrated a high frequency of diabetic nephropathy among patients with type 2 diabetes mellitus. Significant associations were observed between nephropathy and indicators of poor glycemic control, including elevated fasting blood sugar and HbA1c levels. Furthermore, nephropathy was more frequently noted in patients with coexisting microvascular complications such as retinopathy and neuropathy. Declining eGFR corresponded with increasing albuminuria, indicating progressive renal impairment. These findings emphasize the importance of early detection and routine monitoring to mitigate disease progression. Future researches should embed longitudinal follow-ups, multicenter studies and interventional strategies to assess nephropathy progression and evaluate targeted preventive measures for high-risk diabetic populations.

Authors Contribution

Conceptualization: MIJ

Methodology: YH, AS, AA, IN

Formal analysis: MIJ, MSNK, AS, AI, AA, IN

Writing, review and editing: MIJ, YH, MSNK, AS, AI, AA, IN

All authors have read and agreed to the published version of the manuscript

Conflicts of Interest

All the authors declare no conflict of interest.

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