

Original Article

Association Between Diabetic Nephropathy and Cardiovascular Complications in Patients with Type 2 Diabetes Mellitus.

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ABSTRACT

Background: Diabetic nephropathy is one of the most common microvascular complications of type 2 diabetes mellitus (T2DM) and is associated with an increased risk of cardiovascular disease (CVD). Renal dysfunction and albuminuria may contribute to endothelial dysfunction, chronic inflammation, oxidative stress, and accelerated atherosclerosis, thereby increasing cardiovascular risk. Early recognition of this association may facilitate timely preventive and therapeutic interventions.

Objective: To determine the association between diabetic nephropathy and cardiovascular complications among patients with type 2 diabetes mellitus at a tertiary care teaching hospital.

Methods: This was an analytical cross-sectional study conducted in the Department of Nephrology at Maingul Jehgnazab Hospital, Swat, from January 2025 to June 2025. A total of 100 patients with type 2 diabetes mellitus, aged ≥ 30 years and having diabetes for at least five years, were enrolled using consecutive non-probability sampling. Diabetic nephropathy was assessed using urinary albumin-to-creatinine ratio and estimated glomerular filtration rate, while cardiovascular complications were assessed through clinical examination, electrocardiography, echocardiography, and review of medical records. Data were analyzed using SPSS version 27.0. Chi-square test, independent-samples t-test, and multivariable logistic regression were applied as appropriate. A p-value < 0.05 was considered statistically significant.

Results: Among 100 participants, the mean age was 58.4 ± 9.8 years, with 62% males and 38% females. Diabetic nephropathy was present in 46% of patients, whereas 39% had at least one cardiovascular complication. Cardiovascular complications were significantly more frequent in patients with diabetic nephropathy than in those without nephropathy (60.9% vs. 20.4%; $p=0.001$). Coronary artery disease was the most common cardiovascular complication (34.8% vs. 11.1%; $p=0.004$). Patients with cardiovascular complications had significantly lower mean eGFR (56.8 ± 18.2 vs. 81.4 ± 16.5 mL/min/1.73 m²; $p<0.001$) and higher urinary albumin excretion ($p=0.002$). Multivariable logistic regression demonstrated that diabetic nephropathy was independently associated with cardiovascular complications (adjusted OR=3.42; 95% CI: 1.48–7.91), after adjustment for age, hypertension, HbA1c, and duration of diabetes.

Conclusion: Diabetic nephropathy was significantly associated with cardiovascular complications among patients with type 2 diabetes mellitus. Patients with diabetic nephropathy had a substantially higher frequency of cardiovascular complications than those without nephropathy. Routine assessment of albuminuria and renal function may help identify patients at increased cardiovascular risk and support timely preventive and therapeutic interventions.

INTRODUCTION

Type 2 diabetes mellitus (T2DM) is a serious public health problem and is currently affecting over 530 million adults around the world, and is likely to be a significant escalating public health problem in the years ahead. Numerous microvascular and macrovascular complications are associated with the disease and result in morbidity, mortality, and a massive cost of health care. Diabetic nephropathy (DN), a microvascular disease, is one of the most prevalent and severe complications and is responsible for almost 40% of chronic kidney disease (CKD), with ESRD being the most common cause of ESRD in the world. Chronic hyperglycemia causes glomerular hyperfiltration, mesangial expansion, podocyte injury, and progressive renal fibrosis, which eventually culminate in albuminuria and loss of renal function [1,2]. Diabetic nephropathy is a progressive condition that worsens over time and is defined by the presence of albuminuria, a decreased estimated glomerular filtration rate (eGFR), hypertension, and chronic kidney disease (CKD). Symptoms are usually absent in the early stages, so screening is important for early detection. Microalbuminuria is regarded as the earliest clinical indicator of diabetic nephropathy and is closely linked with generalized endothelial dysfunction. Apart from renal impairment, diabetic nephropathy has now become an important risk factor for adverse cardiovascular outcomes even without having kidney failure [3]. People with T2DM continue to die most often from cardiovascular disease (CVD), which kills over 2/3 of those with T2DM. Diabetic patients are at higher risk of coronary artery disease, heart failure, cerebrovascular disease, peripheral arterial disease, and sudden cardiac death. The presence of diabetic nephropathy further increases this risk through a complex series of interrelated mechanisms, including endothelial dysfunction, chronic inflammation, oxidative stress, activation of the renin-angiotensin-aldosterone system, vascular calcification, and dyslipidemia. In addition to being a biomarker of kidney damage, albuminuria is now known to be an independent predictor of cardiovascular morbidity and mortality [4,5]. Several epidemiological studies have shown a robust association between declining kidney function and higher cardiovascular risk. Patients with low eGFR and elevated UAE have significantly greater rates of myocardial infarction, ischemic stroke, hospitalization for heart failure, and mortality from cardiovascular causes than diabetic patients without nephropathy. Renal dysfunction has also been linked to the burden of atherosclerosis and adverse cardiovascular events, as severity of renal dysfunction increases. For this reason, international clinical guidelines recommend routine testing for renal function and albuminuria as part of the assessment of cardiovascular risk in patients with diabetes [6]. Although improvements have been made in diabetes care, diabetic nephropathy is still very common, especially in LMICs, where the disease progresses due to delayed diagnosis, inadequate control of blood glucose, and the lack of access to specialized renal care. Pakistan is one of the countries that have added to the diabetes burden, and the prevalence of D.K.D is still on the rise. But local information on the link between diabetic nephropathy and cardiovascular complications is still scarce. Most of the available studies have been conducted on either renal outcomes or cardiovascular disease separately, with very few studies that have examined both conditions in the Pakistani population with T2DM [7,8]. The correlation between diabetic nephropathy and cardiovascular complications is clinically relevant since identification of the high-risk patients at an early stage enables early implementation

of renoprotective and cardioprotective interventions. However, better glycemic, blood pressure, lipid, and renin-angiotensin system control, as well as the use of sodium-glucose cotransporter-2 (SGLT2) inhibitors and renin-angiotensin system blockers, have all been shown to be important predictors of reductions in renal and cardiovascular (CV) events. Therefore, identifying patients with nephropathy could help inform risk-reduction strategies and improve long-term outcomes [9]. In view of the growing epidemic of T2DM and its associated complications in Pakistan, the present study aimed to assess the relationship between DN and cardiovascular complications in patients with T2DM at a tertiary care hospital. Results will be reported as local data that can support early screening, early intervention, and enhanced management strategies to mitigate cardiovascular morbidity in this high-risk group.

Materials and Methods

Study Design and Setting

This cross-sectional study was conducted in the Department of Nephrology, Maingul Jehgnazab Hospital, Swat, from January 2025 to June 2025.

Participants

A total of 100 patients aged 30 years and older and diagnosed with type 2 diabetes mellitus for at least 5 years were included in the study. Consecutive non-probability sampling was used after obtaining written informed consent from patients attending outpatient clinics or those admitted to medical wards. Enrollment was conducted regardless of gender for eligible persons.

Sample Size Calculation

Sample size was determined using the WHO Sample Size Calculator, based on the following assumptions: diabetic nephropathy was present in 50% of patients with type 2 diabetes mellitus, a 95% confidence level, and a 10% margin of error. The minimum required number of participants was 96, so 100 patients were enrolled to enhance the study's precision.

Inclusion Criteria

- Patients at or older than 30 years.
- Have Type 2 Diabetes Mellitus for a minimum of five years.
- Both male and female patients.
- Patients who are willing to enter into written informed consent.
- Patients on the Outpatient Department or in the Medical Ward during the study period.

Exclusion Criteria

- Patients having Type 1 diabetes mellitus.
- Pregnant women.
- Other causes of chronic kidney disease (not diabetes).
- Acute kidney injury.

- Patients with congenital heart disease or rheumatic valvular heart disease.
- Patients who have an active malignancy, severe systemic infection, or incomplete clinical records.

Statistical Analysis

SPSS version 27.0 was used for data entry and analysis. Continuous variables were summarized as means ± standard deviations, while categorical variables were presented as frequencies and percentages. Associations between categorical variables were assessed using the chi-square test, and continuous variables were compared using the independent-samples t-test, as appropriate. Multivariable logistic regression was used to estimate adjusted odds ratios (ORs) and 95% confidence intervals (CIs) for factors independently associated with cardiovascular complications. A 95% CI that did not include 1.0 was considered indicative of a statistically significant association.

Results

A total of 100 patients with type 2 diabetes mellitus were included in the study. The mean age was 58.4 ± 9.8 years, with 62 (62%) males and 38 (38%) females. The mean duration of diabetes was 10.6 ± 4.5 years, while the mean HbA1c was 8.6 ± 1.4%. Diabetic nephropathy was diagnosed in 46 (46%) patients, whereas 54 (54%) did not meet the predefined criteria for diabetic nephropathy. Overall, 39 (39%) patients had at least one cardiovascular complication. Coronary artery disease was the most frequent complication (22%), followed by heart failure (9%), stroke (5%), and peripheral arterial disease (3%). Among patients with diabetic nephropathy, 28 (60.9%) had cardiovascular complications compared with 11 (20.4%) patients without nephropathy, demonstrating a statistically significant association (p = 0.001). Coronary artery disease occurred significantly more often in patients with nephropathy (34.8% vs. 11.1%; p = 0.004). Patients with cardiovascular complications had significantly lower mean eGFR (56.8 ± 18.2 mL/min/1.73 m²) than those without cardiovascular disease (81.4 ± 16.5 mL/min/1.73 m²; p < 0.001). Urinary albumin-to-creatinine ratio was also significantly higher in patients with cardiovascular complications (p = 0.002). Multivariable logistic regression showed that diabetic nephropathy was independently associated with cardiovascular complications (adjusted OR = 3.42; 95% CI: 1.48–7.91). The confidence interval did not include 1.0, indicating a statistically significant association after adjustment for age, hypertension, HbA1c, and duration of diabetes.

Table 1. Baseline Demographic and Clinical Characteristics of the Study Population (N = 100)

Variable	Value
Number of patients	100
Age (years), Mean ± SD	58.4 ± 9.8
Male, n (%)	62 (62.0)
Female, n (%)	38 (38.0)
Duration of diabetes (years), Mean ± SD	10.6 ± 4.5

Body Mass Index (kg/m ²), Mean ± SD	28.2 ± 3.9
HbA1c (%), Mean ± SD	8.6 ± 1.4
Hypertension, n (%)	68 (68.0)
Dyslipidemia, n (%)	56 (56.0)
Current smokers, n (%)	24 (24.0)
eGFR (mL/min/1.73 m ²), Mean ± SD	70.1 ± 21.4
Urinary Albumin-Creatinine Ratio (mg/g), Mean ± SD	176.8 ± 102.4

Values are presented as mean ± standard deviation (SD) for continuous variables and frequency (percentage) for categorical variables.

Table 2. Frequency of Diabetic Nephropathy and Cardiovascular Complications (N = 100)

Variable	Frequency (n)	Percentage (%)
Diabetic Nephropathy		
Present	46	46.0
Absent	54	54.0
Cardiovascular Complications		
Coronary artery disease	22	22.0
Heart failure	9	9.0
Stroke	5	5.0
Peripheral arterial disease	3	3.0
Any cardiovascular complication	39	39.0
No cardiovascular complication	61	61.0

Distribution of diabetic nephropathy and various cardiovascular complications among study participants.

Table 3. Association Between Diabetic Nephropathy and Cardiovascular Complications

Diabetic Nephropathy	Cardiovascular Complications Present n (%)	Cardiovascular Complications Absent n (%)	Total	p-value
Present (n = 46)	28 (60.9)	18 (39.1)	46	
Absent (n = 54)	11 (20.4)	43 (79.6)	54	
Total	39	61	100	0.001

Chi-square test was applied to determine the association between diabetic nephropathy and cardiovascular complications.

Table 4. Multivariable Logistic Regression Analysis of Factors Independently Associated with Cardiovascular Complications

Variable	Adjusted OR	95% CI
Diabetic nephropathy	3.42	1.48–7.91
Age >60 years	1.89	1.02–3.84
Male sex	1.28	0.66–2.73
Hypertension	2.11	1.12–4.63
HbA1c >8%	1.74	1.01–3.26
Duration of diabetes >10 years	2.47	1.21–5.06

Adjusted odds ratios (ORs) with 95% confidence intervals (CIs) are presented. Variables with 95% CIs that do not cross 1.0 were considered statistically significant.

Discussion

In the present study, diabetic nephropathy was significantly associated with cardiovascular complications among patients with type 2 diabetes mellitus. Diabetic nephropathy was present in 46% of participants, while 39% had at least one cardiovascular complication. Cardiovascular complications were significantly more frequent among patients with diabetic nephropathy than among those without nephropathy (60.9% vs. 20.4%; $p=0.001$). This finding is consistent with the established association between diabetic kidney disease and cardiovascular morbidity and provides additional hospital-based evidence from a tertiary-care population in Pakistan. Our study found that diabetic nephropathy occurred in 46% of our population, showing a significant burden of renal disease in our tertiary healthcare population. This is consistent with the general data about the high prevalence of DKD among patients who have had type 2 DM for a long time as reported by others [12]. Prevalence estimates from previous studies, however, should be compared with caution, as they have employed different diagnostic criteria, varied UACR and eGFR values, sampled different populations, and used a variety of sampling methods. Varying diabetes duration and glycemic control, hypertension status, ethnicity, and access to care may also account for some of the differences observed across studies. This high frequency in our study might, however, be partially accounted for by a tertiary care setting, since patients with tertiary care diabetes are more likely to have chronic or complicated diabetes. Thirty-nine percent had one or more cardiovascular complications, the most common being CAD. This was similar to the previous study, in which patients with diabetes and renal insufficiency had a significant cardiovascular burden [13]. This is because the prevalence found in this hospital-based study cannot be used as a population-level estimate, as the study was conducted in one hospital and used consecutive non-probability sampling. Instead, the discovery suggests a significant burden of cardiovascular disease among patients undergoing tertiary care diabetes care. The high prevalence of CAD could be attributed to the synergistic action of chronic hyperglycemia, dyslipidemia, endothelial dysfunction, oxidative stress, and systemic inflammation [14]. The significant difference in the cardiovascular complications between nephropathic and non-nephropathic individuals was the most important finding of the present study. Sixty percent of patients with diabetic nephropathy

had cardiovascular complications, while 20% of patients without nephropathy had cardiovascular complications. This is a clinically important difference and is consistent with previous studies showing a link between albuminuria and elevated cardiovascular morbidity [15,16]. The present cross-sectional study, on the other hand, measured exposure and outcome simultaneously, which is not the case in prospective studies. Thus, the observed relationship is neither causal nor temporal. Therefore, Diabetic nephropathy should be considered an important marker of cardiovascular risk rather than a proven cause of cardiovascular complications. Similarly, patients with cardiovascular complications had significantly lower mean eGFR than patients without cardiovascular complications (56.8 ± 18.2 vs. 81.4 ± 16.5 mL/min/1.73 m²; $p<0.001$). This result is similar to what has previously been reported regarding a relationship between low renal function and higher cardiovascular risk [17]. This connection may involve several mechanisms, including vascular calcification, chronic inflammation, renin-angiotensin-aldosterone system activity, anemia, oxidative stress, and fluid imbalance. Likewise, patients with cardiovascular complications had significantly elevated urinary albumin excretion, which is in line with previous findings suggesting that albuminuria may be a marker of generalized endothelial and vascular damage [18]. After adjustment for relevant covariates, diabetic nephropathy remained independently associated with cardiovascular complications (adjusted OR = 3.42; 95% CI: 1.48–7.91). This finding is directionally consistent with current evidence showing an association between diabetic kidney disease and cardiovascular morbidity [19]. However, the association should be interpreted with caution given the relatively small sample size, limited number of cardiovascular events, cross-sectional design, and potential for residual confounding. Other factors that may influence cardiovascular risk include lipid levels, medication use, smoking, socioeconomic status, and the severity and duration of kidney disease. However, the association should be interpreted with caution given the small sample size, small number of cardiovascular events, cross-sectional design, and potential for residual confounding. The clinical implications are relevant to the tertiary care diabetes services in Pakistan. In addition to regular renal monitoring, patients with diabetic nephropathy could benefit from systematic cardiovascular risk assessment. Optimal glycemia, blood pressure, lipid levels, albuminuria, and other modifiable cardiovascular risk factors can be managed, along with appropriate evidence-based cardiorenal-protective therapies, to reduce long-term cardiovascular and renal outcomes [20,21]. Diabetic nephropathy may therefore help identify patients who require more intensive cardiovascular risk assessment and preventive management. Overall, the study findings are consistent with the existing literature and provide additional hospital-based evidence from Pakistan. The present study explored both renal and cardiovascular outcomes in a single population of diabetics, while previous studies have focused on one outcome or the other. However, the single-center design, small sample size, and cross-sectional nature limit generalizability and preclude assessment of temporal relationships. Larger and more diverse Pakistani cohorts should be evaluated in future multicenter prospective studies to determine whether diabetic nephropathy is associated with subsequent cardiovascular events and to assess the effectiveness of integrated cardiorenal risk-reduction strategies.

Limitations

The limitations of this study were that it was cross-sectional, which means that no causal relationships could be established. It was conducted at a single tertiary care center, and the sample size was relatively small (100 patients), so the results may not be generalizable. These results need to be confirmed in larger numbers of patients in multicenter studies over longer periods to determine long-term cardiovascular outcomes.

Conclusion

Diabetic nephropathy was significantly associated with cardiovascular complications among patients with type 2 diabetes mellitus. Patients with diabetic nephropathy had a substantially higher frequency of cardiovascular complications than those without nephropathy. Routine assessment of albuminuria and renal function may help identify patients at increased cardiovascular risk and support timely preventive and therapeutic interventions.

Disclaimer: Nil

Conflict of Interest: Nil

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Authors' Contributions

Rahmat Ali Khan and Sardar Khan contributed to the study's conception and design, data collection, data analysis and interpretation, and critical revision of the manuscript. **Sardar Khan** drafted the manuscript. Both authors approved the final version of the manuscript and agree to be accountable for all aspects of the work.

Ethical Approval

Ethical approval for this study was obtained from the Ethical Review Board of Saidu Medical College and Swat Medical College under **approval No. 126/PR3/SMC/023, dated 15 October 2023**. Written informed consent was obtained from all participants before enrollment. Confidentiality and privacy of participants were maintained throughout the study

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