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GLYCEMIC CONTROL AND ITS ASSOCIATION WITH MICROVASCULAR COMPLICATIONS IN TYPE 2 DIABETES

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Abstract

Background: *Type 2 diabetes mellitus is a highly prevalent chronic disorder associated with long-term vascular complications. Poor glycemic control plays a pivotal role in the development of microvascular complications such as retinopathy, nephropathy, and neuropathy, which significantly affect quality of life and increase healthcare burden.*

Objectives: *To determine the association of glycemic control with microvascular complications in patients with type 2 diabetes.*

Study Design & Setting: *An analytical cross-sectional study was conducted at the outpatient endocrinology clinics of a tertiary care teaching hospital over six months.*

Methodology: *A total of 150 patients with type 2 diabetes were enrolled. Glycemic control was assessed by HbA1c levels and categorized as good (<7.0%), suboptimal (7.0–8.9%), and poor (≥9.0%). Microvascular complications were identified through standardized methods: retinopathy by dilated fundus examination, nephropathy by urine albumin-to-creatinine ratio and eGFR, and neuropathy by monofilament and vibration perception testing. Data were analyzed using SPSS version 25. Logistic regression was applied to assess associations.*

Results: *The mean age of patients was 54.8 ± 9.6 years with a male predominance (58.7%). Good glycemic control was present in 28.0%, suboptimal in 37.3%, and poor in 34.7% of patients. Retinopathy, nephropathy, and neuropathy were present in 30.0%, 25.3%, and 34.7% of patients, respectively. Poor glycemic control was significantly associated with higher frequencies of all complications. Each 1% rise in HbA1c increased the odds of retinopathy (OR 1.48, p=0.006), nephropathy (OR 1.42, p=0.021), and neuropathy (OR 1.55, p=0.002).*

Conclusion: *Poor glycemic control was strongly associated with increased risk of microvascular complications in type 2 diabetes. Optimal glycemic management is*

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essential to reduce long-term morbidity.

INTRODUCTION

Type 2 diabetes mellitus (T2DM) is one of the most prevalent metabolic disorders worldwide, characterized by chronic hyperglycemia due to insulin resistance and relative insulin deficiency.[1] According to the International Diabetes Federation (IDF), an estimated 537 million adults were living with diabetes in 2021, and this figure is projected to rise to 643 million by 2030.[2,3] Among these, the majority suffer from T2DM, which poses a significant public health challenge due to its chronic course, lifelong management requirements, and the risk of long-term complications.[4] Glycemic control, primarily measured through glycated hemoglobin (HbA1c) levels, remains the cornerstone in preventing or delaying the onset of diabetes-related complications.[5]

Sustained hyperglycemia in T2DM exerts deleterious effects on blood vessels, leading to both microvascular and macrovascular complications. Microvascular complications, including diabetic retinopathy, nephropathy, and neuropathy, are of particular concern as they are directly linked to prolonged poor glycemic control and can significantly impair quality of life.[6,7] Diabetic retinopathy is a leading cause of blindness among working-age adults, diabetic nephropathy is the most common cause of end-stage renal disease worldwide, and diabetic neuropathy increases the risk of foot ulcers and amputations. Collectively, these complications contribute substantially to the morbidity, disability, and economic burden associated with T2DM.[8]

The relationship between glycemic control and microvascular complications has been well established through landmark clinical trials. The United Kingdom Prospective Diabetes Study (UKPDS) demonstrated that intensive glycemic control reduced the risk of microvascular endpoints by 25% compared to conventional therapy.[9] Similarly, the Diabetes Control and Complications Trial (DCCT), though conducted in type 1 diabetes, reinforced the principle that improved glycemic control significantly reduces microvascular damage, and these findings have been extrapolated to T2DM. Moreover, evidence from epidemiological studies consistently shows that higher HbA1c levels are associated with increased risk and severity of microvascular complications.[10-12]

Despite these findings, achieving and maintaining optimal glycemic targets in real-world settings remains challenging due to factors such as delayed diagnosis, poor adherence to lifestyle modifications, limited access to healthcare resources, and comorbid conditions. Furthermore, ethnic and regional variations in the prevalence and progression of complications highlight the need for context-specific research. In many low- and middle-income countries, including Pakistan, limited awareness, poor follow-up, and inadequate screening programs contribute to a higher burden of diabetes-related complications. Given the global rise in T2DM and its complications, it is crucial to explore the association between glycemic control and microvascular outcomes in diverse populations. Understanding this relationship not only emphasizes the importance of strict glycemic management but also guides clinical decision-making, patient education, and policy formulation aimed at reducing the long-term burden of diabetes.

MATERIALS AND METHODS

Ethical approval was obtained from the institutional review board, and written informed consent was obtained from all participants; confidentiality was maintained throughout. The study was designed as an analytical cross-sectional investigation and was conducted in the outpatient of Shaikh Zayed Hospital Lahore from November 2024 to April 2025. A total of 150 adults with type 2 diabetes mellitus (T2DM) were enrolled by consecutive sampling. Eligibility was defined as age ≥18 years, a confirmed diagnosis of T2DM for ≥1 year, and at least one visit during the study window. Patients with type 1 diabetes, gestational diabetes, acute intercurrent illness, known proliferative retinopathy treated within the last 6 months, advanced chronic kidney disease on dialysis, chronic steroid use, or incomplete records were excluded. Sample size was calculated using the single-proportion formula $n = Z^2 \cdot p(1-p)/d^2$ with Z=1.96, p=0.50, and d=0.08; the

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minimum n was 150 after allowing for ~10% non-response. Data were collected on a structured proforma and were abstracted from the electronic record and a same-day clinical assessment. Glycemic control was assessed by glycated hemoglobin (HbA1c) measured by high-performance liquid chromatography in a College of American Pathologists-accredited laboratory; fasting plasma glucose and lipid profile were recorded when available within 4 weeks of the index visit. Glycemic control was categorized as good (HbA1c <7.0%), suboptimal (7.0–8.9%), and poor (≥9.0%). Microvascular complications were ascertained as follows. Diabetic retinopathy was assessed by dilated fundus examination performed by an ophthalmologist or 2-field fundus photography, and was graded according to ETDRS categories; presence of any non-proliferative or proliferative retinopathy was coded as retinopathy present. Diabetic nephropathy was assessed by spot urine albumin-to-creatinine ratio (ACR) and estimated glomerular filtration rate (eGFR, CKD-EPI); microalbuminuria was defined as ACR 30–300 mg/g and macroalbuminuria as >300 mg/g. Peripheral neuropathy was assessed by 10-g Semmes–Weinstein monofilament at 10 sites per foot and vibration perception with a 128-Hz tuning fork at hallux; neuropathy was defined when ≥1 sensory modality was abnormal bilaterally or when a neuropathy disability score ≥3 was recorded. Covariates including age, sex, duration of diabetes, body mass index, blood pressure, smoking status, antihyperglycemic regimen, and statin/ACEI-ARB use were recorded. Data were entered in SPSS (version 25) and were cleaned prior to analysis. Normality was assessed by the Shapiro–Wilk test. Continuous variables were summarized as mean±SD or median (IQR) and categorical variables as n(%). The association between HbA1c categories and each microvascular complication was tested with chi-square, and p-for-trend across ordered HbA1c groups was estimated. Multivariable logistic regression models were fitted for retinopathy, nephropathy, and neuropathy with HbA1c (continuous per 1% increase and categorical) as the exposure and adjustment for prespecified covariates; adjusted odds ratios with 95% confidence intervals were reported. A two-sided $p<0.05$ was considered statistically significant.

RESULTS

The baseline demographic and clinical characteristics of the study participants are presented in Table 1. The mean age of patients was 54.8 ± 9.6 years, with a male predominance (58.7%). The mean duration of diabetes was 8.7 ± 4.2 years, and the mean BMI was 27.6 ± 3.9 kg/m², indicating that most patients were overweight. Hypertension was found in 64.0% of the study population, while 18.7% were current smokers. Regarding treatment, 34.7% of the patients were on insulin therapy whereas 65.3% were managed with oral hypoglycemic agents only.

The distribution of glycemic control among the study population is shown in Table 2. Out of 150 patients, 28.0% had good control (HbA1c <7.0%), 37.3% had suboptimal control (HbA1c 7.0–8.9%), and 34.7% had poor control (HbA1c ≥9.0%). The overall mean HbA1c level was 8.4 ± 1.2%, reflecting that a majority of patients were unable to achieve recommended glycemic targets.

The frequency of microvascular complications is detailed in Table 3. Diabetic retinopathy was observed in 30.0% of patients, nephropathy in 25.3%, and neuropathy in 34.7%. More than half of the participants (58.0%) had at least one microvascular complication, whereas 42.0% did not exhibit any evidence of such complications.

The association between glycemic control and microvascular complications is summarized in Table 4. Patients with poor glycemic control (HbA1c ≥9.0%) had a higher prevalence of all complications compared to those with good control. Retinopathy was present in 46.2% of poorly controlled patients compared to only 14.3% in those with good control. Similarly, nephropathy was found in 42.3% of poorly controlled patients versus 11.9% in the good control group. Neuropathy was most frequent among poorly controlled patients (53.8%) compared to 19.0% in those with HbA1c <7.0%. Overall, 80.8% of patients with poor glycemic control had at least one microvascular complication, while only 35.7% of patients with good control developed any complication.

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The logistic regression analysis is presented in Table 5. Each 1% increase in HbA1c was significantly associated with higher odds of developing microvascular complications. The adjusted odds ratio (OR) for retinopathy was 1.48 (95% CI: 1.12–1.97, p=0.006), for nephropathy was 1.42 (95% CI: 1.05–1.92, p=0.021), and for neuropathy was 1.55 (95% CI: 1.18–2.05, p=0.002). The combined outcome of any complication showed the strongest association, with an OR of 1.63 (95% CI: 1.24–2.15, p<0.001).

Table 1. Baseline Demographic and Clinical Characteristics of Patients with Type 2 Diabetes (n=150)

Variable	Mean ± SD / n (%)
Age (years)	54.8 ± 9.6
Male	88 (58.7)
Female	62 (41.3)
Duration of Diabetes (years)	8.7 ± 4.2
BMI (kg/m²)	27.6 ± 3.9
Hypertension	96 (64.0)
Current Smokers	28 (18.7)
On Insulin Therapy	52 (34.7)
On Oral Hypoglycemics Only	98 (65.3)

Table 2. Glycemic Control Status of the Study Population (n=150)

HbA1c Category	n (%)	Mean HbA1c ± SD
Good Control (<7.0%)	42 (28.0)	6.5 ± 0.3
Suboptimal (7.0–8.9%)	56 (37.3)	8.1 ± 0.6
Poor (≥9.0%)	52 (34.7)	9.6 ± 0.5
Overall	150 (100)	8.4 ± 1.2

Table 3. Frequency of Microvascular Complications in the Study Population (n=150)

Complication	n (%)
Retinopathy	45 (30.0)
Nephropathy	38 (25.3)
Neuropathy	52 (34.7)
≥1 Complication	87 (58.0)
No Complication	63 (42.0)

Table 4. Association of Glycemic Control with Microvascular Complications (n=150)

Complication	Good Control <7.0% n=42	Suboptimal 7.0–8.9% n=56	Poor ≥9.0% n=52
Retinopathy	6 (14.3)	15 (26.8)	24 (46.2)
Nephropathy	5 (11.9)	11 (19.6)	22 (42.3)
Neuropathy	8 (19.0)	16 (28.6)	28 (53.8)
≥1 Complication	15 (35.7)	30 (53.6)	42 (80.8)

Table 5. Logistic Regression Analysis of HbA1c with Microvascular Complications (n=150)

Complication	Adjusted OR (95% CI) per 1% ↑ HbA1c	p-value
Retinopathy	1.48 (1.12–1.97)	0.006

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Nephropathy	1.42 (1.05–1.92)	0.021
Neuropathy	1.55 (1.18–2.05)	0.002
Any Complication	1.63 (1.24–2.15)	<0.001

DISCUSSION

Type 2 diabetes mellitus is a chronic metabolic disorder with rising prevalence worldwide, leading to significant morbidity and mortality. Poor glycemic control is strongly linked with the development of microvascular complications such as retinopathy, nephropathy, and neuropathy.[13] These complications reduce quality of life and increase healthcare costs. HbA1c remains the standard biomarker for assessing long-term glycemic control. Previous trials like UKPDS and DCCT have established its role in reducing complication risks.[14] However, data from local populations remain limited, necessitating this study.

In our study, the mean age of patients was 54.8 ± 9.6 years, with a male predominance of 58.7%, closely resembling the findings of Ali et al. (2023), where the mean age at diagnosis was 55.6 ± 10.2 years, although they reported a slightly higher proportion of females (52%).[16] Our results showed that 28.0% of patients had good glycemic control, 37.3% had suboptimal, and 34.7% had poor control, whereas Ali et al. reported much lower rates of good control (12%) and markedly higher rates of poor control (64%, HbA1c ≥8%).[16] Similarly, Muhammad et al. (2021) found that 78.1% of their 300 patients had poor glycemic control, which was higher than in our population. These differences highlight variation in healthcare access, adherence, and awareness across different study populations.[17]

Regarding complications, our study showed retinopathy in 30.0%, nephropathy in 25.3%, and neuropathy in 34.7% of patients, with 58.0% having at least one complication. These findings were lower compared to Memon et al. (2025), who reported markedly higher rates: retinopathy 73.3%, neuropathy 63.3%, and nephropathy 40%, possibly due to their younger but poorly controlled cohort (mean age 24.23 ± 3.45 years; HbA1c 7.65 ± 1.15%).[15] Their study also demonstrated very strong correlations of HbA1c with KDIGO (r=0.839), ETDRS (r=0.864), and TCNS (r=0.870), stronger than those reported in Ali et al. (2023), where correlations were moderate—retinopathy (r=0.42), neuropathy (r=0.39), nephropathy (r=0.34), and CVD (r=0.28), all p<0.01. Our regression analysis similarly showed HbA1c as an independent predictor, with each 1% increase associated with higher odds of retinopathy (OR 1.48), nephropathy (OR 1.42), and neuropathy (OR 1.55), comparable to the independent predictive role of HbA1c in Ali et al.'s logistic regression.[16]

The prevalence of complications in our study was also comparable to the ranges highlighted in the review by Taimur et al. (2024), where retinopathy (14.5–43.0%), nephropathy (14.0–31.0%), and neuropathy (10.8–59.6%) were most frequently observed.[18] Similarly, our findings align with Muhammad et al. (2021), who reported retinopathy 44.4%, neuropathy 36.9%, and nephropathy 31.6%, though their rates were slightly higher, likely influenced by a longer diabetes duration.[17] Vankwani et al. (2024) also confirmed the link between microvascular complications and nephropathy progression, showing retinopathy and neuropathy significantly associated with CKD stages (p<0.05), supporting our observation that nephropathy was strongly related to poor control (42.3% in HbA1c ≥9.0% vs. 11.9% in HbA1c <7.0%).[19]

Furthermore, Jabeen et al. (2023) emphasized the metabolic link of HbA1c with cardiovascular risk through triglyceride-glucose index and triglyceride-HDL ratio, showing very strong correlations with HbA1c (r=0.963 and r=0.757, p=0.01). While our study did not assess lipid indices, their findings reinforce HbA1c as a robust biomarker not only for microvascular but also macrovascular outcomes.[20]

A major strength of this study was the use of standardized diagnostic methods for assessing microvascular complications. Another strength was the inclusion of a reasonably sized sample (n=150) representative of a typical tertiary-care diabetic population. The study also provided local evidence that adds to the existing global literature. However,

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being a cross-sectional design, it could not establish causality. Single-center recruitment may limit generalizability of findings. Additionally, some variables such as adherence to therapy and lifestyle factors were not fully explored.

CONCLUSION

Poor glycemic control was significantly associated with higher frequency of microvascular complications in patients with type 2 diabetes. HbA1c remained a strong predictor of risk across all complications. Optimal glycemic management is essential to prevent long-term diabetes-related morbidity.

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