DOI: https://doi.org/10.54393/pjhs.v6i3.2650

PAKISTAN JOURNAL OF HEALTH SCIENCES
(LAHORE)
https://thejas.com.pk/index.php/pjhs
ISSN (E): 2790-9352, (P): 2790-9344
Volume 6, Issue 03 (March 2025)

Original Article

OPEN ACCESS

The Correlation between Glycemic Control and Microvascular Complications in Type 1 Diabetes Mellitus Patients

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ARTICLE INFO

Keywords:

Type 1 Diabetes Mellitus, Glycemic Control, Hba1c, Microvascular Complications

How to Cite:

Memon, Y., Fareed, G., Qureshi, K. A., Kumar, M., Baig, M. S., Memon, Z. H., & Karim, I. (2025). The Correlation between Glycemic Control and Microvascular Complications in Type 1 Diabetes Mellitus Patients : Glycemic Control and Microvascular Complications in Type 1 Diabetes Mellitus Patients. Pakistan Journal of Health Sciences, 6(3), 18-22. https://doi.org/10.54393/pjhs .v6i3.2650

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Received date: 15th February, 2025
Acceptance date: 28th March, 2025
Published date: 31st March, 2025

ABSTRACT

Type 1 Diabetes Mellitus (T1DM) is a chronic condition that destroys pancreatic beta cells, leading to persistent hyperglycemia. Prolonged high levels resulted in an increased risk of microvascular complications. Glycemic control, indicated by HbA1c, plays a critical role in reducing these risks. **Objective:** To examine the strength of the relationship between HbA1c levels and the severity of microvascular complications in individuals with T1DM. **Methods:** A cross-sectional study was conducted on 30 patients with T1DM at Liaquat University Hospital, Hyderabad, from December 2024 to February 2025. HbA1c levels were recorded, and microvascular complications were evaluated using KDIGO criteria for nephropathy, ETDRS for retinopathy, and TCNS for neuropathy. Data were analyzed using descriptive statistics and inferential methods, including Spearman's correlation and linear regression, through SPSS version 22.0. **Results:** The average age of participants was 24.23 ± 3.45 years, with a mean HbA1c level of 7.65 ± 1.15%. Retinopathy was the most frequent complication (73.3%), followed by neuropathy (63.3%) and nephropathy (40%). Combined complications were present in 40% of cases. HbA1c levels were significantly correlated with the severity of all microvascular complications, showing positive associations with KDIGO (r=0.839), ETDRS (r=0.864), and TCNS (r=0.870). HbA1c values also progressively increased with complication severity (p<0.001). **Conclusions:** It was concluded that poor glycemic control was strongly associated with the presence and severity of microvascular complications in T1DM patients. These findings highlight the importance of maintaining optimal HbA1c levels to mitigate complications. Further longitudinal studies are warranted to explore these associations in greater depth.

INTRODUCTION

Diabetes mellitus is a global epidemic with reported cases of 578 million people worldwide by the year 2030 and affects both microvascular and macrovascular [1]. The most common complications include diabetic Nephropathy, retinopathy, and neuropathy [2]. The development of complications begins early and can occur late after diagnosis in young people with type 1 diabetes (T1D) [3]. This is the most common form of diabetes with 90% of cases in children and adolescents age group. Although the global variation is large, the incidence is increasing by 3–4% per year worldwide [4]. The Diabetes Control and Complications Trial (DCCT) and Epidemiology of Diabetes Interventions and Complications (EDIC) provide significant evidence for intensive insulin treatment to achieve controlled glycemic levels and avoidance of long-term consequences [5]. Some studies suggest the prevalence of Retinopathy (82–100%) which resulted in a leading cause of blindness, Nephropathy (20–40%), and Neuropathy which resulted in most non-traumatic amputations [6-8]. The prevalence of microvascular complications among the Pakistani population includes Diabetic retinopathy (DR) 32.4% was the most prevalent

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one followed by nephropathy (30.6%), neuropathy (DN) (28.1%), and gastroparesis (DG) 22.3% but patients are mostly with metabolic syndrome [9]. Glycemic control for the prevention of complications is necessary. It should be primarily assessed using HbA1c, a well-known and reliable biomarker that reflects average glycemic levels over time. Current international guidelines recommend HbA1c levels below 53 mmol/mol (7%) for the majority of adults, or below 47.5 mmol/mol (6.5%) when safely achievable [10]. Indeed, it is a chronic disease characterized by the autoimmune destruction of beta cells in the pancreas, resulting in absolute insulin deficiency. Insulin deficiency in T1DM can lead to poor glycemic control resulting in the development of retinopathy, nephropathy, and neuropathy, with a significant impact on patient morbidity and quality of life. The data regarding microvascular complications is scarce in Pakistan and this study will help us to direct attention regarding the prevalence and measurements of microvascular complications.

This study aims to see the correlation of glycemic control with the presence of microvascular complications in T1DM patients.

METHODS

This cross-sectional study was conducted at the Department of Medicine, Liaquat University of Medical and Health Sciences (LUMHS), Hyderabad, Pakistan. Ethical approval was obtained under (Reference No. LUMHS/REC/-548). Following the IRB approval, prospective data collection was performed from December 2024 to February 2025. Telephonic communication was made with patients and a request for follow-up was made. The sample size was calculated using Open Epi software. The study employed consecutive sampling, enrolling 30 patients with Type 1 Diabetes Mellitus (T1DM) who met the inclusion criteria of being over 18 years of age, diagnosed with T1DM for at least five years, and having HbA1c records available for the past year. Patients with incomplete medical records, TIDM not more than five years, or Type 2 Diabetes Mellitus were excluded. Data collection was carried out systematically. Patients were recruited from outpatient clinics, including diabetic and medical clinics. After obtaining informed consent, participants underwent detailed clinical evaluations. HbA1c levels were measured using high-performance liquid chromatography (HPLC), following standardized laboratory protocols to ensure precision in glycated hemoglobin assessment. The presence and severity of microvascular complications were assessed through referrals to specialized departments. Diabetic nephropathy was evaluated using Kidney Disease: Improving Global Outcomes (KDIGO) guidelines, involving glomerular filtration rate and albuminuria measurements. Diabetic retinopathy was assessed using the Early Treatment Diabetic Retinopathy Study (ETDRS) scale through fundoscopic examinations. Neuropathy severity was determined using the Toronto Clinical Neuropathy Score (TCNS), which included symptom evaluation, reflex testing, and sensory testing. Statistical analysis was conducted using SPSS version 22.0. Descriptive statistics were performed to summarize patient demographics and clinical characteristics. Continuous variables were presented as mean ± standard deviation, while categorical variables were expressed as frequencies and percentages. The Chi-square test was used to analyze categorical data, and independent t-tests or Mann-Whitney U tests were applied for continuous data. The association and effect size between HbA1c levels and microvascular complications were evaluated using Spearman's correlation and linear regression. A p-value of <0.05 was considered statistically significant.

RESULTS

A total number of 30 patients were enrolled and the mean age was 24.23 ± 3.45 and 53.3% were male. Mean glycemic control and duration of disease were 7.65 ± 1.15 and 6.26 ± 1.46 respectively. The HbA1c levels were normality distributed (Parametric) as compared to the Duration of disease, which was not normally distributed (Non-parametric)(Table 1).

Table 1: General Data Distribution

Variables	Mean ± SD/ n (%)
Age	24.23 ± 3.45
Gender	
Male	53%
Female	47%
Duration of Disease	6.26 ± 1.46 years
Mean Glycemic Control	7.65 ± 1.15
Micro-Vascular Complication	
Nephropathy	12 (40%)
Retinopathy	22 (73.3%)
Neuropathy	19 (63.3%)
Combined	12 (40%)

The mean HBA1c in Nephropathy, Neuropathy, Retinopathy, and combined was 8.75 ± 0.89, 8.27 ± 0.97, 8.10 ± 1.0 and 8.75 ± 0.89 respectively. The mean duration of disease in nephropathy, neuropathy, retinopathy, and combined was 7.0 ± 1.65, 6.3 ± 1.6, 6.5 ± 1.5, and 7.0 ± 1.65 years respectively. The nephropathy and combined Microvascular complications show similar patterns in Mean HBA1c levels and Mean duration of Diabetic Type 1 Complications. Mean HBA1c was significantly associated with Microvascular complication (p-0.001) and it is calculated by One Way ANOVA. On the other hand, the duration of the disease was nonparametric and the association with nephropathy (p-024), Neuropathy (p-0.92), retinopathy (0.21), and Combined (0.024) was calculated by Mann Whitney U test (Figure 1).

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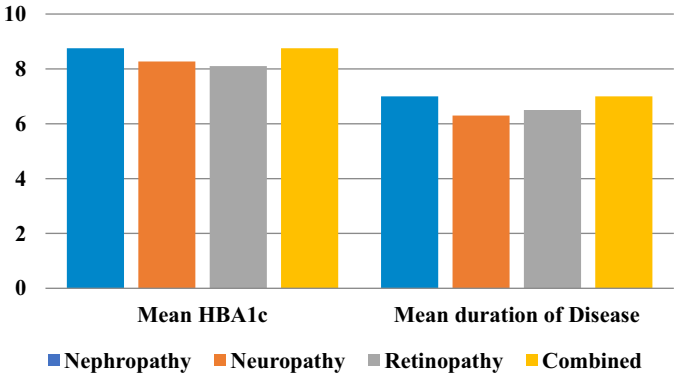

Figure 1: Change in Mean HBA1c and Duration of Disease according to Micro-vascular complication

The detailed assessment of Microvascular complications, from the evaluation of the Nephrology Department 60% of patients have G1 (GFR>90) and A1 (<30 mg/g). 16.7% of patients have G2 (GFR 60-89 ml/min/1.73m2) A2 (30-300 mg/g). 13.3% of patients have G3a (GFR: 45-59 ml/min/1.73m2) A2. 3.3% of patients have G3b (GFR: 30-44 ml/min/1.73m2) and A3 (>300mg/g). 6.7% of patients have G4 (GFR: 15-29 ml/min/1.73m2) and A3 (Figure 2).

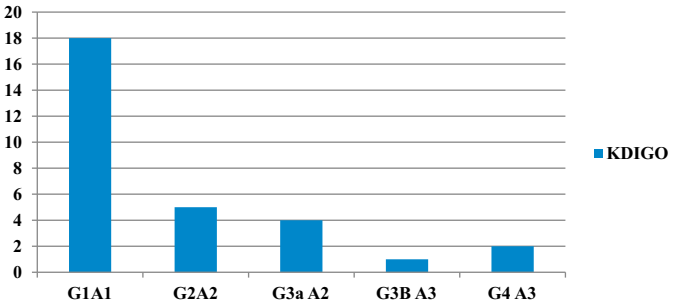

Figure 2: Kidney Disease Improving Global Outcome Scale (KDIGO)

In the case of retinopathy, the moderate non-proliferative diabetic retinopathy was most common one (30%) as compared to other subcategories of ETDRS score (Figure 3).

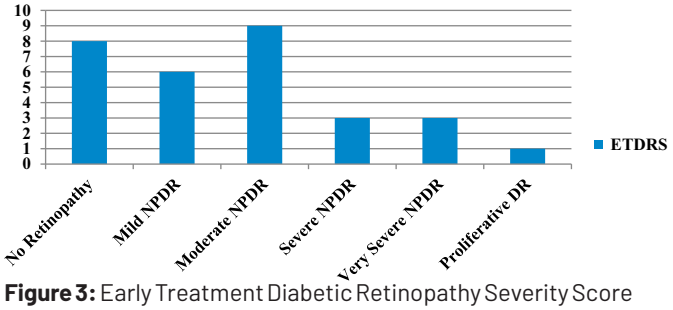

Figure 3: Early Treatment Diabetic Retinopathy Severity Score

In the case of neuropathy, (46.7%) have moderate neuropathy on TCNS score (Figure 4).

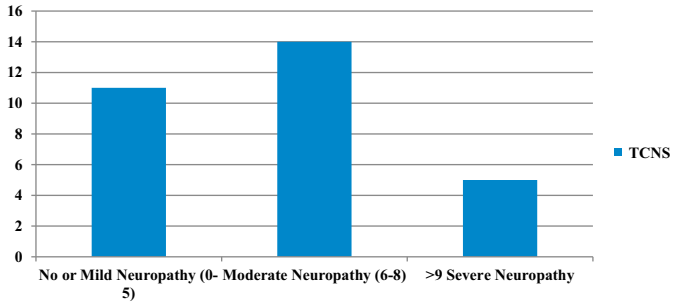

Figure 4: Toronto Clinical Neuropathy Score (TCNS)

Results show a positive correlation between HBA1c and KDIGO, which was significant and it was calculated with Spearman rho correlation, it has been shown a 0.839% increase in HBA1c levels could result in KDIGO change (Table 2).

Table 2: Kidney Disease Improving Global Outcome Scale with HBA1c Levels

KDIGO	Mean ± SD
G1 A1	6.92 ± 0.60
G2 A2	8.00 ± 0.35
G3a A2	9.00 ± 0.81
G3b A3	9.00
G4 A3	10.00

Results show a positive correlation between HBA1c and ETDRS, which was significant and it was calculated with Spearman rho correlation on linear regression, it has been shown that a 0.864 % increase in HBA1c levels could result in ETDRS change (Table 3).

Table 3: Early Treatment Diabetic Retinopathy Score with HBA1c Levels

ETDRS	Mean ± SD
No retinopathy	6.43 ± 0.41
Mild NPDR	7.20 ± 0.40
Moderate NPDR	8.16 ± 0.90

It shows a positive correlation between HBA1c and TCNS, which was significant and it was calculated with Spearman rho correlation, it has been shown that a 0.870% increase in HBA1c levels could result in TCNS change (Table 4).

Table 4: Toronto Clinical Neuropathy Score with HBA1c Levels

TCNS	Mean ± SD
No or Mild Neuropathy	6.59 ± 0.43
Moderate neuropathy	7.87 ± 0.64
Severe Neuropathy	9.40 ± 0.89

DISCUSSION

The findings emphasize the significant impact of glycemic control (HbA1c levels) on the prevalence and severity of microvascular complications in patients with Type 1 Diabetes Mellitus (T1DM) [1]. The mean age of the study participants was 24.23 ± 3.45 years, with 53.3% males and 47% females. This aligns with global epidemiological data

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showing T1DM as a condition commonly affecting young adults and adolescents. The mean HbA1c of 7.65 ± 1.15% and mean disease duration of 6.26 ± 1.46 years highlight the challenges in achieving optimal glycemic control in this population. According to the DCCT and EDIC trials, a similar pattern of poor glycemic control has been linked to microvascular complications even in younger cohorts [5]. The prevalence of complications with HBA1c values was retinopathy (73.3%, 8.10 ± 1.0), neuropathy (63.3%, 8.27 ± 0.97), nephropathy (40%, 8.75 ± 0.89), and combined complications (40%, 8.75 ± 0.89) demonstrates the burden of micro-vascular complications in this cohort. These results support findings which demonstrate that each 1% rise in HbA1c significantly increases the risk of microvascular complications [11]. Current findings are consistent with studies in both developed and developing countries, including those from Pakistan, where retinopathy was reported as the most prevalent microvascular complication in T1DM [9]. Regional studies have shown that socioeconomic barriers, limited access to healthcare, and inadequate follow-up contribute to poor glycemic control [12, 13]. In comparison with cohorts of developed countries, LMIC faces a disproportionately higher risk of complications, emphasizing the need for tailored diabetes management strategies in resource-limited settings [14, 15]. The distribution of nephropathy according to KDIGO classification revealed that 60% of patients were in the early stages (G1 and A1), with only 6.7% in advanced nephropathy (G4 A3). This aligns with studies reporting nephropathy as a late complication, usually progressing with longer disease duration and poor glycemic control [16]. A positive correlation between HbA1c and KDIGO stages, calculated using Spearman's rho correlation, indicated that even small increments in HbA1c (rs=0.839, CI 95% [0.584, 0.918], r2=0.704) significantly worsen kidney function. Moderate non-proliferative diabetic retinopathy (NPDR) was the most common subtype, affecting 30% of participants [17]. For Retinopathy, the mean HbA1c values increased progressively across ETDRS categories, from 6.43 ± 0.41% in patients without retinopathy to 9.33 ± 0.57% in those with very severe NPDR. Our findings are consistent with the Early Treatment Diabetic Retinopathy Study and similar research showing that retinopathy severity correlates strongly with poor glycemic control (rs=0.864, CI 95% [0.733, 0.935], r2=0.746) [18]. Neuropathy severity, as assessed by TCNS, revealed that 46.7% of participants had moderate neuropathy. The mean HbA1c levels increased with the severity, from 6.59 ± 0.43% (mild neuropathy) to 9.40 ± 0.89% (severe neuropathy). This trend highlights the critical role of maintaining optimal HbA1c levels to prevent or delay neuropathy progression (rs=0.870, CI 95% [0.762, 0.927], r2=0.757) [19]. These findings align with study by Sheleme *et al.*, which emphasize the linear relationship between hyperglycemia and nerve damage [7].This reinforces the synergistic impact of poor glycemic control on multiple organ systems. Studies include the association of retinopathy with nephropathy resulting in poor kidney function, and intensive glycemic control can reduce the cumulative risk of combined complications by over 60% [18, 20]. Future directions include longitudinal studies, expanding sample size and diversity, including a broader patient population, assessing other risk factors, and exploring intervention strategies. The future practical recommendations include enhancing HbA1c monitoring, introducing structured diabetes education programs, implementing early screening for complications, adapting multidisciplinary care, promoting access to resources, and longitudinal monitoring with proper data collection.

CONCLUSIONS

It was concluded that reaffirms the pivotal role of maintaining HbA1c levels below 7 to reduce the risk and severity of microvascular complications in T1DM patients. The strong association between HbA1c and the severity of complications emphasizes the necessity of strict glycemic control.Targeted interventions,such as frequent monitoring, patient education, and timely adjustment to insulin therapy are vital for achieving these glycemic goals. Our findings support integrating individualized treatment plans into routine care to minimize complications and improve long-term outcomes.

Authors Contribution

Conceptualization: KAQ
Methodology: YM, KAQ, MK, MSB
Formal analysis: IK
Writing review and editing: GF, ZHM

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

Conflicts of Interest

All the authors declare no conflict of interest.

Source of Funding

The author received no financial support for the research, authorship and/or publication of this article.

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