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ASSOCIATION BETWEEN GLYCEMIC VARIABILITY AND MICROVASCULAR COMPLICATIONS IN PATIENTS WITH TYPE 2 DIABETES ATTENDING A TERTIARY CARE HOSPITAL

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Abstract

Background: Chronic hyperglycemia is a well-established risk factor for diabetic microvascular complications; however, increasing evidence suggests that glycemic variability may independently contribute to vascular damage. ***Aims:*** This study aimed to evaluate the association between glycemic variability indices and microvascular complications in patients with type 2 diabetes mellitus. ***Methods:*** This hospital-based observational cross-sectional study was conducted in the Department of General Medicine at Prakash Institute of Medical Science and Research, Maharashtra (415409), over a defined study period. The study population comprised patients with type 2 diabetes mellitus attending both outpatient and inpatient departments. A total of 80 patients with confirmed type 2 diabetes mellitus were included in the study. ***Results:*** The mean age of the study population was 54.6 ± 9.8 years, with males constituting 60%. The mean duration of diabetes was 8.2 ± 4.6 years, and mean HbA1c was 8.4 ± 1.2%, indicating suboptimal glycemic control. More than half of the patients had at least one microvascular complication, with diabetic neuropathy being the most prevalent. Patients with microvascular complications exhibited significantly higher HbA1c levels and glycemic variability indices compared to those without complications ($p < 0.001$). Glycemic variability indices demonstrated stronger correlations with microvascular complications than HbA1c alone. ***Conclusion:*** Increased glycemic variability is significantly associated with diabetic microvascular complications, independent of mean glycemic control. Targeting glycemic fluctuations, in addition to HbA1c reduction, may help mitigate the risk of microvascular complications in type 2 diabetes mellitus.

Keywords: Type 2 diabetes mellitus; Glycemic variability; Microvascular complications; HbA1c; Fasting blood glucose.

INTRODUCTION

Type 2 diabetes mellitus (T2DM) is a major global public health challenge, characterized by chronic hyperglycemia resulting from insulin resistance and relative insulin deficiency. The prevalence of T2DM has increased dramatically over recent decades, particularly in low- and middle-income countries, including India, owing to rapid urbanization, sedentary lifestyles, and dietary transitions [1]. Persistent hyperglycemia in patients with T2DM is associated with the development of long-term complications, which are broadly classified into macrovascular and microvascular complications. Microvascular complications—namely diabetic retinopathy, diabetic nephropathy, and diabetic neuropathy—are major contributors to morbidity, reduced quality of life, and increased healthcare burden [2].

Traditionally, glycemic control has been assessed using glycated hemoglobin (HbA1c), which reflects the average blood glucose concentration over the preceding two to three months. Landmark clinical trials such as the Diabetes Control and Complications Trial (DCCT) and the UK Prospective Diabetes Study (UKPDS) established the strong association between elevated HbA1c levels and the risk of microvascular complications [3,4]. However, HbA1c does not provide information regarding acute glucose fluctuations, daily glycemic excursions, or hypoglycemic episodes. Increasing evidence suggests that patients with similar HbA1c levels may experience significantly different patterns of glucose variability, leading to varying risks of diabetic complications [5].

Glycemic variability (GV) refers to fluctuations in blood glucose levels over time and includes both short-term variability (within-day and day-to-day fluctuations) and long-term variability (visit-to-visit changes in glycemic parameters). Measures of GV include standard deviation

(SD), coefficient of variation (CV), mean amplitude of glycemic excursions (MAGE), and continuous glucose monitoring (CGM)-derived indices [6]. Emerging data indicate that GV may play an independent role in the pathogenesis of diabetic microvascular complications, beyond the effect of sustained hyperglycemia reflected by HbA1c [7].

The proposed mechanisms linking GV to microvascular damage include increased oxidative stress, activation of inflammatory pathways, endothelial dysfunction, and enhanced formation of advanced glycation end products (AGEs). Acute glucose fluctuations have been shown to induce greater oxidative stress than sustained hyperglycemia, leading to cellular injury and vascular dysfunction [8]. These pathophysiological processes contribute to capillary basement membrane thickening, microvascular ischemia, and neuronal damage, thereby accelerating the progression of diabetic retinopathy, nephropathy, and neuropathy.

Several observational and experimental studies have demonstrated a significant association between increased GV and the prevalence or severity of microvascular complications in patients with T2DM. Long-term variability in fasting plasma glucose and HbA1c has been linked to higher risks of diabetic nephropathy and retinopathy, independent of mean glycemic levels [9]. However, the evidence remains heterogeneous, with differences in study design, population characteristics, and methods used to assess GV. Moreover, data from Indian populations, particularly those attending tertiary care centers, remain limited.

In a country like India, where T2DM often presents at a younger age and with poor glycemic control, identifying additional modifiable risk factors for microvascular complications is crucial. Evaluating the association between GV and microvascular complications may help refine risk stratification, guide individualized treatment strategies, and improve long-term outcomes. Understanding this relationship in a tertiary care hospital setting, where patients often have longer disease duration and multiple comorbidities, can provide valuable insights into real-world clinical practice [10].

The present study aims to evaluate the association between glycemic variability and microvascular complications in patients with type 2 diabetes mellitus attending a tertiary care hospital. Objectives include assessing glycemic variability indices and determining their relationship with diabetic retinopathy, nephropathy, and neuropathy.

MATERIALS AND METHODS

Study Design: Hospital-based, observational, cross-sectional study.

Study Setting: Department of General Medicine, Prakash Institute of Medical Science and Research, Maharashtra 415409.

Study Duration: Conducted over a defined study period.

Study Population: Patients with type 2 diabetes mellitus attending the outpatient and inpatient departments.

Sample Size: Total of 80 patients with type 2 diabetes mellitus.

Inclusion Criteria: Adults aged ≥18 years with diagnosed type 2 diabetes mellitus and regular follow-up.

Exclusion Criteria: Type 1 diabetes mellitus, gestational diabetes, acute infections, severe systemic illness, and unwillingness to participate.

Statistical Analysis: Data were entered into Microsoft Excel and analyzed using SPSS software version 27.0 (SPSS Inc., Chicago, IL, USA) and GraphPad Prism version 5. Continuous variables were expressed as mean ± standard deviation, while categorical variables were presented as frequencies and percentages. The unpaired t-test was used to compare continuous variables between independent groups, and the paired t-test was applied for within-group comparisons. Categorical variables were analyzed using the Chi-square test or Fisher's exact test as appropriate. A p-value of <0.05 was considered statistically significant.

RESULTS

Table 1: Baseline Demographic and Clinical Characteristics (n = 80)

Parameter	Mean ± SD / n (%)
Age (years)	54.6 ± 9.8
Male	48 (60%)
Female	32 (40%)
Duration of diabetes (years)	8.2 ± 4.6
BMI (kg/m²)	26.1 ± 3.4
HbA1c (%)	8.4 ± 1.2

Table 1 shows the baseline demographic and clinical characteristics of the study population. A total of 80 patients with type 2 diabetes mellitus were included, with a mean age of 54.6 ± 9.8 years. Males constituted 60% of the study population. The mean duration of diabetes was 8.2 ± 4.6 years, and the mean HbA1c level was 8.4 ± 1.2%, indicating suboptimal glycemic control in the majority of patients.

Table 2: Distribution of Glycemic Variability Indices

Glycemic Parameter	Mean ± SD
Mean fasting blood glucose (mg/dL)	156.4 ± 32.5
SD of FBG (mg/dL)	38.6 ± 11.2
Coefficient of variation (%)	24.7 ± 6.8
Mean postprandial glucose (mg/dL)	228.9 ± 45.6

Table 3: Prevalence of Microvascular Complications

Complication	Present n (%)	Absent n (%)
Diabetic retinopathy	28 (35%)	52 (65%)
Diabetic nephropathy	22 (27.5%)	58 (72.5%)
Diabetic neuropathy	30 (37.5%)	50 (62.5%)

Table 4: Comparison of Glycemic Variability in Patients with and Without Microvascular Complications

Parameter	Complications Present (n=46)	Complications Absent (n=34)	p-value
HbA1c (%)	8.9 ± 1.1	7.7 ± 0.9	<0.001
SD of FBG (mg/dL)	44.2 ± 9.8	31.4 ± 8.6	<0.001
CV (%)	28.6 ± 5.9	19.8 ± 4.7	<0.001

Table 5: Association Between Glycemic Variability and Individual Microvascular Complications

Complication	Mean SD of FBG (mg/dL)	Mean CV (%)	p-value
Retinopathy present	46.1 ± 10.2	29.4 ± 6.1	<0.001
Nephropathy present	43.8 ± 9.6	28.1 ± 5.4	0.002
Neuropathy present	45.3 ± 10.8	29.0 ± 6.3	<0.001

Table 6: Correlation Between Glycemic Parameters and Microvascular Complications

Parameter	Correlation coefficient (r)	p-value
HbA1c vs complications	0.52	<0.001
SD of FBG vs complications	0.61	<0.001
CV vs complications	0.58	<0.001

Figure: 1. Prevalence and pattern of microvascular complications

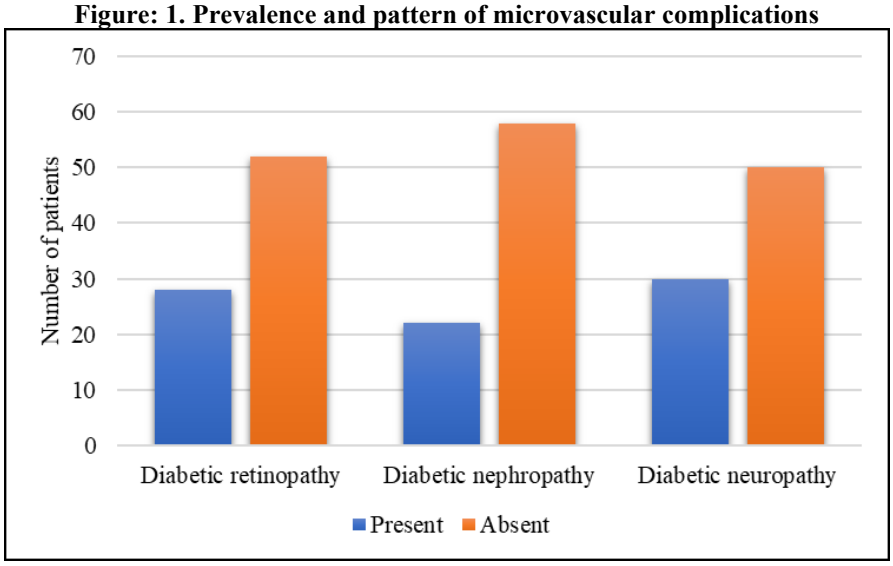

Table 2 depicts the distribution of glycemic parameters and indices of glycemic variability. The mean fasting blood glucose level was 156.4 ± 32.5 mg/dL, while the mean postprandial blood glucose level was 228.9 ± 45.6 mg/dL. The mean standard deviation of fasting blood glucose was 38.6 ± 11.2 mg/dL, and the mean coefficient of variation was 24.7 ± 6.8%, reflecting considerable glycemic fluctuations among the study subjects.

Table 3 summarizes the prevalence of microvascular complications among the study population. Diabetic neuropathy was the most common microvascular complication, observed in 37.5% of patients, followed by diabetic retinopathy in 35% and diabetic nephropathy in 27.5% of patients. Overall, more than half of the patients exhibited at least one microvascular complication.

Table 4 compares glycemic parameters between patients with and without microvascular complications. Patients with microvascular complications had significantly higher mean HbA1c levels (8.9 ± 1.1% vs 7.7 ± 0.9%; $p < 0.001$). Similarly, indices of glycemic variability, including standard deviation of fasting blood glucose and coefficient of variation, were significantly higher in patients with complications compared to those without ($p < 0.001$), indicating a strong association between increased glycemic variability and microvascular involvement.

Table 5 demonstrates the association between glycemic variability indices and individual microvascular complications. Patients with diabetic retinopathy, nephropathy, and neuropathy exhibited significantly higher mean standard deviation of fasting blood glucose and coefficient of variation values. This association was statistically significant for all three complications, with the strongest association observed in patients with diabetic retinopathy and neuropathy.

Table 6 illustrates the correlation between glycemic parameters and microvascular complications. A moderate to strong positive correlation was observed between HbA1c and microvascular complications ($r = 0.52$; $p < 0.001$). Stronger correlations were noted between microvascular complications and indices of glycemic variability, particularly standard deviation of fasting blood glucose ($r = 0.61$; $p < 0.001$) and coefficient of variation ($r = 0.58$; $p < 0.001$), highlighting the independent role of glycemic variability in the development of diabetic microvascular complications.

DISCUSSION

The present study demonstrates that, in patients with type 2 diabetes mellitus, both chronic hyperglycemia and increased glycemic variability are strongly associated with the presence of microvascular complications. The mean HbA1c of 8.4 ± 1.2% in our cohort reflects suboptimal long-term glycemic control, comparable to findings reported in earlier Indian and Asian studies, where mean HbA1c values ranged between 8% and 9% in tertiary-care populations [11,12]. Similar to the observations of Monnier et al. and Nalysnyk et al., our results indicate that indices of glycemic variability, such as standard deviation and coefficient of variation of fasting blood glucose, show a stronger association with microvascular complications than HbA1c alone [13,14].

Diabetic neuropathy emerged as the most prevalent microvascular complication in our study, followed by retinopathy and nephropathy. This pattern aligns with findings by Vinik et al. and Tesfaye et al., who reported neuropathy as the most frequent microvascular manifestation in long-standing type 2 diabetes [15,16]. Importantly, patients with microvascular complications in our study had significantly higher HbA1c and glycemic variability indices, supporting earlier evidence that glucose fluctuations contribute to endothelial dysfunction and oxidative stress beyond mean glucose levels [17]. Studies by Hirakawa et al. and Kilpatrick et al. have similarly demonstrated that greater glycemic variability independently predicts retinopathy and nephropathy progression [18,19].

The strong correlations observed between glycemic variability indices and microvascular complications in our cohort further reinforce the concept that variability is an independent pathogenic factor. Our findings are consistent with the work of Suh and Kim, who highlighted glycemic variability as a critical therapeutic target alongside HbA1c reduction [20]. Overall, these results suggest that strategies aimed at minimizing glucose fluctuations, in addition to improving average glycemic control, may play a crucial role in reducing the burden of diabetic microvascular complications.

CONCLUSION

The present study highlights a significant association between poor glycemic control and increased glycemic variability with the development of microvascular complications in patients with type 2 diabetes mellitus. A substantial proportion of the study population exhibited at least one microvascular complication, with neuropathy being the most prevalent. Patients with complications had significantly higher HbA1c levels as well as elevated indices of glycemic variability, including standard deviation and coefficient of variation of fasting blood glucose. Importantly, glycemic variability showed a stronger correlation with microvascular complications than mean glycemic measures alone, underscoring its independent pathogenic role. These findings suggest that reliance solely on HbA1c may underestimate the risk of diabetic complications. Therefore, comprehensive glycemic assessment incorporating variability indices should be considered in routine clinical practice. Targeting both sustained hyperglycemia and glucose fluctuations may help reduce the burden of microvascular complications and improve long-term outcomes in patients with type 2 diabetes mellitus.

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