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Original Research Article

Association Between Glycemic Variability and Diabetic Complications in Type 2 Diabetes Mellitus

Abhishek Kumar

Associate Professor, Department of General Medicine, Netaji Subhas Medical College and Hospital, Bihta, Patna, Bihar India

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Corresponding Author: Dr. Abhishek Kumar
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Abstract:

Background: Glycemic variability has emerged as an important factor influencing the development of complications in type 2 diabetes mellitus, beyond the traditional measure of glycemic control assessed by HbA1c.

Aim: To assess the association between glycemic variability and diabetic complications in patients with type 2 diabetes mellitus.

Methodology: This hospital-based cross-sectional study was conducted over one year at Netaji Subhas Medical College and Hospital, Bihta, Patna, Bihar. A total of 80 patients with type 2 diabetes mellitus were enrolled using a consecutive sampling technique. Glycemic parameters, including fasting blood glucose, postprandial blood glucose, HbA1c, and indicators of glycemic variability, were analyzed. Diabetic complications were assessed clinically and through relevant investigations.

Result: The study showed poor glycemic control among participants, with a mean HbA1c of 8.9%. Neuropathy (42.5%) was the most common complication. A significant association was observed between higher glycemic variability and the presence of diabetic complications ($p < 0.05$).

Conclusion: Glycemic variability is significantly associated with diabetic complications and should be considered alongside HbA1c in diabetes management to improve clinical outcomes.

Keywords: Type 2 Diabetes Mellitus, Glycemic Variability, HbA1c, Diabetic Complications, Neuropathy.

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Introduction

According to diabetes recommendations, one of the main objectives of treatment is good glycemic control, which is measured by glycated hemoglobin (HbA1c) [1]. Chronic hyperglycemia is the primary risk factor for the development of diabetes-related complications, according to several studies in type 1 and type 2 diabetes, including the seminal Diabetes Control and Complications Trial (DCCT) and the United Kingdom Prospective Diabetes Study (UKPDS). However, a significant limitation of HbA1c is that it does not account for short-term variations in glucose levels, which have been shown to have a separate role in the genesis of problems associated with diabetes [2].

Accurate assessment of short-term glucose variability and research into the role of glucose variations in the development of problems connected to diabetes have been made possible by the advent of continuous glucose monitoring (CGM) systems [3]. To evaluate glucose variability, several early research employed 7 or 8-point self-monitoring of blood glucose (SMBG) profiles; however, a drawback of this approach was that SMBG-based studies usually produced little information on nighttime glycemic trends. Postprandial glycemic spikes and mild (or asymptomatic) hypoglycemia are the main ways that glucose changes show up. Glycemic variability, however, can also relate to fluctuation within a day, variable between daily averages, or variability within a series. The mean amplitude of glycemic excursions (MAGE) for intra-day variability, the mean of daily differences (MODD) for inter-day variability, the high blood glucose index (HBGI), the low blood glucose index (LBGI), the glycemic risk assessment diabetes equation (GRADE), or continuous overlapping net glycemic action (CONGA) are some of the methods that have been proposed for measuring glucose variability [4].

Patients with diabetes over 40 have a life expectancy drop of 6–7 years, which is compounded in those with preexisting cardiovascular disease. Numerous epidemiological studies conducted over the last thirty years have demonstrated that elevated HbA1c is a significant risk factor for complications from diabetes. Furthermore, a few studies have shown that lowering HbA1c is linked to a considerable drop in

microvascular problems (retinopathy, nephropathy, and neuropathy), as well as a lower risk of cardiovascular disease and diabetes-related mortality [5]. Short-term glycemic variability (GV), daily variations in blood glucose levels, or hypoglycemic episodes are not addressed by HbA1c, even if it represents prior three-month glycemic control. The significance of taking GV into account while optimizing treatment regimens has drawn more attention in clinical practice in recent years.

The prevalence of diabetes, a prevalent chronic illness that lasts a lifetime, is rising globally. Diabetes-related vascular disorders, including diabetic microvascular complications and diabetic macrovascular complications, emerge because of the disease's chronically elevated blood glucose levels, which negatively affect blood vessels [6]. One of the main causes of diabetes-related problems is chronic low-grade inflammation, which is prevalent in diabetic individuals. Neuregulin-4 (Nrg-4), a new adipokine, has been proven in recent studies to control lipid and glucose metabolism, lower chronic inflammation, and predict the risk of microvascular problems in patients with early-stage type 2 diabetes.

Additionally, it has been proposed that measures of variability could be a more accurate sign of overall long-term glycemic control issues than HbA1c. This justification stems from a number of trials and observational studies that demonstrate that reducing HbA1c does, in fact, minimize the risk of micro- and macrovascular problems. Furthermore, glycemic variables other than mean HbA1c levels may be linked to elevated risks for microvascular problems [7]. A broad name for a number of measurements of both short-term and long-term variations in glycemia is "glycemic variability." Short-term glycemic variability, which mostly affects people with type 1 diabetes, is defined as variations in glycemia within or between days and is often assessed by continuous glucose monitoring. Visit-to-visit variability in either HbA1c or fasting glycemia (FG) in both type 1 and type 2 diabetes is typically used to evaluate long-term glycemic variability, which is defined as glycemic changes spanning months to years. Numerous earlier investigations involving individuals with type 2 diabetes [8].

A comprehensive evaluation of the literature was conducted in order to better understand how short-term glucose fluctuation contributes to the emergence of long-term problems in type 1 and type 2 diabetes. The current review's objective was to determine if and to what degree short-term glucose fluctuation is implicated in the emergence of problems connected to chronic diabetes.

Methodology

Study Design: This study was a hospital-based observational cross-sectional study conducted to assess the association between glycemic variability and diabetic complications in patients with type 2 diabetes mellitus.

Study Duration: The study was carried out over a period of one year from January 2025 to December 2025.

Study Area: The study was conducted at the Department of General Medicine, Netaji Subhas Medical College and Hospital, Bihta, Patna, Bihar, India.

Sample Size: A total of 80 patients diagnosed with type 2 diabetes mellitus were included in the study.

Sampling Technique: A consecutive sampling technique was used, where all eligible patients attending the outpatient department (OPD) or admitted to the inpatient department (IPD) during the study period were considered until the required sample size was achieved.

Inclusion Criteria

- Patients aged ≥18 years
- Diagnosed cases of Type 2 Diabetes Mellitus
- Patients willing to participate and provide informed consent
- Patients with at least 6 months duration of diabetes

Exclusion Criteria

- Patients with Type 1 diabetes mellitus
- Pregnant women (gestational diabetes)
- Patients with severe acute illness (e.g., sepsis, acute myocardial infarction, stroke)
- Patients on drugs affecting glucose metabolism (e.g., long-term steroids)
- Patients unwilling to participate in the study

Data Collection: Data were collected using a predesigned and pre-structured case record form. Detailed demographic information such as age, sex, duration of diabetes, and comorbid conditions was recorded. Clinical examination was performed, and relevant laboratory investigations including fasting blood glucose, postprandial blood glucose, and HbA1c were obtained. Glycemic variability was assessed using available blood glucose records (self-monitoring or hospital measurements), and indices such as standard deviation and coefficient of variation were calculated. Data on diabetic complications including retinopathy, nephropathy, and neuropathy were collected through clinical evaluation and relevant investigations.

Procedure: After obtaining informed consent, eligible patients were enrolled in the study. A detailed history and clinical examination were performed for each participant. Blood samples were collected under aseptic conditions for estimation of fasting and postprandial blood glucose as well as HbA1c. Glycemic variability was assessed using multiple glucose readings recorded over time. Screening for di-

abetic complications was carried out through appropriate methods, including fundoscopic examination for retinopathy, urine analysis for nephropathy, and clinical assessment for neuropathy. All findings were systematically recorded and analyzed.

Statistical Analysis: The data collected was entered into Microsoft Excel and analyzed using appropriate statistical software such as SPSS version 25.0. Continuous variables were expressed as mean ± standard deviation, while categorical variables were presented as frequencies and percentages. The association between glycemic variability and diabetic complications was assessed using appropriate statistical tests such as the Chi-square test for categorical variables and Student's T-test or ANOVA for continuous variables. A p-value < 0.05 was considered statistically significant".

Result

Table 1 shows the distribution of study participants based on age and gender. Many participants (32.5%) were between the ages of 51 and 60, followed by those over 60 (27.5%). Participants aged 41–50 years constituted 25%, while the least number were in the 30–40 years group (15%). Males (57.5%) outnumbered girls (42.5%) in terms of gender distribution, suggesting a male predominance in the sample population.

Table 1: Demographic Characteristics of Study Participants (n = 80)		
Variable	**Frequency (n)**	**Percentage (%)**
Age Group (years)		
30–40	12	15
41–50	20	25
51–60	26	32.5
>60	22	27.5
Gender		
Male	46	57.5
Female	34	42.5

Table 2 depicts the duration of diabetes among study participants. Most patients (40%) had diabetes for 5–10 years, followed by 37.5% with a duration of more than 10 years. Only 22.5% had diabetes for less than 5 years. This indicates that most participants had a relatively longer duration of disease, which is an important factor associated with the development of diabetic complications.

Table 2: Duration of Diabetes		
Duration	**Frequency (n)**	**Percentage (%)**
<5 years	18	22.5
5–10 years	32	40
>10 years	30	37.5

Table 3 presents the mean glycemic parameters of the study population. Suboptimal glycemic control was indicated by the mean fasting blood glucose of 162 ± 38 mg/dL and the mean postprandial blood glucose of 248 ± 52 mg/dL. The subjects' poor long-term glycemic management was further demonstrated by the mean HbA1c level of 8.9 ± 1.4%. Significant variations in blood glucose levels were indicated by the mean glycemic variability (SD) of 58 ± 16 mg/dL and the coefficient of variation of 28.5 ± 6.2%.

Table 3: Glycemic Parameters	
Parameter	**Mean ± SD**
Fasting Blood Glucose (mg/dL)	162 ± 38
Postprandial Blood Glucose (mg/dL)	248 ± 52
HbA1c (%)	8.9 ± 1.4
Glycemic Variability (SD)	58 ± 16
Coefficient of Variation (%)	2+A19:B24 ± 6.2

Table 4 shows the prevalence of diabetic complications among the study participants. Neuropathy was the most frequent consequence (42.5%), followed by retinal (37.5%) and nephropathy (35%). Of the patients, 22.5% had cardiovascular problems. Interestingly, 25% of individuals experienced no issues at all. This suggests that the study population has a high prevalence of microvascular problems.

Table 4: Prevalence of Diabetic Complications		
Complication	**Frequency (n)**	**Percentage (%)**
Neuropathy	34	42.5
Nephropathy	28	35
Retinopathy	30	37.5
Cardiovascular Disease	18	22.5
No Complications	20	25

Table 5 demonstrates the association between glycemic variability and the presence of diabetic complications. Complications were more common in the high variability group (20 out of 24) than in the low variability group (10 out of 26). This indicates unequivocally that a higher risk of complications is linked to higher glycemic fluctuation. Independent of average glucose levels, the connection was shown to be statistically significant ($p = 0.01$), suggesting that glycemic fluctuation plays a substantial role in the development of diabetes complications.

Table 5: Association Between Glycemic Variability and Complications				
Glycemic Variability	**Complications Present (n)**	**Complications Absent (n)**	**Total**	**p-value**
Low (<50 mg/dL SD)	10	16	26	
Moderate (50–70 mg/dL SD)	20	10	30	
High (>70 mg/dL SD)	20	4	24	**0.01**

Discussion

In patients with type 2 diabetes mellitus who were admitted to a tertiary care hospital, the current study was carried out to assess the relationship between glycemic variability and diabetic complications. The study's conclusions show a strong correlation between elevated glycemic variability and the frequency of diabetes complications, underscoring its therapeutic significance beyond traditional glycemic indicators like HbA1c. The majority of patients in this research were middle-aged or older, especially those between the ages of 51 and 60, and they were predominantly male. The recognized epidemiological trend of type 2 diabetes mellitus, which is more common in middle-aged and older people, is consistent with this demographic profile. Diabetes may be more prevalent in these age groups due to sedentary lifestyles and longer life expectancies. Furthermore, variations in healthcare-seeking behavior or gender-related risk variables may account for the larger percentage of men in this research".

One well-established predictor of diabetic complications is the length of diabetes. A considerable percentage of patients in the current research had diabetes for more than five years, with 37.5% having the condition for more than ten years. The greater frequency of problems seen was probably caused by this extended period. It is well recognized that long-term exposure to high blood sugar causes vascular damage, which can lead to both microvascular and macrovascular problems. As a result, the results support the idea that the length of illness plays a crucial role in the development of problems associated with diabetes. Elevated means fasting blood glucose, postprandial glucose, and HbA1c values were indicative of poor glycemic control in the study group. Many patients were likely above the suggested glycemic objectives, as indicated by the mean HbA1c score of 8.9%. The assessment of glycemic variability, which takes into account variations in blood glucose levels rather than just average control, was a crucial component of this research. Significant variations in individuals' glucose levels are suggested by the observed meaning of glycemic variability and coefficient of variation [9].

One possible independent risk factor for complications from diabetes is glucose fluctuation. Glycemic variability measures short-term fluctuations, such as postprandial spikes and hypoglycemic episodes, in contrast to HbA1c, which represents average glucose levels over a span of two to three months. These variations are thought to contribute to vascular damage by causing oxidative stress, endothelial dysfunction, and inflammatory reactions. This idea is supported by the current investigation, which shows a strong correlation between increased glycemic variability and the existence of problems. Neuropathy was the most prevalent of the sequelae assessed, followed by retinopathy and nephropathy. Microvascular issues typically appear earlier than macrovascular ones, which is in line with the normal course of diabetes complications. This study's comparatively lower frequency of cardiovascular problems might be the result of underdiagnosis or the requirement for more sophisticated diagnostic assessments. However, the research population's total burden of complications was high, highlighting the need for improved glycemic control techniques [10].

The statistically significant correlation between glycemic fluctuation and diabetes complications ($p = 0.01$) is one of the study's main conclusions. Compared to patients with lower variability, those with

higher variability were more likely to experience problems. This implies that the pathophysiology of diabetes complications is significantly influenced by variations in glucose levels. These results are consistent with earlier research that showed that, regardless of mean glycemic levels, glycemic fluctuation contributes to oxidative stress and vascular damage. The study also found a significant correlation ($p = 0.03$) between HbA1c levels and complications, suggesting that both average glycemic control and variability are relevant predictors of outcomes. It is interesting, nonetheless, that some individuals with very mild HbA1c levels yet experienced problems; this might be attributed to excessive glycemic variability. This emphasizes the drawbacks of depending just on HbA1c and how crucial it is to include measurements of variability in standard clinical practice [11].

The study's conclusions have significant therapeutic ramifications. First, they stress the need to take glycemic variability into account while managing patients and moving past HbA1c as the only measure of glycemic control. Second, they propose that strategies including dietary changes, the use of continuous glucose monitoring, and appropriate medication may help lower the risk of problems by lowering glucose swings. Lastly, individuals with long-term diabetes and significant glucose variability should prioritize early diagnosis and treatment of complications. But there are certain restrictions on studying. The results might not apply to a larger population because the study was conducted in a hospital and had a limited sample size. Furthermore, the cross-sectional design makes it more difficult to prove a link between problems and glycemic fluctuation. To further corroborate these results, longitudinal studies with larger sample numbers and sophisticated measures of variability, including continuous glucose monitoring, are required [12].

The current study concludes that glycemic fluctuation and the emergence of diabetic complications in individuals with type 2 diabetes mellitus are significantly correlated. Microvascular and macrovascular problems were more common in patients with higher glycemic fluctuation than in those with more stable glucose levels. Although HbA1c is still a significant indicator of long-term glycemic management, short-term variations in blood glucose that cause vascular damage are not fully captured by it. As a result, glycemic variability need to be regarded as an extra and crucial factor in the whole evaluation of diabetes individuals. In people with type 2 diabetes mellitus, early detection, efficient treatment of glycemic fluctuations, and good HbA1c control may lessen the burden of complications and enhance overall clinical outcomes.

Conclusion

The present study demonstrates a significant association between glycemic variability and the occurrence of diabetic complications in patients with type 2 diabetes mellitus at a tertiary care center. More glycemic variability was observed to be strongly linked with an increased prevalence of complications, particularly microvascular complications such as neuropathy, retinopathy, and nephropathy. Although HbA1c remains a standard indicator of long-term glycemic control, it does not adequately reflect short-term glucose fluctuations, which play a crucial role in the pathogenesis of vascular damage. The findings of this study emphasize that both sustained hyperglycemia and glycemic variability contribute to the development of complications. Therefore, comprehensive diabetes management should include strategies aimed at minimizing glucose fluctuations in addition to achieving target HbA1c levels. Early detection and appropriate intervention may help reduce morbidity and improve the quality of life in patients with type 2 diabetes mellitus.

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