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Original Article

Time in Range, Not Just HbA1c: Redefining Glycemic Control and Microvascular Risk

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ABSTRACT

Introduction: Glycated hemoglobin (HbA1c) has long been the standard marker for assessing long-term glycemic control in patients with type 2 diabetes mellitus (T2DM). However, it does not reflect glycemic variability or daily glucose fluctuations. Time in Range (TIR), derived from continuous glucose monitoring (CGM), has emerged as a complementary metric that may better predict diabetes-related complications. This study evaluated the association between TIR and microvascular complications and compared its predictive performance with HbA1c.
Materials and Methods: A hospital-based cross-sectional observational study was conducted from May 2024 to May 2025 among 150 adults with T2DM. Demographic and clinical data, HbA1c, and CGM-derived metrics including TIR, Time Above Range (TAR), Time Below Range (TBR), mean glucose, and glycemic variability were recorded. Participants were evaluated for diabetic retinopathy, nephropathy, and neuropathy. Statistical analysis included Chi-square test, independent t-test, Pearson's correlation, multivariable logistic regression, and receiver operating characteristic (ROC) curve analysis.
Results: The mean HbA1c was 8.32 ± 1.34%, while the mean TIR was 58.4 ± 17.2%. Microvascular complications were present in 54.7% of participants, with neuropathy being the most common (40.7%). Lower TIR showed a significant association with increased microvascular complications ($\chi^2 = 56.92$, $p < 0.001$) and demonstrated a stronger inverse correlation with microvascular risk than HbA1c ($r = -0.71$ vs. $r = 0.54$). Logistic regression identified lower TIR as an independent predictor of microvascular complications. ROC analysis showed that TIR had the highest predictive accuracy (AUC = 0.89), outperforming HbA1c (AUC = 0.77).
Conclusion: Time in Range is a superior indicator of glycemic control and microvascular risk compared with HbA1c alone. Incorporating CGM-derived TIR into routine diabetes management may improve risk stratification, facilitate earlier intervention, and enhance prevention of diabetes-related microvascular complications.

Keywords: *Time in Range; Continuous glucose monitoring; Glycated hemoglobin; Type 2 diabetes mellitus; Microvascular complications.*

INTRODUCTION

Diabetes mellitus is one of the most prevalent chronic metabolic disorders worldwide and remains a major public health concern because of its rapidly increasing incidence and long-term complications [1]. Persistent hyperglycemia contributes to progressive vascular injury, leading to both microvascular and macrovascular complications that substantially increase morbidity, mortality, and healthcare costs [2]. Diabetic retinopathy, nephropathy, and neuropathy are the principal microvascular complications and are major causes of blindness, chronic kidney disease, and disability

among individuals with type 2 diabetes mellitus (T2DM) [3]. Early identification of patients at increased risk of these complications is therefore essential for optimizing glycemic management and improving long-term outcomes [4].

For several decades, glycated hemoglobin (HbA1c) has served as the gold standard for assessing long-term glycemic control and guiding treatment decisions [5]. HbA1c reflects average blood glucose levels over the preceding two to three months and has been shown to correlate with the risk of diabetes-related complications [5]. However, HbA1c has important limitations, as it does not capture daily glucose fluctuations, episodes of hypoglycemia or hyperglycemia, or glycemic variability [6]. Furthermore, patients with similar HbA1c values may exhibit markedly different glucose profiles, resulting in differences in their risk of developing vascular complications [7].

The widespread adoption of continuous glucose monitoring (CGM) has transformed diabetes management by providing detailed information on glucose patterns throughout the day [8]. Among CGM-derived metrics, Time in Range (TIR), defined as the percentage of time spent within the target glucose range of 70–180 mg/dL, has emerged as a clinically meaningful indicator of glycemic control [9]. International expert consensus recommends TIR as a complementary measure to HbA1c because it reflects both the quality and stability of glucose control [10]. Emerging evidence suggests that lower TIR is associated with an increased prevalence and severity of diabetic retinopathy, nephropathy, and neuropathy, independent of HbA1c, indicating that TIR may be a superior predictor of diabetes-related complications [11].

Despite the growing clinical importance of TIR, its role in routine assessment of glycemic control and prediction of microvascular complications remains inadequately explored in many healthcare settings. Comparative data evaluating the predictive utility of TIR and HbA1c for microvascular risk are limited, particularly in the Indian population. Therefore, the present study aimed to evaluate the association between Time in Range and microvascular complications in patients with type 2 diabetes mellitus and to compare its predictive performance with HbA1c in assessing glycemic control and microvascular risk.

MATERIALS AND METHODS

This hospital-based cross-sectional observational study was conducted in the Department of General Medicine at a tertiary care teaching hospital over a period of one year, from May 2024 to May 2025. A total of 150 adult patients with established type 2 diabetes mellitus (T2DM) who fulfilled the eligibility criteria were enrolled after obtaining written informed consent. The study was initiated following approval from the Institutional Ethics Committee and was conducted in accordance with the ethical principles outlined in the Declaration of Helsinki. Adult patients aged ≥18 years with T2DM who underwent continuous glucose monitoring (CGM) during the study period were included. Patients with type 1 diabetes mellitus, gestational diabetes, severe acute illness, advanced hepatic disease, end-stage renal disease requiring dialysis, malignancy, or incomplete clinical or CGM data were excluded.

Baseline demographic and clinical characteristics, including age, sex, body mass index (BMI), duration of diabetes, smoking status, hypertension, dyslipidemia, current antidiabetic treatment, and relevant comorbidities, were recorded using a structured case record form. Anthropometric measurements were obtained using standardized techniques. Laboratory investigations included glycated hemoglobin (HbA1c) estimation using a standardized high-performance liquid chromatography (HPLC)-based assay. Continuous glucose monitoring data were collected using an approved CGM device with adequate sensor wear duration. The CGM-derived metrics analyzed included Time in Range (TIR; 70–180 mg/dL), Time Above Range (TAR; >180 mg/dL), Time Below Range (TBR; <70 mg/dL), mean glucose, and glycemic variability expressed as coefficient of variation (CV%).

All participants underwent evaluation for diabetic microvascular complications. Diabetic retinopathy was assessed by comprehensive ophthalmological examination with dilated fundus evaluation, diabetic nephropathy was evaluated using urinary albumin excretion and renal function parameters, and diabetic neuropathy was diagnosed based on clinical examination with appropriate neurological assessment. The presence of one or more of these complications was considered as evidence of any microvascular complication. Patients were further categorized according to HbA1c levels and Time in Range categories to evaluate their relationship with the prevalence of microvascular complications.

Data were entered into Microsoft Excel and analyzed using IBM SPSS Statistics for Windows, Version 20 (IBM Corp., Armonk, NY, USA). Continuous variables were expressed as mean ± standard deviation (SD), whereas categorical variables were presented as frequencies and percentages. Comparisons between categorical variables were performed using the Chi-square test or Fisher's exact test, while continuous variables were compared using the independent samples t-test. Pearson's correlation analysis was used to evaluate the relationship between glycemic metrics and microvascular risk. Multivariable logistic regression analysis was performed to identify independent predictors of microvascular complications after adjusting for potential confounding variables. Receiver operating characteristic (ROC) curve analysis was used to compare the predictive performance of HbA1c, Time in Range, and other CGM-derived metrics for

identifying microvascular complications. A two-tailed p-value <0.05 was considered statistically significant throughout the analysis.

RESULTS

A total of 150 patients with type 2 diabetes mellitus were included in the study. The majority were aged 50–59 years (34.0%), followed by ≥60 years (28.0%). Males constituted 57.3% of the study population. Most participants were overweight (42.0%) or obese (35.3%), while 36.0% had diabetes for more than 10 years. Hypertension and dyslipidemia were present in 56.0% and 47.3% of patients, respectively, whereas 18.7% were smokers (Table 1).

Table 1. Baseline Characteristics of Study Participants (N = 150)

Variable	Category	n (%)
Age (years)	<40	18 (12.0)
	40–49	39 (26.0)
	50–59	51 (34.0)
	≥60	42 (28.0)
Sex	Male	86 (57.3)
	Female	64 (42.7)
BMI (kg/m²)	Normal (<25)	34 (22.7)
	Overweight (25–29.9)	63 (42.0)
	Obese (≥30)	53 (35.3)
Duration of diabetes	<5 years	37 (24.7)
	5–10 years	59 (39.3)
	>10 years	54 (36.0)
Hypertension	Yes	84 (56.0)
Dyslipidemia	Yes	71 (47.3)
Smoking	Yes	28 (18.7)

The mean HbA1c of the study participants was 8.32 ± 1.34%, while the average Time in Range (TIR) was 58.4 ± 17.2%. The mean Time Above Range (TAR) and Time Below Range (TBR) were 34.7 ± 16.8% and 6.9 ± 4.5%, respectively. The mean glucose level was 182.6 ± 42.5 mg/dL, with a glycemic variability (coefficient of variation) of 33.1 ± 7.8% (Table 2).

Table 2. Glycemic Parameters

Variable	Mean ± SD
HbA1c (%)	8.32 ± 1.34
Time in Range (%)	58.4 ± 17.2
Time Above Range (%)	34.7 ± 16.8
Time Below Range (%)	6.9 ± 4.5
Mean Glucose (mg/dL)	182.6 ± 42.5
Glycemic Variability (CV%)	33.1 ± 7.8

Based on TIR, 32.7% of participants had TIR below 50%, 38.7% had TIR between 50% and 70%, and only 28.6% achieved a TIR greater than 70%, indicating that less than one-third of patients attained the recommended glycemic target (Table 3).

Table 3. Distribution of Participants According to Time in Range

Time in Range	n (%)
<50%	49 (32.7)
50–70%	58 (38.7)
>70%	43 (28.6)

Microvascular complications were observed in more than half of the study population, with any complication present in 54.7% of participants. Diabetic neuropathy was the most common complication (40.7%), followed by diabetic retinopathy (37.3%) and diabetic nephropathy (28.7%) (Table 4).

Table 4. Prevalence of Microvascular Complications

Complication	Present n (%)
Diabetic Retinopathy	56 (37.3)
Diabetic Nephropathy	43 (28.7)
Diabetic Neuropathy	61 (40.7)
Any Microvascular Complication	82 (54.7)

The prevalence of microvascular complications increased significantly with worsening HbA1c levels. Patients with HbA1c ≥9% had the highest proportion of complications, whereas those with HbA1c <7% had the lowest prevalence. This association was statistically significant ($\chi^2 = 29.81$, $p < 0.001$) (Table 5).

Table 5. Association Between HbA1c Categories and Microvascular Complications

HbA1c	Complication Present	Complication Absent	Total	χ^2	p value
<7%	11	28	39		
7–8.9%	31	37	68		
≥9%	40	3	43	29.81	<0.001

A strong inverse relationship was observed between TIR and microvascular complications. Patients with TIR below 50% demonstrated the highest prevalence of complications, while those with TIR above 70% had the lowest prevalence. The association was highly statistically significant ($\chi^2 = 56.92$, $p < 0.001$) (Table 6).

Table 6. Association Between Time in Range Categories and Microvascular Complications

Time in Range	Present	Absent	Total	χ^2	p value
>70%	8	35	43		
50–70%	29	29	58		
<50%	45	4	49	56.92	<0.001

Correlation analysis demonstrated that TIR showed the strongest negative correlation with microvascular risk score ($r = –0.71$, $p < 0.001$). In contrast, HbA1c, TAR, and glycemic variability exhibited significant positive correlations with increasing microvascular risk (all $p < 0.001$) (Table 7).

Table 7. Correlation of Glycemic Parameters with Microvascular Risk Score

Variable	r	p value
HbA1c	0.54	<0.001
Time in Range	−0.71	<0.001
Time Above Range	0.63	<0.001
Glycemic Variability	0.46	<0.001

Multivariable logistic regression identified longer duration of diabetes, higher HbA1c, and lower TIR as independent predictors of microvascular complications. Among these variables, TIR remained the strongest independent protective factor, while age, sex, and hypertension were not statistically significant predictors (Table 8).

Table 8. Logistic Regression for Presence of Any Microvascular Complication

Variable	Adjusted OR	95% CI	p value
Age	1.02	0.99–1.05	0.14
Male sex	1.11	0.59–2.10	0.74
Duration of diabetes	1.16	1.07–1.27	<0.001
HbA1c	1.41	1.10–1.80	0.006
Time in Range	0.95	0.93–0.97	<0.001
Hypertension	1.56	0.83–2.94	0.17

Receiver operating characteristic (ROC) analysis demonstrated that TIR had the highest predictive accuracy for microvascular complications (AUC = 0.89), outperforming both TAR (AUC = 0.82) and HbA1c (AUC = 0.77). All three glycemic parameters showed statistically significant discriminatory ability ($p < 0.001$) (Table 9).

Table 9. ROC Analysis for Predicting Any Microvascular Complication

Parameter	AUC	95% CI	p value
HbA1c	0.77	0.70–0.84	<0.001
Time in Range	0.89	0.84–0.94	<0.001
Time Above Range	0.82	0.75–0.88	<0.001

Patients with microvascular complications had significantly higher HbA1c, TAR, and glycemic variability, along with markedly lower TIR, compared with those without complications. All comparisons were statistically significant ($p < 0.001$), highlighting the close association between adverse glycemic profiles and microvascular disease (Table 10).

Table 10. Comparison of Glycemic Metrics Between Patients With and Without Microvascular Complications

Variable	Complication Present (n=82)	Complication Absent (n=68)	t value	p value
HbA1c (%)	9.01 ±1.16	7.48 ±0.94	8.92	<0.001
Time in Range (%)	45.8 ±12.3	73.6 ±10.4	14.87	<0.001
Time Above Range (%)	45.9 ±13.1	21.5 ±9.8	12.64	<0.001
Glycemic Variability (%)	36.4 ±7.1	29.2 ±5.8	6.83	<0.001

DISCUSSION

The present study demonstrated that Time in Range (TIR) was more strongly associated with microvascular complications than HbA1c alone among patients with type 2 diabetes mellitus. More than half of the participants had at least one microvascular complication, and individuals with lower TIR exhibited a significantly greater prevalence of retinopathy, nephropathy, and neuropathy. Although HbA1c remained significantly associated with complications, TIR showed a stronger inverse correlation with microvascular risk and superior predictive performance on ROC analysis. These findings support the growing concept that glycemic control should be assessed using both average glucose exposure and the quality of glucose control, rather than HbA1c alone. Similar observations have been reported by Beck et al., who demonstrated that every 10% reduction in TIR was associated with a substantial increase in the risk of retinopathy progression and microalbuminuria, validating TIR as a clinically meaningful marker of microvascular outcomes [12,13].

In the present study, patients with TIR <50% had the highest burden of microvascular complications, whereas those achieving TIR >70% had the lowest prevalence. These findings are consistent with the study by Lu et al., who evaluated over 3,000 patients with type 2 diabetes and reported that lower CGM-derived TIR was independently associated with increasing severity of diabetic retinopathy [14]. Likewise, Beck et al. demonstrated a strong inverse relationship between TIR and HbA1c, while emphasizing that patients with similar HbA1c values may have markedly different glucose profiles and clinical risks [13]. These findings indicate that TIR captures glycemic excursions and day-to-day glucose variability that are not reflected by HbA1c alone, making it a valuable complementary metric in routine diabetes management.

Another important finding of the present study was that TIR remained an independent predictor of microvascular complications even after adjustment for conventional risk factors, whereas HbA1c showed comparatively lower predictive ability. Furthermore, ROC analysis demonstrated a higher area under the curve for TIR than HbA1c, suggesting superior discrimination for identifying patients at risk of microvascular disease. These findings are supported by the systematic review by Raj et al., which summarized evidence from observational studies and concluded that lower CGM-derived TIR is consistently associated with diabetic retinopathy, nephropathy, and peripheral neuropathy across diverse populations [15]. International consensus recommendations have also recognized TIR as a clinically meaningful outcome that complements HbA1c in evaluating overall glycemic control and therapeutic effectiveness.

The clinical implications of the present study are substantial. While HbA1c remains an established marker of long-term glycemic control, it does not adequately reflect glycemic variability, duration of hyperglycemia, or hypoglycemic exposure. Incorporating TIR into routine clinical practice may enable earlier identification of patients at high risk for diabetes-related complications and facilitate individualized therapeutic interventions. Increasing availability and affordability of continuous glucose monitoring systems are likely to enhance the integration of TIR into routine diabetes care. Future prospective multicenter studies with longer follow-up are warranted to establish standardized TIR thresholds for predicting long-term microvascular outcomes and to determine whether interventions aimed at improving TIR translate into reduced complication rates.

CONCLUSION

The present study demonstrates that Time in Range (TIR) is a stronger indicator of glycemic control and microvascular risk than HbA1c alone in patients with type 2 diabetes mellitus. Lower TIR was significantly associated with a higher prevalence of diabetic retinopathy, nephropathy, and neuropathy and remained an independent predictor of microvascular complications after adjustment for conventional risk factors. These findings highlight the added clinical value of continuous glucose monitoring-derived metrics in identifying patients at increased risk of diabetes-related complications. Incorporating TIR alongside HbA1c into routine diabetes assessment may facilitate more comprehensive glycemic evaluation, enable timely therapeutic interventions, and ultimately improve long-term microvascular outcomes.

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REFERENCES

1. Hossain MJ, Al-Mamun M, Islam MR. Diabetes mellitus, the fastest growing global public health concern: Early detection should be focused. Health Sci Rep. 2024 Mar 22;7(3):e2004. doi: 10.1002/hsr2.2004. PMID: 38524769; PMCID: PMC10958528.
2. Zakir M, Ahuja N, Surksha MA, et al. Cardiovascular Complications of Diabetes: From Microvascular to Macrovascular Pathways. Cureus. 2023 Sep 24;15(9):e45835. doi: 10.7759/cureus.45835. PMID: 37881393; PMCID: PMC10594042.
3. Kulkarni A, Thool AR, Daigavane S. Understanding the Clinical Relationship Between Diabetic Retinopathy, Nephropathy, and Neuropathy: A Comprehensive Review. Cureus. 2024 Mar 21;16(3):e56674. doi: 10.7759/cureus.56674. PMID: 38646317; PMCID: PMC11032697.
4. Schwartz SS. Optimizing glycemic control and minimizing the risk of hypoglycemia in patients with type 2 diabetes. Drugs Context. 2013 May 22;2013:212255. doi: 10.7573/dic.212255. PMID: 24432042; PMCID: PMC3884850.
5. Sherwani SI, Khan HA, Ekhzaimy A, Masood A, Sakharkar MK. Significance of HbA1c Test in Diagnosis and Prognosis of Diabetic Patients. Biomark Insights. 2016 Jul 3;11:95-104. doi: 10.4137/BMI.S38440. PMID: 27398023; PMCID: PMC4933534.
6. Lazar S, Ionita I, Reurean-Pintilei D, Timar R, Luca SA, Timar B. To What Extent Is Hb_{A1c} Associated with Glycemic Variability in Patients with Type 1 Diabetes? A Retrospective, Noninterventional Study. J Clin Med. 2024 Jan 13;13(2):450. doi: 10.3390/jcm13020450. PMID: 38256584; PMCID: PMC10816236.
7. Belli M, Bellia A, Sergi D, Barone L, Lauro D, Barillà F. Glucose variability: a new risk factor for cardiovascular disease. Acta Diabetol. 2023 Oct;60(10):1291-1299. doi: 10.1007/s00592-023-02097-w. Epub 2023 Jun 21. PMID: 37341768; PMCID: PMC10442283.
8. Ghosh N, Verma S. Technological advancements in glucose monitoring and artificial pancreas systems for shaping diabetes care. Curr Med Res Opin. 2024 Dec;40(12):2095-2107. doi: 10.1080/03007995.2024.2422005. Epub 2024 Nov 14. PMID: 39466337.
9. Aleppo G. Clinical Application of Time in Range and Other Metrics. Diabetes Spectr. 2021 May;34(2):109-118. doi: 10.2337/ds20-0093. Epub 2021 May 25. PMID: 34149251; PMCID: PMC8178724.
10. Danne T, Nimri R, Battelino T, et al. International Consensus on Use of Continuous Glucose Monitoring. Diabetes Care. 2017 Dec;40(12):1631-1640. doi: 10.2337/dc17-1600. PMID: 29162583; PMCID: PMC6467165.
11. Battelino T, Danne T, Bergenstal RM, et al. Clinical Targets for Continuous Glucose Monitoring Data Interpretation: Recommendations From the International Consensus on Time in Range. Diabetes Care. 2019 Aug;42(8):1593-1603. doi: 10.2337/dci19-0028. Epub 2019 Jun 8. PMID: 31177185; PMCID: PMC6973648.
12. Beck RW, Bergenstal RM, Riddlesworth TD, Kollman C, Li Z, Brown AS, Close KL. Validation of Time in Range as an Outcome Measure for Diabetes Clinical Trials. Diabetes Care. 2019 Mar;42(3):400-405. doi: 10.2337/dc18-1444. Epub 2018 Oct 23. PMID: 30352896; PMCID: PMC6905478.
13. Beck RW, Bergenstal RM, Cheng P, Kollman C, Carlson AL, Johnson ML, Rodbard D. The Relationships Between Time in Range, Hyperglycemia Metrics, and HbA1c. J Diabetes Sci Technol. 2019 Jul;13(4):614-626. doi: 10.1177/1932296818822496. Epub 2019 Jan 13. PMID: 30636519; PMCID: PMC6610606.
14. Lu J, Ma X, Zhou J, Zhang L, Mo Y, Ying L, Lu W, Zhu W, Bao Y, Vigersky RA, Jia W. Association of Time in Range, as Assessed by Continuous Glucose Monitoring, With Diabetic Retinopathy in Type 2 Diabetes. Diabetes Care. 2018 Nov;41(11):2370-2376. doi: 10.2337/dc18-1131. Epub 2018 Sep 10. PMID: 30201847.
15. Raj R, Mishra R, Jha N, Joshi V, Correa R, Kern PA. Time in range, as measured by continuous glucose monitor, as a predictor of microvascular complications in type 2 diabetes: a systematic review. BMJ Open Diabetes Res Care. 2022 Jan;10(1):e002573. doi: 10.1136/bmjdrc-2021-002573. PMID: 34980591; PMCID: PMC8724710.