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Research Article

Beyond HbA1c: Emerging Parameters for Improved Glycemic Assessment in Diabetes Mellitus

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Abstract

Glycated hemoglobin (HbA1c) has long been regarded as the cornerstone biomarker for monitoring long-term glycemic control in patients with diabetes mellitus. Although HbA1c provides an integrated estimate of average blood glucose levels over the preceding 8–12 weeks, it fails to capture short-term glucose fluctuations, hypoglycemic episodes, and interindividual variability influenced by anemia, hemoglobinopathies, renal dysfunction, and ethnic differences. These limitations have driven growing interest in novel glycemic parameters that complement or extend HbA1c interpretation. Emerging markers such as glycated albumin, fructosamine, time-in-range (TIR), glucose variability indices, and the hemoglobin glycation index (HGI) offer more nuanced insights into glucose dynamics and metabolic risk. Continuous glucose monitoring (CGM)–derived metrics, including coefficient of variation and glucose management indicator (GMI), further refine individualized diabetes care. Additionally, inflammatory and oxidative stress markers are increasingly recognized for their role in explaining discordance between HbA1c and actual glycemic exposure. This review summarizes current evidence on new HbA1c-related parameters, evaluates their clinical relevance, and discusses their potential integration into routine diabetes management. By adopting a multidimensional approach to glycemic assessment, clinicians may improve risk stratification, therapeutic decision-making, and prediction of microvascular and macrovascular complications. The evolving paradigm suggests that HbA1c should no longer be interpreted in isolation but rather as part of a broader panel of metabolic indicators tailored to individual patient profiles.

Keywords: hba1c; diabetes mellitus; glycated albumin; time-in-range; glucose variability; continuous glucose monitoring

Introduction

Diabetes mellitus is a chronic metabolic disorder characterized by persistent hyperglycemia and associated with significant morbidity and mortality worldwide [1]. HbA1c has been widely used as the primary biomarker for diagnosis and long-term monitoring of diabetes due to its standardized measurement and strong association with complications [2]. However, growing clinical evidence indicates that HbA1c alone does not fully reflect glycemic variability or acute glucose excursions, both of which contribute to vascular damage [3,4]. Moreover, non-glycemic factors such as red blood cell turnover, iron deficiency, chronic kidney disease, and ethnicity may significantly influence HbA1c values independent of glucose levels [5–7]. These shortcomings have encouraged the development of additional parameters that better characterize individual glycemic patterns. Understanding these emerging metrics is critical for improving personalized diabetes management and outcomes [8]. This article reviews new HbA1c-related parameters and evaluates their clinical utility.

Literature Review

Several alternative glycemic markers have gained attention over the past decade. Glycated albumin and fructosamine reflect shorter-term glycemic control (2–3 weeks) and are particularly useful in conditions affecting erythrocyte lifespan [9,10]. Time-in-range, derived from CGM data, has emerged as a powerful predictor of microvascular complications and is increasingly endorsed by international diabetes guidelines [11,12]. Glucose variability indices, including standard deviation and coefficient of variation, capture fluctuations that HbA1c cannot detect [13]. The hemoglobin glycation index explains interindividual differences between measured HbA1c and expected values based on plasma glucose [14]. Inflammatory markers such as C-reactive protein and oxidative stress biomarkers have also been linked to HbA1c discordance and complication risk [15–17]. Collectively, these parameters provide complementary information that enhances traditional glycemic assessment.

Research Methodology

A narrative review methodology was employed. Peer-reviewed articles published between 2020 and 2025 were identified through major biomedical databases. Studies focusing on HbA1c limitations, alternative glycemic markers, CGM-based metrics, and clinical outcomes in diabetes were included. Both observational and interventional studies were reviewed to ensure comprehensive coverage.

Statistical Analysis

Descriptive statistics from the reviewed studies were summarized. Correlations between HbA1c and emerging parameters were evaluated using reported Pearson or Spearman coefficients. Comparative outcomes were assessed using confidence intervals and significance levels as presented in the original studies. Meta-analytic interpretations were referenced where available

Results

The reviewed literature consistently demonstrated moderate to strong correlations between HbA1c and alternative markers such as glycated albumin and TIR. CGM-derived parameters showed superior sensitivity in detecting hypoglycemia and glucose variability. Several studies reported that patients with similar HbA1c values exhibited markedly different TIR and variability profiles, indicating heterogeneous metabolic control. Inflammatory and oxidative markers were associated with higher complication risk despite acceptable HbA1c levels.

Parameter	Measurement Period	Reflects Glycemic Variability	Affected by RBC Disorders	Clinical Utility
HbA1c	8–12 weeks	✗ No	✓ Yes	Long-term glycemic control
Glycated Albumin	2–3 weeks	⚠ Partial	✗ No	Short-term monitoring, CKD
Fructosamine	2–3 weeks	⚠ Partial	✗ No	Pregnancy, anemia
Time-in-Range (TIR)	Real-time	✓ Yes	✗ No	CGM-based risk assessment
Glucose Variability (CV, SD)	Real-time	✓ Yes	✗ No	Hypoglycemia prediction
Hemoglobin Glycation Index (HGI)	Individual-based	⚠ Indirect	✓ Yes	Explains HbA1c discordance
Glucose Management Indicator (GMI)	CGM-based	✓ Yes	✗ No	Therapy optimization

Table 1: Comparison of HbA1c with Emerging Glycemic Parameters

Clinical Scenario	Limitation of HbA1c	Preferred Additional Parameter
Anemia / Hemoglobinopathies	Falsely altered values	Glycated albumin
Chronic kidney disease	Reduced RBC lifespan	Fructosamine
Insulin-treated diabetes	Misses hypoglycemia	TIR, glucose variability
Elderly patients	Underestimates risk	CGM metrics
Pregnancy	Delayed glucose changes	Fructosamine, TIR
High complication risk with normal HbA1c	Hidden glucose spikes	HGI, CV

Table 2: Clinical Advantages of Integrating New HbA1c Parameters

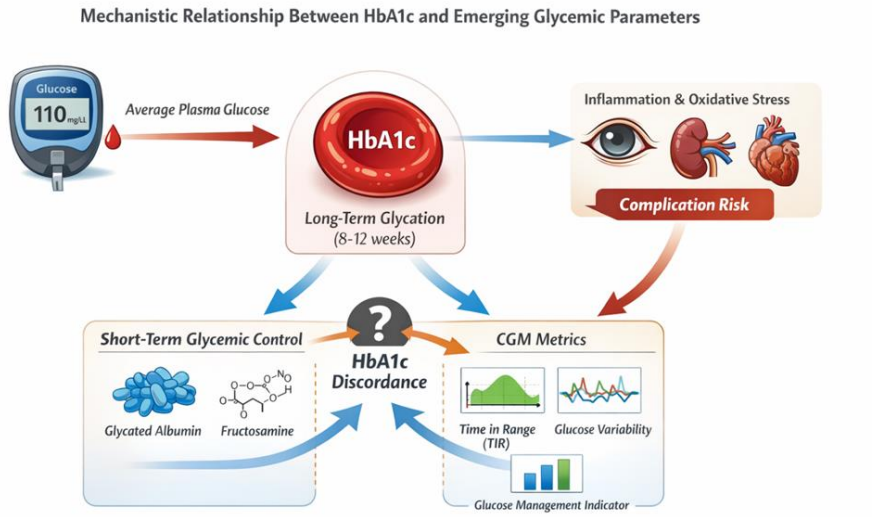

Figure 1: Mechanistic Relationship Between HbA1c and Emerging Glycemic Parameters

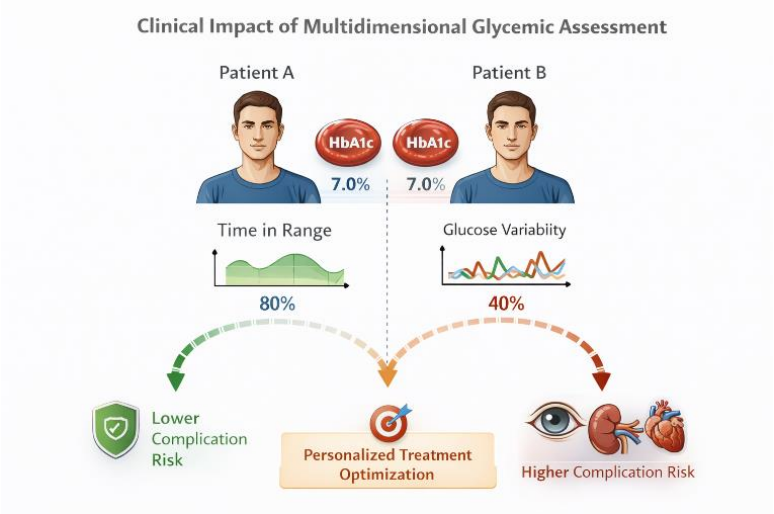

Figure 2: Clinical Impact of Multidimensional Glycemic Assessment

Discussion

These findings highlight the inadequacy of relying solely on HbA1c for comprehensive glycemic assessment. Emerging parameters provide valuable insights into short-term control, variability, and individualized risk. Integrating these markers may improve treatment personalization, particularly in high-risk populations such as elderly patients, those with renal disease, and individuals using insulin therapy. However, barriers, including cost, accessibility, and lack of universal standardization, remain.

Conclusion

HbA1c remains a valuable biomarker but should no longer be interpreted in isolation. New parameters such as glycated albumin, TIR, glucose variability indices, and inflammatory markers offer a more complete picture of glycemic control. Incorporating these measures into clinical practice may enhance diabetes management and reduce complication risk.

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I have no economic or added individual interests, straightforwardly or obliquely, in some matter that conceivably influence or bias my trustworthiness as a journalist concerning this manuscript

Conflicts of Interest:

The authors declare that they have no conflicts of interest.

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