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Research Paper

Beyond Blood Sugar: The Clinical Significance of HbA1c Measurement in Diabetes Diagnosis and Management

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Abstract

Background: Diabetes mellitus is one of the fastest-growing chronic diseases worldwide, requiring reliable methods for diagnosis and long-term monitoring. While daily blood glucose measurements provide immediate information, they do not reflect overall glycemic control. Glycated hemoglobin (HbA1c) has become the gold standard for assessing average blood glucose levels over the preceding two to three months

Objective: This article reviews the principles, clinical applications, measurement techniques, advantages, limitations, and future perspectives of HbA1c testing in diabetes care.

Methods: A narrative review of current scientific literature and clinical guidelines was conducted to summarize the role of HbA1c in diagnosis, monitoring, and treatment decision-making.

Results: HbA1c provides a standardized measure of long-term glycemic control and correlates with the risk of diabetes-related complications. Various laboratory methods, including high-performance liquid chromatography (HPLC), immunoassays, enzymatic assays, capillary electrophoresis, and boronate affinity chromatography, are used for HbA1c estimation. Despite its advantages, HbA1c interpretation may be influenced by conditions affecting red blood cell lifespan, hemoglobin variants, anemia, chronic kidney disease, and recent blood transfusions.

Conclusion: HbA1c remains an indispensable biomarker for diabetes diagnosis and management. Understanding its strengths and limitations enables healthcare professionals to interpret results accurately and optimize patient care. Continued advancements in analytical technologies are expected to improve the precision and accessibility of HbA1c testing worldwide

Introduction

Diabetes mellitus is a chronic metabolic disorder characterized by persistent hyperglycemia resulting from impaired insulin secretion, insulin resistance, or both. According to the International Diabetes Federation, the global prevalence of diabetes continues to increase, posing significant health and economic challenges. Effective diabetes management depends on accurate assessment of long-term glycemic control to minimize complications such as retinopathy, nephropathy, neuropathy, and cardiovascular disease.

Among various biomarkers available, glycated hemoglobin (HbA1c) has emerged as the most reliable indicator of average blood glucose concentration over approximately 8–12 weeks. Unlike fasting plasma glucose or random blood glucose testing, HbA1c reflects cumulative glucose exposure and is unaffected by short-term dietary changes or daily glucose fluctuations.

Formation of HbA1c

The formation of HbA1c involves several biochemical steps:

1. Glucose enters circulating red blood cells.
2. Glucose binds reversibly to hemoglobin, forming a Schiff base.
3. The Schiff base undergoes molecular rearrangement to form a stable ketoamine known as HbA1c.
4. The glycated hemoglobin remains throughout the lifespan of the erythrocyte.

Since this reaction is irreversible, HbA1c accumulates proportionally to blood glucose concentration.

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Methods of HbA1c Measurement

Several laboratory techniques are available.

High-Performance Liquid Chromatography (HPLC)

HPLC is considered the reference method in many laboratories.

Advantages include:

- High analytical accuracy
- Excellent precision
- Detection of hemoglobin variants
- Automated processing

Limitations include relatively high cost and instrument maintenance.

Factors Affecting HbA1c Measurements

Several physiological and pathological conditions may influence HbA1c results.

Falsely Elevated HbA1c

- Iron deficiency anemia
- Vitamin B12 deficiency
- Reduced red blood cell turnover
- Splenectomy

Falsely Low HbA1c

- Hemolytic anemia
- Acute blood loss
- Pregnancy
- Blood transfusion
- Erythropoietin therapy

Other Influencing Factors

- Chronic kidney disease
- Liver disease
- Hemoglobinopathies
- Recent transfusion
- Ethnicity
- Certain medications

Clinicians should always interpret HbA1c within the patient's clinical context.

Quality Assurance in HbA1c Testing

Accurate HbA1c measurement requires rigorous laboratory quality control

Important quality measures include:

- Regular instrument calibration
- Internal quality control procedures
- Participation in external quality assessment programs
- Use of standardized analytical methods
- Proper specimen handling and storage

Laboratories should adhere to internationally recognized standardization programs to ensure reliable results.

Conclusion

HbA1c measurement has transformed diabetes diagnosis and long-term disease management by providing a reliable indicator of average glycemic control over the previous two to three months. Its strong association with the development of diabetes-related complications makes it an essential biomarker in clinical practice. Although several analytical methods are available, each has unique strengths and limitations that must be considered during result interpretation. Factors such as anemia, hemoglobin variants, chronic kidney disease, and altered red blood cell survival can influence HbA1c values and should be evaluated alongside the patient's clinical history. Continued improvements in laboratory technology, standardization, and point-of-care testing are expected to enhance the accuracy and accessibility of HbA1c measurement, ultimately supporting better patient outcomes through informed clinical decision-making

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