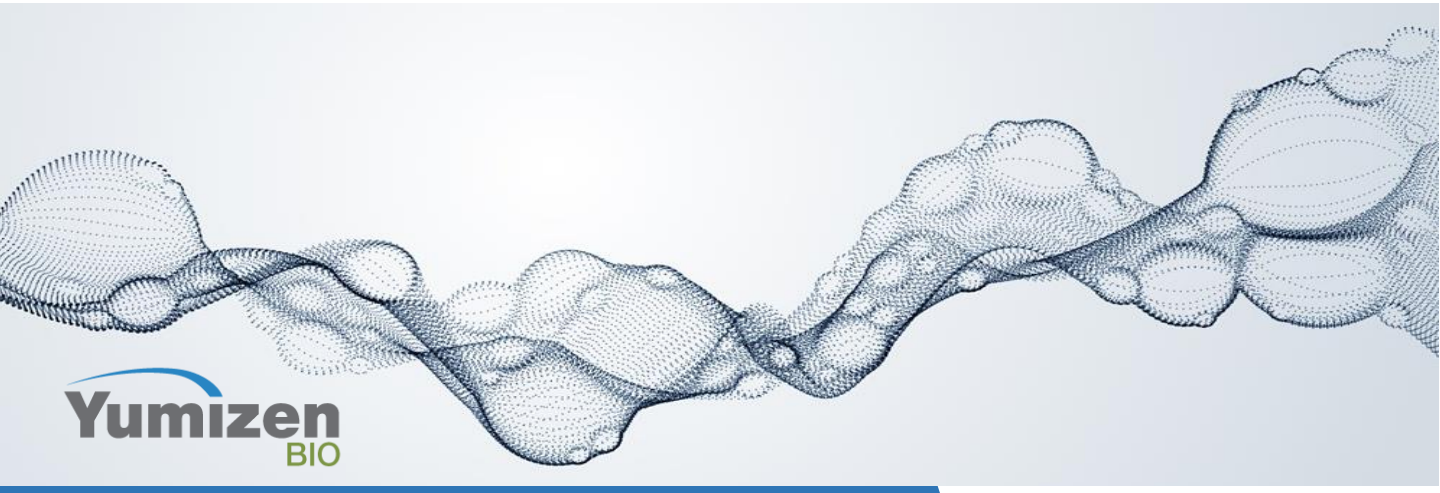


Yumizen BIO

HbA1c Clinical Chemistry Diabetes Assay

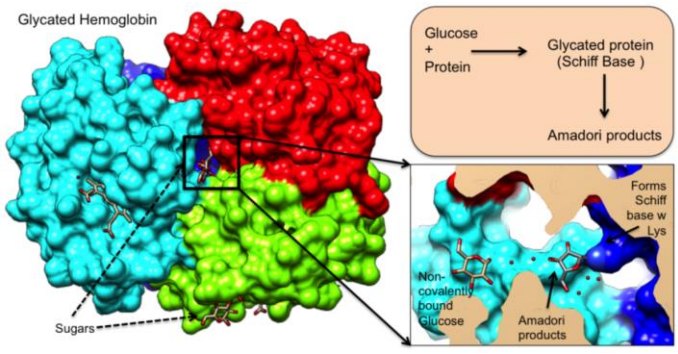
November 2024

Introduction

The hemoglobin A1c (HbA1c) assay is an accurate and precise aid for diagnosing diabetes mellitus by monitoring long-term glucose control in individuals with diabetes mellitus and also for identifying patients who may be at risk of developing diabetes mellitus.

Diabetes is on the rise worldwide. In 2019, an estimated 463 million adults, or 1 in 11 adults, were diagnosed with diabetes, and this number is projected to rise.[1]

To address this critical public health concern, mid- to high-volume laboratories need a modern HbA1c clinical chemistry assay that is simple to install, operate and integrate into their existing testing workflows.



HORIBA POINTE Hemoglobin A1c Reagent Set avoids the inconvenience and expense associated with additional dedicated HbA1c analyzers by opting for precision, efficiency, convenience, and value.

Glycemic Goals in Adult Diabetics

Consistent regulation and monitoring of blood glucose levels is the mainstay of therapeutic diabetic management, achieved through maintaining blood glucose levels at or near the non-diabetic ranges and avoiding significant fluctuations.

By determining long-term (2-3 months) blood glucose control, HbA1c serves as a measurement for the diagnosis and monitoring of diabetes mellitus patients.

High HbA1c levels have been correlated with an increased risk for type 2 diabetes mellitus, as well as cardiovascular disease.

Different methodologies are used in laboratories for measuring HbA1c. These may not yield equitable results due to hemoglobin variants present in patients, establishing a need to standardize HbA1c methodologies.

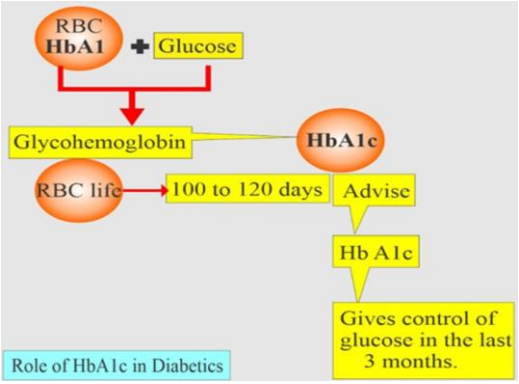
	Hemoglobin A_{1c} (%)	Preprandial Glucose		Postprandial Glucose**	
		mg/dL	mmol/L	mg/L	mmol/L
ADA ↑: Adults	<7.0	80-130	4.4-7.2	<180	<10.0
Pregnant Adults	<6.0	60-99	3.3-5.5	100-129	5.6-7.2
Older Adults					
Healthy	<7.5	90-130	5.0-7.2	90-150	5.0-8.3
Intermediate	<8.0	90-150	5.0-8.3	100-180	5.6-10.0
Poor Health	<8.5	100-180	5.6-10.0	110-200	6.1-11.1
AACE	≤6.5	≤110	≤6.1	≤140	≤7.8

** - 1 to 2 hours after beginning a meal for adults, except bedtime for older adults

↑ - Youth <18 years of age: goal hemoglobin A_{1c} <7.5%

HbA1c is the preferred clinical marker.

Testing with a diagnostic threshold of ≥ 6.5% (≥ 48 mmoL/moL) HbA1c has been recommended for the diagnosis of Type 2 diabetes by the International Expert Committee (IEC)[2], the American Diabetes Association (ADA)[3], and the World Health Organization (WHO)[4].



Different methods for HbA1c testing

HbA1c estimation methods are mainly based on Structural differences or Charge differences of the Hemoglobin molecule. Laboratorians should use a method that has been certified by the National Glycohemoglobin Standardization Program NGSP, standardized or traceable to the Diabetes Control and Complications Trial DCCT reference assay. In cases of high abnormal Hemoglobin, e.g., HbS, HbF, HbC and HbThal, serum fructosamine or glycated albumin levels are the preferred tests for the diagnosis and monitoring of Diabetes Mellitus.

Hb1Ac comparison of different methods

Table 1: Comparison of Various HbA1c Measurement Methodologies

Method	Basis	Advantages	Disadvantages
Immunoassay	Structural differences. Uses antibodies towards glycated N-terminal of Hb's β chain.	Provide quantitative measurements of HbA1c.	HbF produces falsely low results. Hb variants such as Hb S and Hb C may cause false increase in HbA1c measurements.
Affinity Chromatography	Structural differences. Uses borate to bind glycosylate hemoglobin based on HbA1c's chemical structure.	Not TEMPERATURE-DEPENDENT. Usually not affected by variant hemoglobin F, S, or C.	High levels of HbF seen in thalassemia, HPFH, etc. may interfere with results.
Ion Exchange Chromatography (Including HPLC)	Charge differences. A positively charged resin bed separates negatively charged HbA1c.	HPLC has the advantage of separating hemoglobin variants into peaks.	Highly temperature dependent. Some hemoglobin variants may interfere with results.
Electrophoresis	Charge differences.	Separates various hemoglobin variants and allows for identification of variants.	Hemoglobin F over 7% interferes with results.
Isoelectric Focusing	Charge differences. Variation of electrophoresis using an isoelectric point to separate hemoglobin variants.	Sensitive, economical, quick.	Pre-HbA1c interferes with results.
Enzymatic	Oxidations & proteolysis.	Cost effective, simple	Interferences from Hb variants, hemolytic anemia can lead to lower values.

HORIBA POINTE Hemoglobin A1c Reagent Set Enhanced Turbidimetric Immunoassay

An accurate, efficient aid for the diagnosis and monitoring of Diabetes Mellitus

HORIBA POINTE was introduced to the market in 2003 as one of the only direct measurement systems for HbA1c. Other test methods use an HbA1c value derived from the measurement of total hemoglobin, then a second measurement of hemoglobin A1c levels from patient samples, whereupon a calculation is performed. The HORIBA POINTE method, however, gives a direct value in percentage HbA1c.

Methodology, Enhanced performance, Greater efficiency

This method is a direct immunoturbidimetric system which utilizes the interaction of antigen and antibody to directly determine the HbA1c in whole blood. Total hemoglobin and HbA1c have the same unspecific absorption rate to latex particles. When mouse antihuman HbA1c monoclonal antibody is added (R2), latex-HbA1c-mouse anti human HbA1c antibody complex is formed.

Agglutination is formed when goat anti-mouse IgG polyclonal antibody interacts with the monoclonal antibody. The amount of agglutination is proportional to the amount of HbA1c absorbed onto the surface of latex particles. The amount of agglutination is measured as absorbance. The HbA1c value is obtained from a calibration curve.

Specificity

Hemoglobin variants HbA2, HbC, and HbS do not interfere with this method.

It has been reported that high levels of HbF may lead to underestimation of HA1c and that uremia does not interfere with HbA1c determination by immunoassay.

Conclusion

HbA1c testing is an accurate, user-oriented & accessible method, representing an effective tool for screening, diagnosis and monitoring diabetes. The prognostic potential of HbA1c lies in its unique ability of estimating retrospective glycemic control.

The test can be carried out using a variety of techniques, depending on workload capacities.

It is highly recommended that the test is authorized by the National Glycohemoglobin Standardization Program (NGSP) or the International Federation of Clinical Chemistry (IFCC).

As the epidemic of diabetes continues to grow worldwide, HbA1c testing may be implemented as part of the diagnostic, prognostic and monitoring process, leading to better patient care and successful clinical outcomes.

The fully HORIBA automated HbA1c hemoglobin assay kit eliminates the need for manual sample pre-treatment, enabling you to deliver results simply, with less risk of error.

For more details:
https://www.horiba.com/int/medical/products/detail/action/show/Product/abx-pentra-400-reagents-572/

Emerging biomarker for Diabetes Mellitus

The quantification of serum glycated albumin (GA) can serve as an alternative. In fact, serum albumin may undergo structural changes by glycation, which impairs its function and plays a major role in the genesis of diabetes mellitus complications. GA can be measured accurately either on serum or plasma collected on tubes containing lithium heparin or EDTA as an anticoagulant. The introduction of a new enzymatic assay has increased the diffusion of this test, in both research and clinical settings.

This enzymatic assay is rapid, sensitive, and adaptable to routine clinical chemistry analyzers. GA allows an evaluation of the glycemic balance over a period of approximately three weeks and is particularly interesting for diabetic patients with chronic kidney disease.

References:

1.IDF
Diabetes Atlas 9th edition 2019. (2019). International Diabetes Federation. https://diabetesatlas.org/en/

2. International Expert Committee, 2009. International Expert Committee report on the Role of the A1C assay in the Diagnosis of Diabetes. Diabetes Care, 32(7), pp. 1327-1334.

3. American Diabetes Association, 2010. Diagnosis and Classification of Diabetes Mellitus. Diabetes Care, Volume 33, pp. 62-69.

4. WHO, World Health Organization (WHO). [Online] http://www.who.int/diabetes/publications/diagnosis_diabetes2011/en/ [Accessed 01 May 2017]

5. https://www.aacc.org/science-and-research/scientific-shorts/2023/what-is-the-difference-between-fructosamine-and-glycated-albumin

Authors:

George Ferrandi, PharmD, Head of Clinical Chemistry, International Marketing, HORIBA

Dr. Prakash Suvasia, Scientific & Medical Officer, HORIBA

Brooke Bradley, Product Manager, Medical (Chemistry), HORIBA