

# HbA1c Assay as Diagnostic and Prognostic Biomarker for Diabetic Patients

**Khalid Abdelsamea Mohamedahmed\***

Department of Medical Laboratory Sciences, Faculty of Applied Medical Sciences, Jerash University, Jerash, Jordan.  
Department of Hematology and Immunohematology, Faculty of Medical Laboratory Sciences, University of Gezira, Wad Medani, Sudan.  
Department of Immunology, Faculty of Medical Laboratory Sciences, University of Gezira, Wad Medani, Sudan.

**\*Correspondence**

Dr. Khalid Abdelsamea Mohamedahmed  
khalid.gu89@gmail.com

Received: 10 August 2025 / Accepted: 21 November 2025 / Published: 31 December 2025

Hemoglobin A1c (HbA1c) is one of the most for detection and long-term tracking diabetes mellitus due to measuring average blood glucose levels during the preceding 2-3 months. It is crucial for determining glycemic control and forecasting the likelihood of long-term diabetic consequences, especially microvascular illness. This mini-review focusing in the biochemical basis of glycosylated hemoglobin. its diagnostic and prognostic value, and major factors affecting its reliability. Although HbA1c minimizes the impact of short-term glucose fluctuations, its accuracy may be compromised by non-glycemic factors such as altered erythrocyte turnover, hemoglobin variants, comorbid conditions, and genetic polymorphisms. Awareness of these limitations is crucial for appropriate interpretation of HbA1c results. Understanding these restrictions is essential for correctly interpreting HbA1c findings. HbA1c remains a cornerstone in diabetes care, but optimal use requires integration with clinical context and complementary glycemic assessments.

**Keywords:** *HA1C, Diabetes mellitus, Diagnostic biomarker, Prognostic biomarker*

The primary protein in erythrocytes and the pigment that distributed oxygen, hemoglobin, is what gives blood its red hue. Hemoglobin adult (Hb A) makes up around 90% of hemoglobin. about 8% of Hb A is composed of small contents that differ chemically, even though 92% of hemoglobin A is composed of a single chemical component. Among these trace elements are HbA1c, A1b, A1a1, and A1a2 (Abdalla et al., 2023). A tiny portion of hemoglobin that has glucose bound to it is called HbA1c (Glycosylated or glycated hemoglobin). HbA1c levels are influenced by the concentration of blood glucose. In other words, elevated blood glucose levels correspond to increased HbA1c levels, which reflect the average blood glucose levels over the previous six to eight weeks rather than being impacted by daily variations in blood glucose (Al Ali et al., 2025). A slow, irreversible, non-enzymatic process of adding sugar residue to hemoglobin results in HbA1c, which is defined by the International Federation of Clinical Chemistry working group (IFCC) as hemoglobin that has been irreversibly glycated at one or both N terminal valines of beta chains. The rate of production of HbA1c is directly correlated with the levels of ambient glucose (Awad et al., 2025). Evaluating glycated hemoglobin in blood offers insights into a person's blood sugar levels over the past 2 to 3 months, reflecting the expected half-life of RBCs. Within the typical 120-day lifespan of RBCs, glucose molecules attach to Hb, creating glycated Hb. Within people inadequately managed diabetes, elevations in levels of this HbA1c are observed. After hemoglobin undergoes glycosylation, it stays in that state. An accumulation of glycated hemoglobin in the RBCs indicates the glucose levels the cell was subjected to throughout its life span (Sherwani et al., 2016). The measurement of glycosylated hemoglobin evaluates therapy effectiveness by tracking long-term regulation of serum glucose levels. The HbA1c level correlates with the average blood sugar levels observed over the past 1 to 3 months, with some studies suggesting that a significant portion of its value is associated with a shorter duration of two to four weeks (Leow, 2016; Sherwani et al., 2016). Diabetes mellitus has reached epidemic levels globally due to its numerous complications, resulting in significant morbidity and mortality from chronic vascular issues

such as retinopathy, nephropathy, and cardiovascular disease (Mohamedahmed et al., 2016). HbA1c, an indicator of blood sugar control, signifies sugar levels from the prior months. HbA1c levels foretell the likelihood of microvascular complications in diabetic patients (Ibrahim et al., 2021). The HbA1c examination is presently one of the most effective methods for diagnosing diabetes. It is advised to measure glycated hemoglobin for assessing blood sugar regulation in individuals at risk of pre-diabetes and for tracking blood sugar control in those with higher levels, known as diabetes mellitus. The HbA1c test assesses long-term average blood sugar levels, aiding both diabetics and their doctors by establishing treatment objectives to minimize the risks linked to the onset and advancement of diabetes-related chronic complications (Ibrahim & Mohamedahmed, 2022; Ibrahim et al., 2022). Research indicates that A1C serves as a measure of blood sugar levels during the previous weeks or months. Glycated hemoglobin does not accurately represent glycemic control as is often asserted. Various elements contribute to differences in A1C outcomes (Radin, 2014). Factors influencing HbA1c measurement such as erythrocyte turnover rate, alcohol use, specific medications for cancer treatment, and infections like HIV or hepatitis C are recognized to yield inaccurate results. Hemoglobin variants arise from single nucleotide mutations in the hemoglobin globin genes, leading to an amino acid change. More than 700 silent variants exist, with the majority affecting HbA1c (Shimazaki et al., 2007). HbA1c assesses blood sugar levels over the past 2–3 months and is utilized to determine if a person has diabetes (HbA1c  $\geq$  6.5%) or to evaluate diabetes management. Recent studies on genome-wide association with HbA1c have successfully discovered several genomic loci affecting HbA1c via glycemic (elements that impact blood glucose levels) and erythrocytic (elements that influence red blood cells) pathways (Leong & Wheeler, 2018). HbA1c inaccuracies caused by non-glycemic factors might result in inadequate care or negative health effects. A recently reported case is the erythrocytic variant G6PD, which causes a false reduction in HbA1c and results in missed diabetes diagnoses with existing thresholds (Ahmed et al., 2022).

## **Conclusion**

HbA1c is a practical and widely accepted biomarker for evaluating glycemic control and predicting diabetic complications. Despite its clinical value, HbA1c levels may be influenced by several non-glycemic and genetic factors, potentially leading to diagnostic inaccuracies in certain populations. Therefore, HbA1c should be interpreted cautiously and, when necessary, supported by additional glycemic markers and clinical evaluation. A comprehensive approach enhances diagnostic accuracy and supports effective diabetes management.

## **Acknowledgement**

Clinical Chemistry Staff in Faculty of Medical Laboratory Sciences, University of Gezira were thanked.

## **Author contributions**

Author made a significant intellectual contribution, reviewed and approved the final manuscript version, and consented to take responsibility for all elements of the work.

## **Funding**

No funding.

## **Conflict of interest**

Author has stated that there are no competing interests.

## **Ethics approval**

Ethical approved was obtained from the Research and Ethic Committee in Faculty of Medical Laboratory Sciences, University of Gezira.

## **AI tool usage declaration**

The author has declared that no AI and associated tools are used for writing scientific content in the article.

## References

- Abdalla AA, Elmukashfi STA, Hassan AY, et al. (2023). The Effect of Aspirin on HbA1c Assay Among Diabetic Hypertensive Patients Attending Abu Aqulah Centre in Wad Madani, Gezira State, Sudan. *International Journal of Diabetes and Endocrinology*. 8(1):1-5.
- Ahmed AK, Elsiddig YM, Mohamedahmed KA; et al. (2022). Assessment of G6PD Activity among Diabetic Patients and Its Relationship with Hyperglycemia, Wad Madani, Gezira State, Sudan. *Open Access Library Journal*. 9: e9399.
- Al Ali MAO, Mohamedahmed KA, Babker AM. (2025). Role of platelet indices and vitamin D in forecasting deterioration of glycemic control and vascular complications in type 2 diabetes. *Italian Journal of Medicine*. 19(1):1875.
- Awad RA, Mohamed OO, Barakat ME, et al. (2025). Assessment of Iron Profiles among Patients with Type 2 Diabetes Mellitus Attending Kassala Teaching Hospital, Kassala State, Sudan (2024). *IJAHRM*. 9(2):19-233.
- Ibrahim RE, Ibrahim SE, Abdalsamea K, et al. (2021). Evaluation of Common Coagulation Tests in Type 2 Diabetic Patients and Association with Diabetic Pre-cardiovascular Complications, Gezira State–Sudan, 2020-2021. *Asian Hematology Research Journal*. 5(4):1-6.
- Ibrahim RE, Mohamedahmed KA. (2022). The Role of 4G Allele in *Plasminogen Activator Inhibitor-1 (rs1799889)* Gene as Biomarker for Thrombophilic States among Patients with Type 2 Diabetes. *GMJ*. 11: e2247.
- Ibrahim RE, Ibrahim SHE, Mohamedahmed KA; et al. (2022). The Frequency of rs1799889 in Plasminogen Activator Inhibitor Type -1 Gene in Sudanese Type 2 Diabetic Patients, Gezira State, Sudan, 2020-2021. *Open Journal of Applied Sciences*. 12(1):165-174.
- Leong A, Wheeler E. (2018). Genetics of HbA1c: a case study in clinical translation. *Curr Opin Genet Dev*. 50:79-85.
- Leow MK. (2016). Glycated Hemoglobin (HbA1c): Clinical Applications of a Mathematical Concept. *Acta Inform Med*. 24(4):233-238.
- Mohamedahmed KA, Mohammed RM, Talha AA. (2022). Prevalence of Anemia among Patients with Type II Diabetes Mellitus, Alkhair Medical Center, Wad Medani, Gezira State, Sudan (2020). *International Journal of Healthcare and Medical Sciences*. 8(3):13-18.
- Radin MS. (2014). Pitfalls in hemoglobin A1c measurement: when results may be misleading. *J Gen Intern Med*. 29(2):388-94.
- Sherwani SI, Khan HA, Ekhzaimy A, et al. (2016). Significance of HbA1c Test in Diagnosis and Prognosis of Diabetic Patients. *Biomark Insights*. 11:95-104.
- Shimazaki T, Kadowaki T, Ohyama Y, et al. (2007). Hemoglobin A1c (HbA1c) predicts future drug treatment for diabetes mellitus: a follow-up study using routine clinical data in a Japanese university hospital. *Translational Research*. 149(4):196-204.