CHEARS Chronical
CHEARS
Volume 13 · Issue 1 · Jan–Mar 2026

GENERAL

Affect of fortuitous Hemoglobin variants on the accuracy of HbA1c estimation by HPLC method.

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Received: 03 June 2025 **Published:** 27 February 2026 **Volume 13, Issue 1** (Jan–Mar 2026)
Article no.: e151 **Open access** · free to read

The Diabetes Mellitus (DM) is one of the most common chronic lifestyle diseases widely prevalent around the globe. As per recent WHO r?port, more than 366 million people will be effected by 2030.This rising trend requires a long term monitoring of glycemic control in diabetic population.

HbA1c testing is widely and commonly recommended by doctors as it gives a measure of average blood glucose levels over the past 2 -3 months. Thus making it a crucial biomarker for diagnosing and managing diabetis.

Different methodologies are available for HbA1c estimation like HPLC, enzymatic ,turbidimetric , immunoassay and capillary electrophoresis. Of all the methods ,High Performance Liquid Chromatography (HPLC) is the reference ?gold standard? method.

Basically this article will raise awareness about various hemoglobnopathies which are coincidental finding during HbA1c testing.Thus picking up hidden hemoglobin variants which would otherwise have gone unnoticed and helping health care professionals and patients to have a better understanding of their glycemic control.

American diabetes association (ADA) has recommended HbA1c for long term monitoring of glycemic control. Therefore, accurate and precise measurement of HbA1c is extremely important .

Many Hemoglobin variants are found in people from South East Asia and India. These Hb variants are a fortuitous finding when HbA1c is analysed. However, their presence may affect the accuracy of the test causing a spurious increase or decrease in the HbA1c result, depending on the methodology and properties of the haemoglobin.

When a patient?s chromatogram shows a hemoglobin variant during HbA1c testing , it is reported to ordering clinician who then explains the patient about the presence of the variant and asks for HPLC testing in order to identify and quantify the Hemoglobin variant HbA1c is strongly correlated with complications of Diabetes , so its measurement must be be accurate and precise. This will benefit the patients in keeping a track of their blood glucose levels thereby achieving better glycemic control.

Although cation exchange HPLC is the reference method , the accuracy of HbA1c testing by this method can be adversely affected by the presence of variant Hb. The variant Hb may interfere with glycated form of Hb either giving falsely high / low values or sometimes HbA1c fraction cannot be detected at all .

Ideally, treating doctor should detect the presence of Hb variant in chromatogram and decide if HbA1c measurement can be accepted at face value. HbA1c cannot be reported by HPLC method if the variant window is >50% of the total hemoglobin in chromatogram. Hetrogenous variants like HbS and HbC do not affect the assay .In contrast, if the Homozygous Hb variant or compound Heterozygous variant is detected , it invalidates HbA1c results.

In such cases patients are advised and samples are analysed by alternative methods that is not affected by method based interference . Fructosamine is usually recommended in such cases but since it reflects only 20 days glucose control, clinicians are not preferring it . Immunoassay involving antigen antibody interaction between first six amino acids of A1c is another alternate method of HbA1c testing .If there is no choice or availability of

alternate methods ,ADA (American diabetic association) recommends reporting of calculated A1c, NGSP has published approved calculator to calculate A1c from fasting /random blood sugar result.

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Thus, in managing diabetic patients , accurate interpretation of HbA1c results and appropriate treatment of diabetes is crucial.As ignoring the presence of Hb variants results in mismanagement of diabetes leading to over or under treatment of the disease resulting in long-term development of complications.

Competing interests

The authors declare that they have no competing interests.

How to cite this article (Vancouver)
Osman SF. Affect of fortuitous Hemoglobin variants on the accuracy of HbA1c estimation by HPLC method. CHEARS Chronical. 2026;13(1):e151. Available from: https://chears.in/journal/volume-13/issue-1/affect-of-fortuitous-hemoglobin-variants-on-the-accuracy-of-hba1c-estimation-by-151
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https://chears.in/journal/volume-13/issue-1/affect-of-fortuitous-hemoglobin-variants-on-the-accuracy-of-hba1c-estimation-by-151