A Patient with Undetectable Hemoglobin A1c

Sutirtha Chakraborty1* and Debkishore Gupta2

CASE DESCRIPTION

A blood sample from a 39-year-old female patient with newly diagnosed type 2 diabetes was assayed for hemoglobin (Hb) A1c on a Bio-Rad D10 HPLC platform. No peak for A1c was seen on the chromatogram (Fig. 1A), and the result was reported as 0%. A complete blood count was clinically significant for an Hb concentration of 10.9 g/dL (reference interval 12–15 g/dL) and a mean corpuscular volume of 77 fl (reference interval 80–96 fl).

QUESTIONS

1. What was the reason for the absent A1c peak?
2. Can A1c be measured in this patient by an alternative method?
3. What other factors can affect A1c measurement?

The answers are on the next page.

---

Fig. 1. Bio-Rad D10 Chromatogram in A1c mode (A) and extended A2F mode (B).
The sample was reanalyzed in the extended mode, which revealed 95.5% of an Hb that eluted with Hb A2 and an Hb F of 2.2% (Fig 1B). The likely diagnosis was homozygosity for Hb E, a clinically benign condition common in Southeast Asia (1). Because there is no Hb A, ion exchange HPLC will not detect glycated Hb E, although there may be differences between assays. In this case, the result was 7.2% by Roche Tina-quant Hb A1c (2). There are several other factors that affect A1c results, such as any condition that shortens erythrocyte survival (recovery from acute blood loss, hemolytic anemia). Increased fetal Hb and carbamylated Hb also influence A1c measurement (3).

**Author Contributions:** All authors confirmed they have contributed to the intellectual content of this paper and have met the following 3 requirements: 
(a) significant contributions to the conception and design, acquisition of data, or analysis and interpretation of data; (b) drafting or revising the article for intellectual content; and (c) final approval of the published article.

**Authors’ Disclosures or Potential Conflicts of Interest:** No authors declared any potential conflicts of interest.

**References**


**News & Views**

**2011 Consensus Meeting on the Worldwide Standardization of Hemoglobin A1c Measurement**

David B. Sacks

The measurement of hemoglobin A1c (Hb A1c) is integral to the management of patients with diabetes. Hb A1c is used in the evaluation of long-term (8–12 weeks) glucose control, to alter therapy and predict the risk for development of microvascular complications, and as a criterion to diagnose diabetes. Early Hb A1c assays measured different forms of glycohemoglobin and lacked standardization. The publication of the Diabetes Control and Complications Trial (DCCT) in 1993 motivated the development of standardization programs in Japan, Sweden, and the US. The National Glycohemoglobin Standardization Program (official name later shortened to the acronym NGSP) was by far the most widely implemented program around the world, being used in the vast majority of countries that had Hb A1c standardization. The subsequent development of a reference measurement system by the IFCC led to several meetings to effect universal standardization of Hb A1c. At the initial meeting in 2004, participants reached consensus for the adoption of the IFCC reference method as the global standard for calibration of Hb A1c assays. All participants agreed that the same Hb A1c values should be reported globally.

These decisions were endorsed at subsequent meetings in 2007 and 2009. Additional recommendations, published in 2010 in *Clinical Chemistry* (1), were:

1. Hb A1c results should be reported by clinical laboratories worldwide in Système International (SI) units (mmol/mol, no decimals) and derived NGSP units (%), 1 decimal, using the IFCC–NGSP master equation (DCCT units).
2. Hb A1c conversion tables including both SI (IFCC) and NGSP units should be easily accessible to the diabetes community.

---

1 Department of Laboratory Medicine, NIH, Bethesda, MD.
2 Nonstandard abbreviations: Hb A1c, hemoglobin A1c; DCCT, Diabetes Control and Complications Trial; NGSP, National Glycohemoglobin Standardization Program; SI, Système International.