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# Abnormal Hb A<sub>1c</sub> Result from a Diabetic Patient Leads to Unexpected Diagnosis

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## CASE DESCRIPTION

A 70-year-old male with a history of type 2 diabetes mellitus (T2DM) presented to an outpatient laboratory for routine venipuncture to evaluate glycemic management and cardiovascular disease risk. The patient arrived at the laboratory alert, with no apparent distress. Hemoglobin A<sub>1c</sub> (Hb A<sub>1c</sub>) testing was performed along with a lipid panel for routine screening of lipid disorders. The lipid panel results demonstrated mixed hyperlipidemia, showing increased triglycerides and decreased HDL cholesterol. The Hb A<sub>1c</sub> analysis by capillary electrophoresis (CE) on the Sebia CAPILLARYS 3 TERA instrument resulted with a flag for an atypical profile in the electropherogram and no Hb A<sub>1c</sub> value was reported. Prior Hb A<sub>1c</sub> measurements throughout the past year demonstrated Hb A<sub>1c</sub> concentrations  $\geq 6.5\%$ , consistent with his diagnosis of T2DM, and revealed a downward trend in the Hb A<sub>1c</sub> concentration (Table 1). The patient was not receiving medical treatment or medications known to affect red blood cells or Hb A<sub>1c</sub> measurement (1). The inconclusive Hb A<sub>1c</sub> result was repeated with a different instrument and another sample from the patient, collected at a different phlebotomy location, showed similar inconclusive results as the previous specimen (Table 1). Compared to typical hemoglobin and Hb A<sub>1c</sub> migration patterns, this patient's specimens resulted in unusual shifts in hemoglobin peak migration times as observed upon close review of the electropherogram, suggesting a potential analytical interference of the Hb A<sub>1c</sub> measurement (Fig. 1).

## PATIENT FOLLOW-UP

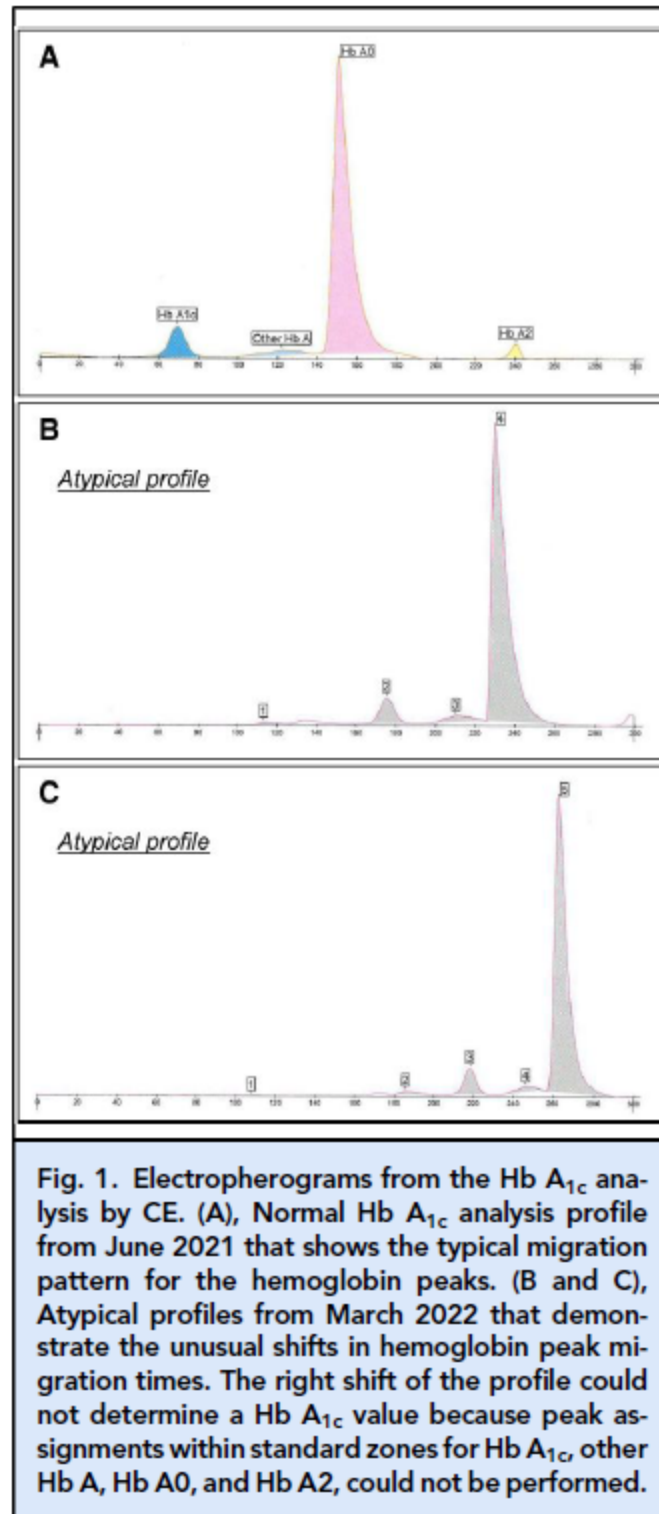
In communications with the assay manufacturer, it was suggested that a potential cause of this type of interference could be markedly increased leukocyte counts. In sharing this information with the clinical team, it was recommended to the patient to return to the hospital to obtain a complete blood count (CBC) for evaluation. Simultaneously, we opted to test Hb A<sub>1c</sub> in 2 unrelated specimens with markedly elevated white blood cell counts ( $>100$  k/ $\mu$ L; reference interval: 4.30 to 11.30 k/ $\mu$ L), wherein we observed similar peak shifts in the electropherograms. The patient's follow-up test at the hospital revealed a CBC with a highly elevated leukocyte count of 175.80 k/ $\mu$ L, suggesting the abnormal Hb A<sub>1c</sub> result could be due to an interference caused by leukocytosis. A manual differential confirmation demonstrated elevations in myelocytes, metamyelocytes, promyelocytes, blasts, and basophils. During this hospital visit, another Hb A<sub>1c</sub> measurement was performed by CE and showed a Hb A<sub>1c</sub> concentration of 7.8%. This value correlated well with previous Hb A<sub>1c</sub> measurements and was consistent with the patient's history of T2DM. A fasting blood glucose (FBG) was also ordered and revealed an impaired fasting glucose concentration of 144 mg/dL (reference interval: 64 to 128 mg/dL). The FBG concentration was consistent with the elevated Hb A<sub>1c</sub> concentration. Due to the significantly elevated leukocyte count, the patient was referred to the emergency department for further workup.

**QUESTIONS TO CONSIDER**

- What are common and uncommon interferences in Hb A<sub>1c</sub> assays?
- What are known interference issues with the Hb A<sub>1c</sub> CE assay?
- What patient-related preanalytical factors could influence Hb A<sub>1c</sub> and its measurement?
- How can the laboratory rule out interferences?
- How could incorrect Hb A<sub>1c</sub> results be misinterpreted or lead to unnecessary testing?

**Table 1. Hb A<sub>1c</sub> measurements from May 2021 to March 2022**

Date of Hb A <sub>1c</sub> measurement	Hb A <sub>1c</sub> value, %
May 2021	9.0
June 2021	8.1
September 2021	7.3
March 2022—1st collection	"Atypical profile"; no value
March 2022—2nd collection	"Atypical profile"; no value



## REFERENCE

1. Mitchell K, Mukhopadhyay B. Drug-induced falsely low A1c: report of a case series from a diabetes clinic. *Clin Diabetes* 2018;36:80–4.

### Final Publication and Comments

The final published version with discussion and comments from the experts will appear in the July 2023 issue of *Clinical Chemistry*. To view the case and comments online, go to <https://academic.oup.com/clinchem/issue/69/7> and follow the link to the Clinical Case Study and Commentaries.

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