COMMENT ON LI ET AL.

Visual Inspection of Chromatograms Assists Interpretation of HbA_{1c}: A Case Report. Diabetes Care 2018;41:1829–1830

Jie Li,[1] Jie Lei,[2] An-ping Xu,[1] Yong Xia,[1] and Ling Ji[1]

Diabetes Care 2019;42:e9 | https://doi.org/10.2337/dc18-1836

We read with interest the article by Li et al. (1). The authors reported a case with an extremely abnormal HbA_{1c} value due to interference of a hemoglobin (Hb) variant. We agree with the authors regarding the necessity of visual inspection of chromatograms of HbA_{1c} prior to reporting the results, especially in the scenario of discordance between HbA_{1c} and other clinical findings. However, we believe some comments and suggestions for future investigation are important for exploring this issue.

Li et al. (1) should double-check their gene sequencing data, which were not included in the case report. We note that they identified a heterozygous mutation (c.242T>A, Leu81His) in the *HBB* gene. However, according to the record of human hemoglobin variants in database HbVar (http://globin.bx.psu.edu/hbvar/menu.html) and the National Center for Biotechnology Information (NCBI), the nucleotide at position c.242 in the *HBB* gene is A instead of T. The mutation reported by Li et al. is more likely to have been c.245T>A in the *HBB* gene, which results in a transition of leucine to histidine. Besides, the clinical features of the reported case were similar to those in the proband with hemoglobin variant Hb La Roche-sur-Yon (β81[EF5]Leu→His, *HBB*: c.245T>A) (2).

Apart from cation-exchange high-performance liquid chromatography (HPLC) used for the HbA_{1c} measurement in the case report (1), other common methods based on different principles include capillary electrophoresis (CE), immunoassay, enzymatic assays, and boronate affinity HPLC (3). Based on our clinical practice and research, we want to emphasize the following points: *1*) Recognition of the interference is crucial in order to prevent reporting erroneous results, especially in populations with a high prevalence of Hb variants such as in southern China. However, recognition of Hb variants depends on testing methods and the features of the Hb variants. For instance, we found that the common α- and β-globin variants in China, including Hb E, Hb New York, Hb J-Bangkok, Hb G-Coushatta, Hb Q-Thailand, Hb G-Honolulu, Hb Ube-2, and Hb G-Taipei, all can be separated by CE. Determination of HbA_{1c} levels using CE showed less interference than cation-exchange HPLC instruments (4). The degree of impact on the measurement of HbA_{1c} depends on the separation of Hb variants from Hb A (4,5). *2*) For newly identified Hb variants, the degree of interference with HbA_{1c} might be case dependent. Unlike the case reported by Li. et al. (1) with a low level of HbA_{1c} (initially measured at 2%), some Hb variants may present with a normal level of HbA_{1c}. These Hb variants may be hard to discover if the analytical methods have a limited capacity to prevent interference by Hb variants. For these patients, their geographic origins and the other indices of metabolic control should be carefully checked before any crucial treatment regimen is begun. *3*) For those suspicious cases with Hb variants, repeat analysis of HbA_{1c} should ideally be performed using a method based on a different analytical principle from the initial assay.

Duality of Interest. No potential conflicts of interest relevant to this article were reported.

References

1. Li Q, Xiao Y, Shah AD, Li S. Visual inspection of chromatograms assists interpretation of HbA_{1c}: a case report. Diabetes Care 2018;41:1829–1830
2. Wajcman H, Kister J, Vasseur C, et al. Structure of the EF corner favors deamidation of asparaginyl residues in hemoglobin: the example of Hb La Roche-sur-Yon [β81 (EF5) Leu→His]. Biochim Biophys Acta 1992;1138:127–132
3. Little RR, Rohlfing CL, Hanson S, et al. Effects of hemoglobin (Hb) E and HbD traits on measurements of glycated Hb (HbA_{1c}) by 23 methods. Clin Chem 2008;54:1277–1282
4. Xu A, Chen W, Xia Y, Zhou Y, Ji L. Effects of common hemoglobin variants on HbA_{1c} measurements in China: results for α- and β-globin variants measured by six methods. Clin Chem Lab Med 2018;56:1353–1361
5. Ji L, Yu J, Zhou Y, et al. Erroneous HbA_{1c} measurements in the presence of β-thalassemia and common Chinese hemoglobin variants. Clin Chem Lab Med 2015;53:1451–1458

[1]*Department of Laboratory Medicine, Peking University Shenzhen Hospital, Shenzhen, Guangdong, China*
[2]*Department of Laboratory Medicine, Maternity and Child Healthcare Hospital of Nanshan District, Shenzhen, Guangdong, China*

Corresponding author: Ling Ji, 1120303921@qq.com