https://doi.org/10.4082/kjfm.18.0164 • Korean J Fam Med 2019;40:282-283

KJFM
Korean Journal of Family Medicine

eISSN: 2092-6715

■ Letter

Pitfalls of Measuring Hemoglobin A1c in a Patient with Sickle Cell Trait in South Korea

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To the Editor

International medical service is not uncommon in South Korea since the number of patients from abroad has increased annually. According to a report by the Ministry of Health and Welfare, a total of 364,000 foreign patients visited Korea in 2016. Therefore, it is worth recalling that relatively uncommon clinical situations in Korea may be quite common in other countries. We herein report the case of a 46-year-old African-American patient with poorly controlled diabetes who presented with unusually low hemoglobin A1c (HbA1c).

A 46-year-old African-American male with past medical history of poorly controlled type 2 diabetes mellitus (DM) presented complaining of severe pain in both feet due to distal sensory neuropathy. He also admitted erectile dysfunction and blurry vision. He stated that diabetes was neglected until 6 months before presentation, when he started oral hypoglycemic agents and gabapentin. He did not know his paternal medical history. His mother had type 2 DM and rheumatoid arthritis and two of his brothers had hypertension. The patient's examination revealed a blood pressure of 146/91 mm Hg, and the heart rate was 74 bpm. His height was 172 cm and weight 101 kg. Vibration sense was mildly reduced in the great toes.

His fasting glucose (FBS) was 179 mg/dL, while HbA1c with ion-exchange high-performance liquid chromatography (Tosoh HLC-723 G7; Tosoh Corp., Tokyo, Japan) was 4.7%. Other laboratory tests, including the complete blood count, blood urea nitrogen, and creatinine were normal. Follow-up HbA1c was also discordantly low at 4.3% although FBS was 135 mg/dL and 2-hour postprandial glucose was 200 mg/dL. When he was questioned again about family history of sickle cell disease, he reported that only his sister was affected. Subsequent hemoglobin (Hb) electrophoresis showed that he had sickle cell trait with sickle hemoglobin (Hb S) of 42.6%. Glycoalbumin was measured to monitor blood glucose for longer periods instead of HbA1c and ranged from 18%–22% (reference range, 11%–16%). After his medication was changed to insulin, he was able to achieve good glycemic control and his symptoms resolved.

Sickle cell anemia or trait is rarely encountered in Korea. However, Hb S is the most common Hb variant in the United States and worldwide. The prevalence is especially high in African-Americans, reaching about 8%–10%, and is also high in sub-Saharan Africa, Latin America, Mediterranean countries, the Middle East, and parts of India.

HbA1c provides a predictable correlation with blood glucose and estimation of average glucose for the prior 2–3 months.[1,2] However, Hb variants may invalidate HbA1c results *in vitro* through analytical interference or *in vivo* by altering the red blood cell lifespan or glycation rate.[3-6] When the result is not correlated with the clinical impression, the possibility of interference by Hb variants should be considered,[4,7,8] and the interpretation of HbA1c values should be based on the patient's medical history and other laboratory results. Effort should be made to identify the Hb variant, and other HbA1c methods that do not cause interference should be considered to monitor glycemic control. Testing for other indicators of average blood glucose levels, such as glycoalbumin or fructos-

Received: September 17, 2018, Revised: November 6, 2018, Accepted: November 7, 2018
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amine, can be considered. If there is no appropriate method for a particular Hb variant, glycoalbumin, daily multiple testing of capillary glucose or continuous glucose monitoring may be used to monitor diabetes.[9,10]

CONFLICT OF INTEREST

No potential conflict of interest relevant to this article was reported.

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