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An Emerging Diabetes Mellitus Diagnosis Modality: HbA_{1c}

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Classically, the diagnosis of diabetes has been made using the fasting plasma glucose, random plasma glucose, or a 2-hr 75-g oral glucose tolerance test. There are many problems with the definition of diabetes based on blood glucose levels, such as the high intra-individual biological variability, variability in the collection and storage methods, and difficulty in ensuring a fasting state before measuring the blood glucose [1].

Recently, the hemoglobin A_{1c} (HbA_{1c}) assay has also been recommended for the diagnosis of diabetes. The HbA_{1c} concentration is a good indicator of glycemic control over the previous 8-12 weeks; the time period is dictated by the 120-day lifespan of erythrocytes. HbA_{1c} is used as the standard biomarker for the adequacy of glycemic management since it correlates well with both microvascular and, to a lesser extent, macrovascular complications based on a large epidemiological study [2,3]. In the past, expert committees have rejected the proposed use of HbA_{1c} for the diagnosis of diabetes mainly because of the lack of assay standardization. However, HbA_{1c} assays are now highly standardized, and an international expert committee recommended the use of the HbA_{1c} test to diagnose diabetes, with a threshold of ≥ 6.5%, in 2009 [4]. The American Diabetes Association (ADA) affirmed this decision in 2010. The diagnostic test should be performed using a method that is certified by the National Glycohemoglobin Standardization Program (NGSP) and standardized or traceable to the Diabetes Control and Complications Trial reference assay [5]. An HbA_{1c} cut-off of ≥ 6.5% is associated with an increase in the prevalence of moderate retinopathy [6].

A few attempts to verify the validity of glycated hemoglobin in diagnosing type 2 diabetes mellitus in different ethnic populations have been published [7]. Since many studies have found that ethnicity influences the HbA_{1c} level [8], it is necessary to confirm the utility of HbA_{1c} in different races. Recently, Yu et al. [9] investigated the validity of glycated hemoglobin in diagnosing type 2 diabetes mellitus in 497 Chinese subjects, and checked the fasting plasma glucose, oral glucose tolerance test (OGTT), and HbA_{1c}. In their study, an HbA_{1c} level of 6.5% had a sensitivity of 62.7% and a specificity of 93.5% as a diagnostic tool. They concluded that the optimal cut-off point of HbA_{1c} was 6.3% with a sensitivity of 79.6% and specificity of 82.2%. HbA_{1c} ≥ 6.5% has reasonably good specificity for diagnosing diabetes in Chinese, in concordance with the ADA recommendation [9]. These results, in terms of Asians, are meaningful. Yun et al. [10] also reported on the difference between the HbA_{1c} assay and fasting plasma glucose level for making the diagnosis of diabetes in Korean adults; the kappa index of agreement between the fasting plasma glucose level and HbA_{1c} was 0.50.

Since HbA_{1c} is associated with the risk of diabetes, HbA_{1c} is superior to the glucose level for assessing chronic complications of diabetes and a study of Koreans found agreement between glycosylated hemoglobin and fasting

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plasma glucose [10]. The 2011 diabetes guidelines of the Korean Diabetes Association (KDA) included using HbA_{1c} ≥ 6.5% for diagnosing diabetes [11].

To date, many studies support the use of glycosylated hemoglobin for diagnosing diabetes. The HbA_{1c} level is a reliable indicator of chronic glycemia and correlates well with the risk of diabetes complications. Nevertheless, HbA_{1c} is also affected by hemoglobinopathies, recent hemolysis, high triglyceride levels, pregnancy, and some drugs, including salicylates and vitamins C and E [12]. In addition, HbA_{1c} does not reflect acute elevations in the glucose level [12]. Clinicians must be aware of these limitations.

Conflict of interest

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

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