DIABETES

Prognostic validity of HbA$_{1c}$ levels in nondiabetic adults

HbA$_{1c}$ levels ≥6% may be a clinically useful marker for the identification of individuals at risk of diabetes mellitus, as well as for the prediction of cardiovascular disease and all-cause mortality, say researchers of a community-based population study published in the *New England Journal of Medicine.*

In January 2010, the American Diabetes Association revised their clinical practice guidelines to include the use of HbA$_{1c}$ levels for the diagnosis of diabetes mellitus. Accordingly, an HbA$_{1c}$ value ≥6.5% is considered diagnostic of diabetes mellitus, and individuals with an HbA$_{1c}$ level between 5.7% and 6.4% are considered at high risk of developing this condition.

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Elizabeth Selvin, an Assistant Professor of Epidemiology and Medicine at the Johns Hopkins Bloomberg School of Public Health in Baltimore (MD, USA), was interested in determining whether levels of HbA$_{1c}$ rather than fasting glucose concentration—the standard measure used in clinical practice for the diagnosis of diabetes mellitus—are more accurate predictors for the identification of individuals at high risk of long-term

adverse health outcomes. Selvin led an ancillary study to the ARIC study, a large ongoing NIH-funded longitudinal study of middle-aged adults. "Long-term prognostic information on HbA$_{1c}$ values can help inform the use of the HbA$_{1c}$ test in clinical practice," she explains.

The researchers measured HbA$_{1c}$ levels from frozen whole-blood samples of 11,092 individuals, who did not have a history of diabetes mellitus or cardiovascular disease, with high-performance liquid chromatography and examined the association of HbA$_{1c}$ concentration with long-term health complications, such as diabetes mellitus, coronary heart disease, stroke and all-cause mortality. During the follow-up period of 15 years, 2,251 participants developed diabetes mellitus. In addition, 1,198 cases of coronary heart disease and 358 cases of ischemic stroke were reported and 1,447 deaths occurred in the study cohort.

HbA$_{1c}$ values at baseline were similarly associated with the risk of diabetes mellitus and more strongly associated with risks of cardiovascular disease and all-cause mortality than baseline levels of fasting glucose.

An HbA$_{1c}$ level <5.0% was associated with approximately half the risk of developing diabetes mellitus compared with a value of 5.0% to <5.5%, whereas an HbA$_{1c}$ level of 6.0–6.4% related to an approximately 10-fold risk of diabetes mellitus compared with a value of 5.0%

to <5.5%, even after adjustment for major diabetes risk factors. Furthermore, an HbA$_{1c}$ value ≥6.0%, when compared with HbA$_{1c}$ levels of 5.0% to <5.5%, was associated with approximately twice the risk of coronary heart disease, stroke and all-cause mortality, independent of other risk factors and/or baseline fasting glucose level.

In other words, "higher HbA$_{1c}$ values were associated with a progressively higher risk of diabetes mellitus in a continuous manner," summarises Selvin, "[with] no evidence of a risk threshold."

On the other hand, no association could be determined between fasting glucose concentration and coronary heart disease, stroke or death after adjustment for all risk factors and baseline HbA$_{1c}$ level, suggesting that HbA$_{1c}$ might be superior to fasting glucose concentration for the prediction of long-term complications.

"Persons with HbA$_{1c}$ values ≥6.0% are at high risk of developing diabetes mellitus, even after adjustment for other risk factors and independently of baseline fasting glucose," concludes Selvin.

The findings add to the growing body of evidence that supports the use of HbA$_{1c}$ as a diagnostic test for the diagnosis of diabetes mellitus.

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