

Fasting Glucose and HbA1c May Both Be Useful to Predict Diabetes

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Disclosure: Penny Murata, MD, has disclosed no relevant financial relationships

September 24, 2010 - Fasting glucose and glycated hemoglobin (HbA1c) levels may both be useful to predict diabetes, according to the results of population-based analyses reported online September 20 in *Diabetes Care*.

“Although ...HbA1c is now recommended to diagnose diabetes, its test performance for diagnosis and prognosis is uncertain,” write Elizabeth Selvin, PhD, MPH, from the Johns Hopkins Bloomberg School of Public Health in Baltimore, Maryland, and colleagues. “Our objective was to assess the test performance of HbA1c against single and repeat glucose measurements for diagnosis of prevalent diabetes and for prediction of incident diabetes.”

The study sample consisted of 12,485 participants enrolled in the Atherosclerosis Risk in Communities (ARIC) Study and a subpopulation of 691 participants in the Third National Health and Nutrition Examination Survey (NHANES III) who had repeated glucose test results available.

For detection of prevalent diabetes against a single fasting glucose level of 126 mg/dL or more, the sensitivity of an HbA1c level of at least 6.5% was 47%, and the specificity was 98% (area under the receiver operator characteristic curve [AUC], 0.892). Against fasting glucose measurements of 126 mg/dL or more repeated at an interval of 3 years, the sensitivity of an HbA1c level of at least 6.5% improved to 67%, whereas the specificity was still high at 97% (AUC, 0.936).

In NHANES III, findings were similar with use of fasting glucose measurements repeated 2 weeks apart. For groups based on age, body mass index, and race, HbA1c had consistent accuracy. The 10-year risk for diagnosed diabetes was 88% for persons with a fasting glucose level of at least 126 mg/dL and an HbA1c level of at least 6.5% at baseline vs 55% for those persons with a fasting glucose level of at least 126 mg/dL and an HbA1c level of 5.7% to less than 6.5%.

“HbA1c performs well as a diagnostic tool when diabetes definitions that most closely resemble those used in clinical practice are used as the gold standard,” the study authors write. “The high risk of diabetes among initially undiagnosed persons with both elevated fasting glucose and HbA1c suggests a dual role for fasting glucose and HbA1c for prediction of diabetes.”

Limitations of this study include lack of head-to-head comparison of the accuracy of glucose vs HbA1c; small number of cases of diabetes in the NHANES III subsample, resulting in imprecise estimates and preventing further subgroup analyses; and lack of 2-hour glucose data at the time of HbA1c measurement in the ARIC Study.

“In conclusion, we found HbA1c performs best when more stringent glucose criteria are used to define diabetes (i.e., fasting glucose ≥ 126 mg/dl on two separate occasions), similar to clinical practice,” the study authors conclude. “Our data support current recommendations for use of HbA1c in the diagnosis of diabetes and demonstrate that an HbA1c cut-off of 6.5% is highly

specific and may be reasonably sensitive in the context of evidence linking HbA1c to risk of long-term microvascular and macrovascular outcomes in nondiabetic adults. We also found that HbA1c and fasting glucose both strongly predict subsequent risk of diagnosed diabetes but the very high risk observed for persons with both elevated fasting glucose and HbA1c suggests a dual role for fasting glucose and HbA1c for prediction of diabetes.”

This research was supported by the National Institutes of Health/National Institute of Diabetes and Digestive and Kidney Diseases (NIH/NIDDK). The ARIC Study is carried out as a collaborative study supported by the National Heart, Lung, and Blood Institute. One of the study authors (Frederick L. Brancati, MD, MHS) was supported by NIH/NIDDK and by the Johns Hopkins Diabetes Research and Training Center.

Diabetes Care. Published online September 20, 2010. [Abstract](#)

Clinical Context

According to the July 2009 issue of *Diabetes Care*, HbA1c measurement is recommended to diagnose diabetes. However, the accuracy of HbA1c might depend on whether the comparison gold standard is a single fasting glucose measurement, a 2-hour glucose measurement, or repeated glucose measurements.

This population-based analysis uses data from the ARIC Study described by the ARIC investigators in the April 1989 issue of the *American Journal of Epidemiology* and NHANES III data files, documentation, and codebooks to evaluate the performance of HbA1c against single vs repeated glucose measurements to diagnose prevalent diabetes and predict incident diabetes.

Study Highlights

- ◆ The ARIC Study included 15,792 black or white adult subjects aged 45 to 64 years.
- ◆ Participants from ARIC had fasting glucose tests and clinical examinations every 3 years for 3 visits.
- ◆ ARIC exclusion criteria were self-reported physician diagnosis of diabetes, diabetes medication use, missing data, or nonfasting status.
- ◆ The NHANES III Second Exam, a substudy of the NHANES III, included 2596 subjects selected nonrandomly from the original NHANES III.
- ◆ Subjects from the NHANES III Second Exam underwent repeated plasma glucose and HbA1c testing 2 weeks (mean, 17 days) after the first examination.
- ◆ 317 subjects aged 40 to 74 years from NHANES III had valid data for oral glucose tolerance tests.
- ◆ Exclusion criteria for the NHANES III Second Exam were age younger than 18 years, fasting less than 8 hours, prior physician diagnosis of diabetes, and missing data on glucose or HbA1c.
- ◆ The current study included 12,485 subjects from the ARIC Study and 691 subjects in NHANES III.
- ◆ Prevalent diabetes was defined as a single fasting glucose level of at least 126 mg/dL at baseline or a fasting glucose level of at least 126 mg/dL at 2 separate examinations.
- ◆ HbA1c level was categorized as less than 6.5% or 6.5% or more.
- ◆ ARIC subgroup analysis was conducted for age (< 60 years vs ≥ 60 years), race or ethnicity (white or African American), and body mass index.
- ◆ Of subjects from the ARIC Study with a baseline fasting glucose level of at least 126 mg/dL, 60% had a fasting glucose level of at least 126 mg/dL at the 3-year follow-up.
- ◆ Of subjects from NHANES III with a baseline HbA1c level of at least 6.5%, 80% had an HbA1c level of at least 6.5% at the 17-day follow-up.
- ◆ Of subjects from NHANES III with a baseline fasting glucose level of at least 126 mg/dL, 70% had a fasting glucose level of at least 126 mg/dL at the 3-year follow-up.

- ◆ With a single fasting glucose level of 126 mg/dL or more, HbA1c had a sensitivity of 47% and a specificity of 98% for detection of prevalent diabetes (AUC, 0.892).
- ◆ With a repeated fasting glucose level of at least 126 mg/dL measured 3 years apart, HbA1c had a sensitivity of 67% and a specificity of 97% (AUC, 0.936).
- ◆ Use of a repeated fasting glucose level of at least 126 mg/dL measured 2 weeks apart and HbA1c had similar results.
- ◆ The results for HbA1c levels were similar for different age groups and ethnic groups.
- ◆ The highest AUC for HbA1c identification of diabetes was 0.936 if based on repeated glucose levels of at least 126 mg/dL 3 years apart.
- ◆ On the basis of a small sample size of 29 cases of diabetes, NHANES III analysis showed high AUCs for (1) baseline single fasting glucose levels, (2) baseline fasting glucose levels of at least 126 mg/dL plus 2-hour glucose levels of at least 200 mg/dL, and (3) fasting glucose levels of at least 126 mg/dL and 2-hour glucose levels of at least 200 mg/dL at baseline or 2-week follow-up.
- ◆ HbA1c accuracy was lower for normal-weight vs overweight and obese subjects if diabetes was defined by single instead of repeated measurement.
- ◆ For incident diabetes, the AUC was 0.827 for cases detected during visits up to 6 years of follow-up vs 0.733 for cases detected through visits or annual telephone interviews at up to 15 years of follow-up.
- ◆ The 10-year risk for diabetes in persons with a fasting glucose level of at least 126 mg/dL was higher if the HbA1c level was 6.5% or more vs 5.7% to less than 6.5% (88% vs 55%).
- ◆ Study limitations included lack of direct comparison between glucose and HbA1c and small number of diabetes cases in the NHANES III Second Exam sample.

Clinical Implications

- ◆ An HbA1c level of at least 6.5% has a sensitivity of 47% and a specificity of 98% for detection of prevalent diabetes with a single fasting glucose level of 126 mg/dL or more.
- ◆ An HbA1c level of at least 6.5% has a sensitivity of 67% and a specificity of 97% for detection of prevalent diabetes with repeated fasting glucose levels of 126 mg/dL or more.