Hemoglobin $A_1c$ As a Screen for Previously Undiagnosed Prediabetes and Diabetes in an Acute-Care Setting

**OBJECTIVE**—Hemoglobin $A_1c$ ($HbA_{1c}$) is recommended for identifying diabetes and prediabetes. Because $HbA_{1c}$ does not fluctuate with recent eating or acute illness, it can be measured in a variety of clinical settings. Although outpatient studies identified $HbA_{1c}$-screening cutoff values for diabetes and prediabetes, $HbA_{1c}$-screening thresholds have not been determined for acute-care settings. Using follow-up fasting blood glucose (FBG) and the 2-h oral glucose tolerance test (OGTT) as the criterion gold standard, we determined optimal $HbA_{1c}$-screening cutoffs for undiagnosed dysglycemia in the emergency-department setting.

**RESEARCH DESIGN AND METHODS**—This was a prospective observational study of adults aged $\geq 18$ years with no known history of hyperglycemia presenting to an emergency department with acute illness. Outpatient FBS and 2-h OGTT were performed after recovery from the acute illness, resulting in diagnostic categorizations of prediabetes, diabetes, and dysglycemia (prediabetes or diabetes). Optimal cutoffs were determined and performance data identified for cut points.

**RESULTS**—A total of 618 patients were included, with a mean age of 49.7 ($\pm$ 14.9) years and mean $HbA_{1c}$ of 5.68% ($\pm$ 0.86). On the basis of an OGTT, the prevalence of previously undiagnosed prediabetes and diabetes was 31.9 and 10.5%, respectively. The optimal $HbA_{1c}$-screening cutoff for prediabetes was 5.7% (area under the curve [AUC] = 0.659, sensitivity = 55%, and specificity = 71%), for diabetes $HbA_{1c}$ 5.8% (AUC = 0.717, sensitivity = 57%, and specificity = 79%), and for diabetes 6.0% (AUC = 0.868, sensitivity = 77%, and specificity = 87%).

**CONCLUSIONS**—We identified $HbA_{1c}$ cut points to screen for prediabetes and diabetes in an emergency-department adult population. The values coincide with published outpatient study findings and suggest that an emergency-department visit provides an opportunity for $HbA_{1c}$-based dysglycemia screening.

There are 26.8 million people with diabetes in the U.S., and by the year 2030, it is estimated to increase to 36 million people (1). Current estimates are that 25% of individuals with diabetes remain undiagnosed, and by the time of diagnosis, there often are microvascular and macrovascular abnormalities found (2–4). Early recognition is important because lifestyle modifications and medications can reduce the incidence of diabetes in people at high risk (5), and the treatment of diabetes can prevent or delay microvascular end–organ complications.

The use of hemoglobin $A_{1c}$ ($HbA_{1c}$) to diagnose prediabetes and diabetes recently was recommended by the American Diabetes Association (ADA) (6). $HbA_{1c}$ testing has an advantage over glucose-based testing because it does not require fasting, and the test can be performed at any time. Guidelines recommend an $HbA_{1c}$ $\geq 6.5$% to diagnose diabetes and $HbA_{1c}$ between 5.7 and 6.4% for identifying prediabetes. These cutoff values for $HbA_{1c}$ are derived in part from outpatient studies and are based on populations of those not acutely ill at the time of testing (7–9).

Less attention has been given to screening and diagnosing diabetes and prediabetes in acute-care settings such as the emergency department, where blood is routinely drawn to manage acute illness and clinicians are available to interpret the results. The $HbA_{1c}$ test can be quickly performed in many different clinical settings, including the hospital. However, it is not known whether $HbA_{1c}$ thresholds differ between the higher-risk acute-care and the general outpatient populations. The purpose of this study was to determine optimal $HbA_{1c}$-screening cutoff points for undiagnosed dysglycemia in the emergency-department setting using follow-up fasting blood glucose (FBG) and 2-h oral glucose tolerance tests (OGTTs) as the criterion gold standard.

From the 1Department of Emergency Medicine, Long Island Jewish Medical Center, North Shore–Long Island Jewish Healthcare System, Long Island, New York; and the 2Department of Environmental Medicine, New York University School of Medicine, New York, New York.

Corresponding author: Robert Silverman, rsilverm@lij.edu.

Received 24 May 2010 and accepted 13 June 2011.

DOI: 10.2337/dc11-0287

This article contains Supplementary Data online at http://care.diabetesjournals.org/lookup/suppl/doi:10.2337/dc10-0996/-/DC1.

© 2011 by the American Diabetes Association. Readers may use this article as long as the work is properly cited, the work is educational and not for profit, and the work is not altered. See http://creativecommons.org/licenses/by-nc-nd/3.0/ for details.
HbA1c and undiagnosed diabetes in acute care

with the assay), those who underwent chemotherapy in the past 6 months, those who used systemic steroids in the past 4 weeks, and those who received intravenous glucose or sympathomimetics before emergency-department blood was drawn. The study was approved by the North Shore–Long Island Jewish Institutional Review Board.

After written informed consent was obtained in the emergency department, a detailed medical history was obtained from the patient. HbA1c was measured using the Tosoh G7 (Tosoh Bioscience) high–performance liquid chromatography analyzer. The instrument is certified by the National Glycohemoglobin Standardization Program and International Federation of Clinical Chemistry, and the interassay and intra-assay coefficient of variation was <3% for HbA1c (http://www.diagnostics.eu.tosohbioscience.com/solutions/hplc-solutions/G7+analyser/).

The assay was performed in a National Glycohemoglobin Standardization Program level 1–certified laboratory, which also participates in CAP proficiency–testing surveys, including linearity studies. Quality-control testing was performed at the start and end of each batch or shift. Patients were scheduled to undergo follow-up at the general clinical research center after recovering from their acute illness for an FBS and a 2-h OGTT. Study subjects were instructed to fast overnight for at least 8 h before their testing day and increase carbohydrate intake the day before testing. Diagnostic categories of normal, prediabetes (impaired fasting glucose and impaired glucose tolerance), and diabetes were determined from the results of the FBS and 2-h OGTT using the ADA criteria (10).

Receiver-operating characteristic curves were developed, and the area under the curve (AUC) with 95% CIs were determined. Data analyses were conducted for three clinical entities, including individuals with OGTT-diagnosed diabetes compared with those without OGTT-diagnosed diabetes, those with OGTT-diagnosed dysglycemia (either diabetes or prediabetes) compared with those with a normal OGTT, and those with OGTT-diagnosed prediabetes compared with those with a normal OGTT. Optimal HbA1c cutoffs were determined by taking the greatest sum of the sensitivity and specificity for measured HbA1c values among each of the three newly diagnosed groups (diabetes, dysglycemia, and prediabetes). The positive predictive value and negative predictive value were reported for the optimal cutoff values. Additional analyses included in the online Supplementary Data are test-performance data for all HbA1c values for which there was sufficient data. This included positive- and negative-likelihood ratios and true- and false-positive and true- and false-negative values. SPSS version 16 and XLSTAT software were used to analyze the data.

RESULTS—A total of 2,082 patients consented to participate in the emergency department, and 618 of these patients returned to the general clinical research center, met all inclusion criteria, had full laboratory data for analysis, and were included in the study. The mean age was 49.7 years (±14.9), 343 (55.5%) were male, 275 (44.5%) were female, and the mean overall HbA1c was 5.68% (±0.86). Other clinical history is noted in Table 1. The prevalence of diabetes and prediabetes on the basis of emergency-department HbA1c testing was 33.0 and 10.2%, respectively, and the prevalence of diabetes and prediabetes on the basis of follow-up glucose-based testing was 31.9 and 10.5%, respectively (Table 2).

The AUC for the group with diabetes was 0.868 (95% CI 0.814–0.922), for the group with prediabetes was 0.659 (0.638–0.679), and for those with dysglycemia was 0.717 (0.704–0.731). Performance criteria, including sensitivity, specificity, and predictive values, also are shown in Table 3. We found the optimal HbA1c-cutoff value for diabetes to be 6.0% and that for prediabetes to be 5.7%, and an HbA1c of 5.8% was found to optimally identify individuals with dysglycemia (Table 3). As noted, 42% of patients with an HbA1c of ≥6.0% will have diabetes on the basis of the follow-up OGTT (the positive predictive value), and 97% of patients with an HbA1c <6.0% will not have diabetes (the negative predictive value). In screening for prediabetes, 51.4% of patients with an HbA1c of ≥5.7% will have the disorder on the basis of the follow-up OGTT, and 74.1% of patients with an HbA1c ≤5.7% will not have prediabetes.

In screening for dysglycemia, among those with an HbA1c of ≥5.8%, 66.5% of patients will have the disorder on the basis of the OGTT, whereas 71.3% of individuals with HbA1c values <5.8% will not have dysglycemia.

We also evaluated the performance of an emergency-department HbA1c cutoff of 6.5% for identifying individuals with diabetes and found a sensitivity of 54%, a specificity of 96%, and a positive predictive value and negative predictive value of 64 and 95%, respectively. It is not a surprise that the higher cutoff HbA1c of 6.5% led to fewer false-positives than the HbA1c cutoff of 6.0% (20 vs. 70, respectively) but more false negatives.

Table 1—Patient characteristics

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Yes</th>
<th>No</th>
<th>Unknown</th>
<th>Yes</th>
<th>No</th>
<th>Unknown</th>
<th>Yes</th>
<th>No</th>
<th>Unknown</th>
<th>Yes</th>
<th>No</th>
<th>Unknown</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>49.7 ± 14.9</td>
<td>29.2 ± 6.83</td>
<td></td>
<td>310 (50.2)</td>
<td>308 (49.8)</td>
<td></td>
<td>109 (17.6)</td>
<td>509 (82.4)</td>
<td></td>
<td>22 (3.6)</td>
<td>596 (96.4)</td>
<td></td>
</tr>
<tr>
<td>Sex</td>
<td>Male</td>
<td>343 (55.5)</td>
<td>Female</td>
<td>275 (44.5)</td>
<td></td>
<td></td>
<td>81 (13.1)</td>
<td>376 (60.8)</td>
<td></td>
<td>4 (0.6)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ethnicity</td>
<td>African American</td>
<td>154 (24.9)</td>
<td>White</td>
<td>295 (47.7)</td>
<td></td>
<td></td>
<td>57 (9.2)</td>
<td>57 (9.2)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hospitalized</td>
<td>Yes</td>
<td>310 (50.2)</td>
<td>No</td>
<td>308 (49.8)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Time to follow-up (days)</td>
<td>55 ± 56.2</td>
<td></td>
<td></td>
<td>38 (6.3)</td>
<td></td>
<td></td>
<td>106 (17.6)</td>
<td>509 (82.4)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Relative with diabetes</td>
<td>Yes</td>
<td>109 (17.6)</td>
<td>No</td>
<td>509 (82.4)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Past medical history</td>
<td>High cholesterol</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Coronary artery disease</td>
<td>Yes</td>
<td>109 (17.6)</td>
<td>No</td>
<td>509 (82.4)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Other cardiac§</td>
<td>Yes</td>
<td>55 (8.9)</td>
<td>No</td>
<td>563 (91.1)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stroke/transient ischemic attack</td>
<td>Yes</td>
<td>22 (3.6)</td>
<td>No</td>
<td>596 (96.4)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Data are means ± SD or n (%). n = 618. *Other = Caribbean, Guinean, other South American; †Yes = parents or siblings; ‡History of coronary artery disease; §Other cardiac = congestive heart failure, dysrhythmia, cardiomyopathy, pacemaker, AICD.
large pool of all types of individuals who can potentially be screened. Our study concluded that HbA1c cutoffs were similar to patients screened in outpatient settings and suggest that the HbA1c results can be used in a range of clinical settings and that illness acuity also should not preclude screening for dysglycemia. Regarding the prevalence of undiagnosed disease, our study differs from most other studies in that it took place in an acute-care setting and that there was a relatively high frequency of undiagnosed prediabetes and diabetes. In a recent report of the National Health and Nutrition Examination Survey data, the frequency of undiagnosed diabetes using HbA1c was 1.8%, which is lower than in our findings (22). This also differs from data obtained on the inpatient service of an inner-city hospital, where 24% of adults without known diabetes had an HbA1c of ≥6.5% (23). It is possible that the inclusion of patients with a baseline higher diabetes risk profile, as well as acute medical illness, which may be associated with underlying dysglycemia (such as cardiovascular disease), led to a higher frequency of diabetes in the acute-care studies. It also may reflect patients who do not obtain routine outpatient care and, therefore, remain undiagnosed, although in our study, most patients did have some type of medical insurance, suggesting that access to care was less of an issue.

The goal of screening for dysglycemia in the acute-care setting should be earlier diagnosis leading to timely outpatient follow-up with a provider. Although counseling for management of chronic disease may be challenging in acute-care settings, individuals will sometimes show greater interest in their health during times of illness, and opportunities for early diagnosis should not be lost. During a brief discussion, patients with elevated HbA1c could be encouraged to partner with a provider and maintain long-term care as well as attempt lifestyle modifications. The concept of the “teachable moment” has been demonstrated in the case of smoking

Table 3—Optimal HbA1c screening cutoffs for determination of dysglycemia

<table>
<thead>
<tr>
<th>Receiver-operating characteristic curve cutoff value (HbA1c) (%)</th>
<th>AUC (95% CI)</th>
<th>Sensitivity (%)</th>
<th>Specificity (%)</th>
<th>Positive predictive value (%)</th>
<th>Negative predictive value (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prediabetes</td>
<td>5.7</td>
<td>0.659 (0.638–0.679)</td>
<td>54.8</td>
<td>71.3</td>
<td>51.4</td>
</tr>
<tr>
<td>Diabetes</td>
<td>6.0</td>
<td>0.868 (0.814–0.922)</td>
<td>76.9</td>
<td>87.3</td>
<td>41.7</td>
</tr>
<tr>
<td>Prediabetes/diabetes</td>
<td>5.8</td>
<td>0.717 (0.704–0.731)</td>
<td>56.9</td>
<td>78.9</td>
<td>66.5</td>
</tr>
</tbody>
</table>

Prediabetes/diabetes = combination of either prediabetes or diabetes.

CONCLUSIONS—In an acute-care setting, we found that an HbA1c of 5.7% is the optimal screening cutoff for prediabetes, and 6.0% is the optimal screening cutoff for diabetes. These findings are very similar to a number of previous studies in which individuals from different ethnic and racial groups and geographic regions were tested in outpatient settings. This includes HbA1c cutoffs for prediabetes that have been identified, respectively, from Asian Indian, Chinese, and British populations (11–13). In addition, our findings are consistent with reports from more recent studies that use retinopathy as the criterion for identifying glycemic-related vascular disease (14,15). It is important to note that our HbA1c findings of 5.7% as a screen for prediabetes coincide with recent ADA recommendations for identifying individuals at risk for incident diabetes (6).

Our findings indicating an HbA1c of 6.0% as the optimal diabetes-screening cutoff are consistent with data from other studies that use the FBS or 2-h OGTT to define diabetes (11,12,16–19). The diabetes-screening cutoff that we and others have identified is lower than the diagnostic mark of 6.5% that the ADA guidelines now recommend. The difference in cutoffs can be explained in part by the desired outcome of a screening test to miss a few people with the target disease, and, therefore, screening cutoffs typically are lower than diagnostic cutoffs. Differences also may occur because of known inconsistencies between the use of glucose and HbA1c-based testing to diagnose diabetes because there will be patients with HbA1c values <6.5% who have an FBS >126 mg/dL or a 2-h OGTT >200 mg/dL (20). Regardless, a diabetes-screening cutoff of 6.0% effectively identifies higher-risk individuals who require referral for additional evaluation and management.

With nearly 120 million emergency-department visits annually in the U.S. (21), the emergency department provides a very

Table 2—Determinations on the basis of emergency-department HbA1c and follow-up OGTT

<table>
<thead>
<tr>
<th>HbA1c-based emergency-department diagnosis*</th>
<th>n (%)</th>
<th>HbA1c-based emergency-department diagnosis using higher-risk cutoffs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal (HbA1c &lt;5.7%)</td>
<td>351 (56.8)</td>
<td>Normal/lower risk (HbA1c &lt;6.0%)</td>
</tr>
<tr>
<td>Prediabetes (HbA1c 5.7–6.4%)</td>
<td>204 (33.0)</td>
<td>High risk for diabetes (HbA1c 6.0–6.4%)</td>
</tr>
<tr>
<td>Diabetes (HbA1c ≥6.5%)</td>
<td>63 (10.2)</td>
<td>Diabetes (HbA1c ≥6.5%)</td>
</tr>
<tr>
<td>Glucose-based follow-up diagnosis†</td>
<td>356 (57.6)</td>
<td>Glucose-based follow-up diagnosis†</td>
</tr>
<tr>
<td>Normal</td>
<td>197 (31.9)</td>
<td></td>
</tr>
<tr>
<td>Prediabetes</td>
<td>65 (10.5)</td>
<td></td>
</tr>
</tbody>
</table>

*Based on the 2010 ADA guidelines: HbA1c 5.7–6.4% = prediabetes, HbA1c ≥6.5% = diabetes. †Based on FBS and/or 2-h OGTT findings from the general clinical research center follow-up visit.
cessation in which patients are more likely to quit smoking after health events, such as pregnancy, hospitalizations, or a diagnosis of cancer (24). Such health events represent opportunities for health care providers to educate patients and encourage behavior modifications. Medical triggers are associated with better short- and long-term weight loss, which could be one component of a diabetes intervention (25).

Among limitations for the study, patients were not consecutively screened through the emergency department, and enrollment depended upon the availability of dedicated research associates who generally worked 8-h shifts. Attempts were made to have the investigators rotate through the emergency department during the day, evening, and weekend hours, but there was no overnight coverage. In addition, patients had to sign consent at the time of the emergency-department visit to participate and follow-up at the general clinical research center for additional testing. Patients with a previous history of hyperglycemia were excluded from this study; however, some patients may not correctly recall this information, leading to potential misclassification errors. We also did not collect information on the last time patients had outpatient glucose testing before their emergency-department visit, and, therefore, we were unable to determine whether there were other recent missed opportunities for diagnosis. As with most laboratory tests, unless the diagnosis is obvious on the basis of clinical presentation, abnormal test findings need to be repeated at a later time to confirm a diagnosis of prediabetes or diabetes (6).

In summary, optimal HbA1c cutoff values for screening for prediabetes and diabetes in an acute-care setting are similar to cutoffs from populations tested in outpatient settings. There is potential to identify large numbers of emergency-department patients with dysglycemia using HbA1c, and an elevated HbA1c should prompt referral for long-term management.

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

R.A.S. designed the protocol, supervised the data collection and the data analysis, wrote the final draft of the manuscript, had full access to all of the data in the study, and takes responsibility for the integrity of the data and the accuracy of the data analysis. U.T. and T.E. assisted with data analysis and drafting the manuscript. I.W., K.S., and K.G. obtained study specimens and related clinical data from the patient population. K.I. analyzed the study data.

Parts of this article were presented in abstract form at the Society of Academic Emergency Medicine Annual Meeting, Phoenix, AZ, 5 June 2010.

The authors also acknowledge the following additional investigators for their study contributions and help with data collection: Christine Demers, RN; Randi Clarke, RN; Julie Martucciolo, RN; Christine Dolinski, RN, and Melanie Marcano, RN, of the Feinstein Institute for Medical Research, NS–LIJ Health System; James Kelson, PhD, of the NS–LIJ Core Laboratory; and Benjamin Bernstein, MD, Finbar Foley, Nathan Sandalow, Josh Schechter, Jennifer Vreeland, Emily Berkman, and Tara Wedin of the Department of Emergency Medicine, NS–LIJ Health System.

References
19. Perry RC, Shankar RR, Fineberg N, McGill J, Baron AD. Early Diabetes Intervention Program (EDIP). HbA1c measurement improves the detection of type 2 diabetes in high-risk individuals with nondiagnostic levels of fasting plasma glucose: the Early

Acknowledgments—This work was supported in part by the Feinstein Institute for Medical Research, North Shore–Long Island Jewish (NS–LIJ) General Clinical Research Center (National Institutes of Health grant M01-RR018535). U.T. and T.E. are supported by a New York State Department of Health, Empire Clinical Research Investigator Program fellowship.
Diabetes Intervention Program (EDIP). Diabetes Care 2001;24:465–471