Etiology of Hyperglycemia in Hospitalized Patients Using the A1C Test

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Diabetes is a condition associated with high morbidity, elevated mortality, and a decreased quality of life. In the United States, diabetes affects 25.8 million people and is estimated to exceed $174 billion annually in costs. Diabetes may be present for > 7 years before it is diagnosed, and delays in diagnosis can lead to higher glucose levels at the time of diagnosis.4,5 There are various challenges when screening for diabetes in outpatient settings. Therefore, the hospital setting may be a more optimal venue. It is a controlled environment, and test results can be obtained quickly. Moreover, there is an opportunity to diagnose patients who otherwise may not have access to the health care system.

In hospitalized patients, hyperglycemia is a common but abnormal response to a disease state, surgery, or glucocorticoids. It is associated with the development of diabetes and provides an opportunity to identify individuals with undiagnosed diabetes. Although studies have attempted to use blood glucose values to identify undiagnosed diabetes in hospitalized patients, these values are affected by a number of factors, including stress, medications, and diet. Recently, the A1C test has become accepted as a tool to diagnose diabetes. Moreover, the American Diabetes Association (ADA) recently updated its screening diagnostic criteria for prediabetes to include A1C within a range of 5.7–6.4%. Individuals with an A1C in this range are at high risk for developing overt diabetes. To that end, this study evaluated patients with hyperglycemia in a hospital setting, using A1C levels to analyze the prevalence of undiagnosed diabetes and prediabetes.

Study Methods

Design, setting, and participants
We performed a cohort study of patients randomly admitted to the medical wards of Stony Brook University Medical Center, a 500-bed tertiary care center in Suffolk County, Long Island, New York. A total of 611 patients were included in the study. The patients were treated in the general medicine wards or the cardiac and medical intensive care units and their respective step-down units; patients on surgical, obstetrics and gynecology, and pediatric units were excluded, as were patients receiving a dextrose infusion.

Patients were categorized as having “known diabetes” if any of the following criteria were met: 1) mention of diabetes in the admission note or discharge note, 2) listing of diabetes in the problem list, or 3) evidence in the information system of prior use of outpatient medication to treat diabetes. The study was approved by our institutional review board.

Diagnosis of diabetes and hyperglycemia
Of the total number of patients randomly selected, those who had a random glucose level of ≥ 200 mg/dl during their hospital stay (n = 145) were considered to have hyperglycemia. Those with a known diagnosis of diabetes (n = 106) were then excluded. An A1C was obtained on the remaining patients (n = 39) during their stay using a high-performance liquid chromatography method, which is the primary method for the National Glycohemoglobin Standardization Program.

A diagnosis of possible undiagnosed diabetes was made if the A1C was ≥ 6.5% and there was no history of diabetes. Patients with an A1C in the range of 5.7–6.4% were identified as possibly having prediabetes. Stress hyperglycemia was defined as a random glucose level ≥ 200 mg/dl with an A1C < 5.7%. Steroid-induced hyperglycemia was defined as a random glucose level ≥ 200 mg/dl in patients who received at least one dose of systemic glucocorticoids intravenously or orally during their hospitalization. All patients who received glucocorticoids during their hospital stay and who had hyper-
glycemia were also examined in a separate analysis according to A1C.

Demographic characteristics and clinical variables
Demographic information, including age, sex, race, length of stay, and admission unit, were obtained from the hospital electronic medical record, along with patients’ BMI, A1C, and blood glucose values. Demographics in patients with or without hyperglycemia were analyzed using the Fisher two-tailed test (Table 1). A physician reviewed all available records of these patients.

Study Results
As shown in Figure 1, of the 611 patients randomly selected during the 5-month study period, 145/611 (23.7%) had elevated random blood glucose levels ≥ 200 mg/dl. A further analysis and chart review identified 106 of those subjects as having known diabetes. The remaining 39 patients with hyperglycemia and no known diagnosis of diabetes were further evaluated by A1C measurement. The clinical characteristics of the patients with known diabetes and those with hyperglycemia without a prior diagnosis of diabetes are shown in Table 1.

Of the 39 hyperglycemic patients having no known diagnosis of diabetes, 18 (46.2%) were found to have an A1C ≥ 6.5% and were classified as possibly having diabetes, whereas 13 (33.3%) were found to have an A1C of 5.7–6.4% and were classified as having possible prediabetes. Given that there was no outpatient A1C repeated on the patients, it was inappropriate to classify these patients as unequivocally having diabetes or prediabetes without a subsequent repeat measurement. Four patients (10.3%) were categorized as having stress hyperglycemia because they were hyperglycemic with an A1C < 5.7%, and four patients (10.3%) treated with glucocorticoids were hyperglycemic with an A1C < 5.7%.

As shown in Figure 2, 18 (46.2%) of the 39 hyperglycemic patients without a history of diabetes were treated with glucocorticoids during their hospitalization. These patients were subdivided further according to their A1C. Half (9/18) had an A1C ≥ 6.5%, whereas 27.8% (5/18) had an

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Table 1. Patient Demographics and Baseline Characteristics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Group 1: Known Diabetes (n = 106)</th>
<th>Group 2: Unrecognized Probable Diabetes (n = 39)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)*</td>
<td>65 ± 17</td>
<td>63 ± 17</td>
<td>0.608</td>
</tr>
<tr>
<td>Female sex (%)</td>
<td>31</td>
<td>36</td>
<td>0.690</td>
</tr>
<tr>
<td>White race (%)</td>
<td>29</td>
<td>67</td>
<td>0.0001</td>
</tr>
<tr>
<td>A1C (%)*</td>
<td>7.88 ± 2.14</td>
<td>6.91 ± 2.13</td>
<td>0.017</td>
</tr>
<tr>
<td>Length of stay (days)*</td>
<td>23.1 ± 41.3</td>
<td>17.2 ± 22.2</td>
<td>0.402</td>
</tr>
<tr>
<td>BMI (kg/m²)*</td>
<td>29.5 ± 7.0</td>
<td>30.7 ± 7.8</td>
<td>0.402</td>
</tr>
<tr>
<td>Average random glucose (mg/dl)*</td>
<td>334 ± 143</td>
<td>331 ± 131</td>
<td>0.888</td>
</tr>
</tbody>
</table>

*Data are presented as means ± SD.
A1C of 5.7–6.4%. Only 22.2% (4/18) had a normal A1C of < 5.7%.

Discussion
Hyperglycemia is extremely common in the inpatient setting. This study found that patients with hyperglycemia with no known diagnosis of diabetes can be stratified using the A1C test. About 50% of hyperglycemic patients without a known diagnosis of diabetes were found to have possible diabetes, and 33.3% were found to possibly have prediabetes. Furthermore, patients on glucocorticoids with hyperglycemia were subdivided into groups based on their A1C. Of those patients, 50% were found to have an A1C ≥ 6.5, which signified that these patients also had possible diabetes. In addition, about 30% of the patients on glucocorticoids were discovered to be in the prediabetic range, with an A1C of 5.7–6.4%.

Our results show that a significant number of patients with hyperglycemia in the inpatient setting potentially have undiagnosed prediabetes and diabetes. These results correlate with previous studies that uncovered a substantial number of patients with hyperglycemia who were found to be without a diagnosis of diabetes at the time of admission.

In contrast to our study, other studies have mainly used fasting glucose levels and the glucose tolerance test to diagnose diabetes. Although measurement of fasting glucose levels is a convenient method of diagnosing diabetes, it is not as sensitive as other methods, such as postprandial glucose levels. We used A1C as a diagnostic marker for diabetes because it is now included as a diagnostic criterion under the ADA guidelines. A1C may be more optimal because it is less cumbersome than the glucose tolerance test or measurement of postprandial glucose levels. Other advantages of using the A1C include the fact that it does not require patients to be fasting, reflects more long-term glycemia than plasma glucose levels, and is a standardized and reliable laboratory test. It should be noted, however, that various confounders such as hemoglobinopathies and red blood cell turnover may affect the validity of A1C testing. Furthermore, certain medications (high-dose salicylates) and vitamins (C and E) have also been found to interfere with A1C measurement. Finally, A1C may be transiently elevated by acute or sub-acute illness, which can affect its accuracy.

Other groups included in our study were patients with stress-induced hyperglycemia and those with steroid-induced hyperglycemia. Stress hyperglycemia is a transient increase in blood glucose concentration during an acute illness but is not a normal response. It resolves after the stress is removed and usually recurs with similar stress. In our study, a relatively small percentage of those with hyperglycemia were identified as having stress hyperglycemia.

Corticosteroid-induced hyperglycemia occurs with the use of high-dose glucocorticoids. Donihi et al. found > 50% of patients without known diabetes to experience hyperglycemia when receiving high-dose glucocorticoids. In our study, 78% of the hyperglycemic patients in the corticosteroid group were found to possibly have prediabetes or diabetes. It has been found that glucocorticoids induce a “diabetic-like state,” and patients receiving glucocorticoids have an increased risk for developing overt diabetes. Although our findings in the steroid group will need to be validated in a larger sample, these results may signify the need for screening patients receiving glucocorticoids.

There are several limitations to our study, including those resulting from the course of routine care. For example, the random glucose levels may have included values that were drawn before breakfast or have been from patients who were on NPO status for tests and procedures, which may have underestimated the number of patients with hyperglycemia. At the same time, the prevalence of possible diabetes in our study may have been overestimated in patients...
who had a prolonged stressful illness or were on chronic glucocorticoid therapy. The patients in our study were hospitalized for an average of 17–23 days, but factors such as receiving glucocorticoids may have affected AIC results, which are a weighted average of blood glucose levels. Any significant fluctuations in mean blood glucose could potentially affect AIC within a 1- to 2-week period.23 Furthermore, AIC was checked only during hospitalization and not repeated. Although to our knowledge there are no data examining the equivalence of inpatient and outpatient AIC results, according to ADA guidelines, AIC should be repeated at a later date before a definitive diagnosis is made.24

This study brings attention to patients with hyperglycemia in the hospital setting and shows that there may be an important role for AIC in screening these patients for prediabetes and diabetes. Early intervention in these previously undiagnosed patients may reduce long-term complications of diabetes and improve health care outcomes.

REFERENCES


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