Many patients who receive care in the hospital have hyperglycemia.\textsuperscript{1,2} Elevated blood glucose levels may be related to existing diabetes mellitus, new-onset diabetes mellitus, physiologic stress, or administered medications.\textsuperscript{1,3} For example, up to 50\% of patients receiving steroid therapy have hyperglycemia without a previously established diabetes diagnosis.\textsuperscript{2} In addition, blood glucose levels can be elevated during critical illnesses such as sepsis\textsuperscript{4} or resulting from treatments such as total parenteral nutrition.\textsuperscript{5} Furthermore, use of vasopressors can
cause wide swings in blood glucose and thus affect the accuracy of glucose testing in critically ill patients. 

Hyperglycemia is often identified at the time of hospital admission as a result of an ostensibly unrelated illness. It is often unclear which patients with hyperglycemia have occult diabetes. Kosiborod et al reported that a quarter of patients with no known history of diabetes (NKHD) who present with an acute myocardial infarction are hyperglycemic at the time of admission. When a patient is admitted for a separate and potentially emergent condition, dysglycemia may not be addressed or managed if proper evaluation of the duration of this problem is not provided.

Inpatient hyperglycemia is an independent predictor of increased morbidity and mortality. Hyperglycemia in diabetes has been shown to predict poor outcomes for hospital admissions. In the absence of a diabetes diagnosis, hyperglycemia has been associated with still poorer outcomes. Patients with hyperglycemia who are admitted to the hospital with NKHD have an 18-fold higher hospital mortality. In addition, such patients have a length of stay that is twice that of those who have hyperglycemia and a prior diagnosis of diabetes. Clinicians may fail to determine whether hyperglycemia is related to or constitutes a presenting sign of diabetes.

Glycated hemoglobin (HbA1c) levels have been demonstrated to be an effective means of distinguishing between hyperglycemia as an isolated event and an unrecognized sign of diabetes. Umpierrez et al estimated that 1 in 5 adults admitted to a large hospital with NKHD have an elevated HbA1c level. The HbA1c test measures the amount of hemoglobin that has been bound to glucose in an irreversible, nonenzymatic reaction. The amount of this glycohemoglobin molecule correlates with the average blood glucose level over the previous 8 to 12 weeks, reflecting the lifespan of red blood cells. The test does not require any preparation by the patient and can be performed in concert with other routine blood chemistry analyses.

According to 2015 American Diabetes Association guidelines, the difficulty distinguishing between [previously undiagnosed diabetes and hospital-related hyperglycemia] may be overcome by measuring [HbA1c], as long as conditions interfering with [HbA1c] equilibrium (such as hemolysis, blood transfusion, blood loss, or erythropoietin therapy) have not occurred.

A diagnosis of prediabetes can be made if the HbA1c value is 5.7% to 6.4% and diabetes if the HbA1c value is 6.5% or higher. When the HbA1c test is used for screening, previously undiagnosed diabetes can be recognized and management initiated. Estimates suggest that patients with NKHD constitute about one-third of patients who have hyperglycemia in the hospital. The use of HbA1c testing therefore provides a mechanism to ensure that a diagnosis is made when appropriate and that intervention begins as soon as possible.

In 2011, the United States spent an estimated $2.9 trillion on health care. One in 5 health care dollars is spent on diabetes care. The American Diabetes Association estimated that the cost associated with type 1 and type 2 diabetes mellitus increased 29.0% from $174 billion in 2007 to $245 billion in 2012. The largest percentage (43%) of this cost is related to inpatient hospital care. Patients with diabetes incur 26% of all hospital costs and 12% of all emergency department costs, and these percentages steadily increase with age. Clinicians may fail to determine whether hyperglycemia is related to or constitutes a presenting sign of diabetes. Glycated hemoglobin (HbA1c) levels have been demonstrated to be an effective means of distinguishing between hyperglycemia as an isolated event and an unrecognized sign of diabetes. Umpierrez et al estimated that 1 in 5 adults admitted to a large hospital with NKHD have an elevated HbA1c level. The HbA1c test measures the amount of hemoglobin that has been bound to glucose in an irreversible, nonenzymatic reaction. The amount of this glycohemoglobin molecule correlates with the average blood glucose level over the previous 8 to 12 weeks, reflecting the lifespan of red blood cells. The test does not require any preparation by the patient and can be performed in concert with other routine blood chemistry analyses.

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Disregard for inpatient hyperglycemia may be a form of clinical inertia in diabetes care. This inertia can come from delays in therapy intensification, pa-
patient nonadherence to a treatment regimen, or failure to identify or respond to an abnormal finding. The resulting persistence of dysglycemia increases the likelihood of complications and readmission. Although standards for outpatient diabetes screening exist, the use of the HbA$_1c$ test in the inpatient setting as a diagnostic tool for diabetes has not been consistent. The low cost and convenience of this test suggest that its use in inpatient hyperglycemia may be a good practice.

In the present study, we explored the use of HbA$_1c$ testing in patients who were treated for hyperglycemia in a rural community hospital inpatient setting. The study specifically examined the use of HbA$_1c$ tests for patients with hyperglycemia and NKHD and whether these patients were more likely than those who did not get the HbA$_1c$ test to receive a diagnosis of diabetes on discharge.

Methods
Design
This retrospective study involved the review and analysis of medical records at a 70-bed rural community teaching hospital in the Midwest. This protocol was approved by Ohio University Institutional Review Board and the hospital executive committee.

Population and Sample Selection
The review included medical records of all patients with hyperglycemia at hospital admission from June 31, 2012, to July 1, 2014. Patients were identified from 2 sources: (1) through the hospital pharmacy, where medical records of patients who received any type of insulin, pioglitazone, glyburide, glipizide, glimepiride, or metformin were pulled, and (2) through hospital medical records, in which records of any patient who had received the diagnosis of diabetes at discharge (either established or new-onset diabetes mellitus) were drawn.

Medical records were excluded for the following reasons: pregnancy, same-day surgical procedures, transfer before treatment, refusal of treatment, admission not in the study timeline, and age younger than 18 years. Patients with glucose levels below 150 mg/dL who did not require any hospital treatment were also excluded from the study. Multiple admissions for a single patient within the study timeline were not excluded, but unique patients were identified (Figure).

Study Variables
Admission, fasting, and random blood glucose readings were collected. Fasting blood glucose readings, for the purpose of this study, were those taken as the first reading of the day before 8 AM. This timing matched the delivery of breakfast trays at 8 AM. Random blood glucose was any blood glucose reading after 8 AM. Patient demographic information included race and admission unit (intensive care unit or medical-surgical floor). Other variables included previous diagnosis of diabetes, total number of at-home medications, total number of diabetes medications, HbA$_1c$ testing, blood glucose readings, length of stay, and discharge diagnosis.

Data Analysis
Final data were organized by patient level rather than admission. For patients who had multiple admissions, a mean value was computed across admissions for appropriate outcome measures. Frequencies were generated for categorical variables, and summary statistics, means, SDs, and ranges were computed for continuous variables. For statistical inference regarding 2 group differences of continuous variables, the independent sample t tests were used. Analysis of variance was used to gauge the statistical significance of multiple group differences with respect to continuous outcome variables. $\chi^2$ tests were used to determine association between categorical variables. No adjustments were made to the level of significance, as this retrospective study was exploratory, not experimental. Hence, statistical significance was set at $P \leq .05$. 

21,22 Although standards for outpatient diabetes screening exist, the use of the HbA$_1c$ test in the inpatient setting as a diagnostic tool for diabetes has not been consistent. The low cost and convenience of this test suggest that its use in inpatient hyperglycemia may be a good practice.
Results
The medical record selection process yielded 630 admission records. The excluded records totaled 148, leaving 482 unique hospital admissions in the study. The 482 hospital admissions included in the study corresponded with 348 unique patients.

Of the 348 patients, 298 patients (85%) had a previous diagnosis of diabetes and 50 (15%) had NKHD. Patients with and without a history of diabetes were similarly aged (mean [SD], 60.2 [17.6] years vs 59.2 [15.5] years). In the group of patients with a history of diabetes, 143 (41.1%) were men, compared with 26 (52%) in the group with NKHD. No statistically significant differences existed between the groups for blood glucose measures. However, differences between the patients with known diabetes and the patients with NKHD were significant in the mean (SD) number of total medications (11.4 [6.1] vs 8.8 [5.8], respectively).
Discussion

The present study provides evidence that the HbA<sub>1c</sub> test can be an effective means of identifying patients with NKHD who have hyperglycemia and occult chronic disease. This study showed that more than three-fourths of patients with NKHD had chronic dysglycemia (as determined by HbA<sub>1c</sub> values), with almost 60% meeting criteria for the diagnosis of diabetes. Study patients with NKHD were 5 times more likely to leave the hospital with a diabetes diagnosis when HbA<sub>1c</sub> levels were measured than when they were not measured.

The 50 patients with NKHD had a 50% longer mean (SD) hospital stay compared with the 298 patients with known diabetes (4.2 [3.1] vs 2.6 [1.8] days). This finding is consistent with that of Umpierrez et al<sup>2</sup> and other studies<sup>3,16,23</sup> that reported increased hospital stays (9.0 vs 5.5 days) in patients with newly recognized hyperglycemia vs patients with known diabetes. In a study by Sleiman et al<sup>24</sup> for every 1% increase in HbA<sub>1c</sub>, patient readmission rates nearly doubled.

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**Table.**
Comparison of Patients With and Without a History of Diabetes (N=348)*

<table>
<thead>
<tr>
<th>Characteristic or Outcome Measure</th>
<th>History of Diabetes</th>
<th>Total Sample</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Yes (n=298)</td>
<td>No (n=50)</td>
<td></td>
</tr>
<tr>
<td>Age, y</td>
<td>60.2 (17.8)</td>
<td>59.2 (15.5)</td>
<td>.725</td>
</tr>
<tr>
<td>Sex, male, No. (%)</td>
<td>143 (48.0)</td>
<td>26 (52.0)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>HbA&lt;sub&gt;1c&lt;/sub&gt;, measured, No. (%)</td>
<td>216 (72.5)</td>
<td>31 (62.0)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>HbA&lt;sub&gt;1c&lt;/sub&gt;, %</td>
<td>8.0 (3.1)</td>
<td>8.4 (3.2)</td>
<td>.508</td>
</tr>
<tr>
<td>No. of total home medications</td>
<td>11.4 (6.1)</td>
<td>8.8 (5.8)</td>
<td>.006</td>
</tr>
<tr>
<td>No. of diabetes medications</td>
<td>1.7 (0.9)</td>
<td>0.1 (0.3)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Blood glucose on admission</td>
<td>275.7 (182.3)</td>
<td>245.2 (212.7)</td>
<td>.287</td>
</tr>
<tr>
<td>Fasting blood glucose</td>
<td>177.5 (62.7)</td>
<td>185.3 (66.5)</td>
<td>.420</td>
</tr>
<tr>
<td>Random blood glucose</td>
<td>217.1 (67.3)</td>
<td>207.8 (74.0)</td>
<td>.375</td>
</tr>
<tr>
<td>Length of stay</td>
<td>2.6 (1.8)</td>
<td>4.2 (3.1)</td>
<td>&lt;.001</td>
</tr>
</tbody>
</table>

* Data presented as mean (SD) except where otherwise noted.

Abbreviations: HbA<sub>1c</sub>, glycated hemoglobin; NA, not applicable.
While the efficacy of HbA1c testing in recognizing occult disease in patients with NKHD was the focus of this study, our findings shed light on the opportunity to identify poor long-term glucose control in patients already being treated for disease. A large majority (298 [86%]) of hyperglycemic patients in this study had known diabetes, but an HbA1c test was not ordered for 101 (29%) of these patients. This observation suggests that even for patients with known diabetes, the HbA1c test is often underused. Potential reasons for this situation may include a lack of protocol to respond to an elevated glucose or HbA1c level, a recent outpatient record of the test, costs associated with ordering additional diagnostic tests, clinicians—especially new ones—not being abreast with current standards of care, or lapses in the admissions process from emergent care to the inpatient setting. Knowledge of an elevated HbA1c level provides an opportunity to adjust therapy. For example, Dungan et al.\textsuperscript{25} showed that patients with an HbA1c level greater than 8% and inpatient intensification of their treatment had a 33% reduction in readmission rate.

Any episode of dysglycemia represents a failure of the body’s ability to maintain euglycemia. One may argue that episodes of hyperglycemia are themselves indicators of disease, notwithstanding other factors. Thus, transient hyperglycemia may exist on a continuum with, rather than distinct from, diabetes. Failure to properly evaluate hyperglycemia is an issue regardless of the context in which it happens—whether clinicians explain the elevated glucose with circumstance or ignore it. In a previous study, only 13% of hyperglycemic inpatients were directed to begin a diabetic diet regimen, 2% were given oral hypoglycemic agents, and 6% received scheduled insulin.\textsuperscript{3} If hyperglycemia is not explained in the emergency department or hospital, it will likely persist.

The implementation of reflex HbA1c testing provides an assurance that those with an isolated episode of hyperglycemia are differentiated from those with chronic disease, and it provides a mechanism to stem clinical inertia in diabetes care. The present study supports the need for standardized protocols that include reflex administration of an HbA1c test. Establishing hospital protocols that include an HbA1c test in response to hyperglycemia will ensure the early identification of new disease and initiation of patient-specific therapy.\textsuperscript{26} Moreover, this test will allow physicians to adjust existing therapeutic regimens for better control of blood glucose. Recognition of chronic dysglycemia can improve short-term and long-term outcomes for these patients, including reduced morbidity, mortality, and surgical site infections.\textsuperscript{3,23,25} Use of HbA1c level to assess all patients with hyperglycemia, regardless of diabetes history, will have a positive impact on health care quality and cost.\textsuperscript{20,27} The test can be done at any time, patients are not required to be fasting, and the results are usually obtained within hours.

The present study had a number of limitations. The data were collected retrospectively from a single center. Hence, a large multicenter study will be warranted to determine the real efficacy of the HbA1c test in inpatients with hyperglycemia and NKHD. Lists were generated from 2 different hospital record systems that did not yield identical results. Although the research team tracked individual admissions and cross-referenced them, some records may have been missed. The number of patients with NKHD was quite small, which reflects the large number of patients with known diabetes (85%) and the limited total number of admissions during the study period. Of special note is the rural geographic location and limited resources of the hospital involved in the study. Patients are often transferred to larger urban institutions, resulting in shortened in-house management. Nonetheless, the results of this study are still provocative to inpatient diabetes care in the “real world.” The diagnosis of diabetes in 17 patients rather than all 18 patients with high HbA1c levels reflects a missed opportunity—at least in documentation—of identifying diabetes in 1 patient. Furthermore, 2 people with NKHD were discharged with a diagnosis of diabetes but without clear HbA1c confirmation.
The HbA₁c test is not perfect, especially because of the existence of hemoglobin variants. Any alteration of red blood cells arising from disease or procedures such as anemia, hemoglobinopathies, or blood transfusion may affect test results. In the 2015 American Diabetes Association Standards of Care, blood loss, hemolysis, blood transfusion, erythropoietin therapy, and iron deficiency were noted as conditions that could compromise the accuracy of HbA₁c test results. In addition, there may be little benefit in obtaining HbA₁c values in patients who have had the test in the past 3 months or in those with known hemoglobinopathies. Furthermore, it may be prudent to only select patients who have more than 1 abnormal glucose reading before ordering an HbA₁c test. However, it is well established that hyperglycemia goes unnoticed and is undertreated for many hospitalized patients despite the evidence that shows undiagnosed diabetes contributes to higher mortality and longer length of stays. The small cost for an HbA₁c test can be easily recouped and the rather high disease-related expenses can be avoided.

It is also important to note that a normal HbA₁c level should not overrule acute hyperglycemia in the hospital. Even with a normal HbA₁c level, acute hyperglycemia must be treated promptly to reduce the risk of the associated adverse outcomes.

Conclusion

Hyperglycemia in the hospital is common—it leads to longer lengths of stay and poorer outcomes, especially in patients with NKHD. Although HbA₁c testing elucidates the chronicity of hyperglycemia, it is often not used enough in the inpatient setting. Patients with NKHD whose HbA₁c level was measured were 5 times more likely to leave the hospital with a diagnosis of new-onset diabetes. For patients with diabetes, HbA₁c levels can reveal opportunities to improve management. Underuse of HbA₁c testing in inpatients with hyperglycemia is a missed opportunity to identify, educate, and intervene for patients who are not optimally treated. Early detection and intervention may reduce additional costs of care resulting from increased incidence of diabetes-related complications and readmissions. The implementation of a hospital protocol whereby hyperglycemia is recognized and automatically triggers a reflex HbA₁c test should become part of normal routines. However, further studies involving multicenter data should be conducted to fully establish the efficacy and cost effectiveness of a reflex HbA₁c test in general inpatient populations.

Author Contributions

All authors provided substantial contributions to conception and design, acquisition of data, or analysis and interpretation of data; all authors drafted the article or revised it critically for important intellectual content; all authors gave final approval of the version of the article to be published; and Drs Dogbey and Shubrook agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

References


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