Initial Management of Septic Patients with Hyperglycemia in the Noncritical Care Inpatient Setting

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ABSTRACT

BACKGROUND: Previous research on the management of hyperglycemia in patients with sepsis has focused primarily on those with established organ failure in the critical care setting. The impact of hyperglycemia and glycemic control in patients with infection before developing severe sepsis or shock remains undefined.

METHODS: This observational, prospective, cohort study investigated the relationship between initial 72-hour time-weighted mean glucose concentrations and in-hospital mortality, intensive care unit transfer, and hospital length of stay in a cohort of patients with an acute infection who were admitted from the emergency department to a non-intensive care unit hospital ward. We used multivariate regression models adjusted for age, diabetes, and disease severity.

RESULTS: A total of 1849 patients were included, of whom 29% had diabetes. In the 1310 nondiabetic patients, we observed hyperglycemia using time-weighted glucose concentrations: 121 to 150 mg/dL (n = 204, 16%), 151 to 180 mg/dL (n = 32, 2.4%), and greater than 180 mg/dL (n = 21, 1.6%). Insulin treatment was infrequent in nondiabetic patients, with 9%, 13%, and 29% of nondiabetic patients in these ranges receiving insulin, respectively. As patient glucose values increased, in-hospital mortality increased in nondiabetic patients, with odds ratios (ORs) of 4.4 (95% confidence interval [CI], 1.8-11), 10.0 (95% CI, 2.5-40), and 9.3 (95% CI, 1.9-44.0). Conversely, hyperglycemia did not confer an increased risk of adverse outcomes in diabetic patients. Likewise, increased risk for unplanned intensive care unit admission from the floor demonstrated ORs of 2.2 (95% CI, 1.1-4.3), 2.0 (95% CI, 0.45-8.9), and 6.3 (95% CI, 1.9-20.6) in nondiabetic patients, whereas no increased risk was found in diabetic patients.

CONCLUSIONS: In this cohort of acutely infected patients without established severe sepsis or shock, higher glucose concentrations within the first 72 hours in the nondiabetic population were associated with worse hospital outcomes and were less likely to be treated with insulin compared with diabetic patients.

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KEYWORDS: Diabetes; Hyperglycemia; Sepsis; Severe sepsis; Noncritical care

Recent randomized controlled trials performed in the intensive care unit setting have assessed the efficacy of impact of preventing or treating hyperglycemia compared with tolerating hyperglycemia. 1-4 Although these studies have produced mixed results, most experts agree that pending further research, targeting moderate glucose values in the range of 140 to 180 mg/dL is the best method to optimize the short term. 5 However, these studies were performed in intensive care unit populations, in whom illness is established and often more severe, but the effect of hyperglycemia in a broader group of infected hospitalized patients remains unanswered. The optimal glucose ranges and risk/benefit of insulin...
therapy remain undefined in these patients. Observational studies and 1 randomized trial reported lower rates of wound infections in surgical patients managed with tighter glucose control. Observational studies have found an association between initial glucose values and higher rates of adverse outcomes, such as in-hospital mortality, in-hospital complications, and a longer hospital length of stay. Similar results also have been reported in patients with community-acquired pneumonia, noncardiac surgical patients with hyperglycemia in the perioperative period, and medical patients admitted to general hospital wards. Furthermore, we recently found an association between initial hyperglycemia in the emergency department and higher rates of in-hospital mortality in a cohort of patients with suspected infection, even after adjusting for disease severity. This association was not apparent in diabetic patients, suggesting an altered response from antecedent hyperglycemic exposure. However, much of the previous data were limited by their use of singular glucose measurements, which is likely not as important as a patient’s glycemic state over time.

We sought to investigate the relationship between time-weighted blood glucose measurements during the first 72 hours of a patient’s hospitalization and adverse outcomes (in-hospital mortality, unplanned transfers to the intensive care unit, and hospital length of stay) from a cohort of acutely infected patients initially admitted from the emergency department to a non-intensive care unit hospital ward. We hypothesized that hyperglycemia would affect patient outcomes, and that the temporal exposure to hyperglycemia and whether or not a patient had preexisting diabetes would be important factors in determining the extent to which patient outcomes were affected.

**MATERIALS AND METHODS**

**Setting and Study Design**

This is a secondary analysis of a prospective, observational cohort study reported previously. We included patients with suspected infection in the emergency department who were admitted to a non-intensive care unit hospital ward (between December 10, 2003, and September 30, 2004) at Beth Israel Deaconess Medical Center, a 600-bed urban, tertiary care, academic medical center in Boston, Massachusetts, with approximately 50,000 annual emergency department visits. The institutional review board at Beth Israel Deaconess Medical Center approved the study and granted waiver of informed consent. The study is in compliance with the Helsinki Declaration.

**CLINICAL SIGNIFICANCE**

- As patient glucose ranges increased, in-hospital mortality and other adverse outcomes increased in nondiabetic patients but not in diabetic patients.
- Nondiabetic patients were less likely to be treated with insulin.
- Clinicians and future research should focus on nondiabetic patients with hyperglycemia as a particularly vulnerable patient population.

**Selection of Participants, Data Collection, and Processing**

We prospectively screened and enrolled patients on presentation to the emergency department. The inclusion criteria were age 18 years or more, a suspected infection (as indicated by an admitting diagnosis and a confirmatory chart review), and initial admission from the emergency department to a non-intensive care unit hospital ward. All records of patients with infection or possible infection underwent a review to confirm a suspicion of infection based on emergency department presentation as documented in the medical decision-making portion of the chart. We defined a clinically suspected infection in patients with any of the following criteria: a documented source of infection, such as a radiologic evidence of pneumonia on a chest x-ray or intra-abdominal infection on a computed tomography scan or urinalysis with greater than 5 white blood cells per high-power field; a documentation of infection by the clinician in the medical decision-making portion of the chart; or administration of antibiotics in the emergency department. Chart abstraction occurred on the basis of emergency department information only and without any subsequent knowledge of the hospital course.

Because we were interested in analyzing mean glucose concentrations in patients admitted from the emergency department to a non-intensive care unit hospital ward, we excluded emergency department patients who were discharged to home, who were admitted directly to an intensive care unit, and without at least 3 blood glucose measurements during their hospitalization. Figure 1 details the patient selection process for the study population.

Trained research assistants reviewed the daily emergency department log for an admission diagnosis consistent with infection (ie, pneumonia) or possibly related to an infectious process (ie, shortness of breath) to identify patients. Inter-rater reliability for this approach was excellent (Cohen’s kappa = 0.9). All medical records of patients with infection or possible infection underwent a confirmatory review to affirm a suspicion of infection based on emergency department presentation as documented in the medical decision-making portion of the chart.

**Definition of Diabetes, 72-Hour Time-Averaged Glucose Concentrations, and Outcome Measures**

We classified patients as having preexisting diabetes based on self-report or documentation in their medical record. We recorded initial blood glucose values in the emergency de-
partment and all subsequent measurements during the first 72 hours of the hospital course. For each patient, we calculated the time-weighted mean glucose concentration (mean glucose) with a previously reported method.\textsuperscript{16,17} We used all measured blood glucose concentrations for the calculations. We assumed a linear trend to calculate the mean glucose and by correlating that measurement to a time value.

The primary end point for this analysis was all cause in-hospital mortality, and the secondary outcome measures were transfer to the intensive care unit and total hospital length of stay in days.

\section*{Statistical Analysis}

Values are expressed as means with standard deviation and frequencies with percentages to describe the populations, as appropriate. We investigated the association of time-weighted glucose values over the first 72 hours and outcomes in patients with and without diabetes in a stratified analysis. Time-weighted mean glucose values were analyzed as categoric variables using the following blood glucose ranges: less than 80 mg/dL, 80 to 120 mg/dL, 121 to 150 mg/dL, 151 to 180 mg/dL, and greater than 180 mg/dL.

Next, we investigated the association between time-weighted mean glucose concentrations and adverse outcomes (in-hospital mortality and unplanned transfer to the intensive care unit) using logistic regression analysis and reported the results using odds ratios (ORs) and 95\% confidence intervals (CIs). We used the glucose range of 80 to 120 mg/dL as our reference range. We adjusted the analysis for age, gender, and disease severity according to the Mortality in Emergency Department Sepsis score.\textsuperscript{18} This score is a validated instrument that incorporates covariates such as nursing home residency, terminal comorbid illness, type of infection, bandemia greater than 5\%, and signs of organ dysfunction (tachypnea, septic shock, thrombocytopenia, or altered mental status). We performed a similar analysis for length of hospital stay using a linear regression model. Finally, we investigated whether there was effect modification for the association between time-weighted mean glucose concentrations and patient outcomes based on preexisting diabetes by inclusion of an interaction term into our multivariate models.

All reported CIs are 2-sided 95\% intervals with 2-sided per-comparison alpha set at 0.05. All analyses were performed with SAS 9.2 (SAS Institute, Inc, Cary, NC).

\section*{RESULTS}

\subsection*{Baseline Characteristics of Patients}

From a total of 2161 eligible emergency department visits, 1849 patients were admitted to a non-intensive care unit hospital ward and included in this analysis (Figure 1). The mean

\begin{table}[h]
\centering
\begin{tabular}{|l|l|}
\hline
\textbf{Parameter} & \textbf{n = 1849} \\
\hline
Demographics & \\
Age (y), mean (SD) & 59.9 (19.9) \\
Female gender, n (%) & 883 (48) \\
Race, n (%) & \\
White & 1408 (76) \\
African American & 252 (14) \\
Asian & 51 (3) \\
Other & 138 (7) \\
Comorbidities, n (%) & \\
Coronary artery disease & 135 (7) \\
Congestive heart failure & 209 (11) \\
Cerebrovascular disease & 145 (8) \\
Chronic obstructive pulmonary disease & 229 (12) \\
Dementia & 111 (6) \\
Chronic kidney disease & 222 (12) \\
History of malignant disease & 220 (12) \\
Preexisting diabetes, n (%) & \\
Any type of diabetes & 539 (29) \\
Type 1 diabetes & 69 (4) \\
Type 2 diabetes & 470 (25) \\
Diabetes-associated medication before hospital admission, n (%) & \\
Insulin therapy & 238 (13) \\
Oral hypoglycemic agents & 182 (10) \\
Statin therapy & 256 (14) \\
Underlying infection, n (%) & \\
Pneumonia & 460 (22) \\
Urinary tract infection & 212 (11) \\
Skin or soft tissue infection & 496 (27) \\
Surgical wound infection & 67 (4) \\
Intra-abdominal infection & 301 (16) \\
Outcomes of the hospital stay & \\
Length of hospital stay (d), mean (SD) & 4.9 (5.8) \\
Transfer to ICU, n (%) & 58 (3.1) \\
Mortality, n (%) & 34 (1.8) \\
\hline
\end{tabular}
\caption{Patient Characteristics and Hospital Outcomes}
\end{table}

\textit{ICU} = intensive care unit; \textit{SD} = standard deviation.
age of the cohort was 60 (20) years, and 48% were women. Twenty-nine percent of the patients (n \( \approx \) 11005) had preexisting diabetes, the majority of whom had type II diabetes. Table 1 shows patient characteristics at baseline and hospital outcomes for the total patient cohort.

**Glucose Management Within the First 72 Hours of Hospital Admission**

Table 2 summarizes the number of glucose measurements, time-weighted glucose values, and insulin management of patients overall, and stratified by preexisting diabetes. In patients with diabetes, more blood glucose measurements were performed, and the 72 hour time-weighted mean blood glucose concentration was higher compared with patients without diabetes. Figure 2 shows detailed glucose values in patients with and without diabetes.

**Insulin Treatment Within the First 72 Hours**

Overall, 26% of the total cohort received insulin therapy during the first 72 hours of their hospital course. Figure 3

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**Table 2** Glucose Management Within the First 72 hours

<table>
<thead>
<tr>
<th></th>
<th>Total Population (n = 1849)</th>
<th>Nondiabetic Patients (n = 1310)</th>
<th>Diabetic Patients (n = 539)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Glucose measurement</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean number of glucose measurements (SD)</td>
<td>3 (±1.5)</td>
<td>2.9 (±1.4)</td>
<td>3.7 (±1.7)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Time weighted glucose concentrations</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean glucose concentration (mg/dL) (95% CI)</td>
<td>122 (119-124)</td>
<td>107 (106-108)</td>
<td>157 (152-162)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Glucose ranges, N (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;80 mg/dL</td>
<td>63 (3.4%)</td>
<td>51 (3.9%)</td>
<td>12 (2.2%)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>80-120 mg/dL</td>
<td>1150 (62.2%)</td>
<td>1002 (76.5%)</td>
<td>148 (27.5%)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>121-150 mg/dL</td>
<td>346 (18.7%)</td>
<td>204 (15.6%)</td>
<td>142 (26.4%)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>151-180 mg/dL</td>
<td>121 (6.5%)</td>
<td>32 (2.4%)</td>
<td>89 (16.5%)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>&gt;180 mg/dL</td>
<td>169 (9.1%)</td>
<td>21 (1.6%)</td>
<td>148 (27.5%)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Insulin treatment</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Any insulin treatment, N (%)</td>
<td>480 (26.0%)</td>
<td>41 (3.1%)</td>
<td>439 (81.5%)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Amount of insulin (units) if treated</td>
<td>66 (±82)</td>
<td>10.3 (±14.8)</td>
<td>70.8 (±83.7)</td>
<td>&lt;.001</td>
</tr>
</tbody>
</table>

CI = confidence interval; SD = standard deviation.

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![Figure 2](image-url)  
**Figure 2** Initial time-weighted glucose values during the first 72 hours of the hospital course in nondiabetic (*upper*) and diabetic (*lower*) patients. Weighted glucose values in nondiabetic (*upper*) and diabetic (*lower*) patients.
shows the proportion of patients who received insulin based on mean glucose ranges. Diabetic patients were more likely to receive insulin independent of mean glucose. Conversely, only 9%, 13%, and 29% of nondiabetic patients in the glucose ranges of 121 to 150 mg/dL, 151 to 180 mg/dL, and greater than 180 mg/dL received insulin, respectively, compared with 77%, 91%, and 96% of diabetic patients, respectively. This association was maintained in a logistic model adjusted for time-weighted mean glucose, age, severity of illness (Mortality in Emergency Department Sepsis score), and home insulin regimen (adjusted OR of receiving insulin for diabetic patients 46.2, 95% CI, 29.9-71.5). Figure 4 shows the association between insulin treatment and time-weighted glucose level for diabetic and nondiabetic patients.

**Association Between Initial 72-Hour Time-Averaged Glucose Concentrations and In-Hospital Mortality**

Overall, the mortality rate was 2.1% (95% CI, 1.5-2.8) and statistically similar in patients with and without diabetes (2.0% vs 2.1%, *P* = .90). When comparing mortality within different 72-hour time-averaged glucose ranges (Figure 5), we found that nondiabetic patients had the lowest in-hospital mortality rates when their mean glucose was in the 80 to

![Figure 3](image-url)  Insulin treatment for different time-weighted mean glucose ranges in patients with (A) and without (B) diabetes.
120 mg/dL range, with a stepwise increase in mortality for glucose concentrations in the higher ranges. In diabetic patients, mortality was similar in all ranges, except for the less than 80 mg/dL range, which included only 12 patients, none of whom died.

We confirmed this association in multivariate logistic regression analysis adjusted for age, preexisting diabetes, and severity of disease. Time-weighted glucose values were associated with mortality in nondiabetic patients (OR per 10 mg/dL increase 1.19, 95% CI, 1.09-1.3) but not in diabetic patients (OR per 10 mg/dL increase 0.98, 95% CI, 0.89-1.08). Including an interaction term in the model provided evidence for effect modification of diabetes on the association of time-weighted glucose values and mortality ($P$ of interaction term < .01). Likewise, compared with the reference glucose range of 121 to 150 mg/dL, higher glu-

**Figure 4** Association of time averaged glucose values and probability for insulin treatment in the diabetic and non-diabetic population. In patients with no history of diabetes (A) insulin treatment was found at a much higher glucose threshold compared to diabetic patients (B).
cose ranges were associated with higher mortality rates (Table 3).

When investigating the association of glucose ranges and mortality within different types of infection, we found no evidence for significant effect modification; specifically, no interaction was found for pneumonia, urinary tract infection, intra-abdominal infections, or soft tissue/skin infections.

We also investigated the effect of insulin treatment on mortality. In a propensity-adjusted logistic regression model, we found no association between insulin treatment and mortality (OR, 1.1; 95% CI, 0.56-2.27; \( P = .75 \)).

**Association Between Initial 72-Hour Time-Averaged Glucose Concentrations and Unplanned Transfer to the Intensive Care Unit**

The rate of transfer to the intensive care unit from a non-intensive care unit hospital ward was 3.1% (95% CI, 2.3-3.9) and higher in diabetic patients (4.6%) compared with nondiabetic patients (2.5%, \( P < .05 \)). Figure 5B shows non-intensive care unit hospital ward to intensive care unit transfer rates for different time-averaged glucose ranges in diabetic and nondiabetic patients. Similar to mortality, the rate of intensive care unit admission was lowest in the 80 to 120 mg/dL glucose concentration range, with a stepwise increase at higher glucose ranges only in nondiabetic patients, whereas in diabetic patients the rates were similar in all glucose ranges, except for the less than 80 mg/dL range. In multivariate logistic regression analysis, mean 72-hour blood glucose concentrations tended to be associated with intensive care unit transfer only in the nondiabetic patients (OR per 10 mg/dL increase 1.08, 95% CI, 0.98-1.19), but not in diabetic patients (OR per 10 mg/dL increase 0.98, 95% CI, 0.91-1.06). Testing for effect modification did not show a significant result (\( P \) interaction term = 0.13). Compared to the reference glucose range of 121 to 150 mg/dL, higher glucose ranges were associated with increased risk for intensive care unit transfer (Table 3).

**Association Between Initial 72-Hour Time-Averaged Glucose Concentrations and Hospital Length of Stay**

The mean length of stay was 4.9 days (95% CI, 4.7-5.1) and longer in diabetic patients compared to nondiabetic patients (6.2 vs 4.4 days, \( P < .01 \)). In multivariate linear regression adjusted for age, diabetes, severity of disease (Mortality in Emergency Department Sepsis score), 72-hour mean glucose concentrations were associated with longer hospital length of stay in nondiabetic patients (linear regression coefficient per 10 mg/dL increase 0.1, 95% CI, 0.0-0.26), but not in diabetic patients (linear regression coefficient per 10 mg/dL –0.01, 95% CI, –0.09-0.08). Testing for effect modification showed a positive trend (\( P \) interaction term = .08).

**DISCUSSION**

Because of the growing worldwide epidemic of diabetes, appropriate management of hyperglycemia in the hospital...
setting has become increasingly important. It is estimated that diabetic patients are responsible for more than 20% of all US hospital inpatient days.\textsuperscript{19} Previous research has noted that hyperglycemia is associated with adverse outcomes in intensive care unit patients, postoperative patients, and in those being treated for myocardial infarctions.\textsuperscript{6,9,20} In the critical care setting, a number of previous studies investigated the impact of treating hyperglycemia compared with tolerating hyperglycemia. Initial studies from Belgium suggested the impact of treating hyperglycemia compared with tolerating hyperglycemia. Initial studies from Belgium suggested a lower overall mortality rate among patients in the non-intensive care unit setting. Unfortunately, outcome studies are lacking.

The most recent consensus guidelines by the American Association of Clinical Endocrinologists and American Diabetes Association regarding inpatient glycemic control in the non-intensive care unit setting specifically states that blood glucose concentrations should be maintained between 140 and 180 mg/dL.\textsuperscript{20} However, only approximately 25% of the nondiabetic patients in our cohort with mean glucose ranges greater than 180 mg/dL during the first 72 hours were treated with insulin, which was due to a knowledge or practice translation gap. Furthermore, our finding that nondiabetic patients had the lowest mortality rate when their mean glucose values were in the 80 to 120 mg/dL range raises some doubt whether the American Association of Clinical Endocrinologists/American Diabetes Association consensus guideline provides optimum glycemic control for nondiabetic patients with sepsis in the non-intensive care unit setting. Unfortunately, outcome studies are lacking.

Although we found that higher mean glucose values in nondiabetic patients were associated with higher rates of in-hospital mortality and intensive care unit transfer, additional studies are needed to confirm whether treating hyperglycemia translates into better patient outcomes and, if so, which glucose values should be specifically targeted to optimize patient outcomes. Our study does provide evidence that hyperglycemia in nondiabetic patients hospital-

### Table 3 Outcomes During Hospital Stay According to Glucose Range

<table>
<thead>
<tr>
<th>Glucose Ranges</th>
<th>Diabetic Patients</th>
<th>Nondiabetic Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Frequency(%, n/total)</td>
<td>Adjusted OR(95% CI)</td>
</tr>
<tr>
<td>Mortality</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Glucose &lt; 80 mg/dL</td>
<td>0% (0/12)</td>
<td>NA</td>
</tr>
<tr>
<td>Glucose 80-120 mg/dL</td>
<td>2.03% (3/148)</td>
<td>reference</td>
</tr>
<tr>
<td>Glucose 121-150 mg/dL</td>
<td>2.82% (4/142)</td>
<td>1.50 (0.30-7.48)</td>
</tr>
<tr>
<td>Glucose 151-180 mg/dL</td>
<td>2.25% (2/89)</td>
<td>0.89 (0.13-6.04)</td>
</tr>
<tr>
<td>Glucose &gt;180 mg/dL</td>
<td>1.35% (2/148)</td>
<td>0.45 (0.05-4.32)</td>
</tr>
<tr>
<td>ICU admission from the medical floor</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Glucose &lt; 80 mg/dL</td>
<td>0% (0/12)</td>
<td>NA</td>
</tr>
<tr>
<td>Glucose 80-120 mg/dL</td>
<td>6.08% (9/148)</td>
<td>reference</td>
</tr>
<tr>
<td>Glucose 121-150 mg/dL</td>
<td>7.75% (11/142)</td>
<td>1.30 (0.52-3.24)</td>
</tr>
<tr>
<td>Glucose 151-180 mg/dL</td>
<td>7.87% (7/89)</td>
<td>1.30 (0.46-3.62)</td>
</tr>
<tr>
<td>Glucose &gt;180 mg/dL</td>
<td>3.38% (5/148)</td>
<td>0.57 (0.18-1.77)</td>
</tr>
<tr>
<td>Length of hospital stay</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Glucose &lt; 80 mg/dL</td>
<td>6.58 (5.18)</td>
<td>0.47 (-3.95-4.9)</td>
</tr>
<tr>
<td>Glucose 80-120 mg/dL</td>
<td>5.93 (7.91)</td>
<td>reference</td>
</tr>
<tr>
<td>Glucose 121-150 mg/dL</td>
<td>6.21 (7.39)</td>
<td>0.21 (-1.52-1.94)</td>
</tr>
<tr>
<td>Glucose 151-180 mg/dL</td>
<td>6.1 (6.03)</td>
<td>0.06 (-1.93-2.04)</td>
</tr>
<tr>
<td>Glucose &gt;180 mg/dL</td>
<td>6.6 (8.12)</td>
<td>0.48 (-1.27-2.23)</td>
</tr>
</tbody>
</table>

ICU = intensive care unit; SD = standard deviation; CI = confidence interval. NA = not available; OR = odds ratio.

\*Adjusted for severity and age.
ized in the non-intensive care unit inpatient setting may be a more significant cause of in-hospital complications than previously believed, and that additional focus on improving glycemic control in this population may not only improve patient outcomes but also reduce the use of valuable and increasingly limited healthcare resources.

Although hypoglycemia and its associated complications were a major cause of morbidity and mortality in many of the previous studies investigating various insulin regimens, mean glucose values in the hypoglycemic range were rare in our cohort and not associated with higher rates of in-hospital mortality. However, our study was not specifically designed to address this issue, and our sample size lacks the power to determine whether an association exists between hypoglycemia and adverse patient outcomes.

This study has a number of limitations. First, this is a secondary analysis of a prospectively enrolled cohort, and our primary purpose was hypothesis generation for future research. Although we adjusted our regression models for age, diabetes status, and disease severity, it is possible that additional factors confounded our results. Furthermore, because we relied on subjective self-report and medical record review to determine whether a patient had a diagnosis of diabetes or not, we may have erroneously included diabetic patients in the “nondiabetic” group and vice versa, potentially resulting in misclassification bias. The external validity of our findings also is unknown because this study was performed at a single institution.

CONCLUSIONS
We observed an association between time-weighted mean glucose concentrations and adverse clinical outcomes in nondiabetic patients with acute infection who were admitted to a non-intensive care unit hospital ward, whereas no such associations were found in diabetic patients. Physicians were less likely to administer insulin for hyperglycemia in patients without preexisting diabetes. Additional studies are needed to confirm the validity of these findings and to further elucidate the most appropriate management of hyperglycemia in nondiabetic patients hospitalized in the non-intensive care unit inpatient setting.

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References