The impact of serum glucose in the outcomes of hospitalized with community-acquired pneumonia (CAP)
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Introduction
Hyperglycemia is associated with alterations in host defenses such as abnormal neutrophil function. Hyperglycemia is frequently present in hospitalized patients with CAP. Although hyperglycemia is considered a risk for poor outcomes in these patients, published studies have conflicting results. The objective of this study was to evaluate the impact of serum glucose on the outcomes of hospitalized patients with CAP.

Methods
This was a secondary data analysis of the Community-Acquired Pneumonia Organization (CAPO) International Cohort Study. The first glucose level at the time of hospital admission was used as the predictor variable. In-hospital and 30-day mortality were used as outcome variables in multivariable logistic regression models.

Results
A total of 3033 patients were included in the analysis. The adjusted predicted in-hospital and 30-day mortality ranged from approximately 7% with a normal glucose value to approximately 20% with a glucose of ≥500 (P<0.85, P<0.04, respectively).

Conclusions
In this study, we documented a non-significant clinical trend toward increased mortality in patients with elevated glucose levels at the time of hospitalization. The trend toward increased mortality likely reflects an immunocompromised state associated with elevated glucose. It is unclear if interventions to improve glucose at the time of hospital admission can improve outcomes or if another factor (e.g. sepsis) increases the glucose and the risk of mortality.

Pneumonia is one of the leading infectious causes of mortality worldwide and ranks second in United States. It accounts for 3.2 million deaths worldwide and is associated with significant increase in the long-term morbidity and mortality. Clinical outcomes in hospitalized community-acquired pneumonia (CAP) patients are affected by a variety of factors including age, existing comorbidities and causative agents. Hyperglycemia has been shown to be associated with increased in the length of stay (LOS) and higher in-hospital mortality in patients with infectious diseases including CAP. About 25% of patients with CAP have diabetes. Hyperglycemia is associated with alterations in host defenses such as abnormal neutrophil function and is frequently present in hospitalized patients with CAP. Although hyperglycemia is considered a risk for poor outcomes in these patients, published studies have conflicting results. While some authors have shown a relationship between hyperglycemia and increased mortality in CAP patients, others were not able to find any association. The objective of this study was to evaluate the impact of serum glucose on the outcomes of hospitalized patients with CAP.

Study design and Study population
This was a secondary analysis of patients enrolled in the Community-Acquired Pneumonia Organization (CAPO) International cohort study. Data were collected between 2009 and 2015. In each participating center, non-consecutive medical records of hospitalized patients with the diagnosis of CAP were reviewed. A sample of the data collection form is available at the study website (www.caposite.com). Validation of data quality was performed at the study center before the case was entered into the CAPO database. Institutional Review Board approval was obtained by each participating center.

Study definitions
CAP: Diagnosis of CAP required the presence of criterion A, B, and C:
A. New pulmonary infiltrate on imaging (CT scan or chest x-ray) at the time of admission to the hospital.
B. Signs and Symptoms of CAP (at least one of the following):
   1. New or increased cough (per the patient)
   2. Fever >37.8°C (100.0°F) or hypothermia <35.6°C (96.0°F).
   3. Changes in WBC (leukocytosis >11,000 cells/ml², left shift > 10% band forms/segmental, or leukopenia < 4,000 cells/ml²)
C. Working diagnosis of CAP at the time of hospital admission with antimicrobial therapy given within 24 hours of admission.

Serum glucose levels: Blood glucose levels were obtained from laboratory work within 24 hours of admission.

Study outcomes
In-hospital mortality: defined as death by any cause during hospitalization.
30 day mortality: defined as death by any cause during the first 30 days after hospital admission.

Statistical Analysis
A logistic regression model was used to adjust for confounding in evaluating the relationship between serum glucose and in hospital mortality. The adjusted predicted probability of mortality from this model was plotted against glucose values to visualize the risk of in-hospital mortality over ranges of serum glucose values on hospital admission. The same was done for 30 day mortality. Baseline categorical explanatory variables were summarized as frequencies and percentages. Continuous variables were summarized as frequencies and interquartile range.

RESULTS
• A total of 3,033 patients’ data were evaluated in this study. Patients’ characteristics are shown in Table 1.
• The adjusted predicted in-hospital mortality and 30-day hospital mortality are shown in figure 1 and 2 respectively.

CONCLUSIONS
• In this study, we documented a non-significant clinical trend toward increased mortality in patients with elevated glucose levels at the time of hospitalization.
• The trend toward increased mortality likely reflects an immunocompromised state associated with elevated glucose.
• Stress induced hyperglycemia is a well-known entity noticed in disease states and has been proven to increase mortality. In stress hormones and cytokines are released which increases the hepatic glucose production, causing an increase in serum glucose levels. CAP is also a disease state that can result in increase in blood glucose levels, thus affecting mortality. Hyperglycemia causes an increase in oxidative stress, electrolyte imbalance and endothelial dysfunction. It stimulates pro-inflammatory pathways, platelet activation and immune dysregulation ultimately resulting in increased mortality. It is unclear if interventions to improve glucose at the time of hospital admission can improve outcomes or if another factor (e.g. sepsis) increases the glucose and the risk of mortality.
• Multiple studies have demonstrated that increase in the serum glucose levels at admission is a predictor for complicated hospital course, longer hospitalization duration and increased rates of infection along with higher mortality as compared to normoglycemia. Lepper et al demonstrated that there was a 20 times increase in mortality in patients with newly diagnosed hyperglycemia as compared to those with normal serum glucose levels.
• However, Bhattacharya et al demonstrated that serum glucose levels at admission don’t have an impact on the mortality. There was no association seen between mortality and serum glucose levels in the study by Godar et al. Thus, there is conflicting evidence in the literature regarding the role of serum glucose in regards to mortality in CAP patients.
• Further, multi-centered randomized controlled trials are necessary to evaluate this effect.

REFERENCES