

ABSTRACT

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 database. 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=0.94, 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.

INTRODUCTION

Pneumonia is one of the leading infectious causes of mortality worldwide and ranks second in United States. It accounts for 3.2 million deaths worldwide¹ 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 increase in the length of stay (LOS) and higher in-hospital mortality in patients with infectious diseases including CAP.¹

About 25% of patients with CAP have diabetes². 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,^{1,2} others were not able to find any association.³

The objective of this study was to evaluate the impact of serum glucose on the outcomes of hospitalized patients with CAP.

MATERIALS AND METHODS

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 in to 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:

- New pulmonary infiltrate on imaging (CT scan or chest x-ray) at the time of admission to the hospital.
- Signs and Symptoms of CAP (at least one of the following)
 - New or increased cough (per the patient)
 - Fever >37.8°C (100.0°F) or hypothermia <35.6°C (96.0°F).
 - Changes in WBC (leukocytosis >11,000 cells/mm³, left shift > 10% band forms/microliter, or leukopenia < 4,000 cells/mm³)
- 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.

Day 30 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.

RESULTS

Table 1: Patient Characteristics

Patient Characteristic Chart n=3033	
Demographics	
Age, Median(IQR)	67 (32)
Sex, n(%)	1778 (58.6)
Nursing home resident, n(%)	173 (5.7)
Comorbid Conditions	
Congestive Heart Failure, n(%)	478 (15.8)
COPD, n(%)	712 (23.5)
Diabetes, n(%)	565 (18.6)
HIV, n(%)	240 (7.9)
Renal Disease, n(%)	286 (9.4)
Liver Disease, n(%)	190 (6.3)
Neoplastic Disease, n(%)	346 (11.4)
Physical Exam	
Altered mental status on admission, n(%)	438 (14.4)
Respiratory Rate, Median(IQR)	22 (10)
Systolic blood pressure, Median(IQR)	125 (30)
Temperature (degrees Celsius), Median(IQR)	37.7 (1.6)
Heart rate, Median(IQR)	99 (27)
Lab/Radiography, Median(IQR)	
pH, Median(IQR)	7.5 (0.1)
PaO2, Median(IQR)	62 (19.4)
Blood Urea Nitrogen, Median(IQR)	32 (32)
Serum sodium, Median(IQR)	137 (6)
Serum glucose, Median(IQR)	120 (51)
Hematocrit, Median(IQR)	38 (8)
Pleural effusion, n(%)	697 (23)
Severity of Disease	
ICU admission, n(%)	315 (10.4)
Pneumonia Severity Index, Median(IQR)	120 (56)

In Hospital Mortality

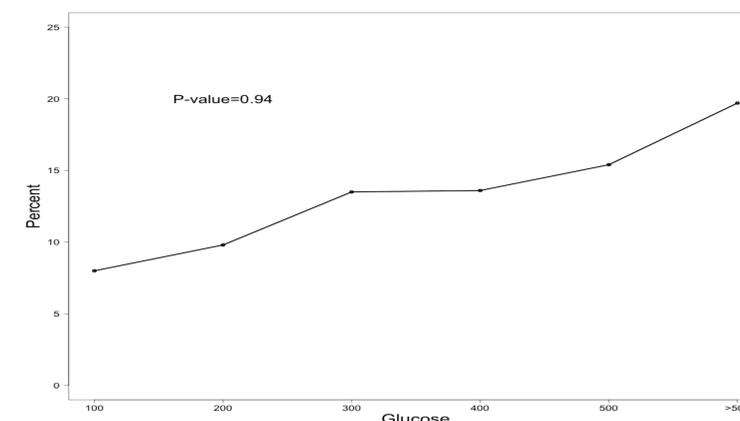


Figure 1: Impact of serum glucose on the in-hospital mortality in community acquired pneumonia patients

30 Day Mortality

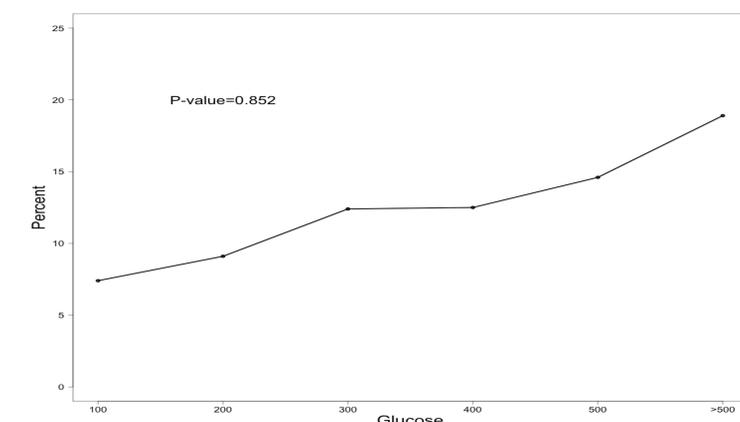


Figure 2: Impact of serum glucose on 30 day mortality in community acquired pneumonia patients

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 levels¹. 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.⁵ 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 compare to normoglycemia⁴. 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 levels².
- However, Bhattacharya et al demonstrated that serum glucose levels at admission don't have an impact on the mortality³. There was no association seen between mortality and serum glucose levels a study by Godar et al⁴. 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

- Koskela HO, Salonen PH, Romppanen J, Niskanen L. Long-term mortality after community acquired pneumonia—impacts of diabetes and newly discovered hyperglycaemia: a prospective, observational cohort study. *BMJ Open*. 2014 Aug 21;4(8):e005715. doi: 10.1136/bmjopen-2014-005715.
- Lepper PM *et al*. Serum glucose levels for predicting death in patients admitted to hospital for community acquired pneumonia: prospective cohort study. *BMJ*. 2012 May 28;344:e3397. doi: 10.1136/bmj.e3397.
- Bhattacharya RK, Mahnken JD, Rigler SK. Impact of admission blood glucose level on outcomes in community-acquired pneumonia in older adults. *Int J Gen Med*. 2013 May 6;6:341-4. doi: 10.2147/IJGM.S42854. Print 2013.
- Godar DA *et al*. The impact of serum glucose on clinical outcomes in patients hospitalized with community-acquired pneumonia. *WMJ*. 2011 Feb;110(1):14-20.
- Dungan KM, Braithwaite SS, Preiser JC. Stress hyperglycaemia. *Lancet*. 2009 May 23;373(9677):1798-807. doi: 10.1016/S0140-6736(09)60553-5.