

Impact of admission blood glucose level on outcomes in community-acquired pneumonia in older adults

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Background: Community-acquired pneumonia (CAP) is a common cause of morbidity and mortality in older adults. Although diabetes mellitus is a risk factor for pneumonia, the clinical impact of blood glucose level at the time of admission is not clear. Our goal was to examine the association between admission hyperglycemia and subsequent mortality, length of stay, and readmission outcomes in older adults with CAP.

Methods: A retrospective observational study was conducted using hospital data for community-acquired pneumonia admissions in 857 persons from January 1, 2008 to December 31, 2010. We examined the effects of admission glucose level on mortality, length of stay, and 30 day readmission, adjusted for demographic factors and comorbidity.

Results: The mean age of the sample was 64 years, and 51% of the subjects were female. Inpatient mortality occurred in 4.6% and the median length of stay was 5 days (interquartile range 3–9 days). Readmission within 30 days occurred in 17%. We found little impact of first glucose measures on in-hospital mortality ($P = 0.94$), length of stay ($P = 0.95$), and 30-day readmission ($P = 0.56$). Subjects 65 years and older trended towards higher in-hospital mortality. Older age, cancer, heart failure, and cirrhosis were associated with adverse outcomes.

Conclusion: Glucose level upon admission for community-acquired pneumonia was not associated with adverse outcomes within 30 days in older adults.

Keywords: community-acquired pneumonia, hyperglycemia, readmission rates, hospital mortality

Introduction

Pneumonia is the eighth most common cause of death in the USA and ranks second among infectious causes of mortality.^{1,2} Over five million people develop pneumonia every year in the US, mostly older adults.³ Diabetes mellitus is a risk factor for pneumonia, and as many as one-quarter of persons with community-acquired pneumonia (CAP) are diabetic.^{3,4} Hyperglycemia has been established as an independent predictor of morbidity and mortality in patients admitted with acute coronary syndromes, ischemic stroke, trauma, heart failure, and coronary artery bypass graft (CABG), as well as admission to surgical and medical intensive care units.^{5,6} Although hyperglycemia leads to impaired host immune responses, the impact of hyperglycemia on concrete clinical outcomes (eg, mortality, length of stay, and readmission) is not clear in CAP. Data on hyperglycemia and CAP are limited. The existing relevant literature shows mixed results, with most studies focused on hospital complications associated with hyperglycemia.^{4–8}

Glycemic status at admission is readily available for all patients, and might provide a potentially useful predictive factor for outcomes and utilization of care. Our goal was to

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examine potential associations of admission hyperglycemia with mortality, length of stay, and readmission rates in patients with CAP.

Methods

Cohort and measures

Retrospective observational data were extracted from admissions to the University of Kansas Medical Center for community-acquired pneumonia (ICD-9-CM code 480–487) from January 1, 2008 through December 31, 2010. Only persons aged 40 years and older were sampled. Our analysis examines the effects of first glucose measure upon admission and age on hospital mortality, length of stay (LoS), and readmission for community-acquired pneumonia (CAP) within 30 days. Data for a total of 1012 CAP admissions were provided. In addition to the primary explanatory measures, demographics (sex and race/ethnicity [American Indian/Eskimo/Aleutian, black, Hispanic, Oriental/Asian/Pacific Islander/Indonesian, white, or other]) were also analyzed. Medical comorbidities, including the presence or absence of cancer, chronic heart failure, chronic renal failure, cirrhosis, HIV, and diabetes were provided in the hospital discharge data. We assigned the patients to three groups. Glucose was categorized as normal glycemia (<126), mild hyperglycemia ($126\text{--}<180$), and uncontrolled hyperglycemia (≥ 180).

Statistical analysis

Univariate descriptive statistics (mean, standard deviation, and percentiles for continuous measures and frequencies and relative frequencies for categorical measures) were derived. Bivariate analyses were also conducted by generating contingency tables with glucose ($<126/126\text{ to }<180/\geq 180$), and Pearson's Chi-square test or exact test alternatives were conducted. Descriptive statistics for age within glucose levels were also generated, and age distributions across these groups was performed using one-way analysis of variance. Comparisons of LoS between strata were performed using the log-rank test. Unconditional logistic regression was used to model in-hospital mortality and 30-day hospital readmission as a function of glucose and age, adjusted for other potential confounding variables such as sex, race/ethnicity, and comorbid conditions. (Diabetes was not included as a covariate due to its strong association with the explanatory measure of interest: glucose.) Models were built using stepwise selection with an entry criterion of a score test P -value less than 0.15 and a retaining criteria of $P < 0.10$ from the Wald test. An interaction term between glucose and age group was also evaluated in a model that was adjusted for the other covariates

selected from this model building process. These enabled the assessment of whether the effects of glucose on mortality and on readmission were different among those ages 65 and older compared to those ages 40–64. The final models were assessed using the Hosmer–Lemeshow goodness-of-fit test. Adjusted odds ratios and corresponding 95% Wald confidence intervals (CI) were generated. Cox proportional hazards regression was used to model LoS as a function of glucose and age, adjusted for other potential confounding variables such as sex, race/ethnicity, and comorbid conditions. Subjects who died; were discharged to hospice; transferred to another institution; or left against medical advice, were treated as right-censored observations for this analysis. A model was built using the same stepwise procedure as described above for the logistic regression models, and analogous testing for an interaction effect between glucose category and age group was conducted. Adjusted hazard ratios and corresponding 95% Wald CI were generated.

All data management and data analysis were performed using SAS version 9.2 (2002–2008, SAS Institute Inc, Cary, NC, USA).

Results

One thousand and twelve community-acquired pneumonia admissions were identified. Missing data required exclusion of 21 records (one hospitalization was missing a valid code for disposition; three records were missing data for the race variable; and 17 were missing a glucose measure for the corresponding admission). After these exclusions, 991 hospitalization records remained which were generated by 857 unique subjects because of repeated hospitalizations in some individuals. Each of these was allowed to contribute only one hospitalization to the analysis. Thus, these 857 subjects comprised the sample for the mortality and length of stay outcome measures (Table 1). However, for the analysis of readmission rates, we further excluded those who died in the hospital or were discharged to hospice, leaving a final sample of 797 persons (Table 2).

The mean age of the sample was 64 years, and 51% were female. Over 70% of the population was non-Hispanic white. Comorbidities are shown in Table 1. Glucose was categorized as normoglycemia in 58.1%, mild hyperglycemia in 27.8%, and uncontrolled hyperglycemia in 14%. Twenty-nine percent had a recognized diagnosis of diabetes mellitus; this diagnosis was associated with higher glucose levels ($P < 0.001$).

In Table 1, inpatient mortality occurred in 4.6%. The median length of stay was 5 days, (inter-quartile

Table 1 Baseline characteristics of all the patients admitted for pneumonia

	All subjects**	Normal	Mild hyperglycemia	Uncontrolled hyperglycemia	P-value****
		<126 mg/dl	126–<180 mg/dl	≥180 mg/dl	
Total	857	498	238	121	
Age					
Years*	64.1 ± 13.3	63.3 ± 13.7	65.4 ± 13.0	64.8 ± 12.2	0.121
65+	401 (46.8)	227 (45.6)	115 (48.3)	59 (48.8)	0.703
Male	416 (48.5)	234 (47.0)	122 (51.3)	60 (49.6)	0.538
Heart failure	183 (21.4)	90 (18.1)	61 (25.6)	32 (26.5)	0.022
Cirrhosis	22 (2.57)	14 (2.81)	3 (1.26)	5 (4.13)	0.231
Chronic renal failure	161 (18.8)	83 (16.7)	50 (21.0)	28 (23.1)	0.154
HIV	4 (0.47)	4 (0.80)	0	0	0.279
Cancer	226 (26.4)	150 (30.1)	58 (24.4)	18 (14.9)	0.002
Diabetes	250 (29.2)	89 (17.9)	70 (29.4)	91 (75.2)	<0.0001
Mortality	39 (4.55)	24 (4.82)	10 (4.20)	5 (4.13)	0.906
Length of stay***	5.0 (3.0, 9.0)	5.0 (3.0, 9.0)	5.0 (3.0, 9.0)	5 (3.0, 10.0)	0.736

Notes: *Mean ± std; **n (%); ***median (25th percentile, 75th percentile); ****P-values are from Pearson's Chi-square test for categorical measures with the exception of HIV (which used the alternative exact test) and analysis of variance for age (continuous).

range 3–9 days). Readmission within 30 days occurred in 17% (Table 2). None of these clinical outcomes differed by glucose category. The length of stay, readmission rate, and inpatient mortality were similar in the three glucose categories.

Multivariable models were built that forced glucose and age group into the model. Covariates included in the model for length of stay were cancer, chronic renal failure, and cirrhosis. Hazard ratios (HRs) for LoS indicated essentially no effect of glucose (HR: 1.03, 95% CI: 0.86–1.23 for 126–<180 versus <126; HR: 0.99, 95% CI: 0.79–1.25 for ≥180 versus <126) and shorter LoS among those ages 40–64 (versus 65 and older; HR: 1.23; 95% CI: 1.04–1.44). The *P*-values for these two factors were 0.95 and 0.01 for glucose and age group, respectively. Thus, age group described

significant variation in the hospital LoS, but glucose did not in this cohort. Controlling for age, no differences in the risk of 30-day readmission between the various levels of glucose were detected (*P* = 0.56). Controlling for age, no differences in the risk of in-hospital mortality between the various levels of glucose were detected (*P* = 0.94). This suggested that no effect for glucose (consistent with the bivariate results) and no interaction effect for glucose with age on length of stay (*P* = 0.20), 30-day readmission (*P* = 0.50), or mortality (*P* = 0.91) were detected.

Discussion

This retrospective observational study of CAP admission data revealed that the first glucose measure upon admission did

Table 2 Baseline characteristics of patients admitted for pneumonia and discharged from the hospital

	Subjects in 30-day readmission	Normal	Mild hyperglycemia	Uncontrolled hyperglycemia	P-value****
		<126 mg/dl	126–<180 mg/dl	≥180 mg/dl	
Total	797	466	219	112	
Age					
Years*	63.8 ± 13.4	63.0 ± 13.8	64.8 ± 12.8	64.8 ± 12.3	0.201
65+**	363 (45.6)	208 (44.6)	102 (46.6)	53 (47.3)	0.822
Male**	387 (48.6)	217 (46.6)	112 (51.1)	58 (51.8)	0.408
Heart failure**	164 (20.6)	81 (17.4)	55 (25.1)	28 (25.0)	0.03
Cirrhosis**	18 (2.26)	10 (2.15)	3 (1.37)	5 (4.46)	0.163
Chronic renal failure**	147 (18.4)	77 (16.5)	45 (20.6)	25 (22.3)	0.234
HIV**	4 (0.5)	4 (0.86)	0	0	0.279
Cancer**	193 (24.2)	132 (28.3)	46 (21.0)	15 (13.4)	0.002
Diabetes**	232 (29.1)	82 (17.6)	64 (29.2)	86 (76.8)	<0.0001
30 day readmission rate**	137 (17.2)	78 (16.7)	36 (16.4)	23 (20.5)	0.596

Notes: *Mean ± std; **n (%); ****P-values are from Pearson's Chi-square test for categorical measures (with the exceptions of cirrhosis and HIV, which used the alternative exact tests) and analysis of variance for age (continuous).

not predict hospital mortality, length of stay, or readmission for community-acquired pneumonia within 30 days in the University of Kansas Medical Center in the USA.

However, there are several limitations to consider. We were not able to follow these patients after discharge from the hospital except to observe readmissions to the same hospital. Mortality during the hospital stay was uncommon, and we were unable to capture post-discharge mortality. Thus, this study sample may be too small to capture possible differences in longer term mortality outcomes across different levels of admission glucose. We were not able to examine changes in serum glucose throughout the hospital stay. There was no structured protocol in treatment for patients with increase serum glucose, which was instead left to the discretion of the health care providers within our center. A single measure of hyperglycemia at admission might reflect the production of stress related counter-regulatory hormones due to acute illness. We are unable to exclude the possibility that severity of illness was differentially distributed across levels of glucose control. This question should be tested in a larger study sample in which measures of severity of illness are available.

A US study reported by Labraere et al⁶ reached similar conclusions to our own. In contrast, our findings differ from a recently published German prospective study by Lepper et al⁷ showing that serum glucose at the time of hospital admission for community-acquired pneumonia (n = 6870) was a predictor of death at 90 days after admission. This prospective study had a longer follow up time period, and captured specific patient-level clinical factors such as confusion, respiratory rate, and blood pressure. Our study population was demographically different and had a three-fold higher rate of malignancy than that in Lepper's trial.⁷ The underlying difference in study population may account in part for disparate conclusions.

Conclusion

Our retrospective observational study of community-acquired pneumonia admission data revealed that first glucose

measure upon admission did not predict hospital mortality, length of stay, or readmission for community-acquired pneumonia within 30 days. Further research on the impact of hyperglycemia needs to be done in larger, diverse samples of CAP patients.

Author contributions

All authors contributed equally to the conception, design and the drafting of the manuscript. Jonathan D Mahnken was responsible for the statistical analysis. All authors read and approved the final manuscript.

Disclosure

Rajib K Bhattacharya is a promotional speaker and involved in an industry sponsored clinical trial for Sanofi Aventis. Sally K Rigler and Jonathan D Mahnken have no competing interests to declare.

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