#### ORIGINAL ARTICLE

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## Association of admission blood glucose level and clinical outcomes in elderly community-acquired pneumonia patients with or without diabetes

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#### Abstract

**Introduction:** Community-acquired pneumonia (CAP) is the major cause of infection-related mortality worldwide. Patients with CAP frequently present with admission hyperglycemia.

**Objectives:** The aim of this study was to evaluate the association between admission blood glucose (ABG) level and clinical outcomes in elderly CAP patients ( $\geq$ 80 years of age) with or without diabetes.

**Methods:** In this single center retrospective study, 290 elderly patients diagnosed with CAP were included. Demographic and clinical information were collected and compared. The associations between admission blood glucose level and the 30-day mortality as well as intensive care unit (ICU) admission and invasive mechanical ventilation (IMV) in elderly CAP patients with or without diabetes were assessed.

**Results:** Of the 290 eligible patients with CAP, 159 (66.5%) patients were male, and 64 (22.1%) had a known history of diabetes at hospital admission. After adjusting for age and sex, the logistic regression analysis had identified several risk factors that might be associated with clinical outcomes in elderly patients with CAP. Multivariable logistic regression analysis revealed that admission glucose level > 11.1 mmol/L was significant associated with ICU admission, IMV, and 30-day mortality both in non-diabetic and diabetic patients. Furthermore, Kaplan–Meier analysis indicated that patients with higher admission glucose level were correlated statistically significantly with 30-day mortality in patients with CAP (P < 0.001).

**Conclusion:** Admission blood glucose is correlated with 30-day hospital mortality, ICU admission, and IMV of CAP in elderly patients with and without diabetes. Specially, admission glucose > 11.1 mmol/L was a significant risk factor for 30-day hospital mortality.

#### **KEYWORDS**

admission blood glucose, clinical outcomes, community-acquired pneumonia, diabetes mellitus, elderly patients

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#### **1** | INTRODUCTION

Community-acquired pneumonia (CAP) is a commonly encountered pulmonary infectious disease in clinical practice.<sup>1</sup> It is related to diverse causes with complicated pathogen, and its severity varies dramatically from one person to another. CAP is responsible for the high rate of morbidity and mortality in adults from both developed and developing countries, with an estimated annual incidence ranging from 1.6 to 11 per 1000 adult population, which claims a considerable number of lives each year.<sup>2,3</sup> More seriously, the number of patients hospitalized with CAP has been increasing in China, especially among the elderly.<sup>4</sup> Sheng et al. reported in a retrospective analysis of 27 723 hospitalized patients with pneumonia in Shanghai in 2011, which showed that older age groups have a higher incidence, accounting for 44.6% of the total.<sup>5</sup> Another study from Hong Kong in 2016 reported that in 197 316 emergency hospital admissions due to pneumonia, patients older than 65 years as the most common population, accounting for 73.8% of cases.<sup>6</sup> Indeed, it contributes to poor clinical outcomes and increased expenditure burden and medical resources for patients and society at large.

Nowadays, identifying risk factors of CAP prognosis and mortality may provide basis for timely and effective treatment of patients with CAP.<sup>7</sup> Diabetes mellitus is a highly prevalent chronic metabolic disorder that occurs in approximately 5–10% in the older population.<sup>8</sup> Moreover, with the increase in the prevalence of diabetes, the incidence of CAP also increases significantly. Interestingly, several studies have reported that hyperglycemia on admission is an independent risk factor for severe clinical outcomes among patients hospitalized with pneumonia or other respiratory diseases.<sup>9–11</sup> Nonetheless, if admission glucose levels with different diabetes statuses could have a significant effects on elderly patients with CAP have not been well characterized. Therefore, the aim of present study was to evaluate the potential relationship between admission glucose level and the clinical outcomes in elderly patients with and without diabetes presenting with CAP in a hospital-based retrospective cohort study.

### 2 | MATERIALS AND METHODS

#### 2.1 | Study design and participants

The present study was a retrospective observational study conducted at Meizhou People's Hospital, which is a large tertiary hospital in the south of China with over 3000 inpatient beds. We observed 2142 consecutive hospitalized CAP patients that were admitted to Meizhou People's hospital from January 2016 to December 2020. The inclusion criterion was the patient discharged with a confirmed diagnosis of CAP according to the 2016 CAP clinical practice guidelines by the Chinese Thoracic Society.<sup>12</sup> The patients were excluded based on the following criteria (Figure 1): (1) aged <80 years; (2) outpatients; (3) with active tuberculosis; (4) patients with incomplete data in medical records. Finally, 290 patients were



**FIGURE 1** Flow chart of patient recruitment

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included for analysis in this study. The study protocol was reviewed and approved by the Meizhou People's Hospital institutional ethical committee. All procedures complied with the ethical guidelines outlined in the 1975 Helsinki Declaration. Patient consent was waived due to the retrospective nature and observational study design.

### 2.2 | Definitions

CAP was defined as the presence of acute illness with features of lower respiratory tract infection and the presence of consolidation in the chest CT or radiography radiograph. The patients were classified into diabetes and nondiabetes groups according to known diabetes status on admission only. All patients that had admission blood glucose measured were also assigned to three groups in terms of admission glucose level (<6.1 mmol/L, 6.1– 11.1 mmol/L, and >11.1 mmol/L) for analysis. Elderly patients were defined as those aged 80 years and above.

# 2.3 | Data collection and clinical outcomes

Initial data after admission contained demographic, baseline clinical characteristics, and laboratory findings were extracted from the electronic medical record system. For the examination of admission plasma glucose, blood samples were collected within the within 3 h once their admission. The primary outcome was defined as 30-day hospital mortality. The secondary outcomes were consisting of intensive care unit (ICU) admission and/or need for invasive mechanical ventilation (IMV). All patients included in this study were followed up for discharge status (survival/death) or death within 30 days.

#### 2.4 | Statistical analysis

Statistical Packages for Social Sciences (SPSS) software version 20.0. (IBM corp., Armonk, NY, USA) was used for the statistical analysis. Continuous variables are described as medians and interquartile ranges (IQRs). Two-group comparisons were analyzed by Mann-Whitney *U* test, and Kruskal-Wallis test was used to compare more than two groups. Categorical variables were presented as numbers and percentages, and  $\chi^2$  test or Fisher's exact test was utilized to compare their difference, as appropriate. Multivariate logistic analysis for clinical outcomes was performed. The model was adjusted for age and sex. Survival was estimated by the Kaplan-Meier method, and the differences in survival

rates were evaluated with a log-rank test. A P value of <0.01 was considered statistical significance.

#### 3 | RESULTS

# 3.1 | Patient demographic and clinical characteristics

Out of 2142 patients who presented with CAP from January 2016 to December 2020, a total of 1826 patients including age <80 years old, outpatients, with active tuberculosis, and death in the first 12 h of admission were therefore excluded. Another, 26 patients without complete clinical data were also ruled out. Finally, 290 elderly patients with CAP were included in the analysis, as shown in Figure 1. The remaining patients consisted of 159 (66.5%) male and 131(33.5%) female aged 80–98 years.

The demographic and clinical characteristics of the study population are summarized in Table 1, among them, 64 (22.1%) patients with a prior diagnosis of diabetes and 226 (77.9%) of the 290 patients without a history of diabetes. The percentages of hypertension in CAP patients with diabetes were higher than those without diabetes (P < 0.001). However, there were no obvious differences in the incidences of IMV, ICU admission, hospital length of stay, and 30-day mortality between patients with and without diabetes (all P > 0.01). Additionally, patients were divided into 3 groups according to the admission blood glucose level ranging from <6.1, 6.1-11.1, and >11.1 mmol/L, respectively. The percentages of chronic kidney disease and chronic liver disease, as well as the incidences of fatigue and impaired consciousness, and CURB-65 score show differences among the three groups. Moreover, significant differences in the severe CAP on admission, IMV, ICU admission, and 30-day mortality were also found among the three groups (P < 0.01).

#### 3.2 | Laboratory parameters

As shown in Table 2, laboratory parameters at admission were compared. CAP patients with diabetes had a higher white blood cell count, neutrophil count, higher level of uric acid, urea nitrogen, and triglycerides, compared with the non-diabetes patients group (P < 0.01). Furthermore, patients with blood glucose levels 6.1–11.1 or >11.1 mmol/L had a trend towards higher white blood cell count, neutrophil count, higher level of uric acid, urea nitrogen, procalcitonin, C-reactive protein (CRP), and D-dimer compared with patients with blood glucose levels <6.1 mmol/L.

Image: problem         (a - z)		Diabetes	Non-diabetes	Р	Blood glucose < 6.1 mmol/L	Blood glucose 6.1-	Blood glucose > 11.1 mmol/L	Р
		(n = 04)	(077 = u)	value	(n = 14/)	(111 = u) T = 100000 T = 111	(07 = u)	value
Age, years         BS 6 ± 4.1         0.03         S5 ± 4.1         0.03         S5 ± 4.1         0.04         0.04           Nowing, r(s)         3 (4.3.1)         13 (5.3.1)         10 (5.3.1)         10 (5.3.1)         10 (4.4)         0.03           Nowing, r(s)         3 (4.3.1)         13 (0.3.1)         6 (9.3.2)         0.03         85 (7.3.1)         10 (4.4)         0.03           Nowing, r(s)         13 (2.0.3)         6 (9.3.1)         0.13         4 (2.0.3)         13 (4.3.1)         11 (4.3)         0.13           Systel blood presure, m         73 4 ± 1.2         7.4 ± 1.13         7.4 ± 1.13         10.6.9         0.03           Hg         R(*1)         R(*1)         85 (7.9)         0.94         13 (2.4.1)         10.05         0.13           Hg         Lateol presure, m         7.4 ± 1.13         7.4 ± 1.13         7.4 ± 1.13         10.05         0.03           Hg         Lateol presure, m         8.4 ± 1.13         7.6 ± 1.13         0.03         0.13           Hg         Lateol presure, m         7.4 ± 1.13         7.4 ± 1.13         10.05         0.13           Lateol presure, m         4 (4.3)         8.7 ± 1.13         7.2 ± 1.13         0.03         0.04           Lateol presure	Demographics							
	Age, years	$85.1\pm4.2$	$85.4\pm4.1$	0.693	$85.0\pm4.1$	$85.6\pm4.1$	$85.6\pm4.5$	0.504
Smoting, $r(\phi)$ 13 (0.1)         6 (62.2)         0.18         4 (2.9)         3 (1.5)         3 (1.5)         0 (1.5)           Atorb Intake, $r(\phi)$ 13 (0.3)         4 (19.9)         0.94         3 (2.3.4)         13 (3.5)         0 (1.5)           Synth blod presure, mm         73 ± ±12.7         7.4 ± 12.8         13 (4.5)         0.94         3 (2.3.4)         13 (3.5)         0 (1.5)           Fig         73 ± ±12.7         7.4 ± 12.8         13 (4.5)         0.68         7.3 ± 11.5         7.8 ± ±13.9         0 (1.5)         0 (1.5)           Presenting         7.4 ± 12.7         7.4 ± 12.9         0.68         7.9 ± 11.5         7.8 ± ±13.9         0 (1.5)         0 (1.5)           High         7.4 ± 12.7         7.4 ± 12.9         0.68         7.9 ± 11.5         7.8 ± ±13.9         0 (1.5)         0 (1.6)           High         41 (6.1)         8 (7.9)         0.07         5 (2.3.6)         0.91         0 (1.6)         0 (1.6)         0 (1.6)           Higher ension         4 (6.3)         4 (1.6)         0.03         5 (2.4)         0 (1.6)         0 (1.6)         0 (1.6)         0 (1.6)         0 (1.6)         0 (1.6)         0 (1.6)         0 (1.6)         0 (1.6)         0 (1.6)         0 (1.6)	Male, $n$ (%)	29 (45.3)	130 (57.5)	0.083	85 (57.8)	65 (55.6)	9 (34.6)	0.089
	Smoking, $n$ (%)	13 (20.3)	66 (29.2)	0.158	44 (29.9)	32 (27.4)	3 (11.5)	0.152
Systelle blood pressure, run $13.4 \pm 2.63$ $14.6 \pm 2.18$ $0.30$ $14.7 \pm 2.03$ $14.6 \pm 2.18$ $0.30$ $14.7 \pm 2.04$ $130.6 \pm 3.40$ $041$ Pirity $7.4 \pm 2.63$ $14.6 \pm 1.23$ $7.5 \pm 1.23$ $0.65$ $7.7 \pm 1.15$ $28.8 \pm 1.39$ $24.4 \pm 1.78$ $0.65$ $7.7 \pm 1.15$ $24.8 \pm 1.53$ $0.66$ Precessing conorbidities, r(s) $4.613$ $8.639$ $0.001$ $9.6401$ $58.8 \pm 1.59$ $0.613$ $0.613$ Hyperension $4.613$ $8.639$ $0.001$ $9.6411$ $8.739$ $0.639$ $0.639$ Chronic obstructive $0.01$ $14.630$ $0.033$ $5.440$ $0.03$ $5.440$ $0.63$ Chronic obstructive $0.01$ $11.430$ $0.033$ $5.440$ $0.63$ $0.63$ Promote obstructive $0.01$ $11.430$ $0.033$ $5.440$ $0.613$ $0.033$ Chronic obstructive $0.01$ $0.01$ $0.01$ $0.01$ $0.01$ $0.023$ Chronic bistructisenes	Alcohol intake, $n$ (%)	13 (20.3)	45 (19.9)	0.944	33 (22.4)	24 (20.5)	1 (3.8)	060.0
	Systolic blood pressure, mm Hg	$137.4\pm26.5$	$134.6\pm21.8$	0.390	$134.7\pm20.8$	$136.9\pm22.4$	$130.6\pm34.0$	0.418
Pre-ossing controlidities, n (6)         R (33)         S (40.1)         S (470)         S (40)         S (40)         S (400)	Diastolic blood pressure, mm Hg	$78.4\pm12.7$	$77.6 \pm 12.9$	0.658	$77.9 \pm 11.5$	$78.8\pm13.9$	$72.4\pm17.8$	0.068
Hypertension $1(64.1)$ $8(38.9)$ $<001$ $9(401)$ $55(470)$ $15(577)$ $019$ Cardiovascular disease $24(37.5)$ $55(24.3)$ $007$ $35(23.8)$ $35(29.9)$ $15(57.7)$ $013$ Cardiovascular disease $1(6.3)$ $4(1.8)$ $007$ $35(2.3)$ $35(2.9)$ $0(2)$ $0133$ Chronic obstructive $0(0)$ $11(4.9)$ $013$ $5(4.4)$ $0.27$ $0.27$ Chronic obstructive $0(0)$ $11(4.9)$ $013$ $5(4.4)$ $0.27$ $0.27$ Chronic obstructive $1(219)$ $12(26)$ $019$ $2(16.3)$ $0(0)$ $01(4.2)$ Chronic lober disease $1(219)$ $12(26)$ $017$ $2(7.5)$ $0.03$ Chronic lober disease $12(18)$ $21(2.6)$ $071$ $2(7.5)$ $0.03$ Structure $1(142)$ $12(19)$ $12(16)$ $0.72$ $1(142.3)$ $0.01$ Chronic lober disease $12(18)$ $21(2.6)$ $0.73$ $2(7.4)$ $1(142.3)$ $0.01$ Structure $12(18)$ $21(2.6)$ $0.73$ $2(17.4)$ $2(2.1)$ $1(142.3)$ $0.01$ Frigue $12(18)$ $21(2.6)$ $0.73$ $2(12.6)$ $2(14)$ $1(142.3)$ $0.01$ Inpaired conscionences $12(18)$ $21(2.6)$ $0.73$ $2(12.4)$ $1(142.3)$ $0.01$ Inpaired conscionences $12(18)$ $21(2.6)$ $0.73$ $2(12.4)$ $1(142.3)$ $0.01$ Inpaired conscionences $12(18)$ $21(2.6)$ $12(2.6)$ $12($	Pre-existing comorbidities, $n$ (%)							
	Hypertension	41 (64.1)	88 (38.9)	<0.001	59 (40.1)	55 (47.0)	15 (57.7)	0.196
	Cardiovascular disease	24 (37.5)	55 (24.3)	0.037	35 (23.8)	35 (29.9)	9 (34.6)	0.336
Chronic obstructive pulmonary disease         (0)         11 (4.9)         013         5 (3.4)         6 (5.1)         0 (0)         0.274           Chronic kidney disease         14 (2.19)         5 (12.6)         0907         24 (16.3)         30 (25.6)         11 (4.23)         0.008           Chronic kidney disease         14 (6.2)         0.196         24 (16.3)         30 (25.6)         11 (4.23)         0.008           Symptoms at presentation, n(%)         7 (10.9)         14 (6.2)         0.782         23 (15.6)         6 (5.1)         6 (23.1)         0.008           Faigue         12 (18.8)         30 (17.3)         0.782         14 (9.5)         5 (21.4)         11 (4.23)         0.001           Faigue         12 (18.8)         30 (17.3)         0.782         14 (9.5)         25 (1.4)         25 (21.4)         12 (46.2)         0.001           Faigue         12 (18.8)         30 (17.3)         0.782         14 (9.5)         25 (1.4)         25 (21.4)         12 (46.2)         0.001           Faigue         12 (18.8)         30 (17.6)         0.782         14 (9.5)         25 (1.4)         12 (46.2)         0.001           Faigue         18 (8.1)         12 (8.1)         0.782         12 (8.30)         12 (8.2) <t< td=""><td>Cardiac failure</td><td>4 (6.3)</td><td>4(1.8)</td><td>0.053</td><td>2 (1.4)</td><td>4 (3.4)</td><td>2 (7.7)</td><td>0.213</td></t<>	Cardiac failure	4 (6.3)	4(1.8)	0.053	2 (1.4)	4 (3.4)	2 (7.7)	0.213
	Chronic obstructive pulmonary disease	0 (0)	11 (4.9)	0.153	5 (3.4)	6 (5.1)	0 (0)	0.274
	Chronic kidney disease	14 (21.9)	51 (22.6)	0.907	24 (16.3)	30 (25.6)	11 (42.3)	0.008
Symptoms at presentation, n(%)Fatigue12 (18.8)51 (22.6)0.51323 (15.6)10 (38.5)0.014Impaired consciousness12 (18.8)51 (22.6)0.51323 (15.6)12 (46.2)0.011Impaired consciousness12 (18.8)39 (17.3)0.78214 (9.5)25 (21.4)12 (46.2)<001	Chronic liver disease	7 (10.9)	14 (6.2)	0.196	9 (6.1)	6 (5.1)	6 (23.1)	0.005
	Symptoms at presentation, $n$ (%)							
	Fatigue	12(18.8)	51 (22.6)	0.513	23 (15.6)	30 (25.6)	10 (38.5)	0.014
URB-65 score, $n$ (%)         1-2       46 (71.9)       172 (76.1)       0.478       122 (83.0)       85 (72.6)       11 (42.3)       <0.001	Impaired consciousness	12 (18.8)	39 (17.3)	0.782	14 (9.5)	25 (21.4)	12 (46.2)	<0.001
	CURB-65 score, $n$ (%)							
3-4 $18 (28.1)$ $54 (23.9)$ $25 (17.0)$ $32 (27.4)$ $15 (57.7)$ Clinical outcomesLinvasive mechanical $14 (21.9)$ $50 (22.1)$ $0.966$ $18 (12.2)$ $33 (28.2)$ $13 (50.0)$ Invasive mechanical $17 (26.6)$ $88 (38.9)$ $0.069$ $60 (40.8)$ $30 (25.6)$ $13 (50.0)$ $-0.001$ ICU admission $17 (26.6)$ $88 (38.9)$ $0.069$ $60 (40.8.0)$ $30 (25.6)$ $15 (57.7)$ $0.002$ Hospital length of stay (days) <sup>a</sup> $60 (4.0-8.0)$ $0.561$ $50 (4.0-8.0)$ $6.0 (4.0-8.0)$ $50 (2.0-12.5)$ $0.591$ $30$ -day mortality (%) $3 (4.6)$ $8 (3.54)$ $0.957$ $3 (2.04)$ $3 (2.56)$ $5 (19.23)$ $0.591$	1-2	46 (71.9)	172 (76.1)	0.478	122 (83.0)	85 (72.6)	11 (42.3)	<0.001
Clinical outcomes         Invasive mechanical $14(21.9)$ $50(22.1)$ $0.966$ $18(12.2)$ $33(28.2)$ $13(50.0)$ $<0001$ ventilation $17(26.6)$ $88(38.9)$ $0.069$ $60(40.8)$ $30(25.6)$ $15(57.7)$ $0.002$ Hospital length of stay (days) <sup>a</sup> $6.0(4.0-8.0)$ $6.0(4.0-8.0)$ $0.561$ $5.0(4.0-8.0)$ $5.0(2.0-12.5)$ $0.501$ $30$ -day mortality (%) $3(4.69)$ $8(3.54)$ $0.957$ $3(2.04)$ $3(2.56)$ $5.(19.23)$ $0.004$	3-4	18 (28.1)	54 (23.9)		25 (17.0)	32 (27.4)	15 (57.7)	
Invasive mechanical $14(21.9)$ $50(22.1)$ $0.966$ $18(12.2)$ $33(28.2)$ $13(50.0)$ $<0.001$ ventilation $17(26.6)$ $88(38.9)$ $0.069$ $60(40.8)$ $30(25.6)$ $15(57.7)$ $0.002$ ICU admission $17(26.6)$ $88(38.9)$ $0.069$ $60(40.8.0)$ $30(25.6)$ $15(57.7)$ $0.002$ Hospital length of stay (days) <sup>a</sup> $6.0(4.0-8.0)$ $0.561$ $5.0(4.0-8.0)$ $6.0(4.0-8.0)$ $0.501$ $0.057$ $3(2.56)$ $5.0(2.0-12.5)$ $0.591$ 30-day mortality (%) $3(4.69)$ $8(3.54)$ $0.957$ $3(2.04)$ $3(2.56)$ $5(19.23)$ $0.004$	Clinical outcomes							
ICU admission $17 (26.6)$ $88 (38.9)$ $0.069$ $60 (40.8)$ $30 (25.6)$ $15 (57.7)$ $0.002$ Hospital length of stay (days) <sup>a</sup> $6.0 (4.0-8.0)$ $6.0 (4.0-8.0)$ $0.561$ $5.0 (4.0-8.0)$ $6.0 (2.0-12.5)$ $0.591$ $30$ -day mortality (%) $3 (4.69)$ $8 (3.54)$ $0.957$ $3 (2.04)$ $3 (2.56)$ $5 (19.23)$ $0.004$	Invasive mechanical ventilation	14 (21.9)	50 (22.1)	0.966	18 (12.2)	33 (28.2)	13 (50.0)	<0.001
Hospital length of stay (days) <sup>a</sup> $6.0 (4.0-8.0)$ $6.0 (4.0-8.0)$ $0.561$ $5.0 (4.0-8.0)$ $6.0 (4.0-8.0)$ $0.51$ $30$ -day mortality (%) $3 (4.69)$ $8 (3.54)$ $0.957$ $3 (2.04)$ $3 (2.56)$ $5 (19.23)$ $0.004$	ICU admission	17 (26.6)	88 (38.9)	0.069	60 (40.8)	30 (25.6)	15 (57.7)	0.002
30-day mortality (%)         3 (4.69)         8 (3.54)         0.957         3 (2.04)         3 (2.56)         5 (19.23)         0.004	Hospital length of stay (days) <sup>a</sup>	6.0 (4.0-8.0)	6.0(4.0 - 8.0)	0.561	5.0 (4.0-8.0)	6.0(4.0-8.0)	5.0 (2.0–12.5)	0.591
	30-day mortality (%)	3 (4.69)	8 (3.54)	0.957	3 (2.04)	3 (2.56)	5 (19.23)	0.004

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*Note:* Values are expressed as the mean  $\pm$  statutation  $\ldots$ . Abbreviation: ICU, intensive care unit.<sup>a</sup>Data were expressed as medians (interquartile range).

LE 2 Comparis	on of laboratory param	aeters among subgroup	os at admis	sion			1
	Diabetes $(n = 64)$	Non-diabetes $(n = 226)$	<i>P</i> value	Blood glucose < 6.1 mmol/L (n = 147)	Blood glucose 6.1– 11.1 mmol/L $(n = 117)$	Blood glucose > 11.1 mmol/L (n = 26)	<i>P</i> value
lood cell t, ×10 <sup>9</sup> /L	11.6(8.43–15.8)	9.10(6.60–12.8)	0.001	8.20(6.30–12.0)	10.6(8.20–14.6)	12.1(9.83–14.8)	<0.001
hil count, /L	9.00(6.18–13.4)	7.10(4.80 - 10.1)	0.002	6.20(4.40–8.80)	8.50(6.40–12.6)	9.40(6.88–12.5)	<0.001
d, μmol/L	379.8(274.0–499.4)	311.6(232.0-405.1)	0.005	319.3(240.8–409.5)	311.9(215.2-422.7)	445.5(282.4–609.6)	0.034
trogen, ol/L	7.82(5.68–11.5)	6.35(4.83–9.01)	0.005	5.91(4.80 - 8.51)	6.98(5.11–9.57)	10.0(6.35-22.3)	0.001
erides, mmol/	1.27(1.00–1.77)	0.96(0.77–1.27)	<0.001	0.97(0.79–1.32)	1.12(0.76–1.38)	1.13(0.74–1.81)	0.535
itonin, ng/ml	0.25(0.05–2.28)	0.21(0.05 - 1.27)	0.474	0.11(0.05-0.65)	0.38(0.06–2.88)	0.65(0.18–5.06)	<0.001
g/L	41.3(10.6–104.3)	44.4(12.2–99.4)	0.982	34.3(8.97–85.0)	62.7(15.9–110.2)	64.4(7.98–106.7)	0.024
r, μg/ml	1.47(0.70 - 3.00)	1.70(0.85 - 3.00)	0.490	1.34(0.66-2.57)	2.06(1.18-3.12)	2.71(1.51-5.00)	<0.001
s were expressed	as the median (interquar	tile range).					

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#### 3.3 **Clinical outcomes**

Of the 290 patients hospitalized with CAP, 185 (63.8%) were admitted to the general ward, and 105 (36.2%) were admitted to ICU, respectively. During the admission, 28 (9.7%) patients had a CURB-65 score  $\geq 4$ , 118 (40.7%) patients required O<sub>2</sub> on arrival, and 43 (14.8%) patients needed IMV. The average length of stays from admission to discharge was 6 days. The average length of ICU stays in the hospital was 5 days, and the average duration of IMV was 4 days, respectively. Of these patients, there were 11 (3.8%) reported death in the patients with CAP, and the average time from admission to death was 2 days. These data are described in detail in Figure 2.

#### **Risk factors for clinical outcomes** 3.4

As shown in Table 3, after adjusting for age and sex, logistic regression analysis was utilized to identify the risk factors that might be associated with clinical outcomes in elderly patients with CAP. From our analysis, several risk factors related to 30-day mortality or the incidence of ICU admission were chronic kidney disease, sepsis, and urea nitrogen > 8.2 mmol/L (P < 0.01). Meanwhile, we also found various risk factors associated with required IMV including chronic kidney disease, chronic liver disease, sepsis, neutrophil count >  $6.3 \times 10^9$ /L, urea nitrogen > 8.2 mmol/L, and procalcitonin > 0.5 ng/ml (P < 0.01).

#### 3.5 | Associations between diabetes, admission glucose level, and clinical outcomes

Among all patients, as is presented in Table 4, after adjusting for age and sex, multivariable logistic regression analysis revealed that admission glucose level > 11.1 mmol/L was significantly associated with ICU admission, IMV, and 30-day mortality both in nondiabetic and diabetic patients (Table 4). In addition, the adjusted odds ratios (ORs) for the association between admission glucose level (>6.1 mmol/L) and IMV in the general population were 2.87 (95% CI: 1.42-5.81, P = 0.003) and 3.20 (95% CI: 1.50–6.82, P = 0.003) in the non-diabetic patients. Furthermore, patients with admission glucose level > 11.1 mmol/L had a significantly higher ICU admission, IMV, and 30-day mortality than in the patients with admission glucose level  $\leq 11.1 \text{ mmol/L}$ , regardless of whether there is a known history of diabetes.

Abbreviation: CRP, C-reactive protein.



**FIGURE 2** Management and outcomes of all patients (n = 290). (A) Percentage (%) of patients admitted to ward and intensive care unit (ICU); (B) percentage (%) of patients who received (X) intervention; (C) median number of days from admission for patients; (D) final outcome of patients

	Outcomes					
	30-day mortality		ICU admission		Invasive mechani	cal ventilation
Risk factor	OR (95% CI)	P value	OR (95% CI)	P value	OR (95% CI)	P value
Pre-existing comorbidities						
Chronic kidney disease	14.8 (3.0–72.6)	0.001	3.85 (2.15-6.89)	< 0.001	6.21 (3.09–12.5)	< 0.001
Chronic liver disease	4.37 (0.80-23.7)	0.088	2.76 (1.11-6.91)	0.030	7.78 (2.94–20.6)	< 0.001
Sepsis	6.82 (1.71–27.3)	0.007	4.30 (1.58–11.7)	0.004	8.58 (3.23-22.8)	< 0.001
Laboratory parameters						
Neutrophil count, >6.3 $\times$ 10 <sup>9</sup> /L	0.93 (0.26-3.37)	0.911	1.41 (0.84–2.34)	0.191	3.06 (1.35-6.93)	0.007
Urea nitrogen, >8.2 mmol/L	20.5 (2.55–164.5)	0.004	2.39 (1.43-3.97)	0.001	3.78 (1.92-7.42)	< 0.001
Procalcitonin, >0.5 ng/ml	14.5 (1.76–119.6)	0.013	1.65 (0.99–2.74)	0.055	3.71 (1.78-7.72)	< 0.001

TABLE 3 Factors for outcomes of interest using the multivariate logistic regression analysis

Abbreviations: CI, confidence interval; ICU, intensive care unit; OR, odds ratio.

The relationship between admission glucose level, diabetic status, and 30-day mortality was also evaluated using a Kaplan–Meier analysis, as shown in Figure 3. No statistically significant difference was found in the 30-day mortality between the patients with and without a history of diabetes (P = 0.724). However, higher admission glucose level was correlated statistically significantly with 30-day mortality in elderly patients with CAP (P < 0.001).

#### 4 | DISCUSSION

The incidence of CAP is increasing and is deemed to be the significant cause of infection-related mortality worldwide. This study investigated the association between admission blood glucose level and clinical outcomes, including 30-day mortality, ICU admission, and IMV, in elderly CAP patients with or without diabetes. Our results identified elevated blood glucose level on 568 WILEY-

TABLE 4 Association between blood glucose levels and severe outcome in patients with and without diabetes mellitus

Variables	Adjusted OR (95% CI)	P value
ICU admission		
Blood glucose >6.1 mmol/L	0.67 (0.41–1.09)	0.110
Blood glucose >11.1 mmol/L	3.02 (1.31-6.99)	0.010
Nondiabetes patients		
Blood glucose >6.1 mmol/L	0.74 (0.42–1.30)	0.292
Blood glucose >11.1 mmol/L	6.78 (1.34–34.2)	0.020
Diabetes patients		
Blood glucose >6.1 mmol/L	0.82 (0.19–3.63)	0.821
Blood glucose >11.1 mmol/L	4.34 (1.20–15.7)	0.025
Invasive mechanical ventilation		
Blood glucose >6.1 mmol/L	2.87 (1.42–5.81)	0.003
Blood glucose >11.1 mmol/L	5.52 (2.20–13.9)	< 0.001
Nondiabetes patients		
Blood glucose >6.1 mmol/L	3.20 (1.50-6.82)	0.003
Blood glucose >11.1 mmol/L	10.1 (2.39–42.5)	0.002
Diabetes patients		
Blood glucose >6.1 mmol/L	-	-
Blood glucose >11.1 mmol/L	8.40 (1.50-46.9)	0.015
In-hospital mortality		
Blood glucose >6.1 mmol/L	3.15 (0.79–12.5)	0.103
Blood glucose >11.1 mmol/L	18.5 (4.21–80. 9)	< 0.001
Nondiabetes patients		
Blood glucose >6.1 mmol/L	2.56 (0.59–11.1)	0.212
Blood glucose >11.1 mmol/L	14.4 (2.12–98.4)	0.006
Diabetes patients		
Blood glucose >6.1 mmol/L	-	
Blood glucose >11.1 mmol/L	-	

The ORs of blood glucose >6.1 mmol/L were with reference to patients with glucose  $\leq$ 6.1 mmol/L; the ORs of blood glucose >11.1 mmol/L were with reference to patients with glucose  $\leq$ 11.1 mmol/L.

Abbreviations: CI, confidence interval; ICU, intensive care unit; OR, odds ratio.



**FIGURE 3** Kaplan–Meier curves of survival rate for patients. (A) Kaplan–Meier curves for community-acquired pneumonia (CAP) patients with or without diabetes. (B) Kaplan–Meier curves for CAP patients with different admission blood glucose level admission as significant predictors in all outcomes of interest (30-day mortality, ICU admission, and IMV). Further, Kaplan–Meier analysis revealed that the 30-day mortality after admission for CAP was related to higher glucose level determined on admission, irrespective of diabetes status at presentation. Therefore, admission blood glucose level might serve as an independent highly significant parameter for the prognosis of elderly CAP patients and particular attention of clinicians should be paid to these patients.

A large population-based study reported that among patients hospitalized with pneumonia, of which 21% were admitted to ICU, 6% required IMV, and 2% died.<sup>2</sup> Our study results found that (36.2%) patients were admitted to the ICU, 14.8% patients required IMV, and 3.8% died, which is higher than that in the aforementioned report. The disease severity of patients admitted with CAP is highly influenced by age and comorbidities.<sup>13</sup> The elderly may be accompanied by a variety of basic diseases, such as cardiovascular and cerebrovascular disease. hypertension, diabetes, and renal that failure may exacerbate the degree of the disease and seriously affect the prognosis of the CAP patient.<sup>14,15</sup> Similar to many studies throughout the world, we found the complications including hypertension and cardiovascular disease were more commonly observed in patients with diabetes. It was noted that chronic kidney disease, chronic liver disease, and sepsis may contribute to the adverse outcomes of elderly CAP patients in this population; this is consistent with previous literature reports.<sup>16</sup>

Patients with infectious diseases frequently present with abnormal blood glucose level, especially in influenza and pneumonia.<sup>10,11</sup> Increasing evidence suggests that hyperglycemia is associated with higher mortality and adverse short-term outcomes across a spectrum of critical illnesses.<sup>17–19</sup> Patients with elevated glucose level are likely to be accompanied by a huge increase of inflammatory mediators and the impaired activation of neutrophils and phagocytosis, which ultimately give rise to exacerbating infection status.<sup>20,21</sup> Besides, stress hyperglycemia is further aggravated by pancreatic islet cell injury or hepatogenic insulin resistance.<sup>22</sup> It is likely then, these conditions will become the major risk factor for critical illnesses and their poor prognosis. However, despite numerous studies that have documented these associations, shreds of evidences on the relationship between hyperglycemia on admission and the prognosis in patients with acute respiratory illness remain elusive, especially in patients with the presence or absence of diabetes.

Importantly, there is also debate on the relationship between admission glucose fluctuation and CAP. For

example, one earlier study found that admission hyperglycemia was a strong predictor of 30-day mortality in both pneumonia patients with and without diabetes.<sup>23</sup> Similar to the above study, our results suggested that elevated admission glucose level was significantly associated with a higher risk of ICU admission, IMV, and 30-day hospital mortality in elderly patients with CAP, regardless of the presence of diabetes. Further Kaplan-Meier survival analysis also demonstrated that elderly CAP patients with admission glucose >11.1 mmol/L had an increased risk of death. However, Jensen et al. reported that only in patients without diabetes, an elevated admission blood glucose was associated with risk for ICU admittance and a trend towards higher in-hospital mortality.<sup>24</sup> Lepper et al. also reported that an increased serum glucose level at admission was an independent predictor of death at 28 and 90 days in patients with CAP without pre-existing diabetes.<sup>25</sup> A recent study reported by Cheng et al. indicated that hyperglycemia is one of the factors for in-hospital mortality among patients with diabetes mellitus and concomitant CAP.<sup>26</sup> Conversely, Bhattacharya et al. found that admission glucose level was not associated with adverse outcomes within 30 days in older patients with CAP.<sup>27</sup> As the above studies were limited to the specific geographical area or single healthcare system, therefore, it is difficult to reach a unanimous conclusion on the research results. The reasons for these discrepancies are presumed to be multifactorial, such as the study population, absence of standard definitions, lack of control cohorts and selection or information biases makes it difficult to consistently determine.

The following limitations of the study have to be mentioned. Firstly, our study is a retrospective study with relatively small sample at a single center; therefore, our findings may not be broadly applicable. In addition, we measured only blood glucose at admission, not dynamic blood glucose during hospitalization nondynamic observation of blood glucose during hospitalization may be another reason for this result. Further clinical research of larger samples is still needed to confirm our results.

In conclusion, we found that admission blood glucose is correlated with in-hospital mortality, ICU admission, and IMV of CAP in elderly patients with without diabetes. In addition, admission and glucose > 11.1 mmol/L was a significant risk factor for death in elderly patients with CAP. Our study suggests that admission blood glucose may be used as an important and useful clinical tool for early and effective risk assessment of CAP in elderly patients, and further studies should be conducted to evaluate this possibility.

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#### **CONFLICT OF INTEREST**

The authors declare that they have no competing interests. No conflict of interest exits in the submission of this manuscript, and all the authors listed have approved the manuscript that is enclosed. The manuscript has been approved by all authors for publication.

#### ETHICS STATEMENT

All procedures complied with the ethical guidelines outlined in the 1975 Helsinki Declaration and approved by the Ethics Committee of Meizhou People's Hospital (Huangtang Hospital) (number: 2020-C-118). Patients' consent was waived due to the retrospective nature and observational study design.

#### **AUTHOR CONTRIBUTIONS**

Author WZ contributed to study design and interpretation of results and revised the final manuscript for publication. XH and WZ contributed to the analysis of results and wrote the manuscript. WL and MC supervised patients' recruitment and collected the clinical data. All authors read and approved the final manuscript.

#### DATA AVAILABILITY STATEMENT

The datasets generated and/or analyzed during the current study are not publicly available due to the fact that individual privacy could be compromised but are available from the corresponding author on reasonable request.

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#### REFERENCES

1. Estimates of the global. Regional, and national morbidity, mortality, and aetiologies of lower respiratory tract infections in 195 countries: a systematic analysis for the Global Burden of Disease Study 2015. *Lancet Infect Dis.* 2017;17(11): 1133-1161.

- Jain S, Self WH, Wunderink RG, et al. Community-acquired pneumonia requiring hospitalization among U.S. Adults N Engl J Med. 2015;373(5):415-427. doi:10.1056/NEJMoa1500245
- Han X, Chen L. Cost effectiveness of different initial antimicrobial regimens for elderly community-acquired pneumonia patients in general ward. *Infect Drug Resist.* 2021;14:1845-1853.
- Çelikhisar H, Daşdemir Ilkhan G, Arabaci Ç. Prognostic factors in elderly patients admitted to the intensive care unit with community-acquired pneumonia. *Aging Male.* 2020;23(5): 1425-1431. doi:10.1080/13685538.2020.1775192
- 5. Song SF, Lu YE, Shan-Lian HU, Li-Xia DU, Shi Q. The analysis for inpatients cost of pneumococcal diseases in Shanghai. *Chin Health Res.* 2014;17(4):277-280.
- 6. Qiu H, Sun S, Tang R, Chan KP, Tian L. Pneumonia hospitalization risk in the elderly attributable to cold and hot temperatures in Hong Kong. *China Am J Epidemiol.* 2016;184(8): 555-569.
- Ma CM, Wang N, Su QW, Yan Y, Yin FZ. The performance of CURB-65 and PSI for predicting in-hospital mortality of community-acquired pneumonia in patients with type 2 diabetes compared with the non-diabetic. *Population*. 2021;14: 1359-1366.
- Mao W, Yip CW, Chen W. Complications of diabetes in China: health system and economic implications. *BMC Public Health*. 2019;19(1):269. doi:10.1186/s12889-019-6569-8
- Popovic M, Blum CA, Nigro N, Mueller B, Schuetz P, Christ-Crain M. Benefit of adjunct corticosteroids for communityacquired pneumonia in diabetic patients. *Diabetologia*. 2016; 59(12):2552-2560. doi:10.1007/s00125-016-4091-4
- Arias Fernández L, Pardo Seco J, Cebey-López M, et al. Differences between diabetic and non-diabetic patients with community-acquired pneumonia in primary care in Spain. *BMC Infect Dis.* 2019;19(1):973. doi:10.1186/s12879-019-4534-x
- Wang S, Ma P, Zhang S, et al. Fasting blood glucose at admission is an independent predictor for 28-day mortality in patients with COVID-19 without previous diagnosis of diabetes: a multi-centre retrospective study. *Diabetologia*. 2020; 63(10):2102-2111. doi:10.1007/s00125-020-05209-1
- Cao B, Huang Y, She DY, et al. Diagnosis and treatment of community-acquired pneumonia in adults: 2016 clinical practice guidelines by the Chinese Thoracic Society, Chinese Medical Association. *Clin Respir J.* 2018;12(4):1320-1360. doi:10. 1111/crj.12674
- Cillóniz C, Dominedò C, Pericàs JM, Rodriguez-Hurtado D, Torres A. Community-acquired pneumonia in critically ill very old patients: a growing problem. *Eur Respir Rev.* 2020;29(155): 190126.
- Blanc E, Chaize G, Fievez S, et al. The impact of comorbidities and their stacking on short- and long-term prognosis of patients over 50 with community-acquired pneumonia. *BMC Infect Dis.* 2021;21(1):949. doi:10.1186/s12879-021-06669-5
- Luna CM, Palma I, Niederman MS, et al. The impact of age and comorbidities on the mortality of patients of different age groups admitted with community-acquired pneumonia. *Ann Am Thorac Soc.* 2016;13(9):1519-1526. doi:10.1513/AnnalsATS. 201512-848OC
- 16. Aston SJ, Ho A, Jary H, et al. Etiology and Risk Factors for Mortality in an Adult Community-Acquired Pneumonia

Cohort in Malawi. *Am J Respir Crit Care Med.* 2019;200(3): 359-369. doi:10.1164/rccm.201807-1333OC

- Lazzeri C, Bonizzoli M, Cianchi G, Ciapetti M, Socci F, Peris A. The prognostic role of peak glycemia and glucose variability in trauma: a single-center investigation. *Acta Diabetol.* 2020;57(8):931-935. doi:10.1007/s00592-020-01493-w
- 18. Yazawa Y, Ohira T, Itabashi R, et al. Association of Admission Hyperglycemia with clinical outcomes in Japanese patients with acute large vessel occlusion stroke: a post hoc analysis of the recovery by endovascular salvage for cerebral ultra-acute embolism Japan registry 2. *Cerebrovasc Dis.* 2021;50(1):12-19. doi:10.1159/000511679
- Lin S, He W, Zeng M. Association of diabetes and admission blood glucose levels with short-term outcomes in patients with critical illnesses. J Inflamm Res. 2020;13:1151-1166. doi:10. 2147/JIR.S287510
- Baker EH, Baines DL. Airway glucose homeostasis: a new target in the prevention and treatment of pulmonary infection. *Chest.* 2018;153(2):507-514. doi:10.1016/j.chest.2017. 05.031
- 21. Zhang W, Li C, Xu Y, et al. Hyperglycemia and correlated high levels of inflammation have a positive relationship with the severity of coronavirus disease 2019. *Mediators Inflamm*. 2021; 2021:8812304.
- Sharma RB, Landa-Galván HV, Alonso LC. Living Dangerously: Protective and Harmful ER Stress Responses in Pancreatic β-Cells. *Diabetes*. 2021;70(11):2431-2443. doi:10.2337/ dbi20-0033
- Kornum JB, Thomsen RW, Riis A, Lervang HH, Schønheyder HC, Sørensen HT. Type 2 diabetes and pneumonia outcomes: a population-based cohort study. *Diabetes Care*. 2007;30(9):2251-2257. doi:10.2337/dc06-2417

- 24. Jensen AV, Egelund GB, Andersen SB, Trier Petersen P, Benfield T. The impact of blood glucose on communityacquired pneumonia: a retrospective cohort study. *ERJ Open Res.* 2017;3(2):00114-02016.
- Lepper PM, Ott S, Nuesch E, et al. Serum glucose levels for predicting death in patients admitted to hospital for community acquired pneumonia: prospective cohort study. *BMJ*. 2012;344(may28 4):e3397. doi:10.1136/bmj.e3397
- Cheng S, Hou G, Liu Z, et al. Risk prediction of in-hospital mortality among patients with type 2 diabetes mellitus and concomitant community-acquired pneumonia. *Ann Palliat Med.* 2020;9(5):3313-3325. doi:10.21037/apm-20-1489
- 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;6:341-344. doi: 10.2147/IJGM.S42854

#### SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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