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LETTER TO THE EDITOR

WILEY

Admission fasting blood glucose predicts 30-day poor outcome in patients hospitalized for COVID-19 pneumonia

To the Editor:

The rapid spread of coronavirus disease 2019 (COVID-19) has posed a major and urgent threat to global health. As of 23 June 2020, there were more than 9.17 million confirmed cases with 473 266 deaths.[1] The clinical spectrum of COVID-19 ranges from mild to critically ill. While most patients with COVID-19 had mild acute

TABLE 1 Risk factors associated with poor 30-day outcome in univariable and multivariable logistic regression analysis

	Univariable		Multivariable	
	OR (95% CI)	*P* value	OR (95% CI)	*P* value
Age (years)	1.075 (1.054, 1.096)	<.001	1.060 (1.019, 1.103)	.006
Male	1.728 (1.031, 2.896)	.038	1.232 (0.416, 3.651)	.706
Co-morbidities (number)	2.296 (1.749, 3.014)	<.001	1.454 (0.914, 2.313)	.114
Laboratory findings				
WBC ($\times 10^9$/L)	1.223 (1.122, 1.334)	<.001	1.390 (0.448, 4.319)	.569
Neutrophil ($\times 10^9$/L)	1.305 (1.190, 1.432)	<.001	0.907 (0.282, 2.919)	.869
Lymphocyte ($\times 10^9$/L)	0.129 (0.067, 0.248)	<.001	1.268 (0.274, 5.857)	.761
LDH (U/L)	1.010 (1.007, 1.012)	<.001	1.008 (1.003, 1.013)	.002
Hemoglobin (g/L)	1.002 (0.989, 1.015)	.812		
Platelet (g/L)	0.994 (0.990, 0.997)	.001	0.994 (0.987, 1.002)	.147
Albumin (g/L)	0.827 (0.783, 0.873)	<.001	1.022 (0.906, 1.153)	.727
AST (U/L)	1.029 (1.017, 1.041)	<.001	1.017 (0.991, 1.043)	.200
ALT (U/L)	1.004 (0.996, 1.011)	.344		
DBIL (μmol/L)	1.176 (1.078, 1.284)	<.001	1.163 (0.993, 1.361)	.061
IBIL (μmol/L)	0.932 (0.873, 0.994)	.032	0.882 (0.741, 1.049)	.155
TBIL (μmol/L)	1.016 (0.986, 1.046)	.299		
APTT (s)	1.017 (0.979, 1.058)	.381		
PT (s)	1.038 (0.996, 1.081)	.080	1.032 (0.993, 1.073)	.108
D-dimer (μg/ml)	1.002 (0.999, 1.004)	.285		
Creatinine (μmol/L)	1.023 (1.012, 1.034)	<.001	1.004 (0.992, 1.017)	.510
CK (U/L)	1.004 (1.002, 1.006)	<.001	1.003 (0.999, 1.006)	.142
CK-MB (U/L)	1.078 (1.044, 1.112)	<.001	1.001 (0.944, 1.061)	.972
Hs-CRP (mg/L)	1.013 (1.007, 1.019)	<.001	0.989 (0.978, 1.000)	.047
Procalcitonin (ng/ml)	1.124 (1.036, 1.220)	.005	1.043 (0.906, 1.201)	.558
Urea nitrogen (mmol/L)	1.293 (0.909, 1.839)	.153		
FBG (mmol/L)	1.316 (1.206, 1.435)	<.001	1.155 (1.013, 1.317)	.032
CT score	0.953 (0.887, 1.024)	.188		

Abbreviations: ALT, alanine aminotransferase; APTT, activated partial thromboplastin time; AST, aspartate aminotransferase; CK, creatine kinase; CK-MB, creatine kinase MB; DBIL, direct bilirubin; FBG, fasting blood glucose; hs-CRP, high-sensitivity C-reactive protein; IBIL, indirect bilirubin; LDH, lactate dehydrogenase; PT, prothrombin time; TBIL, total bilirubin; WBC, white blood cells. Co-morbidities included diabetes, hypertension, coronary heart disease, chronic liver diseases, chronic lung diseases and surgical history. The total number of co-morbidities per patient was summed up.

respiratory infection symptoms, some could rapidly develop fatal complications, such as acute respiratory distress syndrome (ARDS) or respiratory failure, multiple organ dysfunction (MOD), septic shock, or even death.[2] To date, no specific treatments have been recommended for COVID-19 except for meticulous supportive care[3]; thus, early identification of patients with a high risk of poor outcome may facilitate the provision of timely supportive treatment in advance and reduce mortality. Although several clinical and laboratory variables have been identified as predictors for poor prognosis among COVID-19 patients,[4–6] data regarding the prognostic value of fasting blood glucose (FBG) are scarce. Herein, we evaluated the admission FBG for predicting 30-day outcome in COVID-19 patients.

Patients with laboratory-confirmed COVID-19, who were admitted to six designated hospitals for COVID-19 treatment from 1 January to 31 March 2020, were retrospectively enrolled. We collected clinical and laboratory data at hospital admission. A semi-quantitative computed tomography (CT) scoring system was designed to assess the involvement degree or area of pneumonia for each lung lobe (for a total of five lung lobes): 0 for 0% involvement, 1 for 1%-25% involvement, 2 for 26%-50% involvement, 3 for 51%-75% involvement and 4 for 76%-100% involvement.[7] A CT score (range: 0-20) was assigned by summarizing the total scores of the five lung lobes. CT images were reviewed independently by two radiologists, each with more than 10 years of experience. Poor 30-day outcome was defined as composite adverse endpoints, including ARDS, intensive care unit (ICU) admission, septic shock, MOD, or death within 30 days of admission. ARDS was defined according to the Berlin definition.[8] Criteria for MOD included multilobar infiltrates and other organ damage, such as damage to the cardiovascular system, acute liver function damage and acute kidney injury.[9] Baseline features were compared between patients with poor and good 30-day outcomes (Appendix **S1**). The optimal cutoff FBG for discriminating COVID-19 patients with poor and good outcomes was determined by receiver operating characteristic analysis (Appendix S2) and by maximizing the Youden index. To identify predictors for poor 30-day outcome, baseline variables with $P < .10$ in univariable analysis were entered into multivariate logistic regression.

A total of 461 COVID-19 patients were included, of whom 61 (13.2%) developed ARDS, eight (1.7%) developed septic shock, seven (1.5%) developed MOD, 21 (4.6%) required ICU care and 41 (8.9%) died within 30 days of admission. Forty-six patients (10.0%) had pre-existing diabetes, 18 (23.1%) had a poor outcome and 28 (7.3%) had a good outcome ($P < .001$). Patients with a poor outcome had a higher FBG level (9.91 ± 7.61 mmol/L) than those with a favourable outcome (5.92 ± 2.30 mmol/L, $P < .001$). The optimal FBG for predicting poor 30-day outcome was ≥6.23 mmol/L, with an area under the curve of 0.817 (95% CI: 0.765-0.868), sensitivity of 75.6% and specificity of 77.0%. On multivariate analysis, admission FBG was associated with poor 30-day outcome (odds ratio [OR] 1.155, 95% CI: 1.013-1.317, $P = .032$) (Table 1). After adjusting for pre-existing diabetes, the OR of FBG increased to 1.217 (95% CI: 1.054-1.405, $P = .008$).

We found that admission FBG was an independent predictor for 30-day outcome of COVID-19 patients. Hyperglycaemia is mainly caused by diabetes and stress or acute hyperglycaemia.[10] According to a recent meta-analysis, the pooled prevalence for diabetes in patients with COVID-19 was 11.5%.[11] Diabetes has been identified as a crucial risk factor for mortality and progression in hospitalized patients with COVID-19.[12] COVID-19 patients with diabetes may also experience severe complications, such as ketosis, ketoacidosis or diabetic ketoacidosis.[13] Patients with newly diagnosed diabetes had poorer outcomes than those with known diabetes.[14] Acute hyperglycaemia has frequently been observed in patients without diabetes, which may be induced by a decrease of insulin secretion and the appearance/worsening of insulin resistance.[15] Acute hyperglycaemia may cause organ damage by inducing endothelial dysfunction and thrombosis through the glycation process and oxidative stress generation.[16] Continuous glucose monitoring is necessary for patients with diabetes and acute hyperglycaemia. Glucose control helps to prevent and control infections and their complications. Therefore, well-controlled blood glucose may lead to improved outcomes for patients with COVID-19.[16,17]

PEER REVIEW

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SUPPORTING INFORMATION

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