Letters to the editor

Elevated fasting blood glucose at admission is associated with poor outcomes in patients with COVID-19

To the Editor:

We read with great interest the research article by Dr Targher et al. in *Diabetes & Metabolism* entitled 'Patients with diabetes are at higher risk for severe illness from COVID-19' [1], published online in May 2020. The authors found that diabetes was an independent high-risk factor for severe coronavirus disease 2019 (COVID-19) infection. However, hyperglycaemia is more common in non-diabetic than in diabetic patients [2] and, thus, deserves more attention in clinical practice. To date, data about the prognostic value of different levels of admission fasting blood glucose (FBG) in patients with COVID-19 are scarce. Therefore, we aimed to explore the association between stratified FBG levels and poor outcomes in patients hospitalized for COVID-19.

A total of 449 patients admitted to six designated hospitals with laboratory-confirmed COVID-19 were enrolled in the study. All cases were diagnosed according to World Health Organization (WHO) interim guidelines [3]. Data on the patients' demographics, comorbidities, laboratory variables and chest computed tomography (CT) images at admission were collected from 1 January to 31 March 2020. Poor outcomes were defined as composite endpoints including at least one of the following conditions: intensive-care-unit (ICU) admission; respiratory failure requiring mechanical ventilation; shock; and/or death.

To identify risk factors for adverse outcomes, variables with $P < 0.10$ on univariable analyses were included in multivariable logistic regression analyses. Patients were categorized into three groups according to FBG levels: <6.1 mmol/L (n = 291, 64.8%); 6.1–6.9 mmol/L (n = 52, 11.6%); and ≥ 7.0 mmol/L (n = 106, 23.6%). We used Kaplan–Meier curves to evaluate time from admission to death within 30 days in the three FBG groups.

Our institutional ethics committee approved the study and waived informed consent.

Median age of all enrolled patients was 52 years (interquartile range: 38–64), and 259 (57.7%) were male. A total of 45 (10.0%) patients reported having previous diabetes, of which nine (3.1%) had FBG < 6.1 mmol/L, six (11.5%) had FBG at 6.1–6.9 mmol/L and 30 (28.3%) had FBG ≥ 7.0 mmol/L. Compared with patients with normal FBG levels, patients with elevated FBG were older and more likely to have comorbidities. On multivariable analyses, patients with FBG at 6.1–6.9 mmol/L [odds ratio (OR): 5.38, 95% confidence interval (CI): 1.18–24.52; $P = 0.030$] had a higher risk of progression to critical illness than those with FBG ≥ 7.0 mmol/L (OR: 3.94, 95% CI: 1.03–15.15; $P = 0.046$; Table 1). Patients with FBG ≥ 7.0 mmol/L had the worst 30-day survival, followed by patients with FBG at 6.1–6.9 mmol/L (76.4% and 84.6%, respectively; $P < 0.001$ by log-rank test).

In conclusion, FBG levels at 6.1–6.9 mmol/L and ≥ 7.0 mmol/L at admission are both independent predictors of poor outcomes in patients with COVID-19. Therefore, serial FBG monitoring should be recommended for patients with COVID-19 infection, even in those with no known previous diabetes. During this pandemic of COVID-19, the timely identification of patients with hyperglycaemia can facilitate early symptomatic treatment to reduce the adverse outcomes of COVID-19 [4].

Table 1
Risk factors associated with poor outcomes during hospitalization on univariable and multivariable logistic regression analyses.

?	Univariable		Multivariable	
?	OR (95% CI)	*P*	OR (95% CI)	*P*
Age (years)	1.073 (1.053–1.094)	< 0.001	1.058 (1.011–1.108)	0.015
Gender:				
Female	Reference		Reference	
Male	1.780 (1.054–3.005)	0.031	2.187 (0.574–8.338)	0.252
Comorbidities:				
Hypertension	3.679 (2.144–6.314)	< 0.001	1.230 (0.359–4.210)	0.742
Coronary heart disease	3.150 (1.325–7.490)	0.009	0.891 (0.151–5.277)	0.899
Diabetes	3.898 (2.020–7.521)	< 0.001	1.301 (0.303–5.590)	0.724
Hepatitis	1.120 (0.311–4.027)	0.863		
Chronic lung disease	1.938 (0.825–4.553)	0.129		
Previous surgery	3.608 (1.884,–6.910)	< 0.001	1.402 (0.302–6.509)	0.666
Laboratory findings:				
WBC count ($\times 10^9$/L)	1.225 (1.123–1.337)	< 0.001	1.171 (0.416–3.295)	0.765
Neutrophils ($\times 10^9$/L)	1.308 (1.191–1.436)	< 0.001	1.085 (0.389–3.029)	0.876
Lymphocytes ($\times 10^9$/L)	0.128 (0.066–0.247)	< 0.001	1.875 (0.372–9.453)	0.446
LDH (U/L)	1.010 (1.007–1.012)	< 0.001	1.007 (1.001–1.012)	0.012
Haemoglobin (g/L)	1.002 (0.989–1.015)	0.783		
Platelets ($\times 10^9$/L)	0.994 (0.990–0.997)	0.001	0.997 (0.989–1.005)	0.452
Albumin (g/L)	0.826 (0.783–0.872)	< 0.001	0.921 (0.799–1.061)	0.254
AST (U/L)	1.028 (1.016–1.040)	< 0.001	1.005 (0.975–1.036)	0.750
ALT (U/L)	1.003 (0.996–1.011)	0.383		
DBIL (μmol/L)	1.182 (1.081–1.293)	< 0.001	1.007 (0.851–1.191)	0.938
IBIL (μmol/L)	0.935 (0.876–0.998)	0.044	0.913 (0.757–1.101)	0.340
TBIL (μmol/L)	1.018 (0.988–1.049)	0.245		
APTT (s)	1.014 (0.974–1.054)	0.503		
PT (s)	1.037 (0.995–1.081)	0.082	1.046 (1.005–1.090)	0.027
D-dimer (μg/mL)	1.001 (0.999–1.004)	0.285		
Creatinine (μmol/L)	1.024 (1.013–1.035)	< 0.001	1.013 (0.999–1.027)	0.074
CK (U/L)	1.004 (1.002–1.006)	0.001	1.002 (0.998–1.006)	0.247
CK-MB (U/L)	1.076 (1.043–1.110)	< 0.001	1.044 (0.984–1.107)	0.153
hs-CRP (mg/L)	1.012 (1.006–1.018)	< 0.001	0.978 (0.964–0.992)	0.002
Procalcitonin (ng/mL)	1.127 (1.039–1.223)	0.004	1.036 (0.871–1.233)	0.688
Potassium (mmol/L)	0.493 (0.305–0.799)	0.004	0.450 (0.162–1.252)	0.126
Sodium (mmol/L)	0.840 (0.779–0.906)	< 0.001	0.945 (0.765–1.169)	0.604
Chlorine (mmol/L)	0.901 (0.854–0.951)	< 0.001	0.779 (0.648–0.936)	0.008
Admission fasting blood glucose				
<6.1 mmol/L	Reference		Reference	
6.1–6.9 mmol/L	6.534 (3.012–14.176)	< 0.001	5.383 (1.182–24.522)	0.030
≥7.0 mmol/L	11.890 (6.376–22.173)	< 0.001	3.944 (1.027–15.145)	0.046
Computed tomography (CT) score	0.960 (0.894–1.032)	0.268		

Each of the five lung lobes was evaluated for degree of involvement, and classified/scored as 0 (0%), 1 (1–25%), 2 (26–50%), 3 (51–75%) or 4 (76–100%); sum severity CT scores of the total lung were obtained by summing the five lobe scores (maximum: 20); CT images were reviewed independently by two radiologists, each with >10 years' experience; WBC, white blood cell; LDH, lactate dehydrogenase; AST/ALT, aspartate/alanine aminotransferase; TBIL/DBIL/IBIL, total/direct/indirect bilirubin; APTT, activated partial thromboplastin time; PT, prothrombin time; CK, creatine kinase; MB, myocardial band; hs-CRP, high-sensitivity C-reactive protein.

Conflicts of interest

None.

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Shuyi Liu[a,1], Bin Zhang[a,1], Jingjing You[a], Luyan Chen[a],
Huanchu Yuan[b,**], Shuixing Zhang[a,*]
[a]*The First Affiliated Hospital of Jinan University, Guangzhou, Guangdong, China*
[b]*Dongguan People's Hospital, Dongguan, Guangdong, China*

*Corresponding author at: No. 613 Huangpu West Road, Tianhe District, Guangzhou, Guangdong, 510627, China***Corresponding author at: No. 3 South Wandao Road, Wanjiang District, Dongguan, Guangdong, 523000, China
E-mail addresses: 13686178013@139.com (H. Yuan).,
shui7515@126.com (S. Zhang).

[1]Both these authors contributed equally to this work.