# Correlation between Fasting Blood Glucose Level at Admission and Mortality in COVID-19 Patients: A Retrospective Study

**Bin Zhu**
Beijing Tiantan Hospital
**Chunguo Jiang**
Beijing Chaoyang Hospital
**Xiaokai Feng**
Beijing Chaoyang Hospital
**Yanfei Zheng**
Beijing University of Chinese Medicine
**Jie Yang**
China Pharmaceutical University
**Feng Wang**
Beijing Chaoyang Hospital
**Shi Liu**
Huazhong University of Science and Technology
**Fenghua Xu**
Huazhong University of Science and Technology
**Liming Zhang**
Beijing Chaoyang Hospital
**Zhigang Zhao**
Beijing Tiantan Hospital
**Ziren Tang** ( tangziren2020@163.com )
Beijing Chaoyang Hospital

**Research Article**

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# Abstract

**Background:** Coronavirus disease-19 (COVID-19) has spread rapidly, with a growing number of cases confirmed around the world. This study explores the relationship of fasting blood glucose (FBG) at admission with mortality.

**Methods:** In this retrospective, single-center study, we analyzed the clinical characteristics of confirmed cases of COVID-19 in Wu Han from 29 January 2020 to 23 February 2020. Cox proportional hazard regression analysis was performed to evaluate the relationship between FBG and mortality.

**Results:** A total of 107 patients were enrolled in our study. The average age was 59.49 ± 13.33 and the FBG at admission was 7.35 ± 3.13 mmol/L. There were 16 people died of COVID-19 with an average age 68.1 ± 9.5 and the FBG was 8.94 ± 4.76 mmol/L. Regression analysis showed that there were significant association between FBG and death (HR = 1.13, 95%CI: 1.02-1.24). After adjusting for covariables, the significance still exists. In addition, our result showed that FBG > 7.0 mmol/L or diabetic mellitus can significantly increase mortality after adjusting for the age and gender.

**Conclusions:** This study suggests that FBG at admission is an effective and reliable indicator for disease prognosis in COVID-19 patients.


# Background

Coronavirus disease 2019 (COVID-19) was first reported from Wuhan, China, in late December, 2019 [1]. To date, 81238 cases have been confirmed and 3250 cases were died in China up to March 18, 2020 [2]. It has spread rapidly, with a growing number of cases now confirmed in 72 countries over South East Asia, Europe, North America, Australia and the Middle East [3-5]. As a newly identified pathogen, there is no known pre-existing immunity in humans and symptoms are non-specific at early stage (mild respiratory symptoms and fever, 5-6 days after infection on an average) [6]. Once exacerbating, patients developed acute respiratory distress syndrome (ARDS), septic shock, metabolic acidosis coagulation dysfunction and organ failure that are difficult to control [7, 8]. Most patients showed increased inflammation-related biomarkers such as C-reactive protein (CRP) and interleukin, while the pulmonary computed tomography (CT) revealed bilateral distribution of patchy shadows and ground glass opacity [9, 10]. There is no effective medicine or vaccine other than comprehensive clinical intervention.

Based on the epidemiologic characteristics observed, most patients with COVID-19 were 30 to 79 years of age and mortality increases with age [6, 11]. Although COVID-19 is aggressive, the majority of patients can recover shortly after appropriate clinical intervention, except that a small number of patients died. Patients aged over 60 years and those with underlying conditions such as hypertension, diabetes, cardiovascular disease are found with highest risk for severe disease and death [12]. An outline of the most representative laboratory abnormalities found in patients with COVID-2019 infection is still lacking.

As a type of beta coronavirus, the genomic characterization and the epidemiological of this novel virus had been clearly elucidated [13]. Although much has been learned in the past few weeks, crucial knowledge gap remains in clinical. The clinical investigation of risk factors especially the fasting blood-glucose (FBG) with death is scarce. Therefore, this study retrospectively analyzed the FBG level on admission and disease progression of 107 patients with confirmed COVID-2019.

# Methods

### Patients

This was a retrospective study of the clinical characteristics of prospectively collected series of patients diagnosed with COVID-19 in West Branch of Union Hospital affiliated to Tongji Medical College of Huazhong University of Science and Technology between January 2020 and 23 February 2020. All patients who were diagnosed as having COVID-19 pneumonia according to WHO interim guidance (Clinical management of severe acute respiratory infection when novel coronavirus (2019-nCoV) infection is suspected: interim guidance, January 28, 2020). Those who received hormone therapy before admission were excluded from our study. The study was approved by the Ethics Committee of West Branch of Union hospital, Tongji Medical College, Huazhong University of Science and Technology and written informed consent was obtained from patients involved before enrolment when data were collected retrospectively.

### Laboratory Assays

Fasting blood samples at admission were collected. The biochemical parameters comprising FBG, serum lipid profiles were examined in the Laboratory department of West Branch of Union hospital.

Throat swab specimens were collected at admission and the laboratory nucleic acid tests using real time polymerase chain reaction (RT-PCR) for COVID-19 RNA were conducted immediately in the Laboratory department of West Branch of Union hospital. In addition, all patients were given chest X-rays or chest CT to further identify the bilateral ground-glass opacity of infiltrates of lung.

### Date Collected

Medical records including clinical, demographic, laboratory parameters, chest CT/X-ray, length of hospitalization and death time of enrolled patients were extracted using a standardized case report form. If information was not clear, we would consult with the doctor or other healthcare providers responsible for the treatment of the patient.

### Statistical Analysis

Data were presented as Means (SD) or medians (25th percentile-75th percentile) and proportions were calculated for population characteristics. Cox proportional hazard regression analysis was performed to evaluate the relationship between FBG and death. In addition, we adjusted for age, gender, body mass

index (BMI), systolic blood pressure, diastolic blood pressure, total cholesterol, triglycerides, and high-density lipoprotein (HDL) cholesterol in the multivariable model. FBG and death rate were estimated using the Kaplan-Meier method. Survival differences between groups were compared using the log-rank test. All statistical tests were 2-sided with the significant level set at 0.05. Statistical analyzes were performed using Empower Stats (http://www.empowerstats.com) and the R software, version 3.3.1 (http://www.R-project.org/).

# Results

### Demographics, baseline and clinical characteristics of patients

A total of 107 patients were included in this study. The average age were 59.49 ±13.33 and the pneumonia severity index（PSI）was 64.97 ± 38.68. The FBG at admission was 7.35 ± 3.13 mmol/L. Of them 54 were male with an average age 58.2 ± 13.0 and 53 were female with an average 60.6 ± 13.7. The pneumonia severity index (PSI) for male was 70.9 ± 40.2 and 59.1 ± 34.7 for female. There were 16 patients (10 male; 6 female) dead of COVID-19 with an average age 68.1 ± 9.5. The PSI was 105.0 ± 22.7 and the glucose was 8.94 ± 4.76 mmol/L. Of the death case, three patients with diabetes mellitus (DM), 5 patients with hypertension, 2 patients with coronary heart disease and one patient was both with hypertension and coronary heart disease.

### Association of FBG and Death

Associations of FBG level at admission with death are presented in table 2. We found that there were significant association between FBG and death (HR = 1.13, 95%CI: 1.02-1.24). Once adjust for covariables such as age, gender, blood pressure and serum lipid, the significance still exists (model 1: HR = 1.13, 95%CI: 1.03-1.25, p = 0.015 and model 2: HR = 1.33, 95%CI: 1.02-1.73, p = 0.037). To further explore the influence of FBG to death, 7.0 mmol/L was used as a cutoff value to evaluate the relationship (Figure 1). Regression analysis results showed that FBG > 7.0 or DM can significantly increase mortality after adjusting for the age and gender (HR = 2.86, 95%CI: 1.04-7.78, p = 0.043) (Table 3).

Kaplan-meier survival analysis was used to compare the variation trend of survival rate between the FBG < 7.0 and FBG ≥ 7.0 mmol/L during hospitalization. The results showed that compared with patients with FBG under 7.0 at admission, there was a significant decline of the cumulative survival rate in those with FBG over 7.0 (p = 0.043) (Figure 2).

# Discussion

An outbreak of COVID-19 has become a global health concern. Although, the epidemiological and clinical characteristics of patients were well documented, understanding of the clinical spectrum of COVID-19 infection is still limited. As a human-to-human transmission disease, a majority of patients have a favorable prognosis, however, there was still with 3.8% crude fatality ratio (CRF) especially in those over 80 years of age [12, 14]. Thus, explore risk factors related to the prognosis would be helpful. In this study,

we systematically investigated the effect of FBG on mortality. Our results showed that the death risk was associated with the FBG level at admission, which was not reported elsewhere.

Although epidemiology and the genome had been well elucidated, much remain unknown. The risk factors which influence death are still not clear and until now, there is no specific drug for the treatment of patients with COVID-19 [15]. According to WHO guideline, symptoms of COVID-19 are non-specific and the disease presentation can range from no symptoms (asymptomatic) to severe pneumonia and death. The typical signs and symptoms include: fever, dry cough, fatigue, sputum production, shortness of breath, sore throat, headache, myalgia or arthralgia, chills, nausea or vomiting, nasal congestion, diarrhea, and hemoptysis and conjunctival congestion [7, 8, 16]. These symptoms of mild illness in the early stage of COVID-19 infection may be indistinguishable clinically from many other common infectious diseases. However, in our study, we had observed that the FBG level were also increased (> 6.1 mmol/L) when excluded those with diabetes history. Normal human physiology is dependent on a tight control of the FBG levels. Zhang *et al*. had revealed that 57/64 diseases showed with increased FBG [17]. Li *et al.* had reported that patients with FBG ≥ 7.0 mmol/L was one of predictors of all-cause mortality in dilated cardiomyopathy patients [18]. Thus, we believe increased FBG may play an important role in COVID-19 patients' prognosis.

It is noteworthy that most of our study patients did not diabetes but were still with increased FBG level. Before admitted, they had only treated according to syndrome using lopinavir, ritonavir or arbidol. Without considerate psychological factors, we think increased FBG should raise even more attention in the treatment of COVID-19.

This finding of our study is also consistent with published article. In our study, the average age of death cases was older than those recovered patients, which was in accordance with Chen *et al*. and [6, 11]. In addition, we had observed a greater number of men than women in the 107 cases of COVID-19 infection.

Although our results might be helpful in COVID-19 prognosis, the results should be considered as preliminary ones and further research is necessary. Some limitations could not be ignored. First of all, due to the limited number of patients, our conclusions need to be further verified by larger samples and multi-center data. And there was only 16 persons died of COVID-19. Secondly, we did not get a dynamic FBG level during the treatment to complete elucidating the important role of blood glucose in the progress of COVID-19. Thirdly, there were not a long-time follow-up to observe whether those with increased FBG patients developed to diabetes or other metabolic disease when they recovery from COVID-19.

# Conclusion

In conclusion, our study suggests that FBG at admission is an effective and reliable indicator for disease prognosis in COVID-19 patients. Increased FBG should be given more attention in the treatment of COVID-19.

# Abbreviations

COVID-19: Coronavirus disease-19; FBG : Fasting blood glucose; PSI: Pneumonia severity index; ARDS: Acute respiratory distress syndrome; CRP: C-reactive protein; CT: Computed tomography;

# Declarations


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### Authors' Contributions

BZ and XKF designed the study and wrote the first draft. CGJ and XKF guided the methodology, YFZ and JY were responsible for statistics. FW and LS helped in data collection. FHX, LMZ, ZGZ and ZRT critically reviewed, discussed, and modified the manuscript. All authors read and approved the final manuscript for publication.


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### Availability of data and materials

Not applicable.

### Ethics approval and consent to participate

The study was approved by the Ethics Committee of West Branch of Union hospital, Tongji Medical College, Huazhong University of Science and Technology and written informed consent was obtained from patients involved before enrolment when data were collected retrospectively.

### Consent for publication

Not applicable.

### Competing interests

The authors declare that they have no competing interests.

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# Tables

**Table 1** Baseline characteristics of the study participants by sex.

| Variables | Stratified by sex | | |
|---|---|---|---|
| | Male | Female | *P value* |
| N. | 54 | 53 | |
| Age, y | 58.2 ± 13.0 | 60.6 ± 13.7 | 0.201 |
| SBP, mmHg | 24.6 ± 3.2 | 23.1 ± 2.8 | 0.055 |
| DBP, mmHg | 134.4 ± 18.2 | 128.5 ± 17.4 | 0.103 |
| BMI, $kg/m^2$ | 83.1 ± 10.4 | 77.9 ± 11.7 | 0.012 |
| PSI | 70.9 ± 42.0 | 59.1 ± 34.7 | 0.036 |
| CURB.65 | | | 0.663 |
| 0 | 20 (37.0) | 22 (41.5) | |
| 1 | 19 (35.2) | 15 (28.3) | |
| 2 | 11 (20.4) | 14 (26.4) | |
| 3 | 4 (7.4) | 2 (3.8) | |
| DM | | | 0.556 |
| 0 | 46 (85.2) | 48 (90.6) | |
| 1 | 8 (14.8) | 5 (9.4) | |
| CHD | | | 0.526 |
| 0 | 50 (92.6) | 47 (88.7) | |
| 1 | 4 (7.4) | 6 (11.3) | |
| Hypertensive | | | 0.304- |
| 0 | 37 (68.5) | 41 (77.4) | |
| 1 | 17 (31.5) | 12 (22.6) | |
| Laboratory results | | | |
| Fasting blood glucose, mmol/L[†] | 6.4 (5.7-7.6) | 5.9 (5.4-6.8) | 0.156 |
| Total cholesterol, mmol/L[†] | 4.0 (3.5-4.4) | 4.2 (3.8-4.8) | 0.041 |
| Triglycerides, mmol/L[†] | 1.2 (1.0-1.9) | 1.4 (1.1-1.7) | 0.575 |
| HDL cholesterol, mmol/L[†] | 0.9 (0.8-1.0) | 1.0 (0.8-1.2) | 0.033 |
| LDL cholesterol, mmol/L[†] | 2.2 (1.8-2.7) | 2.4 (2.0-2.9) | 0.215 |

BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; HDL, high-density lipoprotein; LDL, low-density lipoprotein

[*] For continuous variables, values are presented as mean ± SD.

[†] Values are presented as median (IQR)

**Table 2** Baseline characteristics of the study participants by death.

| Variables | Stratified by Death | | |
|---|---|---|---|
| | Non-Death | Death | *P value* |
| No. | 91 | 16 | |
| Age, y | 57.9 ± 13.4 | 68.1 ± 9.5 | 0.003 |
| Female, n (%) | 47 (51.6) | 6 (37.5) | 0.417 |
| SBP, mmHg | 131.6 ± 17.9 | 130.6 ± 19.1 | 0.863 |
| DBP, mmHg | 81.3 ± 11.3 | 76.1 ± 10.8 | 0.190 |
| BMI, kg/m2 | 23.9 ± 3.1 | 23.7 ± 2.6 | 0.700 |
| PSI | 58.0 ± 36.9 | 105.0 ± 22.7 | < 0.001 |
| Fasting blood glucose, mmol/L† | 5.9 (5.4-7.3) | 7.0 (6.4-8.2) | 0.003 |
| Total cholesterol, mmol/L† | 4.2 (3.7-4.6) | 3.8 (3.3-4.2) | 0.134 |
| Triglycerides, mmol/L† | 1.3 (1.0-1.8) | 1.3 (1.1-1.9) | 0.906 |
| HDL cholesterol, mmol/L† | 0.9 (0.8-1.2) | 0.8 (0.6-1.0) | 0.046 |
| CURB.65 | | | |
| 0 | 41 (45.1) | 1 (6.2) | |
| 1 | 32 (35.2) | 2 (12.5) | |
| 2 | 16 (17.6) | 9 (56.2) | |
| 3 | 2 (2.2) | 4 (25.0) | |

BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; HDL, high-density lipoprotein;

* For continuous variables, values are presented as mean ± SD.

† Values are presented as median (IQR)

**Table 3** The association between fasting blood glucose and death.

| Fasting blood glucose, mmol/L | N | Case (%) | Crude model | Adjusted model 1* | | Adjusted model 2† | |
|---|---|---|---|---|---|---|---|
| | | | HR (95CI) | HR (95CI) | *P value* | HR (95CI) | *P value* |
| GLU, as continuous | 107 | 16 (15.0) | 1.13 (1.02, 1.24) | 1.13 (1.03, 1.25) | 0.015 | 1.33 (1.02, 1.73) | 0.037 |
| | | | | | | | |
| < 7.0 | 71 | 7 (9.9) | *Ref* | *Ref* | | *Ref* | *Ref* |
| ≥ 7.0 or DM | 36 | 9 (25.0) | 2.65 (0.99, 7.12) | 2.86 (1.04, 7.78) | 0.043 | 3.53 (0.59, 21.15) | 0.1667 |

* Model 1 adjusted for age, sex.

† Model 2 adjusted for age, sex, systolic blood pressure, diastolic blood pressure, fasting blood glucose, total cholesterol, triglycerides, HDL cholesterol.

# Figures

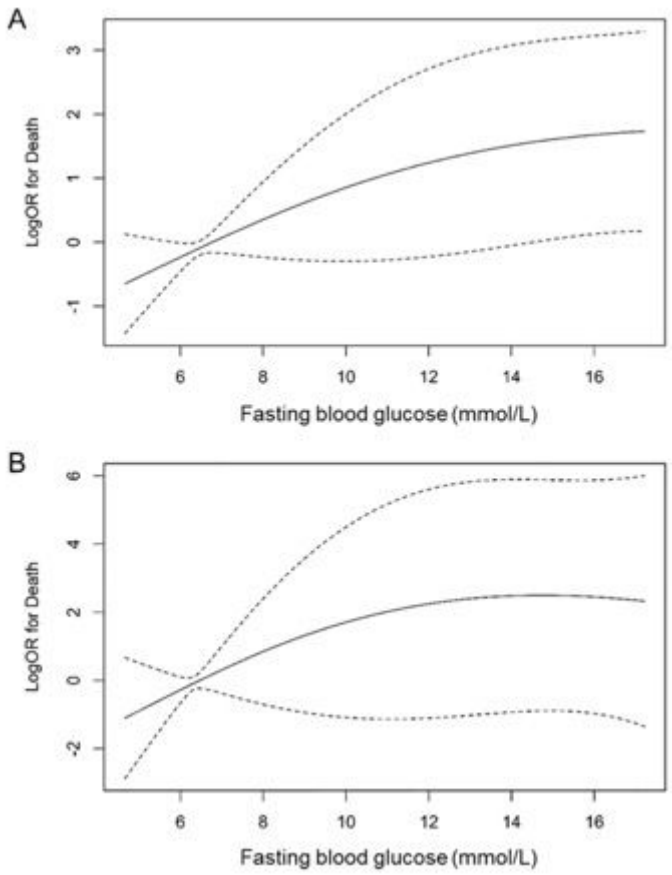


**Figure 1**

Smooth curves between fasting blood glucose and death. (A) Adjusted for age, sex; (B) Adjusted for age, sex, systolic blood pressure, diastolic blood pressure, fasting blood glucose, total cholesterol, triglycerides, HDL.

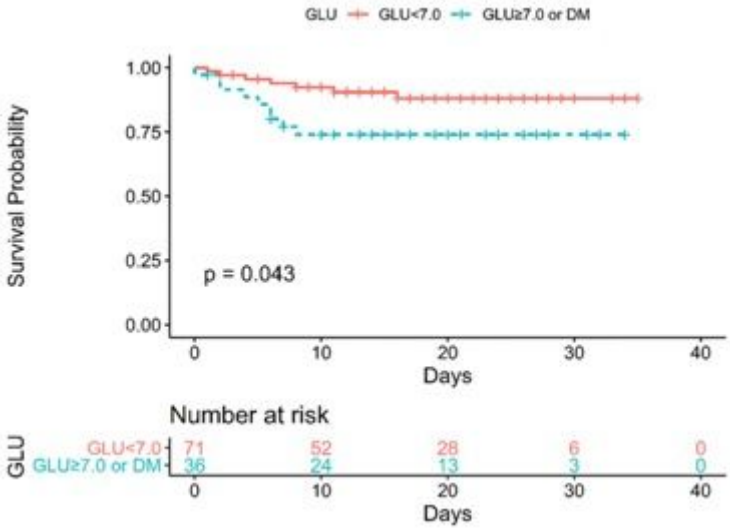


**Figure 2**

The survival rate of patients with COVID-19 between the FBG < 7.0 and FBG ≥ 7.0 mmol/L during hospitalization.