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ASSOCIATION OF FASTING PLASMA GLUCOSE LEVEL ON ADMISSION OF COVID-19 PATIENTS- AN OBSERVATIONAL STUDY

Medical Science

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ABSTRACT

Introduction: The coronavirus disease 2019 (COVID-19) pandemic, which was caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection, is a novel and serious global health threat and has dramatically spread worldwide 1. COVID-19 is transmitted primarily through respiratory droplet and direct contact. At the time of this article's drafting, 188,616,093 confirmed cases and 4,065,804 deaths have been reported worldwide with new confirmed cases and deaths occurring per day

Materials And Methods: All COVID-19 patients consecutively admitted to the hospital between June 1, 2020, and July 31, 2021, were collected. The diagnosis and clinical classification (mild, moderate, severe, and critical) of COVID-19 patients were carried out by two independent doctors based on the Guideline of Novel Coronavirus Pneumonia (8 th revised Edition) issued by the Chinese National Health Commission.

Result: Among 202 diagnosed COVID-19 patients from June 2020 to July 2021, some patients were excluded for age < 18 years (n = 5), pregnant women (n = 3), combined with malignant tumor (n = 1), no available or incomplete laboratory data (n = 120), no FPG data available at admission (n = 44), and patients diagnosed before June or discharged in August (n = 29) were excluded. Finally, 99 cases were included in the study

Conclusion: Higher FPG was an independent predictor of prolonged duration of SARS-CoV-2 RNA shedding/clearance in the present study. Our findings indicate that screening FPG level is an effective and simple method to evaluate the prognosis of patients with COVID-19, and intervention should be taken in time when patients with FPG ≥ 6:1 mmol/l regardless of a history of diabetes.

KEYWORDS

Fasting Plasma Glucose, COVID-19, and SARS-CoV-2

INTRODUCTION

The coronavirus disease 2019 (COVID-19) pandemic, which was caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection, is a novel and serious global health threat and has dramatically spread worldwide [1]. COVID-19 is transmitted primarily through respiratory droplet and direct contact. At the time of this article's drafting, 188,616,093 confirmed cases and 4,065,804 deaths have been reported worldwide with new confirmed cases and deaths occurring per day.

Diabetes mellitus (DM) impacted outcomes of COVID19 patients. A retrospective, single-center study in Iran showed that COVID-19 patients with DM had more comorbidities such as hypertension and complications than those without diabetes. Treatment failure and death were significantly higher in COVID-19 patients with diabetes compared to those without diabetes [2]. Serum levels of inflammationrelated biomarkers such as IL-6, C-reactive protein, serum ferritin and coagulation index, and D-dimer were significantly higher in COVID-19 patients with DM compared with those without DM.

Fasting plasma glucose (FPG) level ≥ 7:0 mmol/l is one of the important criteria for the diagnosis of DM [3]. Regardless of a known history of DM, higher FPG levels significantly predicted mortality of COVID-19 (P < 0:05). Hindawi Journal of Diabetes Research Volume 2022, Article ID 7424748, 8 pages https://doi.org/10.1155/2022/7424748 Among nondiabetic COVID-19 patients, higher FPG remained a significant predictor of mortality [4]. COVID-19 patients with an admission glucose level of >11 mmol/L were more likely to require intensive care unit (ICU), to develop acute respiratory distress syndrome (ARDS) and acute cardiac injury, and they had a higher death rate than patients with an admission glucose level of ≤11 mmol/L. In the multivariable analysis, COVID-19 patients with admission glucose level of >11 mmol/L had an increased risk of death and in-hospital complications, respectively [5].

Combined with some research results mentioned above, both persistent positivity of SARS-CoV-2 RNA and FPG affected outcomes of COVID-19 patients. Currently, there lacks research on the relationship between FPG and persistent positivity of SARS-CoV-2 RNA. We retrospectively analyzed the clinical data of COVID-19 patients in our hospital and further evaluated the relationship between FPG level and duration of SARS-CoV-2 RNA viral shedding/clearance. We tried to find the relevant factors affecting virus clearance and the possible factors that may influence the continuous positive status of SARS-CoV-2 RNA. These results will offer valuable information for the early control of COVID-19 in the real world and help reduce the social burden.

MATERIALS AND METHODS

Study Design and Participants.: All COVID-19 patients consecutively admitted to the hospital between June 1, 2020, and July 31, 2021, were collected from K P C MEDICAL COLLEGE & HOSPITAL, JADAVPUR, KOLKATA-700031. The diagnosis and clinical classification (mild, moderate, severe, and critical) of COVID-19 patients were carried out by two independent doctors based on the Guideline of Novel Coronavirus Pneumonia (8 th revised Edition) issued by the Chinese National Health Commission [6].

Mainly according to the criteria as follows:

(1) patients with epidemiological history of novel coronavirus pneumonia (NCP), in contact with novel coronavirus infected people within 14 days prior to the onset of the disease;
(2) any 2 of the clinical manifestations such as
(i) fever and/or respiratory symptoms;
(ii) the aforementioned imaging characteristics of NCP;
(3) normal or decreased white blood cell count (WBC), and lymphocyte count in the early stage of onset;
(4) positive real-time reverse transcription polymerase chain reaction (RT-PCR) results or highly homologous of viral gene sequence to known new coronaviruses [9].

Exclusion Criterions Included
(1) age < 18 years,
(2) pregnant women,
(3) duplicated cases,
(4) nonavailable or incomplete demographic or clinical data,
(5) malignant tumor status, and
(6) no FPG data available at admission (for example: FPG detected before admission or 24 h after admission, or routine blood glucose tests not being detected for each COVID-19 patient).

Statistical Analysis:
For statistical analysis data were entered into a Microsoft excel spreadsheet and then analyzed by SPSS (version 27.0; SPSS Inc., Chicago, IL, USA) and GraphPad Prism version 5. Data had been summarized as mean and standard deviation for numerical variables and count and percentages for categorical variables. Two-sample t-tests for a difference in mean involved independent samples or unpaired samples. Paired t-tests were a form of blocking and had greater power than unpaired tests..

RESULT AND DISCUSSION

There have been few studies on the correlations between clinical features and the duration of SARS-CoV-2 RNA shedding. In our study, we evaluated the relationship between FPG level and PDVPS or DSRP, and identified factors that may affect the virus clearance and the prognosis of COVID-19.

We retrospectively analyzed the clinical data of COVID19 patients in our hospital and further discussed the relationship between FPG levels and duration of SARS-CoV-2 RNA viral shedding or virus clearance. In our study, the mean duration of SARS-CoV-2 RNA viral shedding was 26:01 ± 6:71 days. In our cohort, patients with the longest viral shedding duration were 42 days. The range of duration SARS-CoV-2 RNA viral shedding was consistent with other studies, which ranged between 11 and 31 days [6].

Among 202 diagnosed COVID-19 patients from June to July 2020, some patients were excluded for age < 18 years (n = 5), pregnant women (n = 3), combined with malignant tumor (n = 1), no available or incomplete laboratory data (n = 120), no FPG data available at admission (n = 44), and patients diagnosed before June or discharged in August (n = 29) were excluded. Finally, 99 cases were included in the study.

The mean age of overall patients was 41:80 ± 10:81 years in our study. In this retrospective analysis, we found that DM patients with senior age and severe inflammatory characteristics of lung had increased incidences of comorbidities compared with those patients without diabetes. DM history was related to the severity of COVID-19 patients, fever, secondary infection, and imaging changes of chest CT (all P < 0:05). However, there was no significant relationship between preexisting diabetes or hypertension and the classification of COVID-19. Consistent with the study from Bennasrallah et al., diabetes and hypertension could not act as predisposing factors for late SARS-CoV-2 viral clearance [7]. In addition, T2DM was not significantly related to prolonged viral RNA conversion time or the proportion of RPV (P > 0:05). The possible reason was that although they had been diagnosed with diabetes before, their blood sugar levels were well controlled, which may be beneficial to themselves.

The Spearman's bivariate correlations showed that women were more likely to have long-term duration of SARS-CoV-2RNA positive. The univariate logistic regression analysis suggested gender was associated with a higher risk of PDVPS. Zhou et al. demonstrated that female sex was an independent predictor for prolonged SARS-CoV-2 RNA shedding. While Xu et al. demonstrated that male sex was an independent predictor for prolonged SARS-CoV2 RNA shedding [8]. Males and females might differ in immune reactivity. However, these inconsistent results of the effect of gender on the duration of SARS-CoV-2 RNA shedding need to be further investigated in the follow-up research. Fu et al. found that D-dimer was related to the severity of COVID-19. However, we found that D-dimer was related to fever in this study. We also found that D-dimer was positively correlated with PDVPS and DSRP (P < 0:05). Moreover, D-dimer was positively related to inflammation-related biomarkers such as SAA, CRP, and ESR (all P < 0:05). Furthermore, D-dimer was negatively correlated to LYM, B cell, T cell, and CD8+ T cell (all P < 0:05). It suggested the potential mechanisms were that D-dimer affected inflammation and immune responses.

Creatinine level was negatively related to PDVPS (P < 0:05). The univariate logistic regression analysis showed that creatinine was also associated with an increased risk of PDVPS. Low serum creatinine (SCr) could reflect to low skeletal muscle mass or sarcopenia and poor nutritional status [9]. The condition of malnutrition could result in weaker cellular mediated immunity and impaired surfactant production. Therefore, patients with low serum creatinine may increase the risk of the inflammatory reaction in lung tissues of COVID-19 patients, which is related to PDVPS.

Although there was a correlation between FPG level and diabetes history in the study population, higher level of FPG was positively related to prolonged duration of SARS-CoV-2 clearance. The univariate logistic regression analysis suggested that FPG levels or FPG≥ULN were significantly associated with higher risk of PDVPS. The multivariate logistic regression analysis further indicated that FPG≥ULN was an independent predictor for PDVPS. There are some mechanisms indicated that higher FPG might play a role in the viral clearance of COVID-19 patients. Since immunity is the first line of defense against SARS-CoV-2, it appears that the disturbed immunity in patients is due to hyperglycemia. Hyperglycemia inhibits neutrophil chemotaxis, decreases phagocytosis by neutrophils, macrophages, and monocytes, and impairs innate cell-mediated immunity [10]. In the present study, the levels of T cell number and CD8+ T cell number were decreased. In addition, CD8+ T cell number was negatively correlated with FPG levels (P < 0:05). Moreover, serum levels of inflammation-related biomarkers such as SAA, CRP, and ESR were significantly elevated among COVID-19 patients with higher FPG (P < 0:05). Furthermore, after controlling for possible confounders, elevated FPG levels were related to the seriousness of COVID-19 accompanied by more severe CT chest findings and inflammation. And the probable mechanisms are that elevated FPG levels increase susceptibility to inflammation due to impaired T cell response, neutrophil function, and humoral immunity.

Recently, Zhao et al. found COVID-19 patients with hypertension had higher risk of recurrent detection of viral RNA by RT-PCR. In the current study, we found that hypertension was associated with repositive of SARS-CoV2 RNA (P < 0:05). The underlying mechanisms might be that hypertension can increase the expression of angiotensin converting enzyme-2 (ACE2). As is known to us, human cells that express ACE2 and transmembrane serine protease 2 (TMPRSS2) receptors act as portal of entry via direct interaction of the human body and immune system. The primary site of infection in COVID-19 is the upper and lower respiratory tract. There, SARS-CoV-2 infects goblet secretory cells of the nasal mucosa and alveolar type II pneumocytes by binding to membrane-bound ACE2, and further strengthening virus entry [11].

There were some limitations of our study. First, the interpretation of our results might be limited by the sample size. Second, owing to the retrospective design of the study, the lack of data did not allow us to analyze the mean inhospital FPG. Third, because the number of critical cases was relatively small, the research on FPG among severe or critical cases may be limited in this study.

CONCLUSION

We found that higher FPG was an independent predictor of prolonged duration of SARS-CoV-2 RNA shedding/clearance in the present study. Our findings indicate that screening FPG level is an effective and simple method to evaluate the prognosis of patients with COVID-19, and intervention should be taken in time when patients with FPG ≥ 6:1 mmol/l regardless of a history of diabetes.

Table: Laboratory Examination Of COVID-19 Patients At Admission According To Different FPG Levels.

	All (n = 99) (%)	Group 1 (n = 51)	Group 2 (n = 13)	Group 3 (n = 35)	P value
FPG (mmol/l)	5.96 (4.89, 7.35)	4.95 (4.51, 5.29)	6.34 (6.27, 6.56)	8.03 (7.24, 9.65)	<0.001
SAA (mg/l)	21.8 (3.2, 75.95)	11.4 (1.4, 38.7)	44.1 (2.4, 137.8)	49 (16.9, 141.15)	0.003
LAC (mmol/l)	2.98 (2.44, 3.65)	2.92 (2.27, 3.6)	2.78 (2.25, 3.6)	3.35 (2.52, 4.03)	0.261
BUN (mmol/l)	4:54 ± 1:20	4:54 ± 1:07	4:16 ± 1:36	4:70 ± 1:33	0.387

Crea (μmol/l)	65.6 (56, 78.2)	66.9 (59.3, 78.9)	60.5 (52.4, 66.95)	62.6 (53.4, 79.6)	0.172
URCA (μmol/l)	317 (256, 382)	343 (267, 417)	286 (220.5, 379)	303 (245, 358)	0.155
WBC ($\times 10^9$/l)	5:12 ± 1:68	5:08 ± 1:63	5:30 ± 1:34	5:11 ± 1:89	0.916
LYM ($\times 10^9$/l)	1.49 (1.1, 1.9)	1.63 (1.23, 2.09)	1.19 (1.09, 1.88)	1.37 (1, 1.82)	0.120
HB (g/l)	144 (130, 153)	148 (134, 160)	128 (119.5, 138)	143 (131, 149)	0.001
PLT ($\times 10^9$/l)	193 (160, 235)	196 (171, 223)	212 (161.5, 251.5)	170 (144, 248)	0.337
ALT (U/L)	19.1 (13.6, 33.3)	19.9 (13.6, 32.7)	14.4 (11.5, 24.25)	19.6 (15.6, 35)	0.191
AST (U/L)	21.3 (17.1, 27.7)	19.5 (16.4, 27)	20.8 (17.7, 24.25)	22.7 (17.9, 30.3)	0.353
CRP (mg/l)	3.50 (0.8, 18.5)	1.7 (0.4, 6)	5 (1, 23.55)	9.1 (1.1, 35.5)	0.004
B cell number (cells/μl)	171.00 (129, 259)	168 (142, 280)	148 (106.5, 233)	186 (122, 247)	0.485
NK cell number (cells/μl)	217 (139, 313)	235 (150, 327)	228 (130.5, 311)	188 (139, 281)	0.379
T cell number (cells/μl)	1004 (655, 1399)	1088 (846, 1497)	822 (540, 1220)	908 (612, 1314)	0.050
$CD4^+$T cell number (cells/μl)	583 (382, 825)	626 (493, 825)	395 (354, 899)	513 (373, 769)	0.159
$CD8^+$T cell number (cells/μl)	348 (220, 469)	396 (288, 483)	221 (146.5, 434)	290 (217, 420)	0.034
D-dimer (mg/l)	0.27 (0.14, 0.45)	0.25 (0.13, 0.42)	0.29 (0.20, 0.53)	0.3 (0.13, 0.45)	0.614
ESR (mm/h)	15 (7, 24)	10 (5, 19)	15 (12, 24.5)	20 (13, 40)	0.001

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