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Characteristics of laboratory findings of COVID-19 patients with comorbid diabetes mellitus

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ABSTRACT

Aims: Coronavirus disease (COVID-19), also referred to as severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), is instigated by a novel coronavirus. The disease was initially reported in Wuhan, China, in December 2019. Diabetes is a risk factor associated with adverse outcomes. Herein, our objective was to investigate the characteristics of laboratory findings of type 2 diabetes mellitus (T2DM) patients infected with SARS-CoV-2.
Methods: This was a retrospective study and included 80 T2DM patients of Jinling Hospital from 2010 to 2020, as well as 76 COVID-19 patients without T2DM and 55 COVID-19 patients with T2DM who were treated at Huoshen hill Hospital from February 11 to March 18, 2020. We then compared the differences in laboratory test results between the three groups.
Results: The levels of lymphocytes, uric acid (UA), and globulin in the T2DM group were significantly higher. In contrast, C-reactive protein (CRP), creatinine, and lactic dehydrogenase (LDH)levels were lower than those in the COVID-19 ($p < 0.05$) and COVID-19 + T2DM groups ($p < 0.05$). No considerable difference was observed regarding the levels of alanine aminotransferase (ALT), white blood cell (WBC), aspartate aminotransferase (AST), globulin, and blood urea nitrogen (BUN) in the three groups ($p > 0.05$).
Conclusion: T2DM patients infected with SARS-CoV-2 showed decreased levels of body mass index (BMI), lymphocytes, UA, and albumin, and increased CRP levels. The decreased BMI, UA, and albumin levels may be associated with oxidative stress response and nutritional consumption. The decreased lymphocyte counts and increased CRP levels may be related to the infection.

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1. Introduction

Since December 2019, reports about mysterious pneumonia in numerous patients came from hospitals in Wuhan City, Hubei Province, China. After laboratory genetic testing and virus isolation, a novel coronavirus was identified as the cause of the disease. The virus was called severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) [1]. Subsequently, it was named coronavirus disease (COVID-19) by the World Health Organization [2]. COVID-19 is very infectious and mainly transmitted through respiratory droplets or contact [3]. The population is generally susceptible, and the number of infected people has increased worldwide.

Studies have shown that people with underlying comorbidities like diabetes are more prone to experience adverse outcomes of COVID-19 [4,5]. This study examined the laboratory results of COVID-19 patients who were either suffering from type 2 diabetes mellitus (T2DM) or not and compared them with patients with T2DM.

2. Methods

2.1. Participants and research design

This was a retrospective study and included two cohorts of adult inpatients (≥45 years old) from Jinling Hospital (Nanjing, China) and Huoshen hill Hospital (Wuhan, China). Approval for this investigation was obtained from the Ethics Committees of both the hospitals. The data of patients with T2DM were collected from the record system of Jinling Hospital from 2010 to 2020. The data of patients with COVID-19 with or without T2DM were collected from the record system of Huoshen hill Hospital from February 11 to March 18, 2020. All COVID-19 patients enrolled herein were diagnosed according to the guidelines of the national health commission of China [6], and the clinical classification was mild pneumonia. Comorbidities in all patients, except the T2DM group, included hypertension.

The following conditions defined T2DM: (1) diagnosis of T2DM in electronic medical records; (2) hypoglycemic agent prescriptions; and (3) random glucose level > 11.1 mmol/L, fasting plasma glucose (FPG) > 7.0 mmol/L, or glucose tolerance test result > 11.1 mmol/L detected during hospitalization. Clinical records of 46 COVID-19 patients with T2DM, 78 COVID-19 patients, and T2DM patients who were age- and sex-matched were used in this study. Hypertension was defined according to the history in electronic medical records, Diastolic blood pressure (DBP) ≥ 90 mmHg, as well as Systolic blood pressure(SBP) ≥ 140 mmHg during hospitalization or antihypertensive medication use. Age matching was within the age range of COVID-19 patients with T2DM, and gender was matched based on frequency matching.

2.2. Data collection

Demographics, laboratory findings, disease duration, and underlying comorbidities were retrieved from electronic medical records of the patients. Body mass index (BMI) was calculated as follows: body weight (kg)/ the square of the height (m). Laboratory tests were performed within 24 h of admission.

2.3. Data analysis

Categorical variables were analyzed using the chi-square test and expressed as percentages. Continuous variables were expressed as the mean ± SD or median with interquartile range (IQR). Parametric data of the three groups were analyzed by one-way ANOVA, followed by LSD-test for mean separation (post-hoc). Nonparametric data were analyzed using the Kruskal-Wallis test. Nemenyi method was used for comparison between two groups. All the analyses were performed using SPSS Statistics version 21.0. Statistical significance was set at $P < 0.05$.

3. Results

3.1. Baseline characteristics

Eighty T2DM patients without COVID-19 were included in the current study. The median age was 61 ± 7.6 years, 37 patients (46.3%) were males and 43 patients (53.7%) were females. The mean BMI was 24.9 kg/m^2 (IQR: 22.9–27.2). Seventy-six COVID-19 patients without T2DM participated in the present study. The median age was 63.3 ± 8.3 years, 43 (56.6%) were males and 33 (43.4%) females. The mean BMI was 21.8 kg/m^2 (IQR: 20.6–23.4). Also included were 55 COVID-19 patients with T2DM. The median age was 62.4 ± 7.7 years, 27 patients (49.1%) were males, and 28 patients (50.9%) were females. The mean BMI was 23.2 kg/m^2 (IQR: 21.8–24.5). No remarkable difference was noted concerning age or gender between the three groups ($p = 0.116$). The BMI in the COVID-19 group was lower compared to that in the T2DM ($p < 0.01$), and T2DM + COVID-19 groups ($p = 0.022$); the BMI in the T2DM + COVID-19 group was markedly lower compared to that in the T2DM group ($p = 0.003$) (see Table 1).

3.2. Comparison of laboratory findings

There were no differences in WBC counts between the three groups. Lymphocyte counts in the T2DM group were considerably higher relative to those in the COVID-19 ($p < 0.001$) and COVID-19 + T2DM groups ($p = 0.001$). However, in COVID-19 and COVID-19 + T2DM groups ($p = 0.134$), there were no notable differences. The levels of CRP in the T2DM group were remarkably lower compared to those in the COVID-19 ($p < 0.001$) and COVID-19 + T2DM groups ($p < 0.001$). However, there was no considerable difference in the COVID-19 vs. COVID-19 + T2DM group ($p = 0.2$). The ALT ($p = 0.923$) and AST levels ($p = 0.055$) in the three groups were statistically the same. The levels of albumin in the T2DM group were higher in comparison to those in the COVID-19 ($p < 0.001$) and COVID-19 + T2DM groups ($p < 0.001$); however, the difference in the COVID-19 vs. COVID-19 + T2DM was insignificant ($P = 0.078$). Although the levels of globulin were lower in the COVID-19 group, as well as the COVID-19 + T2DM group, the difference was not significant ($P = 0.065$). The levels of creatinine in the T2DM group were lower compared to those in

Table 1 – Baseline characteristics of the participants.

Characteristic	T2DM	COVID-19	T2DM + COVID-19
Number	80	76	55
Age (years)	61 ± 7.6	63.3 ± 8.3	62.4 ± 7.7
Gender (M/F)	37/43	43/33	27/28
BMI (kg/m^2)	24.9 (22.9–27.2)	21.8 (20.6–23.4) #	23.2 (21.8–24.5) # *
Duration of DM (years)	8.5 (4.3–12)	NA	6 (4–10)
Comorbidity Of Hypertension (n, %)	43 (56.6%)	28 (36.8%)	30 (54.5%)

BMI, body mass index; #:$p < 0.05$ compared to T2DM group; *: $p < 0.05$ compared to COVID-19 group.

the COVID-19 ($p < 0.001$) and COVID-19 + T2DM groups ($p < 0.001$); the difference in the COVID-19 vs. COVID-19 + T2DM groups was insignificant. No difference was observed in urea nitrogen levels among the three groups ($p = 0.51$). The level of uric acid in the COVID-19 + T2DM group was significantly lower relative to the T2DM group ($p < 0.001$) but higher compared to the levels in the COVID-19 group ($p = 0.033$). The levels of FPG in the COVID-19 group were lower relative to the levels in the T2DM ($p < 0.001$) and COVID-19 + T2DM groups ($p < 0.001$). However, the difference in the T2DM vs. COVID-19 + T2DM groups was trivial ($P = 1$). The levels of LDH in the T2DM group were remarkably lower compared to the levels in the COVID-19 ($p < 0.001$) and COVID-19 + T2DM groups ($p < 0.001$). However, no considerable difference was observed in the COVID-19 vs. COVID-19 + T2DM groups.

Table 2 presents the laboratory findings of the three groups.

4. Discussion

Since the outbreak of COVID-19, many studies have reported diabetes as one of the most common comorbidities of COVID-19. Bornstein reported an important link between metabolic and endocrine mechanisms and COVID-19 [7]. Therefore, in this study, we explored the impact of SARS-CoV-2 infection on patients with T2DM. Based on our literature search, this is the first study to examine and report the differences between T2DM patients, COVID-19 patients without T2DM, and COVID-19 patients with T2DM. The results indicate that COVID-19 patients with and without T2DM showed lower levels of BMI, lymphocytes, albumin, and uric acid, and higher levels of CRP and creatinine than regular patients with T2DM.

Recent studies have reported that most COVID-19 patients show reduced lymphocyte counts and increased CRP levels [8,9]. The virus primarily affects the lymphocytes, especially the T cells [10]. The decrease in lymphocyte counts suggests that SARS-CoV-2 consumes immune cells and inhibits immune function in humans. CRP is an inflammation biochemical indicator. The increase in CRP levels indicates that SARS-CoV-2 introduced cytokine storm which is crucial to the progression of COVID-19.

Although our study reported that patients with COVID-19 showed higher creatinine levels than those with T2DM only, just one case in the COVID-19 group and two cases in the COVID-19 + T2DM group had an abnormal renal function; the rest were within the normal range. Wang et al. [11] reported that acute kidney injury occurred in 5.1% of patients; they thought that COVID-19 infection does not result in acute kidney injury (AKI), and their finding is consistent with our current results. The FPG was higher in patients with T2DM, but we did not observe a poorer control of FPG in COVID-19 patients with T2DM than in T2DM patients. This may be associated with COVID-19 patients with mild illness in the groups.

Viral infection is also closely associated with oxidative injury, and it evokes oxidative stress and intensifies with the pathological process [12]. UA, the final breakdown product

Table 2 – Laboratory findings of participants in the three groups.

	T2DM (n = 80)	COVID-19 (n = 76)	T2DM + COVID-19 (n = 55)
WBC, × 10^9/L	5.7 (5.1–6.8)	5.4 (4.7–6.4)	6.3 (5.3–6.9)
Lyc, ×10^9/L	2.0 (1.6–2.5)	1.4 (1.0–1.7) #	1.6 (1.2–2.1) #
CRP, mg/L	0.7 (0.5–1.5)	2.0 (0.9–5.8) #	2.9 (1.4–11.9) #
ALT, U/L	19 (15–30.5)	22.3 (13.4–33.9)	21.4 (15.6–29.8)
AST, U/L	17 (14.3–24)	20.1 (15.2–25.7)	18.1 (13.8–22.5)
Albumin, g/L	41.7 (39.3–44)	35.4 (33–36.9)#	36.8 (34.1–39.9)#
Globulin, g/L	27.8 (25.0–30.6)	26.1 (24.2–28.0)	26.7 (25.0–29.3)
Creatinine, μmol/L	54.4 (45.2–62.2)	65.1 (55.0–74.8) #	63 (55.0–70.7) #
BUN, mmol/L	5.3 (4.5–6.3)	4.6 (3.8–5.5)	4.8 (4.6–6.0)
UA,μmol/L	310 (264.5–379.5)	253 (218.0–305.8) #	300 (245.0–344.0) #*
FPG, mmol/L	7.1 (6.2–9.2)	4.6 (4.3–5.1) #	7.2 (5.5–8.0) *
LDH, U/L	164.5(145.3–176.8)	214.1(184.1–269.0) #	221.3(178.9–285.5) #

WBC, white blood cell; Lyc, lymphocyte; CRP, C-reactive protein; ALT, alanine aminotransferase; AST, aspartate aminotransferase; BUN, blood urea nitrogen; UA, uric acid; FPG, fasting plasma glucose; LDH, lactic dehydrogenase; #:$P < 0.05$ compared to T2DM group; *:$P < 0.05$ compared to COVID-19 group.

of purine metabolism, is one of the main non-enzyme antioxidants in the plasma [13]. It has a dual identity of an antioxidant and oxidizing agent. UA at the physiological level is a naturally powerful antioxidant, which can remove superoxide and hydroxyl radicals from the plasma. High levels of UA increase the accumulation of reactive oxygen species (ROS), which can result in inflammation and dysfunction in blood vessels [14]. The antioxidant effect of UA is more noticeable outside the cells and in acute stress. Diabetes is often accompanied by hyperuricemia. However, in our study, UA levels were lower in COVID-19 patients and COVID-19 patients with T2DM than in T2DM patients; the levels of albumin showed a similar trend. Albumin is the target of ROS and reactive nitrogen species (RNS), which limits the destruction of other molecules by binding to it. Additionally, albumin can reduce the production of ROS and RNS by combining iron and hemoglobin [15]. Considering the above, we hypothesized that the reduction in the UA levels of patients with COVID-19 was the result of antioxidant reaction and overconsumption of free radicals after SARS-CoV-2 infection. The decrease in UA and albumin levels may be the result of excessive consumption of ROS in oxidative stress response. Moreover, albumin is one of the main markers for assessing nutritional status. People may also increase food consumption after infection with SARS-CoV-2. Anorexia is one of the most common signs and symptoms of patients with COVID-19 [4]. In our study, the BMI of COVID-19 patients complicated with T2DM was lower relative to that of T2DM patients. Therefore, we speculated that the reduction in albumin and UA levels might also be due to malnutrition.

LDH levels are elevated in many pulmonary diseases, including obstructive disease and microbial pulmonary disease [16,17]. In recent studies, LDH levels are increased in COVID-19 patients [17,18] and related to the severity of the disease [4]. The results of the current study also indicated that LDH levels were increased in patients with COVID-19.

This study was limited in the following ways: First, the sample size was small, and this was single-center research. Second, the observed differences could have been due to the confounding effect, because no confounding factors were controlled in the analysis. Third, more studies on metabolic indicators, such as lipids and HbA1C, could not be conducted due to laboratory conditions.

In conclusion, we demonstrated that T2DM patients infected with SARS-CoV-2 showed decreased levels of BMI, lymphocytes, UA, and albumin and increased CRP levels. The decreased BMI, UA, and albumin levels may be associated with oxidative stress response and nutritional consumption. The decreased lymphocyte counts and increased CRP levels may be related to the infection. During treatment, physicians should pay more attention to antioxidant stress and nutritional support therapy.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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