Clinical Characteristics of 538 Novel Coronavirus Disease Patients with Chronic Underlying Diseases in Wuhan, China: A retrospective Study

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Abstract

Background Novel severe acute respiratory syndrome coronavirus 2 causes the novel coronavirus disease (COVID-19) in humans, which has spread rapidly worldwide. Most critical cases of COVID-19 are accompanied by complicated chronic underlying diseases. This retrospective study aims to analyze the clinical characteristics of COVID-19 patients with chronic underlying diseases.

Methods A total of 1,183 COVID-19 patients were divided into the chronic underlying disease (CUD, n = 538) group and the non-underlying disease (non-CUD, n = 645) group. The clinical characteristics and outcomes were collected and compared between the two groups.

Results There were significant differences in age, weight, and SPO2 on admission between the CUD and non-CUP groups. The ratio of severe cases in the CUD group was higher than that in the non-CUD group ($\chi^2 = 35.58$, *p*-value < 0.001). The white blood cell count, neutrophil count, C-reactive protein, urea nitrogen, creatinine, myoglobin, and cardiac troponin in the CUD group were significantly higher than those in the non-CUD group, while the lymphocyte count and albumin in the underlying disease group were significantly lower than those in the non-underlying disease group. No significant difference was found in the total number of tests, the number of positive or negative results in nucleic acid tests between the two groups. The negative rate for both IgG- and IgM-antibody tests in the CUD group was higher than that in the non-CUD group ($\chi^2 = 5.57$, *p*-value = 0.018). No statistical difference in mortality between the CUD (n = 18) and non-CUD groups (n = 13). All surviving patients were cured and discharged. A total of 33 patients had a positive re-examination result for nucleic acid test one week after discharge, including 14 patients with underlying diseases and 19 patients without underlying diseases.

Conclusion: COVID-19 patients with underlying diseases had poorer clinical conditions and had a longer hospital stay, but after active treatment, the mortality had not increased significantly.

Introduction

Novel severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), a positive-sense single-stranded RNA virus of family *Coronaviridae*, genus *Sarbecovirus*, is a newly identified beta-coronavirus to cause human disease[1]. SARS-CoV-2 causes the novel coronavirus disease (COVID-19) in humans, which has spread rapidly worldwide since the first report in December 2019 [2, 3]. By 19:32 Chinese Standard Time, May 11, 2020, a total of 4,123,376 COVID-19 cases had been confirmed globally with 283,055 cases of deaths[4]. It is still urgent to treat the infected patients, block the transmission, and prevent the susceptible populations to control the spread of COVID-19.

SARS-CoV-2 has a highly phylogenetic similarity to severe acute respiratory syndrome coronavirus but demonstrates stronger infectivity than previously known human coronaviruses [1, 5]. Patients with COVID-19 would have clinical symptoms of varying degrees, such as fever, cough, and dyspnea [6]. Because of its rapid spread and strong pathogenicity, the SARS-CoV-2 epidemic has become a global public health emergency without specific drugs for treatment or vaccines for prevention.

Previous studies have shown that most critical cases and the death cases of COVID-19 are accompanied by complicated chronic underlying diseases [7, 8, 9]. Hypertension, cardiovascular diseases, diabetes, smoking, chronic obstructive pulmonary disease (COPD), malignancy, and chronic kidney disease were the most prevalent comorbidities among hospitalized COVID-19 patients [10]. Guan et al investigated 1,590 COVID-19 patients with comorbidity from multicenter and proposed that chronic conditions, including COPD, diabetes, hypertension, and malignancy, were risk factors of poor clinical outcomes [11]. A meta-analysis of 3,027 patients with COVID-19 in 13 studies showed that male, aged, smoking patients might develop into the critical or mortal stage, as well as the patients with comorbidities of hypertension, diabetes, cardiovascular disease, and respiratory diseases [12]. Patients infected with SARS-CoV-2 showed commonness but partial heterogeneity in clinical characteristics and outcomes. Therefore, we believe that it remains valuable to retrospect more COVID-19 patients with underlying diseases for accumulating more medical evidence.

In this study, we retrospectively analyzed the clinical characteristics of 1,183 confirmed novel COVID-19 patients with or without chronic underlying diseases from a single-center, thus further understanding the impact of chronic underlying diseases on the clinical outcome of COVID-19.

Subjects And Methods

Ethics approval

This study was approved by the ethics committee of Guanggu District of Hubei Province Maternal and Child Health Hospital [No. FYGG(L)2020-004], and written informed consent was obtained from patients.

Study Subjects and Data Collection

The subjects included 1,183 confirmed cases of COVID-19 patients admitted to Guanggu Hospital Area of Maternity and Child Healthcare Hospital in China between February 19 and March 16, 2020. All subjects were divided into the chronic underlying disease (CUD, n = 538) group and the non-underlying disease (non-CUD, n = 645) group. The demographics and medical data of the subjects were collected by the retrospective method. The data cutoff for the study was March 31, 2020.

Diagnosis and Classification Criteria

According to the Diagnosis and Treatment Plan for COVID-19 (7^{th} Trial Edition) formulated by the General Office of the National Health Commission of the People's Republic of China, cases with suspected clinical characteristics are confirmed based on any of the following etiological or serological evidence: (1) real-time Polymerase chain reaction (RT-PCR) test of SARS-CoV-2 nucleic acid shows a positive result, (2) the result of virus gene sequencing is highly homologous with a known novel coronavirus, (3) the positive

result for both serum SARS-CoV-2-specific IgM and IgG antibodies; and (4) the result of serum SARS-CoV-2-specific IgG antibody changes from negative to positive or increases by at least four-fold in the recovery period compared to that in the acute phase.

China's classification criteria for COVID-19 is as follows: mild, the clinical symptoms are mild, and no pneumonia is found through imaging; moderate, the patient has a fever, respiratory tract symptoms and other symptoms, and signs of pneumonia can be observed through imaging; severe, one of the following criteria is met: (1) respiratory distress, with a respiratory rate ≥ 30 beats per minute, (2) hypoxemia, with oxygen saturation (SpO_2) ≤ 93% in the resting state, and (3) arterial partial pressure of oxygen (PaO_2)/inhaled oxygen concentration (FiO_2) ≤ 300 mmHg; critical, one of the following conditions is met: (1) respiratory failure occurs and mechanical ventilation is required, (2) shock, and (3) other organ failure requiring intensive care unit (ICU) monitoring and treatment.

Detection Methods

Laboratory tests and SARS-CoV-2 nucleic acid tests for the patients were carried out in Guanggu Hospital Area of Hubei Maternity and Child Healthcare Hospital.

Statistical Analysis

Statistical software SPSS 19 was used for data analysis. Count data were presented as count and percentage, and the χ^2 test was used for intergroup comparison according to the sample size. Measurement data are presented as mean ± standard deviation. For intergroup comparison of the mean, the variance homogeneity test was performed. If the variances were homogeneous, the independent samples t-test was adopted. If the variances were heterogeneous, the separate variance estimation t-test (t'-test) was adopted. A p-value < 0.05 was considered to be statistically significant.

Results

Demographics, General Conditions, and the COVID-19 Classification

A total of 1,183 cases were enrolled, including 538 cases (45.48%) in the CUD group and 645 cases in the non-CUD group. There were 378 cases of hypertension (prevalence rate 31.95%, 378/1183), 164 cases of diabetes (prevalence rate 13.86%, 164/1183), 117 cases of respiratory disease (prevalence rate 9.89%, 117/1183), 81 cases of heart disease (prevalence rate 6.85%, 81/1183), and 40 cases of cerebral infarction (prevalence rate 3.38%, 40/1183) in the CUD group. Some patients presented with multiple underlying diseases. Of the 1,183 cases, 486 were male and 697 were female, with a male-to-female ratio

of 1:1.43. There were 243 males and 295 females in the CUD group, with a male-to-female ratio of 1:1.21, and 243 males and 402 females in the non-CUD group, with a male-to-female ratio of 1:1.65.

The average age of the 1,183 patients was 58.76 ± 15.32 years. There were statistically significant differences in gender, age, weight, systolic blood pressure, and SpO_2 between the two groups upon admission to the hospital. There was no statistically significant difference in height, body temperature, pulse rate, respiratory rate, or diastolic pressure.

In the CUD group, there was one mild case, 418 moderate cases, 100 severe cases, and 19 critical cases. In the non-CUD group, there were two mild cases, 584 moderate cases, 46 severe cases, and 13 critical cases. There was a total of 178 severe and critical cases between the two groups, accounting for 15.05%. The total proportion of severe and critical cases in the CUD group was 21.12%, while the total proportion of severe and critical cases in the non-CUD group was 9.15%, and the difference between the two groups was statistically significant ($\chi^2 = 38.61$, *p*-value < 0.001). Comparisons of the general conditions between the two groups is shown in **table 1**.

Laboratory Findings

The white blood cell count, neutrophil count, C-reactive protein, urea nitrogen, creatinine, and cardiac troponin were significantly higher in the CUD group compared with the non-CUD group, while the lymphocyte count and albumin were significantly lower in the CUD group than that in the non-CUD group. There was no significant difference in procalcitonin, monocyte count, alanine aminotransferase, aspartate aminotransferase, total bilirubin, direct bilirubin, coagulation function indexes, erythrocyte sedimentation rate, or other indicators between the two groups. Details of the results of the two groups are shown in **table 2**.

SARS-CoV-2 Nucleic Acid and Antibody Tests

The average total number of nucleic acid tests for the 1,183 patients during hospitalization was 2.64 ± 1.11, among which the number of positive results was 0.24 ± 0.58, and the number of negative results was 2.39 ± 0.79. There was no significant difference in the total number of nucleic acid tests, the number of positive results, or the number of negative results between the two groups. Of the 1,183 confirmed cases, 458 had negative nucleic acid test results from disease onset to discharge (accounting for 38.72%), including 215 patients in the CUD group (accounting for 39.96%) and 243 patients in the non-CUD group (accounting for 37.67%); the difference between the two groups was not significantly significant ($\chi^2 = 0.65$, *p*-value = 0.421). The conditions of nucleic acid tests in the two groups are shown in **table 3**.

Among the 1,183 patients, 983 patients received tests for both IgG and IgM antibodies against SARS-CoV-2, 108 patients received tests for only IgM antibody, and 92 patients not receive any test for IgG or IgM antibody. As is shown in **table 4**, 734 (74.67%, 734/983) showed positive results for both antibodies while 155 (15.77%, 155/983) patients showed negative results for both antibodies. The 155 cases with negative results for both IgG and IgM antibodies were confirmed for COVID-19 by nucleic acid tests. Among those 155 cases, 80 (14.87%, 80/538) cases had underlying diseases while 75 (11.63%, 75/645) cases had no underlying disease and the difference between the two groups was statistically significant (χ^2 = 5.57, *p*-value = 0.018).

Treatment and Prognosis

In both groups, mild and moderate cases were given symptomatic support treatment, while severe and critical cases were given oxygen inhalation, nutritional support, antiviral treatment, and as necessary, assisted respiration treatment.

The length of hospital stay in the CUD group was 13.15 ± 5.21 days and 11.88 ± 4.84 days in the non-CUD group (t = -4.30, *p*-value < 0.001). A total of 31 patients dead during hospitalization with a mortality rate of 2.62% (31/1183). There were 18 deaths (a mortality rate of 3.35%, 18/538) in the CUD group and 13 deaths (a mortality rate of 2.02%, 13/645) in the non-CUD group, however, the difference was not statistically significant (χ^2 = 2.03, *p*-value = 0.154). All surviving patients were cured and discharged.

Two-week home quarantine was still required for the discharged patients, and SARS-CoV-2 nucleic acid tests were carried out on the 7^{th} day and 14^{th} day after discharge. A total of 33 patients had positive nucleic acid test results in the re-test one week after discharge (an incidence rate of 2.79%), including 14 patients with underlying diseases (an incidence rate of 2.60%, 14/538) and 19 patients without underlying diseases (an incidence rate of 2.95%, 19/645), without a statistically significant difference between the two groups (χ^2 = 0.13, *p*-value = 0.721). Those 33 patients continued to receive treatment.

Discussion

SARS-CoV-2 can infect the respiratory system, digestive system, and central nervous system of humans, mammals, birds, bats, and other animals[13]. The population is generally susceptible to SARS-CoV-2 infection, and the risk of SARS-CoV-2 infection increases especially in middle-aged and elderly people, as well as people with underlying diseases and low immunity [8, 14]. Our research showed that among the 1,183 COVID-19 cases, 45.48% had underlying diseases, and 15.05% were severe and critical cases, most of whom were obese and relatively old, had more severe hypoxia, and were more difficult to treat. In China, Wuhan city was blocked when the SARS-CoV-2 broke out. Therefore, the availability of medical sources was controlled. The population with underlying diseases would be influenced by the short supply of medicine, leading to a vulnerable body condition. To control the spread of SARS-CoV-2 and maximize the use of medical resources, patients with mild disease were admitted to mobile cabin hospitals and

received basic medical care, while patients with multiple underlying diseases and severe disease were admitted to public hospitals and received a complete medical intervention. Thus, on the one hand, the high proportion of patients with underlying diseases in our study might be related to the high risk of COVID-19 of this population; on the other hand, it might due to the policy of prevention and control to the COVID-19 mentioned above.

The proportions of COVID-19 patients with hypertension and diabetes were highest among the novel coronavirus disease cases with complications, which is generally consistent with the nationwide data of COVID-19 with comorbidity in China [11]. Our finding indicates that patients with hypertension and diabetes might be more susceptible to SARS-CoV-2. Research has shown that SARS-CoV-2 infects host cells mainly through the angiotensin-converting enzyme 2 (ACE2) receptor, while the ACE2 receptor is expressed in epithelial cells of the lungs, kidneys, blood vessels, and intestine[15]. The long-term use of ACE inhibitors (ACEIs), angiotensin receptor blockers (ARBs), or the thiazolidinedione (e.g. pioglitazone) in patients with hypertension and diabetic will up-regulate the expression of ACE2 in vivo. A hypothesis has been proposed that the up-regulation of ACE2 expression in hypertension patients who take ACEIs and ARBS will increase the risk of infection of SARS-CoV-2 [16]. However, this hypothesis remained controversial. At present, a large-scale study including 12,594 patients who were tested for SARS-CoV-2 has shown that the use of ACEIs will not increase the prevalence rate of positive results for COVID-19 or the incidence of the severe condition of COVID-19 such as intensive care, mechanical ventilation, or death [17]. Another study suggested that COVID-19 patients using ACEIs and ARBs during hospitalization will not increase the risk of death [18]. As for diabetes, though, people with diabetes might be at increased risk of severe disease, no existing conclusive evidence supports the discontinuation of ACEIs, ARBs, or thiazolidinediones in people with diabetes for precaution of COVID-19 [19, 20]. Katulanda et al. proposed that, in addition to the direct vulnerability to severe COVID-19, people with diabetes should be recognized as a vulnerable group for complicated disease and are at risk since the potential limited access to insulin, blood glucose monitoring equipment, and other healthcare which would be impacted by the COVID-19 [19]. Therefore, we believe that patients with hypertension and diabetes should pay more attention to the prevention against SARS-CoV-2, and sufficient medical support to these vulnerable people is necessary.

The WBC count, neutrophil count, and C-reactive protein levels in the CUD group were higher than those in the non-CUD group, whilst the lymphocyte count was lower than that in the non-CUD group, indicating that COVID-19 patients with chronic underlying diseases have more severe inflammatory reactions. Besides, the indicators of impaired renal function and myocardial injury in the CUD group were higher than those in the non-CUD group in this study. Our finding suggests that patients with chronic underlying diseases are more likely to suffer from renal dysfunction and myocardial injury, which is consistent with the previous studies [21, 22]. Chronic underlying diseases cause chronic damage to corresponding organs, making patients might be more sensitive to ischemia and hypoxia. Therefore, we should actively control blood pressure and blood glucose, as well as protect organ functions while performing routine treatment for COVID-19.

Previous studies have shown that both excessive and impaired immune responses in fighting against SARS-CoV-2 are detrimental to patients [23, 24]. Our study found that the proportion of COVID-19 patients with underlying diseases who could not produce antibodies in time after disease onset was higher. This finding implied that COVID-19 with comorbidity might have a weaker immune response in fighting against SARS-CoV-2. This might be related to the patients' age, multiple underlying diseases, and declined immune function.

In terms of outcomes, the length of hospital stay in the CUD group was significantly longer than that in the non-CUD group. In our study, the mortality of COVID-19 patients with chronic underlying diseases has not increased after receiving active and efficient treatment when compared with. Compared with the global data (mortality of 6.86%, 283,055/4,123,376) [4], our finding showed that the current social and medical strategy for COVID-19 in China is correct. Besides, the positive nucleic acid re-test results of 2.79% of patients were found after discharge, which suggested that precaution during the virus epidemic is also important to people who have been infected by SARS-CoV-2.

Admittedly, there are some limitations in this retrospective study. On the one hand, under the government regulation of medical resources, the medical center in this study mainly admitted patients with the COVID-19 classification higher than mild, thus the selection bias might exist in this study. As a single-center study, the sample size of 1183 might not be large enough to be representative when in the background of current infected cases. On the other hand, there was information bias in data collection. The medical histories of some patients in a coma or the elderly were collected from the social workers and volunteers who transferred the patient from the community to the hospital, not by patients themselves or their families directly. Some incomplete data is not included in this study, such as the history of medication and the diagnosed age of the chronic underlying diseases.

In conclusion, hypertension and diabetes are the relative common comorbidities of COVID-19, and patients with chronic underlying diseases had poorer clinical conditions, but the mortality had not increased significantly after active treatment. The findings of the retrospective analysis of COVID-19 in China would provide evidence-based information for the prevention and treatment of the COVID-19 epidemic in other countries.

Declarations

Ethics approval and consent to participate

This study was approved by the ethics committee of the Guanggu District of Hubei Province Maternal and Child Health Hospital [Number FYGG(L)2020-004]. Written informed consent was obtained from patients.

Consent for publication

Consent for publication from patients were obtained.

Availability of data and materials

The raw data analyzed during the current study are not publicly available as the data is also part of an ongoing study but are available from the corresponding author on reasonable request.

Competing interests

The authors declare that they have no competing interests.

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Author’s contributions

W.Y., X.Y., H.F., and H.Z. contributed to the study design, analyzing data and writing the manuscript. H.F., H.Z., X.F., and Q.Z. were involved in the acquisition of data. Z.L., X.F., and Q.Z. reviewed the manuscript. Z.L. and H.F. obtained funding. All authors read and approved the final manuscript. W.Y., X.Y., H.F., and H.Z. contributed equally to this study.

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