Clinical Characteristics of Patients Infected With the Novel 2019 Coronavirus (SARS-Cov-2) in Guangzhou, China

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Background. The clinical manifestations and factors associated with the severity of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infections outside of Wuhan are not clearly understood.

Methods. All laboratory-confirmed cases with SARS-CoV-2 infection who were hospitalized and monitored in Guangzhou Eighth People’s Hospital were recruited from January 20 to February 10.

Results. A total of 275 patients were included in this study. The median patient age was 49 years, and 63.6% had exposure to Wuhan. The median virus incubation period was 6 days. Fever (70.5%) and dry cough (56.0%) were the most common symptoms. A decreased albumin level was found in 51.3% of patients, lymphopenia in 33.5%, and pneumonia based on chest computed tomography in 86%. Approximately 16% of patients (n = 45) had severe disease, and there were no deaths. Compared with patients with nonsevere disease, those with severe disease were older, had a higher frequency of coexisting conditions and pneumonia, and had a shorter incubation period (all \( P < .05 \)). There were no differences between patients who likely contacted the virus in Wuhan and those who had no exposure to Wuhan. Multivariate logistic regression analysis indicated that older age, male sex, and decreased albumin level were independently associated with disease severity.

Conclusions. Most of the patients infected with SARS-CoV-2 in Guangzhou, China are not severe cases and patients with older age, male, and decreased albumin level were more likely to develop into severe ones.

Keywords. clinical characteristics; epidemiology; risk factors; SARS-CoV-2; viral load.

In December 2019, cases of unexplained pneumonia related to the Huanan seafood market began appearing in Wuhan, Hubei Province, China [1]. It was subsequently determined that the pathogen was a novel coronavirus, and the gene sequence was closely related (with 88% identity) to 2 bat-derived severe acute respiratory syndrome (SARS)–like coronaviruses [2]. The virus is the seventh member of the known coronavirus family that is able to infect humans [3]. As the virus is similar to SARS coronavirus (SARS-CoV), which is a member of the subgenus Sarbecovirus (Beta-CoV lineage B) [4], it was subsequently renamed SARS-CoV-2. The pneumonia caused by the virus was named coronavirus disease 2019 (COVID-19).

The outbreak of SARS-CoV-2 infection has become a global health concern. As of May 6, 2020, there were 82 885 documented cases in China and 4633 deaths due to the disease [http://my-h5news.app.xinhuanet.com/h5activity/yiqingchaxun/index.html].

Although the number of infected persons has increased rapidly, clinical investigations of patients, especially those outside of Wuhan, are lacking. Chen et al. [5] studied the clinical features of 99 patients with COVID-19 and found that SARS-CoV-2 was more likely to infect older men with comorbidities and to lead to acute respiratory distress syndrome (ARDS). Several recent studies [6, 7] have indicated that the rapid spread of the virus is due to human-to-human transmission and have found evidence of familial cluster cases. Wang et al. [8] studied 138 hospitalized patients with COVID-19 in Wuhan: 41% of the patients were suspected to have been infected by in-hospital transmission of SARS-CoV-2, 26% of the patients required treatment in the intensive care unit (ICU), and the mortality rate was 4.3%.

As of May 6, 2020, Guangdong Province, China, has the most confirmed cases outside of Hubei [http://wsjkw.gd.gov.cn/xgzbdk/content/post_2988153.html]. Guangzhou is the economic and health care center of Guangdong Province and is one
of the most popular cities for migrant workers. The Guangzhou Eighth People’s Hospital is the major center for the care of patients with new emerging infectious disease in Guangdong. Thus, the purpose of this study was to examine the epidemiological, clinical, and laboratory characteristics of patients with SARS-Cov-2 infections in Guangzhou.

METHODS

Study Design and Participants

The records of patients with COVID-19 diagnosed by the Guangdong Center for Disease Control (CDC) who were admitted to the Guangzhou Eighth People’s Hospital from January 20, 2020, to February 10, 2020, were retrospectively reviewed. The study was approved by Guangzhou Eighth People’s Hospital Ethics Committee, and written informed consent was obtained from patients involved before enrollment when data were collected retrospectively.

For the analyses, patients were divided into those with severe disease and those with nonsevere disease based on World Health Organization (WHO) interim guidance [9]. Patients were also divided into an “imported” group and a local group. Imported group patients were those who had been to Wuhan within 14 days or who were residents of Wuhan before admission, and the local group included patients who had not left Guangdong during the past month. The incubation period was defined as the duration of time from the contact with the source of transmission to the onset of symptoms. Fitness for discharge was based on abatement of fever for at least 3 days, with improvement of chest computed tomography (CT) findings and viral clearance in upper respiratory tract nasopharyngeal samples.

Data Collection

Data were obtained from the patient medical records database and included demographic and epidemiological characteristics, clinical symptoms and signs, and laboratory test and radiographic imaging results. The laboratory test results collected included complete blood count cell blood count (CBC), tests of coagulation function and liver and kidney function, electrolyte levels, C-reactive protein (CRP), procalcitonin (PCT), lactate dehydrogenase (LDH), and creatine kinase (CK). The primary radiographic assessment was chest CT. If there were missing data or clarifications were needed, the information was obtained by communicating directly with the patient, the attending doctor, or other data providers. All data used in the analyses were checked by 2 doctors.

The end points included the rate of severe infections, complications, the need for ICU admission, the need for mechanical ventilation, and death. These end points were not applied to a fixed time range (ie, within 28 days) as clinical observations were still in progress.

Real-time Reverse Transcription Polymerase Chain Reaction

All patients who were transferred to the Guangzhou Eighth People’s Hospital were diagnosed by a throat swab nucleic acid test administered by the Guangdong CDC. On admission, respiratory samples were taken to determine viral load by a reverse transcription polymerase chain reaction (RT-PCR) assay. In brief, upper respiratory throat swab samples were collected from all patients after admission, and the samples were stored in virus medium. An RNA Isolation Kit (Da An Gene Co., Ltd, Guangzhou, China) was used to extract viral RNA from the samples. RT-PCR was performed using the RNA Detection Kit for SARS-CoV-2 (Da An Gene Co., Ltd). The ORFlab and N genes of SARS-CoV-2 were the amplification target regions. The receiver operating characteristics (ROC) curve method was used to determine the internal standard reference cycle threshold (Ct) value, which was determined to be 40. If the Ct value was ≤40, the sample was considered positive; if the value was >40, the sample was considered negative.

Statistical Analysis

As all the continuous variables in this study were not normally distributed, continuous variables were presented as median and interquartile range (IQR). Categorical variables were described as numbers and percentages. The Wilcoxon-Mann-Whitney U test was used to test differences between groups for continuous variables, as they did not follow a normal distribution. The chi-square test was used to examine differences of categorical variables. Variables with a P value <.10 in bivariate analysis were included in the multivariate logistic regression analysis. Forward stepwise binary logistic regression was used for multivariate analysis. Variables with a P value <.05 were retained in the final regression model. SPSS, version 20.0 (IBM Corp., Armonk, New York, US), was used for data analysis.

RESULTS

Demographic and Clinical Characteristics of Patients

A total of 275 patients with laboratory-confirmed SARS-Cov-2 infections were included in the analysis. The median age of the patients (IQR) was 49 (34–62) years, 41.3% were at least 50 years old, 47.7% were males, and 33.1% had at least 1 coexisting medical condition. None of the patients described exposure to the Huanan seafood market, and none of the patients were health care workers. Based on the WHO definition [9], 230 (83.6%) patients had nonsevere disease and 45 (16.4%) patients had severe disease. Compared with the nonsevere group, patients with severe disease were older and had a much higher frequency of coexisting medical conditions. Additionally, the frequency of imported cases was higher in the severe group than in the nonsevere group (80.0% vs 60.4%; P = .013) (Table 1). The median incubation time for all patients was 6 days; however, the incubation time was significantly shorter in the severe group than in the nonsevere group (4 days...
vs 6 days; \(P = .004\). The median interval between hospital admission and symptom onset was 5 days, but it was significantly longer in the severe group than in the nonsevere group (5 days vs 4 days; \(P = .034\)).

In all patients, the most common symptoms at the onset of illness were fever (70.5%), dry cough (56%), sputum production (22.6%), and sore throat (13.8%). Diarrhea was rare, with only 2.5% of patients reporting this symptom. Compared with the nonsevere group, the frequencies of fever, dry cough, sputum production, fatigue, and shortness of breath were much higher in the severe group (Table 1).

Patients were also divided into imported and local disease groups by epidemiological history. There were no significant differences in the parameters described above between the 2 groups; however, family cluster infections were more common in the local group (Supplementary Table 1).

**Laboratory and Radiographic Findings**

At admission, leukopenia was found in 16.7% of patients, neutropenia in 18.2%, and lymphopenia in 33.5% (Table 2). Other routine blood indices were within the normal ranges. However, the percentages of patients with increased leukocytes and neutrophils and lower levels of lymphocytes were greater in the severe group than in the nonsevere group. In addition, LDH, CK, and aspartate aminotransferase (AST) levels on admission (IQR) were higher in the severe group than in the nonsevere group: LDH: 260 (187–418) U/L vs 179 (148–218) U/L; CK: 114 (68–219.5) U/L vs 69 (49–104) U/L; AST: 32.4 (21.7–49) U/L vs 19.4 (16.2–27.1) U/L.
Albumin (ALB) level was decreased in 51.3% of all patients, and more patients in the severe group had decreased ALB levels than in the nonsevere group (93.1% vs 45.2%; \(P < .001\)).
medical condition, leukocyte count, neutrophil count, lymphocyte count, PCT, LDH, CK, ALB, AST, and D-dimer were associated with disease severity. Thus, these variables were included in the multivariate logistic regression. The multivariate analysis indicated that age 50–64 years (reference, 15–49 years), male sex, and decreased ALB level were independently associated with disease severity (Table 3).

On admission, 38 (14%) patients in the nonsevere group had no abnormalities on chest CT scan, whereas all patients in the severe group had pneumonia. Bilateral pneumonia (67.6%) and multiple small patchy shadows and ground-glass shadows (62.1%) were the most common findings (Table 2). Pneumonia was defined as appearance of symptoms of fever, coughing, or dyspnea and chest CT showing multiple small patchy shadows and interstitial changes in 1 or both lungs at an early stage, which then progressed to multiple ground-glass shadows and infiltration shadows on both lungs. Compared with the nonsevere group, the severe group was more likely to have bilateral involvement (95.6% vs 61.3%; \( P < .001 \)) and pleural effusion (15.6% vs 3.9%; \( P = .007 \)). Chest CT scan patterns were similar between the imported and local disease groups (Supplementary Table 2).

Upper respiratory throat swab samples were collected from all patients at admission, and 151 specimens were positive for the ORF1ab gene, with a median Ct value of 34. Of these patients, 25.8% had higher viral loads (Ct values < 30), whereas 74.2% had low viral loads (Ct values, 30 to 40). A total of 158 specimens were positive for the N gene, with a median Ct value of 32, and 41.8% of the specimens had higher viral loads. The levels of viral RNA were not different between the severe and nonsevere groups. There was no significant difference in viral load between imported and local disease cases (Supplementary Table 2).

Complications and Treatment
During hospitalization, the most common complication was pneumonia (86%), followed by ARDS (7.6%) and disseminated intravascular coagulation (DIC; 1.5%). The rates of all complications were higher in patients with severe disease than in those with nonsevere disease. A total of 237 patients (86.2%) received empiric antibiotic treatment, 226 (82.2%) received antiviral therapy, 64 (23.3%) received systemic corticosteroid treatment, and 26 (9.5%) received immunoglobulin therapy. Additionally, 6 patients (2.2%) were administered antifungal medications (Table 4).

Approximately half of the patients (55.6%) received oxygen, and 10.2% of patients required noninvasive ventilation. Eleven patients (4.0%) required invasive mechanical ventilation, and 6 of the 11 patients received extracorporeal membrane oxygenation (ECMO) and continuous renal replacement therapy (CRRT) as salvage therapy. As expected, these treatments were used in significantly more patients with severe disease as compared with those with nonsevere disease (noninvasive ventilation: 55.6% vs 1.3%; \( P < .001 \); invasive mechanical ventilation: 24.4% vs 0%; \( P < .001 \); ECMO: 13.3% vs 0%; \( P < .001 \); CRRT: 13.3% vs 0%; \( P < .001 \)) because application of these treatments was included in the WHO’s definition of severe disease. As of February 10, 2020, 229 patients (83.3%) were still hospitalized. A total of 38 patients (13.8%) had been discharged, and 8 patients (2.9%) had been transferred to another hospital due to serious illness. As of February 10, no patient had died (Table 4).

**DISCUSSION**

We investigated the epidemiological, clinical, and laboratory characteristics of 275 patients with COVID-19 in Guangzhou, Guangdong, the most affected province outside of Hubei. This is the largest sample size outside Wuhan, the center of the epidemic as we know it so far. The most common symptoms were fever and dry cough, and ~16% of the patients had severe disease. There were no health care workers in the patient sample, no cases of in-hospital infection, and no deaths at the time this report was prepared.

Many studies [10, 11] regarding SARS-CoV-2 have been published recently. In contrast to studies from the city of Wuhan and Zhejiang province, in which most patients were males, slightly more than half of our patients were females (53.3%). Furthermore, the patients in the present study had milder disease with respect to a lower frequency of symptoms such as fever, dry cough, and shortness of breath. The rates of severe cases and mortality in Guangzhou were much lower than reported in Wuhan (16.3% and 0%, respectively), which is similar to the rates reported in Zhejiang [11]. The rate of gastrointestinal symptoms was low in our study, which is consistent with early reports from Wuhan but is contradictory to a recent US study that reported a gastrointestinal symptom rate of 61% [12]. This discrepancy may be attributed to the difference in clinical characteristics between populations or to a change in the virus. However, further studies should be conducted to investigate this issue. The number of infected patients increased sharply in a short period and medical resources were in short supply, which delayed diagnosis and treatment for many patients. In addition, early diagnosis, isolation, and treatment in Guangzhou might have collectively contributed to the marked reduction in the mortality rate.

### Table 3. Association Between Different Parameters and Severe Cases by Multivariate Logistic Regression

| Parameter | OR   | 95% CI  | \( P \) Value |
|-----------|------|---------|---------------|
| Age       |      |         |               |
| <14 y     | 0.000| 0.000   |               |
| 50–64 y   | 23.519| 2.603–212.525| .005         |
| ≥65 y     | 8.878| 0.923–86.414 | .059         |
| Male      | 4.173| 1.151–15.135 | .030         |
| Albumin   | 15.998| 1.833–139.591| .012         |

Abbreviations: CI, confidence interval; OR, odds ratio.

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To further evaluate the relationship between source of infection and disease severity, patients were divided into an imported group and a local group based on epidemiological history. Clinical characteristics and laboratory test results were similar between the groups, but the proportion of imported cases was higher in the severe group (80%). However, this association was not significant in the multiple logistic regression.

SARS-CoV viral particles damage the cytoplasmic component of lymphocytes, which results in lymphocyte apoptosis. Thus, patients infected with SARS-CoV are likely to exhibit lymphopenia. A prior study reported that 35% of patients with nonsevere SARS-CoV infections had mild lymphopenia [13]. Lymphopenia is a prominent feature of severe Middle East respiratory syndrome (MERS) infection [14], and it is common in patients with severe SARS-CoV infection [13]. In our study, 60% of patients with severe infections had some degree of lymphopenia. This suggests that lymphopenia in SARS-CoV-2 infections may be related to the severity of the disease.

Patients who are older and those with multiple underlying diseases are more likely to develop severe disease [15]. Another study demonstrated that patients treated in the ICU were more likely to be older and to have underlying comorbidities, dyspnea, and anorexia than patients who did not require ICU admission [10]. This is consistent with the results of our study. Studies of other viral diseases, such as rabies, have indicated that the incubation period of viral diseases is significantly related to the severity of the disease. Shorter incubation periods are associated with more serious disease, and this is related to the number of cells initially infected by the virus. However, no studies have examined the relationship between the incubation period of COVID-19 and disease severity so far. We found that the incubation period was shorter in patients with severe disease, which suggests that the incubation period of COVID-19 may be related to disease severity. In addition, patients with bilateral pneumonia diagnosed on admission by CT were more likely to develop severe disease [16]. So it is important to process chest CT scans soon after admission.

Multivariate logistic regression analysis indicated that older age, male sex, and lower albumin level were independently associated with severe SARS-CoV-2 infection. ALB is synthesized by hepatocytes and is the most abundant protein in plasma. Gatta et al. [17] reported that hypoalbuminemia was one of the most important factors affecting the prognosis of patients with sepsis. Peires et al. [18] showed that a decrease of ALB level in patients with sepsis indicated worsening of the disease and poor prognosis. The mechanism of ALB reduction due to sepsis is considered to be due to the excessive inflammatory reaction of the body. The inflammatory reaction leads to the release of oxygen free radicals and prostaglandins from Kupffer cells, which can inhibit the synthesis of ALB by the liver and promote the consumption and decomposition of protein, thus leading to hypoalbuminemia. So it is important to evaluate ALB levels dynamically in these patients.

RT-PCR analysis of respiratory or fecal samples, together with serological testing, can confirm the diagnosis of SARS-CoV

| Variable                                           | All Patients (n = 275) | Nonsevere Patients (n = 230) | Severe Patients (n = 45) | P Value |
|----------------------------------------------------|------------------------|-----------------------------|-------------------------|---------|
| Complications                                      |                        |                             |                         |         |
| Septic shock                                       | 1 (0.4)                | 0 (0)                       | 1 (2.2)                 | .164    |
| Acute respiratory distress syndrome                | 21 (7.6)               | 0 (0)                       | 21 (46.7)               | <.001   |
| Disseminated intravascular coagulation             | 4 (1.5)                | 0 (0)                       | 4 (8.9)                 | .001    |
| Administration of antibiotics medications          | 237 (86.2)             | 192 (83.5)                  | 45 (100)                | .002    |
| Administration of antiviral medications            | 226 (82.2)             | 185 (80.4)                  | 41 (91.1)               | .087    |
| Administration of antifungal medications           | 6 (2.2)                | 0 (0)                       | 6 (13.3)                | <.001   |
| Administration of systemic corticosteroids         | 64 (23.3)              | 29 (12.6)                   | 35 (77.8)               | <.001   |
| Administration of immunoglobulin therapy           | 26 (9.5)               | 3 (1.3)                     | 23 (51.1)               | <.001   |
| Oxygen therapy                                     | 153 (55.6)             | 106 (47.0)                  | 45 (100)                | <.001   |
| Mechanical ventilation                             |                        |                             |                         |         |
| Invasive                                           | 11 (4.0)               | 0 (0)                       | 11 (24.4)               | <.001   |
| Noninvasive                                        | 28 (10.2)              | 3 (1.3)                     | 25 (55.6)               | <.001   |
| Use of extracorporeal membrane oxygenation         | 6 (2.2)                | 0 (0)                       | 6 (13.3)                | <.001   |
| Use of continuous renal replacement therapy        | 6 (2.2)                | 0 (0)                       | 6 (13.3)                | <.001   |
| Intensive care unit admission                      | 29 (10.5)              | 1 (0.4)                     | 28 (62.2)               | <.001   |
| Clinical outcomes                                  |                        |                             |                         |         |
| Discharge                                          | 38 (13.8)              | 36 (15.7)                   | 2 (4.4)                 | <.001   |
| Death                                              | 0 (0)                  | 0 (0)                       | 0 (0)                   |         |
| Staying in hospital                                | 229 (83.3)             | 194 (84.3)                  | 35 (77.8)               |         |
| Transfer to another hospital                       | 8 (2.9)                | 0 (0)                       | 8 (17.8)                |         |

Data are presented as No. (%). P values denote the comparison between the nonsevere group and the severe group.
infection in most SARS patients. However, the sensitivity of detecting viral RNA is reported to be 16.4% in nasal swabs, 37.3% in throat swabs, and 66.4% in sputum samples [19]. Testing multiple nasopharyngeal and fecal samples increases the sensitivity of detecting viral RNA [20], and no significant correlation between viral load and severity of SARS-CoV-2 infection has been noted. Considering that Ct values were comparable between the severe group and the nonsevere group, the progression of SARS-CoV-2 respiratory failure might not be due to uncontrolled viral replication, but might be related to immunopathological damage.

This study has several limitations. First, the definition of the incubation period should be the time from when the pathogen invades the body to the earliest onset of clinical symptoms. The uncertainty of the exact dates (recall bias) might have inevitably affected the assessment of incubation period. In addition, by the deadline for data collection of this study (February 10, 2020), 229 patients (83.3%) were still hospitalized. At the time of manuscript submission, the onset time in some patients may have been shorter than the observation period of 28 days, during which these patients could have developed severe disease, resulting in deviation of clinical observation characteristics. At present, there are no further follow-up data for these patients due to the urgent need for information that may guide clinical decision-making. Future study with longer follow-up periods should be conducted to validate the findings of this study. The exposure history was recorded based on patient self-report at admission; all the patients were sober and able to answer questions. Therefore, there may inevitably be a certain degree of subjectivity in the exposure history of the patients. We also found that <10% of patients did not know where they were infected, so there may be other unknown potential exposure. Moreover, viral load from other specimens is a potentially useful marker of disease severity; however, only throat swabs were available in the present study.

CONCLUSIONS

Most of the patients infected with SARS-CoV-2 in Guangzhou, China were not severe cases, with relatively lower severity than that reported in Wuhan, and this may be due to earlier diagnosis and treatment. Moreover, patients with older age, male, and decreased albumin level were more likely to develop into severe ones.

Supplementary Data

Supplementary materials are available at Open Forum Infectious Diseases online. Consisting of data provided by the authors to benefit the reader, the posted materials are not copyedited and are the sole responsibility of the authors, so questions or comments should be addressed to the corresponding author.

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