Clinical features of COVID-19 patients in one designated medical institutions in Chengdu, China

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Abstract

OBJECTIVE: To study the clinical characteristics of patients infected with the 2019 severe acute respiratory syndrome coronavirus 2 (SARS-Cov-2) responsible for coronavirus disease (COVID-2019).

METHODS: Data were collected from 20 patients admitted to the Pidu District People's Hospital in Chengdu from January 26, 2020 to March 1, 2020 with laboratory-confirmed SARS-Cov-2 infection. Clinical data were collected using the World Health Organization (WHO) nCoV CASE RECORDFORM Version 1.2 28JAN2020, which includes parameters such as: temperature, epidemiological characteristics, social network, history of exposure, and incubation period. If information was unclear, the team reviewed the original data and contacted patients directly if necessary.

RESULTS: The median age of the 20 COVID-19 infected patients studied was 42.5 years. In this cohort, four patients became severely ill and one deteriorated rapidly during treatment. This patient was transferred to another medical center with an intensive care unit (ICU) for treatment. This patient died after admission to the ICU. Two of the twenty patients remained positive SARS-Cov-2 more than three weeks, and they were quarantined in a medical facility without medication. According to our analysis, all of the studied cases were infected by human-to-human transmission due to the lack of protective measures; transmission through contact within families requires confirmation. The most common symptoms at onset of illness were fever in 13 (65%) patients, cough in 9 (45%), headache in 3 (15%), fatigue in 6 (30%), diarrhea in 3 (15%), and abdominal pain in 2 (10%). Six patients (30%) developed shortness of breath upon admission. The median time from exposure to onset of illness was

6.5 days (interquartile range 3.25–9 days), and from the onset of symptoms to first hospital admission was 3.5 (1.25–7) days.

CONCLUSION: Compared with patients infected with SARS-Cov-2 in Wuhan (up to the end of February 2020), the symptoms of patients in one hospital in Chengdu, Sichuan Province, were relatively mild and patients were discharged from the hospital after only a short stay. However, the fasting blood glucose of the infected individuals was found to be slightly elevated because of the state of emergency. The dynamic changes in lymphocyte levels can predict disease status of COVID-19. They are also suggestive of changes in mean platelet volume during disease progression. This suggests that the patients had mild cases of COVID-19. However, because there is no effective drug treatment for COVID-19, it is important to detect and identify severe cases from mild cases early.

Introduction

Over the past few decades, there has been a series of respiratory infections caused by emerging viruses, which originated in animals. These viruses—severe respiratory syndrome coronavirus (SARS-CoV), Middle East respiratory syndrome coronavirus (MERS-CoV), and pandemic influenza A (H1N1)—have reached epidemic levels by crossing species barriers. The result has been thousands of human infections and hundreds of deaths[1]. Currently, a mysterious outbreak of atypical pneumonia in late 2019 was traced to a seafood wholesale market in Wuhan, China. Within a few weeks, a novel coronavirus, SARS-CoV–2, was announced by the World Health Organization (WHO)[2]. SARS-CoV–2 is responsible for the outbreak of Coronavirus Disease 2019 (COVID–19).

At the early stages of the outbreak, samples from five patients were submitted for full-length genome sequencing. Patient results that were almost identical to each other were identified as SARS-CoV–2, which is 96% identical at the whole-genome level to a bat coronavirus[3]. There is a worldwide concern about SARS-CoV–2 as a global public health threat[4]. On January 30, 2020, the WHO declared COVID–19 as the sixth public health emergency of international concern. SARS-CoV–2 is spread by human-to-human transmission via droplets or direct contact.[5] As of March 1, 2020, there are 79,972 confirmed COVID–19 cases (including 7,365 severe cases)

and 2,873 deaths in China. In other countries, there are 7,651 confirmed COVID–19 cases and 118 deaths.

Economists estimate that, without urgent global actions to curtail the Wuhan SARS-CoV–2 within the shortest possible time, China is expected to lose up to $62 billion in the first quarter of the year, while the world is likely to lose over $280 billion within the same period[7]. To control COVID–19, effective prevention and control measurements must include early detection, diagnosis, treatment, and quarantine in order to block human-to-human transmission as well as reduce secondary infections among close contacts and health care workers[8]. The local government restricted the import of patients from other provinces and the diffusion of patients internally. In Chengdu, China, 187 medical institutions were designated for the treatment of SARS-CoV–2.

This study was carried out in Pidu District People's Hospital, and it describes the clinical characteristics and laboratory findings of patients in Sichuan Province infected with SARS-Cov–2 to provide insight into the prevention and treatment of COVID–19. In the early stages of the outbreak, the clinical and epidemiological characteristics of COVID–19 were mainly introduced in severe patients in Wuhan[9], but many mild cases can become severe or critical. SARS-Cov–2 will lead to severe infection and death if patients are not identified early enough in the mild stages of the disease.

Methods

Data sources

The working group conducted a retrospective study focusing on the clinical characteristics of confirmed cases of COVID–19 at the Pidu District People's Hospital in Chengdu from January 26, 2020 to March 1, 2020. Since the outbreak of COVID–19 in Wuhan, China, strict precautionary measures have been implemented in Sichuan Province, including the creation of fever clinics that exclusively receive patients with suspected SARS-Cov–2 infection, defined as presenting with a fever, or any respiratory symptoms, including dry cough, especially those with a history of travel to Wuhan or exposure to infected people within two weeks before symptom onset. Case definitions of confirmed human infection with SARS-Cov–2 are in accordance with the interim guidance from the WHO. An Ingenuity CT scanner (Philips (China) Co. Ltd.) was used and set at 210 mA and 120 kV, with the minimum slice thickness of 1 mm.

Only the patients with a laboratory-confirmed infection were enrolled in this study. The working group collected data on 20 patients admitted to the hospital with laboratory-confirmed SARS-Cov–2 infection. Some patients came directly from Pidu District People's Hospital, while other patients were transferred to other medical institutions for treatment by the working group of COVID–19 prevention and control in Chengdu. All of the patients were confirmed as COVID–19-positive. Information was collected on dates of illness onset, visits to clinical facilities, and hospital admissions. Epidemiological data were collected through brief interviews with each patient. Several doctors interviewed each patient to collect exposure histories during the two weeks before illness onset or after the outbreak of COVID–19 in Wuhan, including the dates and times of close contact (gathering, living, or working together) with individuals from Wuhan with confirmed or suspected SARS-Cov–2 infection. Physicians also investigated the social network of the patient, including family social network, friend social network, and colleague social network.

The working group extracted the medical records of patients using WHO nCov CASE RECORD FORM and self-made scale. A team of doctors who had been treating patients with COVID–19 collected and reviewed the data. The design of the study process was based on the Chinese national diagnosis and treatment plan without any intervention measures, concern about privacy of patients, informed patients of specific rules, and conducted with the informed consent of patients. All of the information on the content of the study shall be kept by a special person for inspection, if necessary. Due to the urgent need to collect data on this emerging pathogen. Using a standardized case report form to collect clinical data according to design requirements, the working group contacted the doctor responsible for the treatment of the patient for clarification if the information was unclear.

Laboratory confirmation and treatment

Throat swab specimens were collected from all of the patients before entering the isolation ward and tested by real-time polymerase chain reaction (RT-PCR) for SARS-Cov–2 RNA. Virus detection was repeated twice with at least a 24-hour interval. Throat swab specimens of patient were negative. The patient remained under observation if undiagnosed or returned home for self-monitoring. The patients were admitted to an isolation ward for treatment if they are diagnosed with COVID–19 at a designated facility, or transferred to a designated medical institution. All 20 of the patients in this study came from isolation wards in designated medical institutions.

Laboratory tests were conducted at admission, including a complete blood count, serum biochemistry, and identification of other respiratory pathogens, such as influenza A, influenza B, and nine infectious markers. Early antiviral treatment could alleviate disease severity and prevent illness progression. Lopinavir/ritonavir combined with arbidol showed anti-viral effects in COVID–19. Most patients received anti-viral treatment with interferon alpha inhalation (50 μg twice daily), lopinavir and ritonavir (400 mg twice daily and 100 mg twice daily, respectively), and arbidol (200 mg twice daily) according to the treatment plan. Oral Benadol (400 mg once daily) was administered if the patient's fever lasted for more than three days. The patient was treated with montmorillonite powder for diarrhea. Patients were also treated with integrated Chinese medicine to promote disease rehabilitation. Patients with mild disease symptoms were treated as described above. Patients suspected of being infected with SARS-Cov–2 were discharged from the hospital once the results of two RT-PCR reaction tests taken with 24-hour interval were negative for SARS-Cov–2 antigens.

Statistical analysis

As a previous study has shown that COVID–19 is a self-limited disease and patients generally recover gradually after treatment, the working group collected clinical indicators three times. The first time was one day after admission, the second time was three days after admission, and the third time was five days after admission. Continuous variables were represented as either mean and standard deviations or median with interquartile ranges. For categorical variables, the team calculated the percentages of patients in each category. All of the analyses were done with SPSS software, version 17.0.

Patient and public involvement

This was a retrospective case series study and no patients were involved in the study design, research questions or outcome measures directly. Also, there were no controls or interventions for patients. No patients were asked to advise on interpretation or writing up the results.

Results

Epidemiological characteristics

On March 1, 2020, clinical data were collected on 20 patients with laboratory-confirmed SARS-Cov–2 infection in Sichuan Province. Nine (45%) patients were between 20–39 years of age, seven (35%) cases were between 40–59 years, and four (20%) were aged 60 years or older. The median age was 42.5 years (IQR 29.75–50.25). Half of the patients (50%) were men. No patients had a history of exposure to the Huanan seafood market and all 20 of the patients were exposed to individuals with confirmed SARS-Cov–2 infection. Among the 20 patients, 11 (55%) had a residential history in Wuhan, and the other 9 (45%) had contact with patients from affected areas before illness onset. Of the 11 patients who resided in Wuhan, 4 (36.4%) were aged 20–39 years, 5 (45.5%) were aged 40–59 years, and 2 (18.1%) were older than 60 years. The median age of patients was 43 years (IQR 29–48, Table 1).

Clinical features

In our cohort, four patients (20%) had underlying diseases; two (10%) had lung cancer, one (5%) had scleroderma and diabetes, and one (5%) had diabetes and hypertension. Familial aggregation was present in 4

of 20 patients (20%). All of the patients were able to provide the exact date of close contact with confirmed or suspected COVID–19 cases. The median incubation period from exposure to symptoms onset was 6.5 days (IQR 3.25–9). The median time from onset of symptoms to first hospital admission was 3.5 days (IQR 1.25–7). The median time for *hospital stays* was 14 days (IQR 5.25–19.75). The most common symptoms at illness onset were fever (13, 65%), cough (9, 45%), fatigue (6, 30%), sore throat (10, 50%), chest tightness (2, 10%), headache (3, 15%), diarrhea (3, 15%), and abdominal pain (2, 10%). Seven (35%) patients developed shortness of breath.

Of the 11 patients with a residential history of Wuhan, two (18.2%) had underlying diseases: one patient had diabetes (9.1%) and one patient had lung cancer (9.1%). The median incubation period from exposure to symptoms in this sub-cohort was six days (IQR 3–8). The median time from onset of symptoms to first hospital admission was three days (IQR 1–4). The median time of hospital stays was 15 days (IQR 9–21). The most common symptoms at illness onset were fever (8, 72.7%), cough (4, 36.4%), fatigue (4, 36.4%), sore throat (7, 63.6%), and headache (3, 15%); four (36.4%) patients developed shortness of breath.

On admission, the blood counts of the two (10%) patients showed leucopenia (white blood cell count $< 4 \times 10^9$/L) and eight (40%) showed lymphopenia (lymphocyte count $< 0.8 \times 10^9$/L; Table 2) across the entire cohort. The D-dimer levels were within normal range median 0.345 mg/L (IQR 0.185–0.55mg/L). Levels of aspartate aminotransferase increased in two (10%) patients. Levels of fasting plasma glucose increased in 10 (50%). Over half the patients (82.4%) had normal serum levels of procalcitonin (< 0.1 ng/mL). Abnormalities on chest computed tomograms or radiographs were detected among all of the patients. Seventeen (85%) patients showed more than one lesion site in chest radiographs (Table 1). Typical chest computed tomography findings of infected patients on admission were bilateral or multiple lobular or subsegmental.

In the defined cohort, four patients were transferred to superior medical institutions, one of them was sent into the ICU for acute respiratory distress syndrome and received mechanical ventilation, but the patient expired one day later. Two patients were transferred to an isolation unit because their RT-PCR results remained positive on (Table 1). Of the 20 patients, 16 (80%) were discharged and none died. Two (10%) patients remain quarantined in a medical facility up to now. Discharge standard was based on abatement of fever for at least three days, two negative tests 20 hours apart from pharynx swab nucleic acid, improved evidence on chest radiography, and viral clearance in samples from the lower respiratory tract.

Discussion

As of April 2, 2020, more than 82,722 laboratory confirmed cases of infection with COVID–19 were reported in China. The increasing number of infections is slowing down. However, it is rapidly increasing in other countries. There are 851,537 laboratory-confirmed cases of infection with COVID–19 in more than 200 districts. It is possible that an even greater number of infected patients exist without a diagnosis because their symptoms were less severe and the incubation period is rather long. Only eighty tens of thousands of patients with suspected SARS-Cov–2 infection could eventually receive a diagnosis.

The clinical features of early cases of COVID–19 in Wuhan were not the same as those in other areas of China. According to the data, none of the infected patients in designated medical institutions in Sichuan Province had been exposed to the Huanan seafood market, but most of them lived in Wuhan before the onset of the disease, or they had contact history with people who came back from Wuhan recently. Most infected patients in our study had the same familial cluster, which could be indirect evidence of transmission by contact. It may also suggest human-to-human transmission. At the same time, it is important to be aware of other means of transmission. The SARS-Cov–2 virus was found in anal swabs and blood as well. This suggests shedding and thereby transmission through the oral-fecal route[10]. Doctors tried to find out whether familial aggregation is related to this path of contact transmission, but there was no definitive answer.

It is easy to spread of the disease if protective measures are not taken in the daily life of the patient. Further detailed investigations should aim to ascertain the exact mode of transmission. It is evident that the general population needs to be carefully screened for COVID–19 from the pandemic area. People can effectively stop

SARS-Cov–2 from spreading through the respiratory tract by wearing masks properly. It is important to prevent and control the disease by making sure patients are identified and isolated early. Then, quarantine is one of the oldest and most effective tools of controlling communicable disease outbreaks[11]. We must look at the flow of patients and close contacting people during the prevention and control COVID–19.

The patients in this study have two basic characteristics. First, all of the patients had RT-PCR-confirmed SARS-Cov–2 RNA results. Second, chest CT scan revealed specks or frosted glass. The team isolated the suspected patients if at least one of the two characteristics was present. Some patients can present with a normal chest finding despite testing positive for COVID–19[12]. As a result, many COVID–19 patients will escape confirmed diagnosis, and they can infect people in their daily life if they are not isolated. A combination of repeated swab tests and CT scanning may be helpful for individuals with high clinical suspicion of SARS-Cov–2 infection but negative on RT-PCR screening[13]. In our study, the most common clinical symptoms were fever, cough, fatigue, and chest distress.

Some other symptoms were headache and diarrhea. The laboratory and radiological characteristics were mainly lymphopenia, increased erythrocyte sedimentation rate, increased C-reactive protein, increased lactate dehydrogenase, decreased oxygenation index, normal white blood cell count, and bilateral chest CT involvement. These commonalities have been found in several previous studies[14–16].

However, some clinical features have not been previously reported. Fasting blood glucose of the infected individuals in Sichuan Province was slightly elevated and the glycosylated hemoglobin was normal in the early stages of the disease. These features can gradually become normal until the patient is cured. This may have something to do with the inflammatory response affecting hormonal changes in the body of the patient, which is in a state of emergency. Patients with stress hyperglycemia had more adverse clinical outcomes than patients with normoglycemia[17]. This situation requires us to draw more attention to patients with SARS-Cov–2 infection. Lymphocyte count of the infected individuals is mostly reduced before returning to normal. The dynamic changes in lymphocytes can predict disease status of COVID–19. Alanine aminotransferase (ALT) and aspartate aminotransferase (AST) were abnormally elevated in some patients with novel coronavirus infection, but these levels changes less in people with mild illness. This is consistent with the results of Guan et al.[18] Similarly, it is suggestive of changes in mean platelet volume during disease progression. The result was consistent with previous studies on community-acquired pneumonia[19].

Nevertheless, the working group also found RT-PCR positive patients who had negative chest radiographs, which showed that the lesions had been absorbed. It is not clear how to control these patients according to current the discharge standards. In this study, the pharyngeal swabs of two patients remained positive for a long time and they could not be discharged from the hospital. For these two patients, swabs remain positive for a long time after the clinical symptoms disappeared. It is also not clear if they were infectious to the population. This point is also a challenge to the discharge criteria of cured patients. More evidence needs to be gathered to confirm this phenomenon in the future.

Limitations of study

This study has several limitations. First, only 20 patients were included. Many patients were continually being admitted to hospital as data were being collected, and thus we obtained data on most but not all of the patients with laboratory-confirmed infection in Sichuan Province during the study period. Second, as the patients were only from Sichuan Province, the clinical features might differ from clinical features related to COVID–19 all over the world. Third, the patients were transferred to designated medical institutions after being diagnosed by other medical institutions; therefore, there is a certain bias in the acquisition of clinical data at the initial stage of treatment. Fourth, the patients had mild illness in designated medical institutions. The patients are transferred to the municipal public health center for treatment when they suddenly become critically ill; we did not collect clinical data from these patients. All of these factors could result in biases of clinical observation characteristics. Due to the exploratory nature of the study, which was not driven by formal hypotheses, the sample size calculation was waived.

Conclusion

Compared with the symptoms of the patients with SARS-Cov–2 infection in Wuhan, patients from Sichuan Province were relatively mild. Most of them recovered after treatment and left safely from the hospital. However, the fasting blood glucose of the infected individuals was slightly elevated because of the state of emergency. The dynamic changes of lymphocytes can predict disease status of COVID–19. It is also suggestive of changes in mean platelet volume during disease progression. There is no specific drug available to treat COVID–19 and no specific vaccine to prevent infection. Therefore, we should adopt a multi-strategy prevention and control plan to carry out clinical treatment against SARS-Cov–2 infection as soon as possible.

Declarations

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Ethical approval: In this study, all human enrolled were carried out in accordance with the recommendations of the Medical and Ethical Committees of the Chengdu Fifth People's Hospital (approval No. AF/72/2020-01.0). The study protocol was designed following the guideline of WHO nCov CASE RECORD FORM (Ver. 1.2 28JAN2020) and Chinese Protocol for Prevention and Control of COVID-19 (Edition 1-6), the protocol was approved by the Chengdu Fifth People's Hospital. Written informed consent in accordance with the Declaration of Helsinki was obtained from all participants.

Patient consent: Obtained.

Data sharing: No additional data are available.

Transparency: The lead authors and manuscript's guarantor affirm that the manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned have been explained.

Competing interest: NO

Authors' contribution: ZG and T-YH contributed equally to this article. ZG and L-JC conceptualized the paper. T-YH analyzed the data, with input basic initial data obtained from the study. ZG, FJ, LJ,L-JC,Y-YM and CL wrote the initial draft with all of the authors, providing critical feedback and edits to subsequent revisions. L-YX helped to finalizer the draft. All of the authors approved the final draft of the manuscript. Z-JP is the guarantor. The corresponding author attests that all of the listed authors meet authorship criteria and that no others meeting the criteria have been omitted.

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Tables

Due to technical limitations, Tables 1-2 are available in the Supplementary Files section.

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