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Epidemiological Features of 105 Patients Infected with the COVID-19

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Abstract: Objective: To investigate and evaluate the clinical features of patients infected with the 2019 novel coronavirus (COVID-19) outside of Wuhan.

Methods: 105 patients admitted to our hospital with clinical- and laboratory-confirmed COVID-19 infection were studied. Data were collected from January 17, 2020 to March 5, 2020.

Results: 105 patients (57 male and 48 female) were confirmed to have COVID-19 infection. Among the 105 patients, 55 (52%) had made short trips to Wuhan during the two weeks before the onset of illness, and these were the first-generation confirmed cases. An exact date of close contact with someone in Wenzhou with confirmed or suspected COVID-19 infection from Wuhan (the second-generation confirmed cases) could be provided by 38 (36%) patients. Of the remaining patients, six (6%; the third-generation confirmed cases) were familial clusters of the second-generation confirmed cases, three (3%) had no definite epidemiological features, and 16 (15%) were from the same location as for the case report.

Conclusion: Due to the infectiousness of COVID-19, patients with infections should be diagnosed and treated as early as possible after developing fever symptoms or showing other clinical characteristics or imaging features. With respect to high-risk cases, we must focus on any complications that arise and take effective measures to treat them immediately. This will significantly improve the prognosis of patients with severe infections.

Keywords: 2019 novel coronavirus ■ Outside of Wuhan ■ Epidemiological features ■ Clinical findings

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INTRODUCTION

The current outbreak of the 2019 novel coronavirus, named 2019-novel coronavirus-infected pneumonia (COVID-19) by the World Health Organization (WHO),¹ and the occurrence of numerous pneumonia cases that started in December 2019 in the city of Wuhan, Hubei, China, once again demonstrates the risk of

emerging zoonotic viral infections in general and the spread of pandemic situations in particular. Two months after its first appearance, this epidemic is already larger than the Severe Acute Respiratory Syndrome (SARS) coronavirus (SARS-CoV) outbreak during 2002/2003, and the virus has extended rapidly to most parts of China outside of Wuhan as well as to other countries where case numbers were rapidly increasing. Currently, there is no vaccine or effective antiviral treatment against COVID-19 infection, which has been declared a public health emergency of international concern by WHO and may progress to a pandemic associated with substantial morbidity and mortality.² As cases of human infection increased, quarantine of infected or potentially infected individuals was adopted, and safety guidelines were issued and publicised to the general population to reduce the chance of infection.

Though we have acquired some understanding of the epidemiological, clinical, laboratory, and radiological characteristics, as well as treatment and clinical outcomes of the confirmed cases, it is necessary to conduct further clinical investigations. Also, recent reports showed that a spread of the virus between cities was possible.³ Our hospital, a COVID-19-designated hospital in Wenzhou city in Zhejiang, received its first patient from Zhejiang on January 17, 2020, and this patient had recovered by January 24, 2020. We found that the features of cases for patients outside Wuhan differed from those initially reported by patients in Wuhan. New cases are continually being detected. In order to fully understand the features of the disease as soon as possible, summarise the clinical experiences of curing, and provide insight into the prevention and treatment of COVID-19 across China and elsewhere, the present retrospective case series displays the epidemiological analysis and clinical findings of 105 confirmed cases from the Wenzhou district in detail.

METHODS

Data sources

We conducted a retrospective study focusing on the clinical characteristics of 105 confirmed cases of COVID-19

patients admitted to Wenzhou Central Hospital from the Wenzhou district from January 17, 2020 to February 20, 2020. Of these, 12 were from the First Affiliated Hospital of Wenzhou Medical University, 20 were from the Second Affiliated Hospital of Wenzhou Medical University, 11 were from the People's Hospital of Wenzhou, 13 were from the Integrated Chinese and Western Medicine Hospital, 12 were from the Third People's Hospital of Ou Hai District, nine were from the First People's Hospital of Longwan District and 28 were from our hospital. There were 57 male and 48 female patients. The ages ranged from 22 to 64 years, with a median age of 42 years. Three patients were from out-of-province (Jiangxi province, Shanxi province and Hubei province), and the remainder were local. Of these patients, 53 had underlying diseases, including 34 with hypertension, eight with diabetes, four with fatty liver, seven with chronic hepatitis B, two with chronic gastritis, and two with old tuberculosis.

Outcome measures

Clinical information included epidemiological, clinical, laboratory, and radiological characteristics, respiratory pathogens and treatment and clinical outcomes of the 105 confirmed cases with COVID-19 infection.

Diagnostic criteria

Case definitions of confirmed human infection with COVID-19 are in accordance with 'The Diagnosis and Treatment Plan for New Coronavirus Infected Pneumonia (Trial 5th Edition)' published by the Health Commission of the People's Republic of China in February 2, 2020.⁴ Sputum and throat swab specimens collected from all suspected cases at admission were sent for detection of viral respiratory pathogens and tested positive for COVID-19 RNA by real-time polymerase chain reaction assay within 3 h. Virus detection was repeated twice every 24 h. Common cases are defined as presenting with a fever or any respiratory symptoms and pneumonia on computed tomography (CT), including a dry cough, and especially in those with a history of travel to Wuhan or exposure to infected people within the two weeks before the onset of illness. Patients with a severe illness presented with one of the following conditions: 1. Respiratory distress syndrome, RR \geq 30 times per minute; 2. Oxygen saturation of quiescent status \leq 93%. 3. The ratio of the arterial partial pressure of oxygen (PaO₂) to inspired oxygen concentration (FiO₂) \leq 300 mmHg (1 mmHg = 0.133 kPa). Patients with a critical illness were those who presented with one of the following conditions: 1. Both respiratory failure and mechanical ventilation. 2. Shock. 3. ICU monitoring and treatment combined with other organ failures. Only patients with a laboratory and clinically confirmed

infection were enrolled in this work according to the above classification through related screening assay. Ethical approval for this study was obtained from the ethics committee of our hospital in compliance with the Declaration of China. All participants were informed and gave signed informed consent prior to their inclusion in the study. This was a retrospective case series study, and no patients were involved in the study design, setting the research questions, or the outcome measures directly. No patients asked for advice on interpretation or writing up of results. We used a standardised case report form to collect clinical data.

Treatment plan

1. Symptomatic treatment: the patients were admitted to an airborne-isolation unit at the hospital for clinical observation with health care workers following CDC recommendations for droplets and airborne precautions with eye protection. The patients took rest, drank water, had oxygen therapy and strengthened liquid replenishment. Their low potassium and sodium concentration were corrected under close observation of changes in their condition.
2. Antiviral therapy⁴: Combination therapy was initiated with recombinant human interferon alfa-2b (Anfuron, Tianjin Hualida Bioengineering Co., Ltd, China. 5 million units daily, BID, 7-10 d), medicated with lopinavir and ritonavir tablets (Kaletra, AbbVie Ltd. 800/200 mg daily, BID, 7-10 d), and Abidol hydrochloride tablets (Qixiao, Shiyao Group Ouyi Pharmaceutical Co., Ltd, China. 200 mg, daily, TID, 5-6 d).
3. Chinese medicine therapy: Lianhuaqingwen Jiaonang (Yiling, Shijiazhuang Yiling Pharmaceutical Co., Ltd, China. 4.2 g daily, TID, 7 d).
4. Other therapy: Methylprednisolone (40 mg daily, BID) was used for 16 severe cases and three critical cases. According to clinical symptoms and CT lung imaging, on days 3-5 of treatment, methylprednisolone was reduced to 40 mg daily (QD) and withdrawn on day 7. Also, 16 severe infection cases and three critical cases were treated with intravenous immunoglobulin (IVIG) (20 mg daily, QD) for five days.

Discharge standard

The temperature of patients had returned to normal for three to four days. After markedly improved respiratory function and the repeated negative results of COVID-19

RNA assay for two consecutive tests (the sampling interval should be at least one day), the patients could be discharged.⁴

Statistical analysis

We summarised continuous variables as either means and standard deviations or medians with interquartile ranges. For categorical variables, we calculated the percentages of patients in each category. All analyses were performed with SPSS software, version 22.0.

RESULTS

Epidemiological characteristics

Epidemiological data were collected through brief interviews with each patient. From 17 January to February 20, 2020, clinical data were collected from 105 patients with a laboratory-confirmed COVID-19 infection at Wenzhou Central Hospital in the Wenzhou district. No patients had a history of exposure to the Huanan Seafood Wholesale Market, and 102 (97%) patients had been in close contact (gathering, living, or working together) with individuals with a confirmed or suspected COVID-19 infection. Among the 105 patients, 55 (52%) patients had made short trips to Wuhan in the two weeks before the onset of illness, and these were the first-generation confirmed cases. The second-generation confirmed cases, 38 (36%) of patients, could provide the exact date of close contact with someone in Wenzhou with a confirmed or suspected COVID-19 infection from Wuhan. Six (6%) patients were familial clusters of the second-generation confirmed cases, and these made up the third-generation confirmed cases. A further three patients (3%) had no definite epidemiological features. One confirmed case was connected to 16 (15%) patients from the same location.

Clinical features

Incubation period. The median incubation period from exposure to symptoms was 3.4 days (interquartile range 1-14 days). The median time from the onset of symptoms to the first hospital admission was 4.0 days (1-10 days). The median time from the first hospital admission to confirmation was 5.6 days (2-14 days). The median time from the onset of symptoms to hospitalisation was 5.8 days (2-14 days).

The most common symptoms. The most common symptoms at illness onset (as shown in [Table 1](#)) were fever (98/105, 93.3%) (37.5-40.0 °C) for 6.9 days averaged, dry cough (79/105,75.2%), weak (61/105, 58.1%), expectoration (39/105, 37.1%), shortness of breath (26/105, 24.8%), diarrhoea (22/105, 21.0%), headache (7/105, 6.7%),

Table 1. Clinical characteristics of 105 patients with coronavirus disease 2019 (covid-19).

Classification	Proportion
All patients	105
Age groups (years)	
≤40	32/105 (30.5%)
40-60	63/105 (60.0%)
≥60	10/105 (9.5%)
Sex	
Male	57/105 (54.3%)
Female	48/105 (44.7%)
Clinical symptoms	
Fever	98/105 (93.3%)
Weak	61/105 (58.1%)
Dry cough	79/105 (75.2%)
Expectoration	39/105 (37.1%)
Shortness of breath	26/105 (24.8%)
Nausea	19/105 (18.1%)
Vomit	16/105 (15.2%)
Diarrhoea	22/105 (21.0%)
Haemoptysis	18/105 (17.1%)
Nasal obstruction	8/105 (7.6%)
Sneezing	6/105 (5.7%)
Sore throat	16/105 (15.2%)
Myalgia or fatigue	9/105 (8.6%)
Headache	7/105 (6.7%)

myalgia or fatigue (9/105, 8.6%), sneezing (6/105, 5.7%), and nasal obstruction (8/105, 7.6%).

Laboratory assay

Sputum and throat swab specimens tested positive for COVID-19 RNA by real-time polymerase chain reaction assay. WBC, NEC, LC, Hb, PLT, ALT, AST, CK, LDH, K+, Na+ and CRP are illustrated in [Table 2](#).

Transverse chest computed tomograms

A chest CT is helpful and is more sensitive than an x-ray in identifying viral pneumonia. Imaging of patients with COVID-19 initially revealed characteristic patchy infiltration, progressing to large ground-glass opacities that often present bilaterally. Abnormalities on chest computed tomograms or radiographs were detected amongst all of the patients collected in this study. The chest radiographs of 105 patients were affected to varying degrees. Patients with mild cases mostly showed cloud-like and ground-

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Table 2. Laboratory findings of 65 patients with coronavirus disease 2019 (covid-19).

Classification	Proportion
All patients	105
covid-19 RNA	105/105 (100.0%)
Laboratory findings	
WBC(10 ⁹ /L)	
<3.5	26/105 (24.8%)
3.5-9.5	79/105 (75.2%)
>9.5	0/105 (0.0%)
NEC (10 ⁹ /L)	
<1.8	13/105 (12.4%)
1.8-6.3	89/105 (84.7%)
>6.3	3/105 (2.9%)
LC (10 ⁹ /L)	
<1.1	49/105 (46.7%)
1.1-3.2	57/105 (54.3%)
>3.2	0/105 (0.0%)
Hb (g/L)	
<115	3/105 (2.9%)
115-150	89/105 (84.8%)
>150	13/105 (12.4%)
PLT ((10 ⁹ /L)	
<125	12/105 (11.4%)
125-350	87/105 (82.9%)
>350	6/105 (5.7%)
ALT (U/L)	
<7	2/105 (1.9%)
7-40	82/105 (78.1%)
>40	21/105 (20.0%)
AST (U/L)	
<13	2/105 (1.9%)
13-35	77/105 (73.3%)
>35	26/105 (24.8%)
CK (U/L)	
<40	11/105 (10.5%)
40-200	70/105 (66.6%)
>200	24/105 (22.9%)
LDH (U/L)	
<120	2/105 (1.9%)
120-250	65/105 (61.9%)
>250	38/105 (36.2%)
K+ (mmol/L)	

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Classification	Proportion
<3.5	34/105 (32.4%)
3.5-5.5	71/105 (67.6%)
>5.5	0/105 (0.0%)
Na+ (mmol/L)	
<137	44/105 (41.9%)
137-147	61/105 (58.1%)
>147	0/105 (0.0%)
CRP (mg/L)	
0-8	9/105 (8.6%)
>8	96/105 (91.4%)

glass-like high-density shadows scattered outside the lungs. Small patches of consolidation and air bronchogram were seen locally. The images of patients with severe infections mostly showed diffused high density. Most of the lesions had pulmonary consolidation or cord-like changes, local fibrosis had formed, and the lower lobe of both lungs was more prominent. The high-density plaques of 73 patients involved multiple lung lobes (≥ 3), with early ground-glass, cloud-like or typical of crazy-paving pattern. In the later stage of the disease, at least two lung lobes showed pulmonary consolidation and localised pulmonary fibrosis. The inflammatory response was gradually absorbed after 7-10 days of effective treatment.

Clinical classification

According to ‘The Diagnosis and Treatment Plan for New Coronavirus Infected Pneumonia (Trial 5th Edition)’, issued by the National Health and Health Commission on February 5, 2020, the clinical classification includes 86 cases of a common type, 16 cases of a severe type, and three cases of a critical type.

Electrocardiography (EKG)

EKG was normal in 78 patients. Sinus rhythm and T wave changed in 15 cases, 6 cases showed sinus rhythm and left ventricular high voltage, 2 cases showed sinus tachycardia, 2 cases showed sinus rhythm with left anterior branch block, and sinus rhythm with T wave changed and U waves elevated in 2 cases.

Prognosis

The temperature of 105 patients had returned to normal after treatment for 1-5 days (median length: 2.7 days).

Sputum and throat swab specimens tested negative for COVID-19 RNA undergoing for 10-20 days (median length: 12.8 days) from symptom initiations. All cases were discharged if they fulfilled the criterion of two repeated negative results for COVID-19 RNA assay for two consecutive tests (the sampling interval should be at least one day), and the last patient was discharged by March 5, 2020. The median length of stay was 15.8 days.

DISCUSSION

At the end of December 2019, a group of patients with pneumonia of an unknown cause and linked to Huanan Seafood Wholesale Market were confirmed to be infected with a novel coronavirus, known as 2019-nCoV by WHO. This coronavirus belongs to the same family of viruses responsible for Severe Acute Respiratory Syndrome (SARS) and Middle East Respiratory Syndrome (MERS).⁵ Patients can be afebrile in the early stages of infection, with only chills and respiratory symptoms. High temperature is not a general presentation. The virus quickly spread among the crowd to 23 other countries by travellers from Wuhan. With the spread of the pandemic, there were about 70,000 confirmed cases and 10,000 suspected cases in other parts of China as of January 12, 2020. It was mainly transmitted via airborne droplets from a cough or sneeze and close contact, but little was known about any aspect of other transmissions. As an acute respiratory infectious disease, it has been included in category B infectious diseases in the Law of the People's Republic of China on the Prevention and Treatment of Infectious Diseases and controlled as category A infectious diseases.⁶ Recent reports⁷ about the familial clusters in China indicated that five family members not only had a fever, typical respiratory symptoms, and diarrhoea but tested positive for COVID-19 RNA as well. Our present work indicated that 55 patients were first-generation confirmed cases and 38 patients were second-generation confirmed cases. The local infectious patients were slightly less contagious than imported cases. In other words, 1 s-generation confirmed case infected four cases of third-generation confirmed cases. Additionally, 1 s-generation confirmed case infected two cases of third-generation confirmed cases. Our findings made it completely clear that person-to-person transmission has been occurring and familial clusters (gatherings) are particularly infectious. Inappropriate homecare can be life-threatening for patients and be a detriment to public health. Familial clusters were an important exact transmission pathway that needs to be ascertained. To prevent a superinfection and spread at any time in the community, every confirmed case and close

contact must be isolated and monitored in a health setting, especially for someone with the onset of fever and respiratory symptoms. Diagnostic procedures should be further improved, and strict classified admission practices must be followed. Home care and isolation can relieve the burden on healthcare providers at clinics with infected cases.

Huang C. et al.⁸ reported clinical presentations of a cohort of 41 patients with a laboratory-confirmed COVID-19 infection that greatly resembled SARS-CoV, and the mortality rate was high for COVID-19. It was also noted that patients infected with COVID-19 also had high amounts of IL1B, IFN γ , IP10, and MCP1, probably leading to activated T-helper-1 (Th1) cell responses. The cytokine storm was associated with disease severity. However, COVID-19 infection also initiated increased secretion of T-helper-2 (Th2) cytokines (e.g., IL4 and IL10) that suppress inflammation, which differs from SARS-CoV infection. In the present work, most patients were young or middle-aged, and nearly half of them (57/105, 54.3%) had underlying diseases, especially hypertension. Older people with underlying diseases were usually severely ill after infection. Most of the infected individuals in our study had fever and fatigue as their initial symptom, and some of them presented with an increase of transaminase. The laboratory test results showed that there were some patients with abnormal liver function, 21 with ALT level increases, 26 with AST, 38 with LDH and 24 with CK level increases, which was related to virus infections. Nearly a third of all infected individuals (34/105, 32.4%) showed hypopotassemia, which was connected to decreased consumption after fever, and may be associated with nausea and vomiting after exposure to anti-virus drugs. Half of all patients had diarrhoea during treatment, which was probably related to treatment with lopinavir and ritonavir.

When investigating clinical characteristics and observations of treatment, it was found that patients who developed symptoms after the onset of COVID-19 had relatively mild cases. The toxicity of the virus strain would be diminished with breeding. Changes of CT imaging for patients with mild symptoms mostly showed cloud-like and ground-glass-like high-density shadows scattered outside the lungs. Small patches of consolidation and air bronchograms were seen locally. The images of patients with severe symptoms mostly showed a diffuse high density, where most of the lesions had pulmonary consolidation or rare pleural effusion.

The current study⁹ found that COVID-19 appears to be a recombinant virus between the bat coronavirus and an origin-unknown coronavirus. The recombination occurred

within the viral spike glycoprotein, which recognises cell surface receptors. Interestingly, no similar sequence was found with known sequence databases, suggesting that a putative recombination parent virus was still unknown. Gaining a deeper understanding of the interaction between coronaviruses and the innate immune systems of the hosts may shed light on the development and persistence of inflammation in the lungs, kidneys and other organs and hopefully can reduce the risk of lung, kidneys and other organ inflammation caused by COVID-19.¹⁰ Our study recommends that the toxicity of virus would be attenuated with virus breeding on the basis of the investigations into the alleviation of clinical characteristics and imaging changes of the next generation patients.

In summary, an outbreak of novel coronavirus has spread rapidly and widely, with cases now confirmed in multiple countries. Investigations are underway worldwide to better understand transmission dynamics and the spectrum of clinical illness. COVID-19 is a novel coronavirus, and most people lack resistance or immunity to COVID-19. From our study, despite strong infectivity, the rapid progress of the disease, and lower respiratory tract involvement with server cases, we find patients should be diagnosed and treated as soon as possible after developing fever symptoms combined with clinical characteristics and imaging features. With respect to high-risk cases, the focus must be on being vigilant regarding complications and taking effective measures. In this way, the prognosis for severely ill patients would improve.

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