Clinical Infectious Diseases

MAJOR ARTICLE

Clinical Characteristics of Imported Cases of Coronavirus Disease 2019 (COVID-19) in Jiangsu Province: A Multicenter Descriptive Study

Jian Wu,[1,2,a] Jun Liu,[3,a] Xinguo Zhao,[4,a] Chengyuan Liu,[5,a] Wei Wang,[2] Dawei Wang,[6] Wei Xu,[7] Chunyu Zhang,[8] Jiong Yu,[1] Bin Jiang,[9] Hongcui Cao,[1,10] and Lanjuan Li[1]

[1]State Key Laboratory for the Diagnosis and Treatment of Infectious Diseases, National Clinical Research Center for Infectious Diseases, The First Affiliated Hospital, College of Medicine, Zhejiang University, Hangzhou, China, [2]Department of Laboratory Medicine, The First People's Hospital of Yancheng City, Yancheng, China, [3]Department of Laboratory Medicine, The Fifth People's Hospital of Wuxi, Affiliated to Jiangnan University, Wuxi, China, [4]Department of Respiration, The Fifth People's Hospital of Wuxi, Affiliated to Jiangnan University, Wuxi, China, [5]Department of Infectious Disease, The First People's Hospital of Yancheng City, Yancheng, China, [6]Department of Infectious Disease, The Second People's Hospital of Yancheng City, Yancheng, China, [7]Department of Preventive Medicine and Public Health Laboratory Sciences, School of Medicine, Jiangsu University, Zhenjiang, Jiangsu, China, [8]Department of Laboratory Medicine, The Second People's Hospital of Yancheng City, Yancheng, China, [9]Department of Laboratory Medicine, The Central Blood Station of Yancheng City, Yancheng, Jiangsu, China, and [10]Zhejiang Provincial Key Laboratory for Diagnosis and Treatment of Aging and Physicochemical Injury Diseases, Hangzhou, China

Background. We aimed to report the clinical characteristics of imported cases of coronavirus disease 2019 (COVID-19) in Jiangsu Province.

Methods. We retrospectively investigated the clinical, imaging, and laboratory characteristics of confirmed cases of COVID-19 with World Health Organization interim guidance in 3 grade IIIA hospitals of Jiangsu from 22 January to 14 February 2020. Real-time RT-PCR was used to detect the new coronavirus in respiratory samples.

Results. Of the 80 patients infected with COVID-19, 41 were female, with a median age of 46.1 years. Except for 3 severe patients, the rest of the 77 patients exhibited mild or moderate symptoms. Nine patients were unconfirmed until a third nucleic acid test; 38 cases had a history of chronic diseases. The main clinical manifestations of the patients were fever and cough, which accounted for 63 (78.75%) and 51 (63.75%) cases, respectively. Only 3 patients (3.75%) showed liver dysfunction. Imaging examination showed that 55 patients (68.75%) showed abnormal density shadow and 25 cases (31.25%) had no abnormal density shadow in the parenchyma of both lungs. Currently, 21 cases have been discharged from the hospital, and no patient died. The average length of stay for discharged patients was 8 days.

Conclusions. Compared with the cases in Wuhan, the cases in Jiangsu exhibited mild or moderate symptoms and no obvious gender susceptibility. The proportion of patients having liver dysfunction and abnormal CT imaging was relatively lower than that in Wuhan. Notably, infected patients may be falsely excluded based on 2 consecutively negative respiratory pathogenic nucleic acid test results.

Keywords. coronavirus disease 2019 (COVID-19); clinical characteristics; imported cases; pneumonia.

The coronavirus disease 2019 (COVID-19) has been recently identified to be caused by a type of B-coronavirus [1]. The virus has enveloped virions that appear as round or oval, often polymorphous, with a diameter of 60–140 nm [2]. It is widely distributed in human and other mammals, and its genome is more distant from severe acute respiratory syndrome coronavirus (SARS CoV) [3, 4] and Middle East respiratory syndrome coronavirus (MERS CoV) [5, 6]. Since December 2019, a large number of COVID-19 patients have been reported in Wuhan, Hubei Province [7–9]. Most of them work in or live around the local Huanan seafood wholesale market, where wild animals are illegally on sale. Severe symptoms of acute respiratory infection appeared within the early stage of this pneumonia, with exacerbating cases where patients developed acute respiratory distress syndrome (ARDS), septic shock, metabolic acidosis, and coagulation dysfunction, which are difficult to correct [10].

As of 14 February 2020, 66 577 cases have been confirmed in China, including 54 406 cases in Hubei Province, 37 914 cases in Wuhan City, including medical staff, and several exported cases in Thailand, Singapore, Japan, South Korea, the United States, Australia, and other countries. Considering its highly contagious nature, COVID-19 has been categorized as a class B infectious disease stipulated in the law of the People's Republic of China on the prevention and control of infectious diseases for the first time, and is managed as class A infectious disease [11].

Received 8 February 2020; editorial decision 21 February 2020; accepted 26 February 2020; published online February 29, 2020.

[a]J. W., J. L., X. Z., and C. L. contributed equally to this work.

Correspondence: H. Cao, State Key Laboratory for the Diagnosis and Treatment of Infectious Diseases, National Clinical Research Center for Infectious Diseases, The First Affiliated Hospital, College of Medicine, Zhejiang University, 79 Qingchun Rd, Hangzhou 310003, China (hccao@zju.edu.cn).

Clinical Infectious Diseases® 2020;71(15):706–12

DOI: 10.1093/cid/ciaa199

So far, several studies have described the epidemiological and clinical characteristics of patients with COVID-19, but they are all limited to cases in Wuhan and not in other areas [12, 13]. In this study, the clinical characteristics of 80 patients diagnosed with COVID-19 in 3 grade IIIA hospitals of Jiangsu Province are discussed. We believe our findings will provide further details to the epidemic situation and clinical characteristics of this novel coronavirus.

METHODS

Patients

All enrolled 80 patients, who were referred to the First People's Hospital of Yancheng City, the Second People's Hospital of Yancheng City, and the Fifth People's Hospital of Wuxi from 22 January to 14 February were retrospectively and consecutively analyzed. According to the arrangements by the Chinese government, all 3 tertiary hospitals provide treatment for all patients who were diagnosed as having COVID-19 according to World Health Organization (WHO) interim guidance [14]. We collected all the data including clinical, demographic, laboratory parameters; chest computed tomography (CT); length of hospitalization and intensive care unit stay; and prognosis from patients' medical records and attending doctors. The data endpoint was 14 February 2020. The present study was performed in accordance with the Helsinki Declaration and was approved by the Ethics Committee of the First People's Hospital of Yancheng City. Written informed consent was obtained from participants or their families when data were collected retrospectively.

According to WHO Interim Guidance [14], cases in this study were defined as anyone with the following epidemiological history and consistent with any 2 clinical manifestations and the pathogenic evidence:

1. Epidemiological history: (1) within 14 days before the onset of the disease, there were tourism or residence histories in Wuhan or its surrounding areas, or other communities with confirmed cases; (2) within 14 days before the onset of the disease, there were contacts with confirmed cases of COVID-19; (3) within 14 days before the onset of the disease, there were contacts with suspected cases (having fever or respiratory symptoms) from Wuhan or its surrounding areas, or other communities with confirmed cases; (4) aggregation—within 14 days before the onset of the disease, 1 confirmed case was found in an enclosed environment (eg, a family house, a construction site, an office) with 1 or more cases of fever respiratory tract infection found at the same time, revealing potential interpersonal transmission or joint exposure of the disease.
2. Clinical manifestations: (1) fever and/or respiratory symptoms; (2) imaging indicates multiple mottling and interstitial changes in the lung periphery during the early stage, which subsequently developed into bilateral ground-glass opacity, infiltrates, and lung consolidation; pleural effusion was rarely seen; (3) in the early stage of the disease, the total number of leukocytes was normal or decreased, or the lymphocyte count was decreased.
3. Pathogenic evidence: the nucleic acid test was used to detect the new coronavirus in respiratory fluid.

The patients were clinically classified into 4 types: mild, moderate, severe, or critically ill. The criteria for clinical classifications are shown in Supplementary Table 1.

Strategy for Nucleic Acid Tests

Once a suspected case was admitted to the hospital, the nucleic acid test was carried out immediately. A nose swab and/or throat swab were taken from each patient. The nucleic acid test was considered positive if the result of either of the above samples was positive. If it was negative, the samples would be taken once a day for the next 2 days.

After the treatment, if the patient's condition improved significantly and there were no respiratory symptoms of fever or cough, the patient would be discharged after passing 2 consecutive nucleic acid tests.

Detection of Coronavirus

A total of 150 μL of sample from throat swab and/or nose swab of each patient was used to extract total RNA. On the basis of the manufacturer's instructions, total RNA extracted using the respiratory sample RNA isolation kit (Zhongzhi, Wuhan, China) and each sample obtained 40 μL elution. In order to target the nucleocapsid (N) gene and open reading frame lab (ORF1ab) gene using a 2019 novel coronavirus nucleic acid detection reagent (Bio-germ, Shanghai, China), we used real-time reverse transcriptase–polymerase chain reaction (RT-PCR) with 5 μL RNA. The final reaction mixture concentrations of primer and probe were 500 nm and 200 nm, respectively. The sequences used and real-time RT-PCR performance conditions are listed in Supplementary Table 2.

The lowest detection concentration is 1×10^3 copies/mL. There was no cross-reaction with influenza A virus H1N1, H1N1 (2009), H3N2, H5N1, H7N9, influenza B virus (BV and BY types), human coronavirus (229E/HKU1/OC43/NL63/SARS/MERS), parainfluenza virus (1, 2, 3), or rhinovirus A/B/C. No more than 50% blood and less than 0.9 mg/mL of mucin in the sample will not cause interference.

Statistical Analysis

Statistical analyses were performed with SPSS (version18.0; SPSS Inc, Chicago, IL). If the continuous measurement is a normal distribution, we present it as a mean (±SD); if it is not a normal distribution, we present it as a median (interquartile range [IQR]); the classification variable is presented as a count

(%). We also evaluated whether the laboratory parameters were outside the normal range.

RESULTS

Demographics, Baseline, and Clinical Characteristics of Patients With COVID-19

In this study, 80 cases with COVID-19 in Yancheng City and Wuxi City were investigated, including 5 families. All these cases were imported infections (with an epidemiological history of Wuhan) and had no contact with Huanan seafood market in Wuhan. None of these patients were medical staff. Among them, 41 patients (51.25%) were female, with a median age of 46.1 years (IQR, 30.7–61.5). Twenty-seven patients (33.75%) were aged 25–49 years, 19 patients (23.75%) were aged 50–64 years, 15 patients (18.75%) were aged 18–24 years, 10 patients (12.50%) were under 18 years old, and 9 patients (11.25%) were over 65 years old (Figure 1). Of the 10 patients under 18 years old, the minimum age was 4, 2 patients were between 6 and 8 years old, and 6 patients were between 11 and 13 years; the maximum age was 14. In term of clinical classification, 28 (35.00%) patients were mild type, 49 (61.25%) patients were moderate type, 3 (3.75%) patients were severe type, and no patient was critically ill. During the diagnostic procedure, we found that 41 patients (51.25%) had a positive result in the first test, and 30 patients (37.50%) had a positive result in the second test. Surprisingly, another 9 patients (11.25%) remained negative until a third test. Of all the 80 patients, 38 cases (47.50%) had a history of chronic diseases, including cardiovascular and cerebrovascular diseases, endocrine system diseases, digestive system diseases, respiratory system diseases, malignant tumors, and nervous system diseases (Table 1).

The most common symptoms were fever and cough, which accounted for 63 cases (78.75%) and 51 cases (63.75%), respectively. Thirty cases (37.50%) had shortness of breath. In addition, 18 (22.50%) patients had muscle ache, 13 patients (16.25%) had headache and mental disorder symptoms, and no patients had hemoptysis or diarrhea symptoms. The average time from onset to the emergence of shortness of breath was 8.0 days (IQR, 5.0–13.0). Except for 10 patients (12.50%) with acute respiratory injury and 2 patients (2.50%) with renal injury, there was no other organ damage (Table 1). The intersections of positive nucleic acid test result and clinical characteristic are shown in Supplementary Table 3.

Laboratory Findings of Patients With COVID-19

The white blood cell (WBC) count of 36 patients (45.00%) was lower than the normal range (4×10^9/L), and 26 patients (32.50%) had lymphocytopenia (the lymphocyte count was $<1.0 \times 10^9$/L). Eleven patients (13.75%) had platelets lower than the normal range (125×10^9/L), and no patients had platelets higher than the normal range (350×10^9/L). There were 62 patients (77.50%) with high C-reactive protein (CRP) and 59 patients (73.75%) with a high erythrocyte sedimentation rate (ESR). Only 1 patient (1.25%) had an elevated procalcitonin (PCT) level.

In terms of liver function, only 3 patients (3.75%) showed alanine transaminase (ALT) or aspartate aminotransferase (AST) above the normal range. Two patients (2.50%) had a lower albumin level than the normal range (35 g/L). Eighteen patients (22.50%) had an abnormal myocardial enzyme spectrum, indicating an increase in creatine kinase (CK). The level of lactate dehydrogenase (LDH) was increased in 17 patients (21.25%). Two patients (2.50%) had different degrees of renal function damage, one of them had serious renal function damage (Urea: 26.5 mmol/L, creatinine [CREA]: 1054.4 mmol/L). The blood glucose (GLU) level of 19 patients (23.17%) exceeded the normal range (5.9 mmol/L). The level of D-dimer was increased in 3

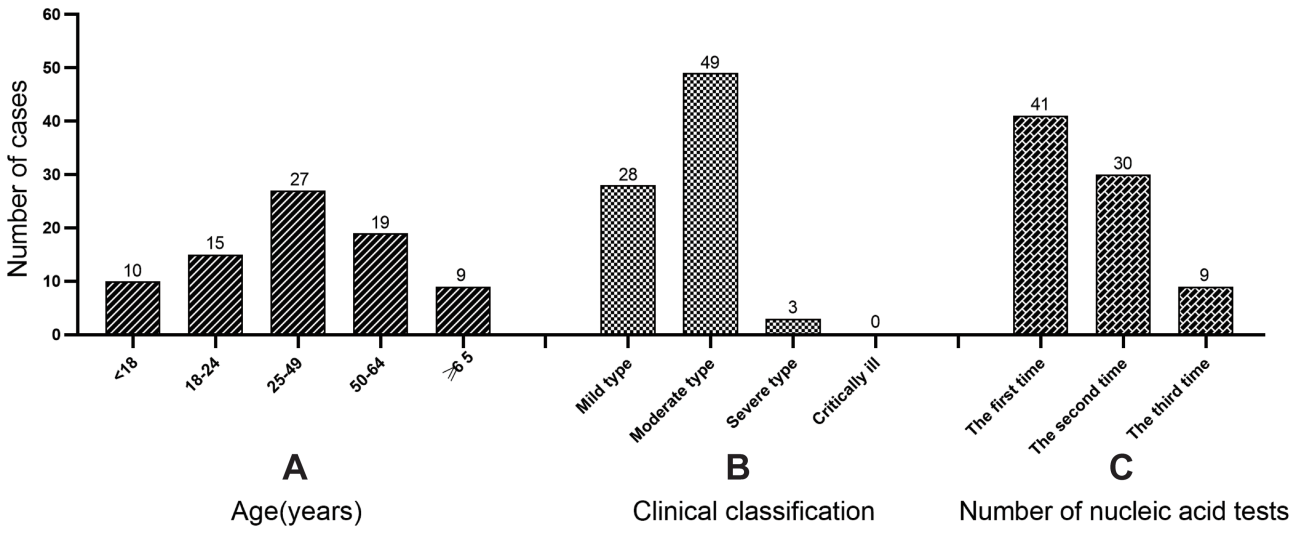

Figure 1. Age distribution, clinical classification, and nucleic acid tests of patients infected with coronavirus disease 2019. *A*, Number of confirmed patients by age group; *B*, number of confirmed patients by different clinical classification; *C*, number of nucleic acid tests used to confirm patients.

Table 1. Demographic, Baseline, and Clinical Characteristics of Patients With COVID-19

Variables	Patients (N = 80)
Age, years	
Mean ± SD	46.10 ± 15.42
Age group, n (%)	
<18 years	10 (12.50)
18–24 years	15 (18.75)
25–49 years	27 (33.75)
50–64 years	19 (23.75)
≥65 years	9 (11.25)
Sex, n (%)	
Female	41 (51.25)
Male	39 (48.75)
Clinical classification, n (%)	
Mild type	28 (35.00)
Moderate type	49 (61.25)
Severe type	3 (3.75)
Critically ill type	0 (0.00)
Types of infection, n (%)	
Huanan seafood wholesale market exposure	0 (0.00)
Imported infections	80 (100.00)
Number of nucleic acid tests, n (%)	
First time	41 (51.25)
Second time	30 (37.50)
Third time	9 (11.25)
Comorbidities, n (%)	38 (47.50)
Cardiovascular and cerebrovascular diseases,cerebrovascular diseasess	25 (31.25)
Endocrine system diseases	5 (6.25)
Digestive system disease	3 (3.75)
Respiratory system diseases	1 (1.25)
Malignant tumor	1 (1.25)
Nervous system diseases	1 (1.25)
Chronic kidney disease	1 (1.25)
Chronic liver disease	1 (1.25)
COPD	0 (0.00)
HIV infection	0 (0.00)
Septic shock	0 (0.00)
Signs and symptoms at admission, n (%)	
Fever	63 (78.75)
Cough	51 (63.75)
Shortness of breath	30 (37.50)
Muscle ache	18 (22.50)
Headache and mental disorder symptoms	13 (16.25)
Sore throat	11 (13.75)
Rhinorrhea	5 (6.10)
Chest pain	3 (3.75)
Diarrhea	1 (1.25)
Nausea and vomiting	1 (1.25)
More than 1 sign or symptom	66 (82.50)
Chest radiograph and CT findings, n (%)	
Bilateral pneumonia	36 (45.00)
Unilateral pneumonia	19 (23.75)
No abnormal density shadow	25 (31.25)
Treatment, n (%)	
Antibiotic treatment	73 (91.25)
Antiviral treatment	80 (100.00)
Hormone therapy	12 (14.63)
Intravenous immunoglobulin therapy	16 (20.00)
Noninvasive (ie,,face mask)	35 (43.75)
Mechanical ventilation	0 (0.00)
ECMO	0 (0.00)
Traditional Chinese medicine	3 (3.75)
Clinical outcome, n (%)	
Remained in hospital	61 (76.25)
Discharged	21 (23.75)
Died	0 (0.00)

Abbreviations: COPD, chronic obstructive pulmonary disease; COVID-19, coronavirus disease 2019; CT, computed tomography; ECMO, extracorporeal membrane oxygenation; HIV, human immunodeficiency virus; SD, standard deviation.

patients (3.75%). Nine types of respiratory pathogens and influenza A and B nucleic acids were examined in all patients, and bacteria and fungi were cultured simultaneously. The results showed that all patients were negative for the above pathogens (Table 2).

Imaging Features of Patients With COVID-19

Of the 80 patients, 55 (68.75%) showed abnormal chest CT images, consisting of 36 cases (45.00%) of bilateral pneumonia and 19 cases (23.75%) of unilateral pneumonia (Table 1). There were no bilateral lobular and subsegmental consolidation areas, bilateral ground-glass shadows, or subsegmental consolidation areas, and only bilateral ground-glass opacity (Figure 2A) and unilateral ground-glass opacity (Figure 2B). Twenty-five cases (31.25%) had no abnormal density shadow in the parenchyma of both lungs (Figure 2C).

Treatment for Patients With COVID-19

All patients were treated empirically with a single antibiotic, mainly moxifloxacin. The duration of antibiotic treatment was 3–12 days (median, 7 days; IQR, 4–9). All patients received ribavirin antiviral therapy for 3–12 days (median, 7 days; IQR, 3–10). Twelve patients (14.63%) also received methylprednisolone sodium succinate or methylprednisolone for 3–12 days (median, 5 days; IQR, 3–8). Thirty-five patients (43.75%) were managed with a noninvasive ventilator (ie, face mask). No patient used an invasive ventilator. One patient was supported with hemodialysis. In addition, 3 patients used traditional Chinese medicine (Jian Wei Xiao Shi oral liquid, Jichuan Pharmaceutical Group Co., Ltd., Taixing, China and Xi Yan Ping, Jiangxi Qingfeng Pharmaceutical Co. LTD, Ganzhou, China) to improve their gastrointestinal function.

Prognosis of Patients With COVID-19

As of 14 February, 21 of the 80 patients (23.75%) had been discharged from the hospital. The average length of stay of discharged patients was 8 days. All other patients were still in the hospital for treatment, and no patient died. The discharge standard reference was as follows: body temperature returned to normal for more than 3 days, respiratory symptoms improved significantly, and

Table 2. Laboratory Findings of Patients With Imported COVID-19

Variables	Normal Range (NR)	Patients (N = 80)		
		Median (IQR)	Above NR, n (%)	Below NR, n (%)
Blood routine examination				
White blood cell count (×10^9/L)	3.5–9.5	4.1 (3.2–5.7)	5 (6.25)	36 (45.00)
Neutrophil count (×10^9/L)	1.8–6.3	4.3 (2.3–5.9)	20 (25.00)	…
Lymphocyte count (×10^9/L)	1.1–3.2	0.6 (0.4–1.0)	…	26 (32.50)
Monocyte count (×10^9/L)	0.1–0.6	0.5 (0.3–0.7)	15 (18.75)	…
Platelet count (×10^9/L)	125.0–350.0	155 (116–188)	0 (0.0)	11 (13.75)
Hemoglobin (g/L)	130.0–175.0	125.3 (13.4)	…	29 (36.25)
Coagulation function				
Activated partial thromboplastin time (s)	21.0–37.0	18.6 (17.2–28.6)	…	2 (2.50)
Prothrombin time (s)	10.5–13.5	10.8 (9.3–13.2)	…	3 (3.75)
D-dimer (μg/L)	0.0–1.5	0.9 (0.4–2.4)	3 (3.75)	…
Blood biochemistry				
Alanine aminotransferase (U/L)	9.0–50.0	24 (12–38)	3 (3.75)	…
Aspartate aminotransferase (U/L)	15.0–40.0	30 (19–39)	3 (3.75)	…
Albumin (g/L)	40.0–55.0	38.3 (37.0–46.2)	…	2 (2.50)
Total bilirubin (μmol/L)	0.0–21.0	6.6 (5.4–12.0)	1 (1.25)	…
Blood urea nitrogen (mmol/L)	3.6–9.5	4.9 (3.4–5.9)	2 (2.50)	…
Serum creatinine (μmol/L)	57.0–111.0	78 (60–90)	2 (2.50)	…
Lactate dehydrogenase (U/L)	120.0–250.0	226 (182–308)	17 (21.25)	…
Glucose (mmol/L)	3.9–6.1	6.8 (4.6–7.7)	19 (23.17)	…
Creatine kinase (U/L)	50.0–310.0	99 (61–191)	18 (22.50)	…
Creatine kinase–muscle/brain (U/L)	<25	22 (15–25)	16 (20.00)	…
Infection-related biomarkers				
C-reactive protein ≥5.0 (mg/L)	0.0–5.0	6.6 (5.3–12.3)	62 (77.50)	…
Procalcitonin ≥5.0 (ng/mL)	0.0–5.0	1.3 (0.4–2.6)	1 (1.25)	…
Erythrocyte sedimentation rate ≥15 (mm/h)	0.0–15.0	11.9 (9.0–17.2)	59 (73.75)	…

Abbreviations: COVID-19, coronavirus disease 2019; IQR, interquartile range; NR, normal range.

respiratory pathogenic nucleic acid test was negative for 2 consecutive times (sampling interval at least 1 day).

DISCUSSION

In this multicenter, multi-sample study, 80 cases with COVID-19 in Yancheng and Wuxi were reported. All patients had imported infections. Most of them received a timely diagnosis and treatment as the government formulated an efficient early-warning and isolation program in time. Except for 3 severe patients, the rest of the 77 patients exhibited mild or moderate symptoms. This report provides the latest information on infected patients in 2 cities of Jiangsu Province.

COVID-19 was mainly transmitted through respiratory droplets and contact [15]. At present, patients with COVID-19 are the main source of infection [16]. What is more remarkable is that asymptomatic infections can also be a source of infection [17]. The 2 cities mentioned in this study, Wuxi and Yancheng, are respectively located in the South and North of Jiangsu Province, and they are representative in population, economic level, and traffic level.

Compared with the results of the 2 studies on Wuhan cases by Chen et al [18] and Huang et al [19], we found that the gender proportion was equal in the 80 patients we included, contradicting the conclusion that men are more susceptible than women. This may be related to the insufficient number of samples in these 3 studies. The results may also be influenced by the spreading mode of the disease, as 5 cases of intrafamilial transmission were included in this study. The age distribution of the patients was consistent with the study by Huang et al [19].

In terms of clinical classification, 3 patients had severe pneumonia, and 77 patients had mild or moderate symptoms. These imported cases diagnosed in a timely fashion and treated in Jiangsu Province. Since most of the cases in this study were mild, the main symptoms were fever and cough. Ten patients had acute respiratory injury, 2 patients had renal injury, and no other organ damage was found.

In terms of laboratory tests, nearly half of the patients had a decreased number of WBCs and one-third of the patients had a decreased number of lymphocytes. In most patients, the CRP level was elevated but the PCT level was normal. All of these changes further illustrated that COVID-19 may exert a major impact on lymphocytes, especially T lymphocytes. The virus spreads and invades through respiratory mucosa, triggers a series of immune responses, and induces the multiple cytokine-release syndrome, resulting in changes in immune components

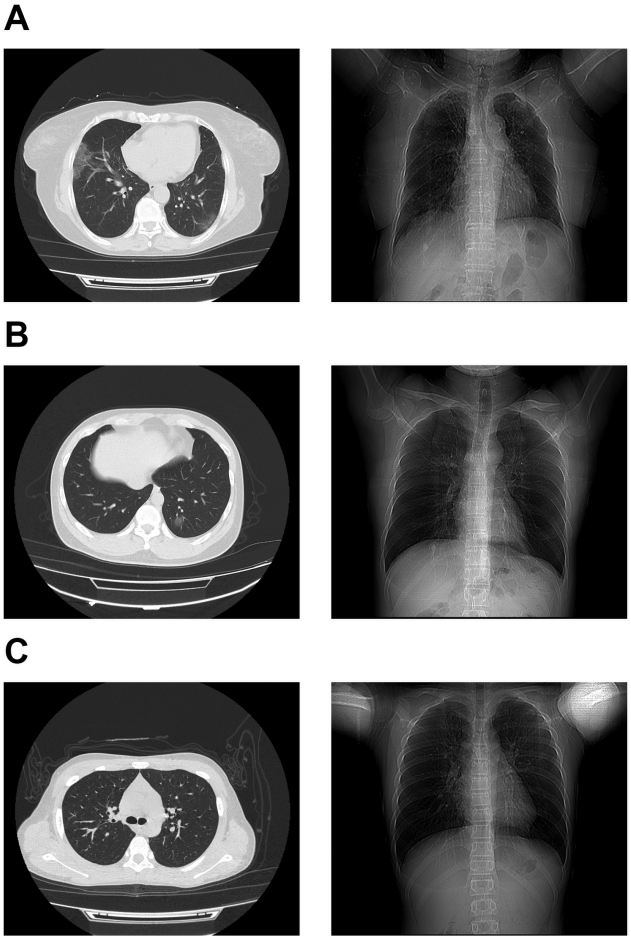

Figure 2. Chest radiograph images and chest computed tomography (CT) images of 3 patients. *A*, Chest radiograph images and chest CT images from a 71-year-old woman showing that there are scattered high-density shadows with fuzzy patches in the lower lobes of the 2 lungs, with ground-glass–like changes, with clear hilar structure, unobstructed trachea, no displacement of mediastinum, no enlarged lymph node shadow, and local thickening of bilateral pleura. *B*, Chest radiograph images and chest CT images from a 38-year-old man showing that there are small patchy ground-glass–like density increasing shadows in the upper and lower lobes of the left lung, with clear hilar structure, unobstructed trachea, no mediastinum displacement, no enlarged lymph node shadow, and no abnormality of pleura on both sides. *C*, Chest radiograph images and chest CT images from a 12-year-old boy showing that there was no abnormal density shadow in the parenchyma of both lungs, the structure of pulmonary hilus was clear, the trachea was unobstructed, mediastinum was not displaced, and no enlarged lymph node shadow was found.

such as peripheral blood leukocytes and lymphocytes [20]. Therefore, intravenous immunoglobulins were used in most patients with decreased WBC and lymphocyte levels.

It has been reported that patients with COVID-19 infection are prone to exhibit liver dysfunction, and the potential mechanism is that COVID-19 may directly bind to angiotensin-converting enzyme 2 (ACE2)-positive bile duct cells [21, 22]. It is suggested that the liver abnormality of patients with SARS and COVID-19 may not be caused by liver cell damage but by bile duct cell dysfunction and other reasons. In our study, 3 patients had abnormal ALT and AST, and 2 patients had decreased protein levels. In addition, 19 patients had an elevated GLU level, and 18 patients had an abnormal muscle zymogram.

In this study, all cases were confirmed by nucleic acid test. The total nucleic acid tests prior to a positive diagnosis for each patient were analyzed. Notably, 9 patients passed 3 tests before they received positive results. Therefore, we consider that if the suspected cases are excluded based on 2 consecutively negative respiratory pathogenic nucleic acid test results (the sampling time is at least 1 day apart), approximately 10% of the infected patients will be missed.

Chest imaging is of great significance for the diagnosis [23]. In the early stage, there were multiple mottling and interstitial changes, especially in the peripheral portion. In severe cases, lung consolidation can occur, but pleural effusion was rare. In the case reports of Wuhan, CT images of all patients were abnormal; 98% of the patients had bilateral involvement. However, in our study, the abnormal rate was relatively lower; 55 patients (68.75%) showed abnormal chest CT images, 36 (45.00%) showed bilateral pneumonia, 19 (23.75%) showed unilateral pneumonia. 25 cases had no abnormality on the first CT, and 23 of them had been diagnosed for more than 4 days. In this regard, we suggest that, when screening patients, clinical manifestations, laboratory examination, and chest imaging should be combined for comprehensive analysis.

Currently, there is no specific drug for the treatment of patients with COVID-19 [24, 25]. A US study showed that remdesivir had good therapeutic effect [26]. China has now carried out preliminary clinical trials on this drug [27]. Currently, the clinical treatment mainly includes empirical antibacterial drugs, antiviral treatment with ribavirin, and an appropriate dose of methylprednisolone to alleviate the shortness of breath. At the same time, it is suggested to use traditional Chinese medicine properly to improve the physical signs of patients. In this study, as there was no critical case, no patient used an invasive ventilator. All 3 hospitals followed the above scheme. At present, 21 cases have been discharged from the hospital, with an average length of stay of 8 days, no death was reported, and all other patients were still in the hospital.

This study is limited by its retrospective nature. First, due to the limited number of patients, our conclusions need to be further verified by large samples and multicenter data. Second, the prognosis is unavailable at the time of analysis, and extended follow-up time would provide more detailed information about potential risk factors that interfere with clinical outcomes. Third, only 2 cities in Jiangsu Province were selected in this study. Although they are representative, more urban cases need to be included to make the research results more accurate.

In conclusion, in-depth study is still needed for patients with COVID-19. Reliable, rapid pathogen detection and practical differential diagnosis based on clinical description are crucial for clinicians to contact suspected patients for the first time, and it is urgent to develop virus vaccines and effective drugs.

Supplementary Data

Supplementary materials are available at *Clinical 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.

Notes

Acknowledgments. The authors thank the authors of the primary studies for their timely and helpful responses to our information requests.

Financial support. This work was supported by Zhejiang University Special Scientific Research Fund for COVID-19 Prevention and Control (grant number 2020XGZX052).

Potential conflicts of interest. H. C. is the recipient of grants from Zhejiang University Special Scientific Research Fund. All other authors report no potential conflicts. All authors have submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Conflicts that the editors consider relevant to the content of the manuscript have been disclosed.

References

1. Peng Z, Yang X-L, Wang X-G, et al. A pneumonia outbreak associated with a new coronavirus of probable bat origin. Nature **2020**; doi:10.1038/s41586-020-2012-7.
2. Zhao S, Lin Q, Ran J, et al. Preliminary estimation of the basic reproduction number of novel coronavirus (2019-nCoV) in China, from 2019 to 2020: a data-driven analysis in the early phase of the outbreak. Int J Infect Dis **2020**; 92: 214–7.
3. Thompson RN. Novel coronavirus outbreak in Wuhan, China, 2020: intense surveillance is vital for preventing sustained transmission in new locations. J Clin Med **2020**; 9: doi:10.3390/jcm9020498.
4. Liu Y, Gayle AA, Wilder-Smith A, et al. The reproductive number of COVID-19 is higher compared to SARS coronavirus. J Travel Med **2020**; doi:10.1093/jtm/taaa021.
5. Hui DS, Azhar EI, Kim Y-J, et al. Middle East respiratory syndrome coronavirus: risk factors and determinants of primary, household, and nosocomial transmission. Lancet Infect Dis **2018**; 18:e217–e227.
6. Cho SY, Kang J-M, Ha YE, et al. MERS-CoV outbreak following a single patient exposure in an emergency room in South Korea: an epidemiological outbreak study. Lancet **2016**; 388:994–1001.
7. Chen L, Liu W, Zhang Q, et al. RNA based mNGS approach identifies a novel human coronavirus from two individual pneumonia cases in 2019 Wuhan outbreak. Emerg Microbes Infect **2020**; 9:313–319.
8. Du Z, Wang L, Cauchemez S, et al. Risk for transportation of 2019 novel coronavirus disease from Wuhan to other cities in China. Emerging Infect Dis **2020**; 26: doi:10.3201/eid2605.200146.
9. Lu R, Zhao X, Li J, et al. Genomic characterisation and epidemiology of 2019 novel coronavirus: implications for virus origins and receptor binding. Lancet **2020**; 395: 565–74.
10. Kofi Ayittey F, Dzuvor C, Kormla Ayittey M, et al. Updates on Wuhan 2019 novel coronavirus epidemic. J Med Virol **2020**; 92: 403–7.
11. Kanne JP. Chest CT findings in 2019 novel coronavirus (2019-nCoV) infections from Wuhan, China: key points for the radiologist. Radiology **2020**; doi:10.1148/radiol.2020200241.
12. Yu F, Du L, Ojcius DM, et al. Measures for diagnosing and treating infections by a novel coronavirus responsible for a pneumonia outbreak originating in Wuhan. China. Microbes Infect **2020**; doi:10.1016/j.micinf.2020.01.003.
13. Eurosurveillance Editorial Team. Note from the editors: World Health Organization declares novel coronavirus (2019-nCoV) sixth public health emergency of international concern. Euro Surveill. **2020**; 25. doi: 10.2807/1560-7917.ES.2020.25.5.200131e.
14. World Health Organization. Clinical management of severe acute respiratory infection when novel coronavirus (nCoV) infection is suspected: interim guidance. **2020**. Available at: https://www.who.int/internalpublications-detail/clinical-management-of-severe-acute-respiratoryinfection-when-novel-coronavirus-(ncov)-infection-is-suspected. Accessed 20 January 2020.
15. Yang F, Liu N, Wu JY, et al. Pulmonary rehabilitation guidelines in the principle of 4S for patients infected with 2019 novel coronavirus (2019-nCoV). Zhonghua Jie He He Hu Xi Za Zhi **2020**; 43:E004.
16. Chen Z-M, Fu J-F, Shu Q, et al. Diagnosis and treatment recommendations for pediatric respiratory infection caused by the 2019 novel coronavirus. World J Pediatr **2020**; doi:10.1007/s12519-020-00345-5.
17. Tuite AR, Fisman DN. Reporting, epidemic growth, and reproduction numbers for the 2019 novel coronavirus (2019-nCoV) epidemic. Ann. Intern. Med **2020**; doi:10.7326/M20-0358.
18. Chen N, Zhou M, Dong X, et al. Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study. Lancet **2020**; 395: 507–13.
19. Huang C, Wang Y, Li X, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. Lancet **2020**; 395: 497–506.
20. Song F, Shi N, Shan F, et al. Emerging coronavirus 2019-nCoV pneumonia. Radiology **2020**; doi:10.1148/radiol.2020200274.
21. Wan Y, Shang J, Graham R, et al. Receptor recognition by novel coronavirus from Wuhan: an analysis based on decade-long structural studies of SARS. J. Virol **2020**; doi:10.1128/JVI.00127-20.
22. Chai X, Hu L, Zhang Y, et al. Specific ACE2 expression in cholangiocytes may cause liver damage after 2019-nCoV infection. bioRxiv **2020**; doi: https://doi.org/10.1101/2020.02.03.931766
23. Chung M, Bernheim A, Mei X, et al. CT imaging features of 2019 novel coronavirus (2019-nCoV). Radiology **2020**; doi:10.1148/radiol.2020200230.
24. Liu W, Morse Jared S, Lalonde T, et al. Learning from the past: possible urgent prevention and treatment options for severe acute respiratory infections caused by 2019-nCoV. Chembiochem **2020**; 21: 730–8.
25. Lu H. Drug treatment options for the 2019-new coronavirus (2019-nCoV). Biosci Trends **2020**; doi:10.5582/bst.2020.01020.
26. Holshue ML, DeBolt C, Lindquist S, et al. First case of 2019 novel coronavirus in the United States. N Engl J Med **2020**; 382: 929–36.
27. Wang M, Cao R, Zhang L, et al. Remdesivir and chloroquine effectively inhibit the recently emerged novel coronavirus (2019-nCoV) in vitro. Cell Res **2020**; 30: 269–71.