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A Comparative Study on the Clinical Features of Coronavirus 2019 (COVID-19) Pneumonia With Other Pneumonias

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Background. A novel coronavirus (COVID-19) has raised world concern since it emerged in Wuhan, China in December 2019. The infection may result in severe pneumonia with clusters of illness onsets. Its impacts on public health make it paramount to clarify the clinical features with other pneumonias.

Methods. Nineteen COVID-19 and 15 other patients with pneumonia (non-COVID-19) in areas outside of Hubei were involved in this study. Both COVID-19 and non-COVID-19 patients were confirmed to be infected using throat swabs and/or sputa with/without COVID-2019 by real-time RT-PCR. We analyzed the demographic, epidemiological, clinical, and radiological features from those patients, and compared the differences between COVID-19 and non-COVID-19.

Results. All patients had a history of exposure to confirmed cases of COVID-19 or travel to Hubei before illness. The median (IQR) duration was 8 (6–11) and 5 (4–11) days from exposure to onset in COVID-19 and non-COVID-19 cases, respectively. The clinical symptoms were similar between COVID-19 and non-COVID-19. The most common symptoms were fever and cough. Fifteen (78.95%) COVID-19 but 4 (26.67%) non-COVID-19 patients had bilateral involvement while 17 COVID-19 patients (89.47%) but 1 non-COVID-19 patient (6.67%) had multiple mottling and ground-glass opacity on chest CT images. Compared with non-COVID-19, COVID-19 presents remarkably more abnormal laboratory tests, including AST, ALT, γ-GT, LDH, and α-HBDH.

Conclusions. The COVID-19 infection has onsets similar to other pneumonias. CT scan may be a reliable test for screening COVID-19 cases. Liver function damage is more frequent in COVID-19 than non-COVID-19 patients. LDH and α-HBDH may be considerable markers for evaluation of COVID-19.

Keywords. novel coronavirus pneumonia; infectious diseases; clinical features; respiratory infection.

At the end of 2019, a novel coronavirus (COVID-19) emerged in Wuhan, Hubei Province, China [1]. Reports showed that the COVID-19 infection caused clusters of onset similar to severe acute respiratory syndrome (SARS) coronavirus [1, 2]. A previous study has shown that coronaviruses can cause respiratory and intestinal infections in animals and humans [3]. Generally, coronaviruses were not considered to be highly pathogenic to humans until the outbreak of SARS in 2002 and 2003 in Guangdong, China [4, 5]. Another highly pathogenic coronavirus, Middle East respiratory syndrome (MERS) coronavirus, emerged in Middle Eastern countries in 2012 [6]. COVID-19 is one more highly pathogenic coronavirus to humans in history.

The virus has raised world concern because of its high transmission capability as well as high mobility and mortality [2, 7–9]. As of 14 February 2020, more than 60 000 cases with over 8000 patients with severe infection with the virus have been reported, and more than 1500 patients died. In addition to China, there have been patients detected in 25 countries globally. Early reports showed that almost all of confirmed patients have evidence of pneumonia [7, 9]. However, pneumonias are very common during a time of year when respiratory illnesses caused by other pathogen infections are highly prevalent [10, 11]. Therefore, it is a difficult time for public health as well as doctors in this outbreak.

In this study, we investigated the clinical features of 19 patients with confirmed COVID-19 pneumonia (COVID-19) and 15 patients with other (COVID-19–negative) confirmed

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pneumonia (non-COVID-19) with a history of travel to Hubei or exposure before illness to COVID-19 patients to describe the potential differences of clinical features between the 2 diseases.

METHODS

Patients

For comparative study, we recruited 19 COVID-19 patients and 15 non-COVID-19 patients from 23 January to 5 February 2020, at the Second Affiliated Hospital of Anhui Medical University and Suzhou Municipal Hospital in Anhui Province, China. COVID-19 or non-COVID-19 cases were confirmed to be infected with or without COVID-19 by real-time reverse transcriptase–polymerase chain reaction (RT-PCR). COVID-19 was defined to be COVID-19 positive by RT-PCR detection. For non-COVID-19 confirmation, we collected a throat swab or sputum sampling every other day. The patient was confirmed as non-COVID-19 if 3 consecutive real-time PCR tests were negative during the first 7 days of admission.

Real-time Polymerase Chain Reaction Detection for Identification of Pathogens

According to the surveillance scheme of pneumonia cases with COVID-19 infection and the guideline of laboratory detection for COVID-19 [12], local Center for Disease Control and Prevention (CDC) collected throat swabs or/and sputa from suspected patients, then shipped them to designated authoritative laboratories to detect the pathogen. RNA was extracted from those collected samples. Specific real-time RT-PCR (rRT-PCR) assays were performed to identify influenza A virus (H1N1, H3N2, H5N1, H7N9), influenza B virus, respiratory syncytial virus, parainfluenza virus, adenovirus, SARS coronavirus (SARS-CoV), and MERS coronavirus (MERS-CoV) using commercial kits or a designated COVID-19 rRT-PCR kit by the Chinese CDC.

Data Collection

We reviewed clinical charts, nursing records, laboratory findings, and chest X-rays for all COVID-19 and non-COVID-19 patients. The admission data of these patients were from 23 January to 5 February 2020. Epidemiological, clinical, laboratory, and radiological data were obtained with standardized data collection forms from electronic medical records. Investigators interviewed each patient and their relatives, where necessary, to determine exposure or close contact histories during the 2 weeks before the illness onset. To ascertain the epidemiological and symptom data, which were not available from electronic medical records, the researchers also directly communicated with patients or their families to ascertain epidemiological or symptom data. If data were missing from the records or clarification was needed, we obtained data by direct communication with attending doctors and other healthcare providers. All data were checked by 2 physicians.

Statistical Analysis

The quantitative blood laboratory tests were compared by Mann-Whitney *U* test. The categorical variables are expressed as numbers (%) and compared by Fisher's exact test. Differences were considered significant at $P < .05$ with a 2-tailed test. All analyses were performed using Instat software (Vision 5.0; GraphPad Prism).

RESULTS

Demographic Characteristics of Cases

As shown in Table 1, 19 COVID-19 patients and 15 non-COVID-19 patients were included in this study. The mean age was 48 (interquartile range [IQR], 27–56) years and 35 (IQR, 27–46) years in COVID-19 and non-COVID-19 patients, respectively. There were 8 (42.11%) female COVID-19 patients and 9 (60%) female non-COVID-19 patients. Serum immunoglobulin M (IgM) detection suggested that 2 (10.53%) of the COVID-19 patients had Coxsackie virus or mycoplasma coinfection. In addition, 3 (18.75%) COVID-19 patients had a history of chronic medical illness. The median duration from exposure to onset is 8 (IQR, 6–11) and 5 (IQR, 4–11) days in COVID-19 and non-COVID-19 patients, respectively. In non-COVID-19 patients, no viral RNA or DNA was detected for targets mentioned in the Methods section, while serological assays showed anti-mycoplasma IgM positive.

Illness-onset Features of Patients

To decrease the possible affects on laboratory results, we selected those patients with similar duration of COVID-19 and non-COVID-19 in this study. The median duration, respectively, was 5 (IQR, 3–9) and 4 (IQR, 2–7) days from onset to admission in COVID-19 and non-COVID-19 patients. There was no statistical difference between patients. On admission, the most common symptoms at onset of illness were fever and cough in both COVID-19 (15 [78.95%] and 9 [47.37%] of

Table 1. Characteristics of COVID-19 and Non-COVID-19 Patients

Variable	COVID-19 Patients (n = 19)	Non-COVID-19 Patients (n = 15)
Age, median (interquartile range), years	48 (27–56)	35 (27–46)
Female, n (%)	8 (42.11)	9 (60.00)
Bacterial/viral coinfection, n (%)	2 (10.53)	2 (13.33)
Coxsackie virus	1 (5.26)	0 (0)
Mycoplasma	1 (5.26)	2 (13.33)
Chronic medical illness, n (%)	3 (15.79)	3 (20.00)
Hypertension	2 (10.53)	1 (6.67)
Ventricular septal defect	0 (0)	1 (6.67)
HBV infection	1 (5.26)	0 (0)
Schizophrenia	0 (0)	1 (6.67)
Duration from exposure to onset, median (interquartile range), days	8 (6–11)	5 (4–11)

Abbreviations: COVID-19, coronavirus 2019; HBV, hepatitis B virus.

19) and non-COVID-19 (14 [93.33%] and 12 [80%] of 15) patients. Less common symptoms of COVID-19 patients were sore throat (4 [21.05%] of 19), headache (2 [10.53%] of 19), fatigue (2 [10.53%] of 19), diarrhea (1 [5.26%] of 19), and chest tightness (1 [5.26%] of 19), whereas non-COVID-19 patients has less common symptoms of sore throat (4 [26.67%] of 15) and diarrhea (1 [6.67%] of 15). All patients had evidence of pneumonia on chest computed tomography (CT) images, but only 2 (10.53%) COVID-19 patients and 5 (30%) non-COVID-19 patients presented abnormal auscultation of the lung (Table 2). In comparison, no significant differences were observed between COVID-19 and non-COVID-19 patients in these onsets.

Features on Computed Tomography Images

On admission, of the 19 COVID-19 patients, 15 (78.95%) had bilateral involvement (Table 2). Similar to previous reports [13], the typical feature was multiple lobular ground-glass opacity (Figure 1A–F) and subsegmental areas of consolidation (Figure 1G) in COVID-19 patients. In addition, sequential CT images from the same patient suggested that the inflammation was rapid infiltration in the lobes of COVID-19 patients (Figure 1A–C, D–G). In comparison, of 15 non-COVID-19 patients, only 4 (26.7%) had bilateral involvement (Table 2). The typical features of non-COVID-19 were patchy shadow or density-increasing shadow (Figure 1H), except for 1 patient (6.67%) who had multiple patchy and mottling shadows with partial ground-glass opacity (Figure 1).

Laboratory Abnormalities of the Patients

On admission, except for 1 non-COVID-19 patient, white blood cell (WBC) counts of the investigated patients were in the normal range, whereas most lymphocytes were decreased in COVID-19 (12 [63.18%] of 19) and non-COVID-19 (10 [66.67%] of 15) patients. An increased ratio of neutrophils was observed in 11 (61.11%) COVID-19 or 9 (64.29%) non-COVID-19 patients. Compared with non-COVID-19 patients, COVID-19 patients had higher levels of aspartate aminotransferase (AST), alanine aminotransferase (ALT), lactate dehydrogenase (LDH), γ-glutamyl transpeptidase (γ-GT), and α-hydroxybutyric dehydrogenase (α-HBDH). In addition, a proportion of COVID-19 but no non-COVID-19 patients had abnormally increased AST (5 [27.78%] of 18), ALT (5 [27.78%] of 18), γ-GT (8 [44.4%] of 18), and LDH (6 [31.58%] of 19). Abnormally increased α-HBDH was seen in 6 (75%) of 8 COVID-19 patients and 3 (20%) of 15 non-COVID-19 patients (Table 3). One of the COVID-19 patients with abnormal LDH also showed abnormal creatine kinase (CK) (365 U/L), while there was no significant difference between CK levels in COVID-19 and non-COVID-19 patients. In addition, most of the COVID-19 and non-COVID-19 patients presented increased levels of C-reactive protein (CRP) and interleukin-6 (IL-6), although no significant difference was observed between the 2 groups of patients. Creatinine levels of all patients were normal (data not shown).

Outcome and Treatments

By 14 February 2020, no patient needed to be admitted to the intensive care unit (ICU) and administered mechanical ventilation in these investigated COVID-19 and non-COVID-19 patients. Except for 2 COVID-19 patients who had a transient decreasing pulse oxygen saturation (SpO_2) (92–93%) on admission, SpO_2 of the other patients remained at 95–99%. All of the COVID-19 patients were treated with the antiviral drug lopinavir and ritonavir tablets and symptomatic supports, while non-COVID-19 patients were treated with antibiotics (moxifloxacin) and other symptomatic supports including enough sleep, nutrition and oxygen therapy if necessary. Besides drug treatments, much of the treatment comprised psychological counseling for these COVID-19 patients because of the panic and anxiety about the illness.

Table 2. Clinical Characteristics of COVID-19 and Non-COVID-19 Patients

Variable	COVID-19 Patients (n = 19)	Non-COVID-19 Patients (n = 15)	*P*
Duration from onset to admission, median (interquartile range), days	5 (3–9)	4 (2–7)	.07
Clinical onset, n (%)			
Fever	15 (78.95)	14 (93.33)	.36
Cough	9 (47.37)	12 (80.00)	.08
Sore throat	4 (21.05)	4 (26.67)	1.00
Headache	2 (10.53)	0 (0)	.49
Fatigue	2 (10.53)	0 (0)	.49
Diarrhea	1 (5.26)	1 (6.67)	1.00
Chest tightness	1 (5.26)	0 (0)	1.00
Abnormal auscultation of lung, n (%)	2 (10.53)	5 (30.00)	.20
Chest CT findings, n (%)			
Unilateral pneumonia	4 (21.05)	11 (23.33)	.005
Bilateral pneumonia	15 (78.95)	4 (26.67)	.005
Multiple mottling and ground-glass opacity	17 (89.47)	1 (6.67)	< .0001

Abbreviations: COVID-19, coronavirus 2019; CT, computed tomography.

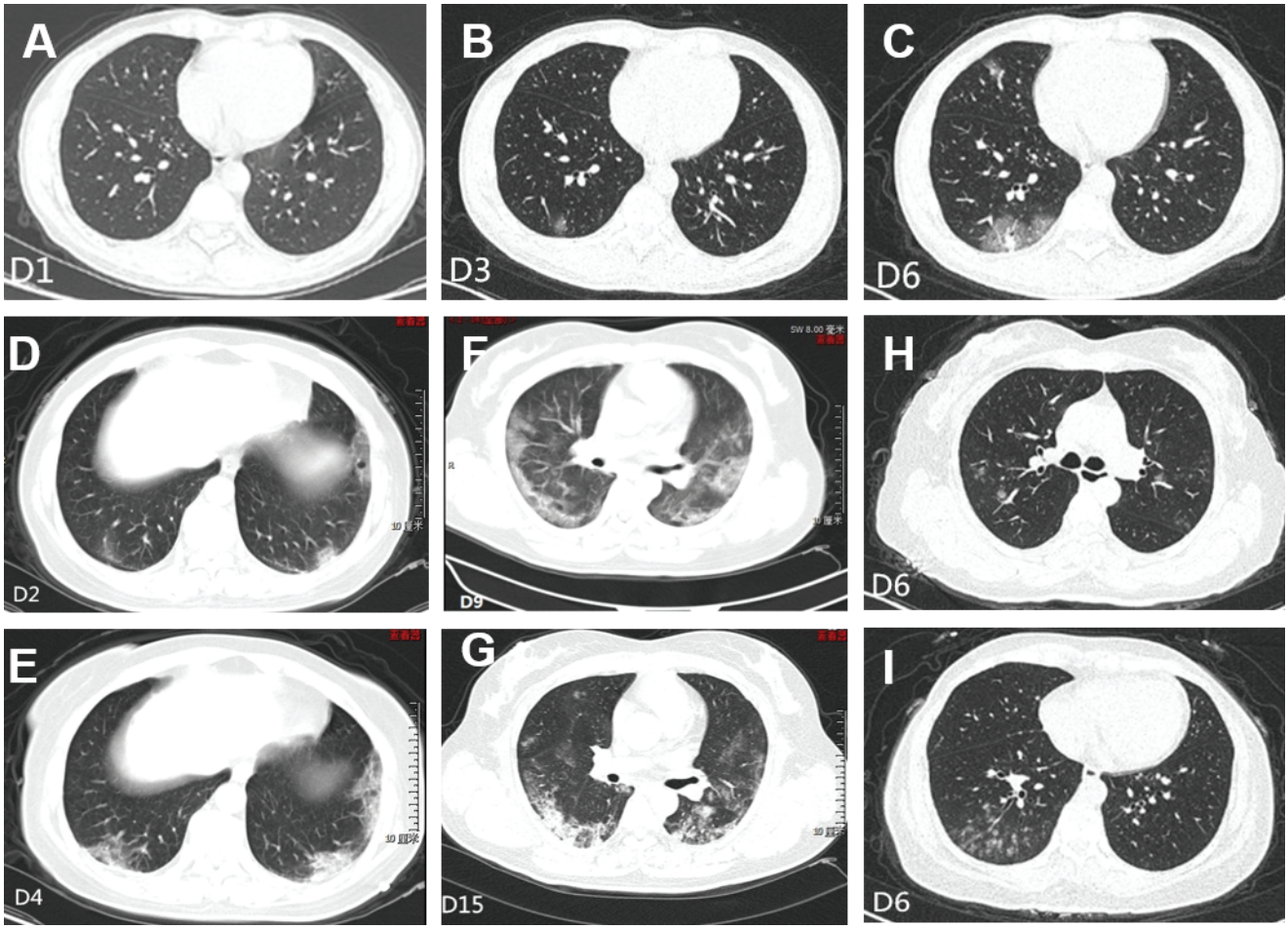

Figure 1. Transverse chest CT images from a 43-year-old male patient with COVID-19 showing no obvious pneumonia change on day 1 after illness (*A*), a mottling and ground-glass opacity in the right lower lobe on day 3 after illness (*B*), and multiple mottling and ground-glass opacity in the right upper and lower lobes on day 6 after illness (*C*). Transverse chest CT images from a 56-year-old female patient with COVID-19 showing bilateral, multiple, lobular mottling and ground-glass opacity on day 2 after illness onset (*D*) and extensively bilateral, lobular, ground-glass opacity on day 4 after illness onset (*E*). Transverse chest CT images from a 52-year-old female patient with COVID-19 showing extensively bilateral ground-glass opacity and subsegmental areas of consolidation on day 9 after illness onset (*F*) and bilaterally reduced, ground-glass opacity, and subsegmental areas of consolidation on day 15 after illness onset (*G*). Transverse chest CT images from a 66-year-old female non-COVID-19 patient showing multiple patchy and mottling shadows (*H*) and partial ground-glass opacity (*I*) on day 6 after illness onset. Abbreviation: COVID-19, coronavirus 2019; CT, computed tomography.

DISCUSSION

COVID-19 has caused severe illness and has impacted multiple countries in the world, and sustained human-to-human transmission has made it a worldwide concern and serious public health threat [14]. So far, it is unclear when this virus will end. However, the symptoms of the virus are similar to those of influenza (eg, fever, cough, or sore throat), and the outbreak is occurring during a time of year when respiratory illnesses from influenza, respiratory syncytial virus, and other respiratory viruses are highly prevalent. It is very important for clinics to identify the infected patients.

We reported here a comparative analysis on 19 patients with pneumonia with laboratory-confirmed COVID-19 infection and 15 patients with pneumonia without COVID-19 infection. All patients had history of exposure to confirmed COVID-19 patients or traveled back from Hubei before their illness. The epidemiology data showed the 2 groups of patients presented onsets of illness after a mean of approximately 1 week. Similar symptoms were presented by both groups of patients. Fever and cough were the most common symptoms. These symptoms are also common in other acute respiratory infections, such as influenza, respiratory syncytial virus, and other respiratory viruses, which may be associated with the difficult control of this epidemic.

Early classification of patients is necessary to prevent and control these epidemics when emergency management has to be conducted in some outbreaks, such as in SARS and COVID-19 [15, 16]. Previously it was suggested that CT scan was a useful tool to screen the suspected cases of COVID-19 infection [13]. In this study, our data also showed that CT images showed remarkably significant differences between COVID-19 and non-COVID-19 patients. Most COVID-19 patients but non-COVID-19 patients

Table 3. Laboratory Results of COVID-19 and Non-COVID-19 Patients

Variable (Normal Range)	COVID-19 Patients (n = 19)	Non-COVID-19 Patients (n = 15)	*P*
WBC (4–10 × 10^9/L), mean (range)	4.92 (1.26–7.63)	6.18 (3.37–12.38)	.30
<4	7/19 (36.84%)	4/15 (26.67%)	.72
>10	0 (0%)	2/15 (13.33%)	.19
Lymphocytes (1.1–3.2 × 10^9/L), mean (range)	0.97 (0.30–2.03)	1.11 (0.62–1.95)	.66
<1.1	12/19 (63.18%)	10/15 (66.67%)	.83
Ratio of neutrophils (45–75%), mean (range)	74.02 (55.30–93)	67.11 (29.7–82.5)	.35
>75	11/18 (61.11%)	9/14 (64.29%)	.85
AST (15–40 U/L), mean (range)	34.9 (17.6–103.8)	21.3 (13–35)	.005
>40	5/18 (27.78%)	0/14 (0%)	.03
ALT (9–50 U/L), mean (range)	36.37 (11.8–85.0)	21.38 (13–35)	.03
>50	5/18 (27.78%)	0/14 (0%)	.03
γ-GT (7–45 U/L), mean (range)	42.17 (17.0–166.8)	23.14 (12–43)	.04
>45	8/18 (44.44%)	0/14 (0%)	.004
LDH (120–250 U/L), mean (range)	256.94 (150–750)	160 (103–227)	.008
>250	6/19 (31.58%)	0/15 (0%)	.02
α-HBDH (72–182 U/L), mean (range)	223.38 (124–373)	169.53 (124–220)	.048
>182	6/8 (75%)	3/15 (20%)	.01
CK (50–310 U/L), mean (range)	92.69 (25–365)	81.87 (36–166)	.93
>310	1/18 (5.56%)	0/15 (0%)	1.00
CRP (0–4 mg/L), mean (range)	26.47 (10–127.1)	21.47 (0.4–142.2)	.64
>4	18/19 (94.73%)	12/15 (80.00%)	.3
IL-6 (0–7 pg/mL), mean (range)	19.34 (8.7–45.3)	15.06 (4.4–33.9)	.65
>7	6/7	8/11	1.00

Abbreviations: ALT, alanine aminotransferase; AST, aspartate aminotransferase; CK, creatine kinase; COVID-19, coronavirus 2019; CRP, C-reactive protein; LDH, lactate dehydrogenase; WBC, white blood cell count; α-HBDH, α-hydroxybutyric dehydrogenase; γ-GT, γ-glutamyl transpeptidase.

had bilateral pneumonia with the feature of multiple mottling and ground-glass opacity on CT images. In addition, similar to severe influenza (eg, H7N9, H1N1pdm 09) [17, 18], inflammation spread quickly in the lungs of COVID-19 patients. CT scan may be a reliable test for screening COVID-19 or non-COVID-19 patients and will allow rapid classification of suspected cases or patients with common pneumonia.

In terms of laboratory tests, the absolute value of lymphocytes in most COVID-19 and non-COVID-19 patients was reduced. This result suggests that COVID-19 infection has similar feature with many other respiratory virus infections, triggered a strong innate inflammatory immune response, and caused depletion of lymphocytes after infection [19–22]. Inflammation is a time-dependent process, usually starting locally, and is recognized centrally later via blood-borne mediators [23]. Previous studies suggested that excessive immune response played an important role in the pathogenesis of severe influenza or SARS [24]. And IL-6 and CRP may be linked to the excessive immune response [25, 26]. In this study, our results also showed abnormally increased CRP and IL-6 in most of both COVID-19 and non-COVID-19 patients. In our results, the ratio of mean of neutrophils was slightly higher in COVID-19 than in non-COVID-19 patients, although there was no statistical difference between them. That might be related to no severe cases being involved in this study because the numbers of neutrophils were much higher in severe COVID-19 than in relatively mild COVID-19 in an early report [2]. Previous studies have shown that excessive neutrophils contributed to acute lung damage, and are associated with severe disease and fatality in patients with influenza infection [27, 28]. Hence, possibly an excessive immune response of the host may be associated with the pathogenesis of COVID-19 in addition to virus-specific factors.

Previous reports showed that a proportion of COVID-19 patients had differing degrees of liver function abnormality [2, 7]. Our data showed that the levels of liver function–associated markers (ALT, AST, and γ-GT) were significantly higher in COVID-19 patients than in non-COVID-19 patients, and a proportion of COVID-19 patients (AST, 26.67%; ALT, 27.78%; γ-GT, 44.44%) but no non-COVID-19 patients presented abnormal levels of these markers, suggesting that acute liver damage was more frequent in COVID-19 patients than in non-COVID-19 patients. This was also observed in patients with SARS or severe influenza (eg, H7N9) [17, 29]. In addition, LDH levels were abnormal in a proportion of COVID-19 patients (31.58%) but in COVID-19 patients. And available data showed that most of the COVID-19 patients (75%) but a few non-COVID-19 patients (20%) had an abnormal α-HBDH. The results suggested that patients with COVID-19 may have multiple tissue or organ damage besides liver injury.

With regard to treatment, all COVID-19 patients were diagnosed and treated outside of the Wuhan area in this study. And none of the COVID-19 patients in this study had severe

complications like acute respiratory distress syndrome or multiple organ failure, which has been reported in Wuhan patients or SARS patients during admission [2, 7, 29, 30]. However, because it is a novel disease, people have more panic and anxiety about it than with other diseases. Psychological counseling should be involved in the treatment.

There are several limitations to this study. First, the sample size was very small. And some laboratory tests were not conducted in some patients because the COVID-19 patients were from 2 hospitals. Second, there was a lack of severe infection to compare findings with severe infection with mild infection. Third, there was a lack of a pediatric population.

Notes

Author contributions. R. G. designed the study and wrote the report. D. Z. and F. Y. gathered data and participated in the clinical treatment. Z. L., Y. J, F. G., and H. Z. participated in the clinical treatment. R. G., D. Z., and L. W. performed data analyses. Y. G. participated in collating data. All authors contributed to the review and revision of the manuscript and have read and approved the final version

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