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RESEARCH ARTICLE

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Clinical characteristics and factors affecting the duration of positive nucleic acid test for patients of COVID-19 in XinYu, China

Jingjing Lu[1] | Qi Yin[1] | Quan Li[2] | Gang Fu[3] | Xueping Hu[1] | Jianhao Huang[1] | Lin Chen[2] | Qiang Li[1] | Zhongliang Guo[1]

[1]Department of Pulmonary and Critical Care Medicine, Shanghai, East Hospital, Tongji University School of Medicine, Pudong, Shanghai, China

[2]Department of Respiratory Medicine, Shanghai East Hospital JiAn Hospital, JiAn, JiangXi, China

[3]Department of Infectious Diseases, XinYu People's Hospital, XinYu, JiangXi, China

Correspondence
Zhongliang Guo, Department of Pulmonary and Critical Care Medicine, Shanghai East Hospital, Tongji University School of Medicine, Pudong, Shanghai 200120, China.
Email: drguozhl@163.com

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Abstract

Background: The outbreak of a new coronavirus, COVID-19, which was earliest reported in Wuhan, China, is now transmitting throughout the world. The aim of this study was to articulate the clinical characteristics of COVID-19 and to reveal possible factors that may affect the persistent time of positive SARS-CoV-2 nucleic acid test, so as to identify which patients may deteriorate or have poor prognoses as early as possible.

Methods: Retrospective cohort study was carried out on 47 patients with confirmed COVID-19 infection admitted to XinYu People's Hospital of JiangXi Province. Epidemiological, demographic, clinical, laboratorial, management, treatment, and outcome data were also collected and analyzed.

Results: In this study, patients were divided into two groups based on whether their SARS-CoV-2 nucleic acid tests in respiratory specimens turn negative within (Group Rapid or Group R) or over (Group Slow or Group S) a week. There was no significant difference in age, sex, travel or exposure history, and smoking history between the two groups. Forty-two patients had been observed with comorbidities. Similar clinical manifestations, for instance fever, cough, sputum, and fatigue, have been observed among patients in both groups, except that patients in Group S were obviously more likely to get fatigue than patients in Group R. Both groups had shown decrease in white blood cell or lymphocyte counts. Chest X-ray or computed tomography scan showed unilateral or bilateral infiltrates. High proportion in both groups has used nasal cannula (89.47% vs. 85.71%) to inhale oxygen. 10.53% of Group S have applied high-flow nasal cannula, while Group R used none. The current treatment is mainly antibiotics, antiviral, and traditional Chinese medicine, while a couple of patients has

Abbreviations: 2019-nCoV, 2019 novel coronavirus; CDC, Center of Diseases Prevention and Control; COVID-19, Coronavirus Disease 2019; CT, Computed tomography; GGO, ground-glass opacities; HFNC, high-flow nasal cannula; IQR, interquartile range; MERS, Middle East respiratory syndrome; NAT, SARS-CoV-2 nucleic acid test; NPPV, non-invasive mechanical ventilation; RT-PCR, real-time reverse transcription–polymerase chain reaction; SARS, severe acute respiratory syndrome; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2; WBC, white blood cell count; WHO, World Health Organization.

Jingjing Lu and Qi Yin contributed equally to the paper.

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used methylprednisolone. Only 1 patient out of both groups got even worse despite this active treatment.

Conclusion: Clinical characteristics of COVID-19 include the exposure history and typical systemic symptoms such as fever, cough, fatigue, decreased WBC and lymphocyte counts, and infiltration in both lower lobes on CT imaging. Among them, fatigue appears to be an important factor that affects the duration of positive SARS-CoV-2 nucleic acid test in respiratory specimens.

KEYWORDS

clinical characteristics, Coronavirus disease, COVID-19, fatigue, SARS-CoV-2

1 | INTRODUCTION

In December 2019, a group of pneumonia patients with unknown pathogeny was found in Wuhan, Hubei Province, China. The clinical manifestation of such pneumonia is very similar to that of viral pneumonia,[1] and the corresponding pathogen was confirmed and named as the 2019 novel coronavirus (2019-nCoV) based on deep sequencing analysis on the lower respiratory tract samples.[2] According to World Health Organization (WHO) interim guidance, the diagnosis of such a disease mainly relies on a positive SARS-CoV-2 nucleic acid test (NAT) in respiratory specimens. Therefore, negative SARS-CoV-2 NAT in respiratory specimens is critical condition for being released from an isolation or hospital. However, what kind of factors may cause the NAT turn from positive to negative, and how that process takes place, still remain unreported.

After analyzing the clinical characteristics of 47 patients diagnosed as COVID-19 infected in XinYu People's Hospital of JiangXi Province, this study aims to articulate the clinical characteristics of COVID-19 and to reveal effective factors as possible that may lead to negative SARS-CoV-2 NAT.

2 | MATERIALS AND METHODS

2.1 | Data sources

This is a retrospective cohort study of 47 patients aged from 13 to 70 years old with confirmed COVID-19 infection hospitalized at XinYu People's Hospital in JiangXi Province, China. All patients were diagnosed with COVID-19 infection according to the World Health Organization interim guidance[3] and were admitted by the hospital between February 4, and February 23, 2020. Epidemiological characteristics, clinical manifestations, laboratory test results, CT images, and clinical treatments were collected from the electronic medical records.

The majority of clinical data used in this study were collected from the first day of hospital admission. Throat swab samples were immediately obtained from all patients at admission and were tested as COVID-19 positive[1] by the RT-PCR at the Jiangxi Provincial Center for Disease Prevention and Control (CDC). Subsequent SARS-CoV-2 NATs in respiratory specimens were taken after 48-72 hours of treatment. Clinical data were sampled only on patients whose NATs show negative in at least two successive tests between which the time interval is at least over one day.

2.2 | Ethical approval

Written informed consent was waived for the retrospective case series, and this study has involved no potential risk to any patient.

2.3 | Statistical analysis

Descriptive analyses of the variables were expressed as median (interquartile range [IQR]) or number (%). Differences in distributions of patient characteristics by subgroups are reported using differences with 95% CIs. All analyses were performed with SPSS version 23.0, and P value <.05 was considered statistically significant.

3 | RESULTS

3.1 | Demographic and epidemiological characteristics

A total of 47 patients, among which 26 (55.32%) were female, were involved in this study (Table 1). Aged from 13 to 70, the median age of the patients is 45 years old. Epidemiological data showed that 1 patient had been traveling to Hubei province, and 30 patients had been exposed to positive infections of COVID-19 (63.8%), including family members and colleagues.

Forty-two patients had comorbidities, including hypertension (n = 10, 21.28%), diabetes (n = 9, 19.15%), coronary heart disease (n = 6, 12.77%), and chronic obstructive lung disease (n = 10, 21.28%). The proportion of patients having underlying diseases seems to be higher in Group S than in Group R. In addition, in both groups most patients were non-smokers.

TABLE 1 Demographic characteristics of patients with COVID-19

Study population	No.(%)
No. of patients	47
Ages, median (IQR), y	45 (34-50)
Gender	
Male	21/47 (44.68)
Female	26/47 (55.32)
Exposure to infected patient	
Yes	30/47 (63.83)
No	17/47 (37.17)
Travel history	
Travel to Hubei province	1/47 (2.13)
No travel history	46/47 (97.87)
Smoke history (packs per year)	
Current (>20)	11/47 (23.40)
Never (≤20)	36/47 (76.60)
Comorbidity	
Hypertension	10/47 (21.28)
Diabetes	9/47 (19.15)
Coronary heart disease	6/47 (12.77)
Chronic obstructive lung disease	10/47 (21.28)
Tumors	0/47 (0.00)
Others	7/47 (14.89)

Note: Except where indicated, data = n/N (%), n is number of patients, where N is the total number of patients with available data.

3.2 | Clinical manifestation and parameter characteristics

For the above 47 patients, time intervals from the onset of some clinical symptom to the date they visited the hospital range from 1 to 18 days (Table 2). The median is 7 days. Most patients have a clear diagnosis within 48 hours after hospitalization. The most common self-reported symptoms at onset of the illness were fever (n = 24, 51.06%), cough (n = 34, 72.34%), sputum (n = 7, 14.89%), fatigue (n = 8, 17.02%), diarrhea (n = 4, 8.51%), and nausea or vomiting (n = 6, 12.77%).

Routine blood tests showed that for most patients (55.32%), the white blood cells (WBC) counts were normal, and normal lymphocyte counts were found in 45 patients. Only 2 patients (4.26%) had decreased lymphocyte counts. A total of 34 patients (72.34%) had findings of bilateral infiltrates on radiographic imaging, while 7 (14.89%) patients had unilateral infiltrates. Additionally, 6 patients have normal imaging.

Forty-three patients out of 47 (91.49%) needed oxygen support during the treatment. The oxygen therapy cases as recorded include nasal cannula (n = 41, 87.23%), HFNC (n = 2, 4.26%), and NPPV (n = 0, 0.00%). Most patients (n = 25, 53.19%) received empirical antibiotic treatment and antiviral therapy (n = 41, 87.23%), including Arbidol and Oseltamivir. Most patients received traditional Chinese medicine

TABLE 2 Clinical manifestation and initial laboratory indices of patients with COVID-19

	No.(%)
Time from illness onset to hospital admission (d)	7 (1-18)
Time from visit hospital to be diagnosed (h)	
<24	10/47 (21.28)
24-48	7/47 (14.89)
>48	30/47 (63.83)
Clinical manifestation	
Fever (T≥37.3)	24/47 (51.06)
Cough	34/47 (72.34)
Sputum	7/47 (14.89)
Fatigue	8/47 (17.02)
Diarrhea	4/47 (8.51)
Nausea or vomiting	6/47 (12.77)
No obvious symptoms	0/47 (0.00)
Hematologic	
White blood cells ($x10^9$/mL)	
<4	21/47 (44.68)
4-10	26/47 (55.32)
>10	0/47 (0.00)
Lymphocytes ($x10^9$/mL)	
<0.8	2/47 (4.26)
LYMPH%	
>40%	12/47 (25.53)
Temperature returns to normal (h)	
< 24	23/47 (48.94)
24-48	14/47 (29.79)
48-72	8/47 (17.02)
>72	2/47 (4.26)
Chest imaging (X-ray or CT scan)	
Unilateral	7/47 (14.89)
Bilateral	34/47 (72.34)
Normal	6/47 (12.77)
Treatment in hospital	
Oxygen therapy	
Nasal cannula	41/47 (87.23)
HFNC	2/47 (4.26)
NPPV	0/47 (0.00)
Methylprednisolone	4/47 (8.51)
Therapy	
Antibiotic	25/47 (53.19)
Antiviral	41/47 (87.23)
Chinese medicine	42/47 (89.36)
Clinical outcomes	
Improve	46/47 (97.87)
Worsen	1/47 (2.13)

Note: Except where indicated, data = n/N (%), n is number of patients, where N is the total number of patients with available data.

therapy (n = 42, 89.36%), including patent and decoction. Four (8.51%) patients received methylprednisolone. Eventually, 46 (97.87%) patients out of 47 recovered after receiving the above treatments.

3.3 | Comparison of the characteristics of Group R and S

In this study, patients were divided into two groups based on whether their SARS-CoV-2 NATs in respiratory specimens turns negative within (Group Rapid, or Group R) or over (Group Slow, or Group S) one week. There were no significant differences in age, gender, travel or exposure history, or smoking history between the two groups of patients (Table 3). However, compared with patients in Group R, patients in Group S had a higher proportion of comorbidities, including hypertension (26.32% vs. 17.86%), diabetes (21.05% vs. 17.86%), coronary heart disease (15.79% vs. 10.71, and chronic obstructive lung disease (31.58% vs. 14.29%).

Table 4 demonstrates that patients in Group S had experienced less hours from visiting the hospital to being diagnosed than those in Group R. Patients in different groups have similar clinical manifestations, such as fever, cough, sputum, fatigue, diarrhea, nausea, or vomiting, except that patients in Group S were more likely to feel fatigue than patients in Group R (difference, 24.44%; 95% CI, 2% to 47.43%; $P = .029$).

Patients in both groups had decreased WBC or lymphocyte counts, but no statistical difference was found between the two groups. Chest X-ray or CT scan discovered unilateral or bilateral infiltrates for these patients. Almost all patients used nasal cannula (89.47% VS 85.71%) to inhale oxygen. 10.53% of the patients in Group S while no patients in Group R had applied high-flow nasal cannula (HFNC). Non-invasive mechanical ventilation (NPPV) was not required to be used since all patients involved here were mild or common type.

TABLE 3 Demographic characteristics of patients with viral nucleic acid detection result

Study population	Group Slow (n = 19)	Group Rapid (n = 28)	Difference (95% CI)	P value
Ages, median (IQR), y	45 (40-50)	44 (29.5-49.75)	3 (−4 to 13)	.26
Gender				
Male	7/19 (36.84)	14/28 (50.00)	13.16 (−14.96 to 37.95)	.37
Female	12/19 (63.16)	14/28 (50.00)		
Exposure to infected patient				
Yes	13/19 (68.42)	17/28 (60.71)	7.71 (−19.67 to 32.16)	.59
No	6/19 (31.58)	11/28 (39.29)		
Travel history				
Travel to Hubei province	0/19 (0.00)	1/28 (3.57)	3.57 (−13.5 to 17.71)	.41
No travel history	19/19 (100.00)	27/28 (96.43)		
Smoke history (packs per year)				
Current (>20)	4/19 (21.05)	7/28 (25.00)	3.95 (−21.52 to 26.18)	.75
Never (≤20)	15/19 (78.95)	21/28 (75.00)		
Comorbidity				
Hypertension	5/19 (26.32)	5/28 (17.86)	8.46 (−14.45 to 33.05)	.49
Diabetes	4/19 (21.05)	5/28 (17.86)	3.20 (−18.53 to 27.61)	.79
Coronary heart disease	3/19 (15.79)	3/28 (10.71)	5.08 (−14.34 to 27.95)	.61
Chronic obstructive lung disease	6/19 (31.58)	4/28 (14.29)	17.29 (−6.36 to 41.29)	.16
Tumors	0/19 (0.00)	0/19 (0.00)	0.00 (−12.06 to 16.82)	.00
Others	2/19 (10.53)	5/28 (17.86)	−7.33 (−15.80 to 26.62)	.49

Note: Except where indicated, data = n/N (%), n is number of patients, where N is the total number of patients with available data.

TABLE 4 Clinical characteristics of patients with viral nucleic acid detection result

	Group Slow (n = 19)	Group Rapid (n = 28)	Difference (95% CI)	P value
Time from illness onset to hospital admission (d)	7 (1-14)	8 (2-18)	−1 (−4 to 1)	.32
Time from visit hospital to be diagnosed (h)				
< 24	5/19 (26.32)	5/28 (17.86)	8.46 (−14.45 to 33.05)	.75
24-48	3/19 (15.79)	4/28 (14.29)	1.50 (−18.5 to 24.91)	
> 48	11/19 (57.89)	19/28 (67.86)	−9.96 (−16.54 to 35.83)	
Clinical manifestation				
Fever (T≥37.3)	11/19 (57.89)	13/28 (46.43)	11.47 (−16.51 to 36.87)	.44
Cough	16/19 (84.21)	18/28 (64.29)	19.92 (−6.52 to 41.04)	.13
Sputum	4/19 (21.05)	3/28 (10.71)	10.34 (−10.37 to 33.69)	.33
Fatigue	6/19 (31.58)	2/28 (7.14)	24.44 (2.00 to 47.43)	.03*
Diarrhea	1/19 (5.26)	3/28 (10.71)	−5.45 (−15.15 to 22.49)	.51
Nausea or vomiting	3/19 (15.79)	3/28 (10.71)	5.08 (−14.34 to 27.95)	.61
No obvious symptoms	0/19 (0.00)	0/28 (0.00)	0.00 (−12.06 to 16.82)	.00
Hematologic				
White blood cell ($\times 10^9$/L)	4.08 (3.64 to 4.96)	4.57 (3.21 to 5.90)	−0.17 (−1.22 to 0.75)	.80
Lymphocytes ($\times 10^9$/L)	1.43 (1.07 to 1.77)	1.56 (1.08 to 2.07)	-0.9 (-0.4 to 0.23)	.67
LYMPH%	30.2 (25.9 to 42.7)	35.00 (30.93 to 41.68)	−3.2 (−8.2 to 2.1)	.21
Temperature returns to normal (h)				
<24	8/19 (42.11)	15/28 (53.57)	−11.47 (−16.51 to 36.87)	.87
24-48	6/19 (31.58)	8/28 (28.57)	3.01 (−21.58 to 29.08)	
48-72	4/19 (21.05)	4/28 (14.29)	6.77 (−14.53 to 30.65)	
>72	1/19 (5.26)	1/28 (3.57)	1.69 (−13.10 to 21.29)	
Chest imaging (X-ray or CT scan)				
Normal	2/19 (10.53)	4/28 (14.29)	−3.76 (−18.81 to 22.56)	.93
Unilateral	3/19 (15.79)	4/28 (14.29)	1.50 (−18.53 to 24.91)	
Bilateral	14/19 (73.68)	20/28 (71.42)	2.26 (−23.87 to 25.76)	
Treatment in hospital				
Oxygen therapy				
Nasal cannula	17/19 (89.47)	24/28 (85.71)	3.76 (−18.81 to 22.56)	.71
HFNC	2/19 (10.53)	0/28 (0.00)	10.53 (−3.73 to 31.39)	.08
NPPV	0/19 (0.00)	0/28 (0.00)	0.00 (−12.06 to 16.82)	.00
Methylprednisolone	3/19 (15.29)	1/28 (3.57)	12.22 (−5.26 to 34.19)	.29
Therapy				
Antibiotic	10/19 (52.63)	15/28 (53.57)	−0.94 (−25.84 to 27.83)	.95
Antiviral	16/19 (84.21)	25/28 (89.29)	−5.08 (−14.34 to 27.95)	.61
Chinese medicine	16/19 (84.21)	26/28 (92.86)	−8.65 (−9.95 to 31.03)	.35
Clinical outcomes				
Improve	18/19 (94.74)	28/28 (100.00)	−5.26 (−7.55 to 24.64)	.22
Worsen	1/19 (5.26)	0/28 (0.00)		

Note: Except where indicated, data = n/N (%), n is number of patients, where N is the total number of patients with available data. *$P < .05$.

Lack of specifically effective treatment, current treatments include antibiotic, antiviral, traditional Chinese medicine, and methylprednisolone. Patients in Group S were less likely to be cured by antibiotic therapy (52.63% vs. 53.57%), antiviral therapy (84.21% vs. 89.29%), or traditional Chinese medicine therapy (84.21% vs. 92.86%), but seemed to be better cured by methylprednisolone (15.29% vs. 3.57%) (Figure 1). Unfortunately, 1 (5.26%) patient in Group S still deteriorated despite of all active treatments.

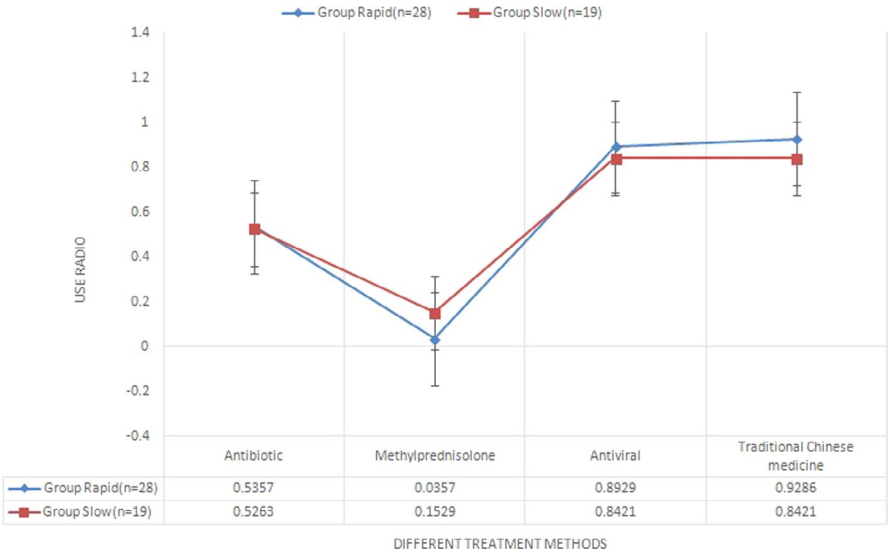

FIGURE 1 The proportion of different treatment methods in the two groups

4 | DISCUSSION

In December 2019, several cases of an unknown pneumonia were found in Wuhan, China. Recently, it has been confirmed that such a disease is caused by SARS-CoV-2, a virus homologous to the viruses that cause severe acute respiratory syndrome (SARS) and Middle East respiratory syndrome (MERS).[4] It is the 7th member of human coronaviruses and belongs to beta coronavirus.[2] Recent studies have shown that it has a characteristics of interpersonal transmission inside families and hospitals.[5,6] As of May 31, 2020, there had been reported 84,570 laboratory-confirmed cases in China, out of which 4,645 had died. Among the deaths, 937 cases were diagnosed in Jiangxi Province. Having hundreds of confirmed cases, XinYu became the city with the second largest number of diagnoses in Jiangxi Province after Nanchang. In this study, we retrospectively analyzed the clinical data of 47 common and mild patients with COVID-19 infection admitted at XinYu People's Hospital between February 4, and February 23, 2020, in order to determine the clinical characteristics and influence factors of the disease.

In order to detect COVID-19, SARS-CoV-2 nucleic acid assay played a vital role in testing oropharyngeal swabs samples and provided a standard and critical condition for confirming recovering and approving discharge. Negative SARS-CoV-2 NAT in respiratory specimens has been believed to indicate viral shedding in respiratory specimens, which allows shorter hospital stay and implies better prognosis. In this study, patients were divided into two groups based on whether or not the NAT turns negative within one week. There was no significant difference in age, gender, travel or exposure history, or smoking history between the two groups. Comorbidities may exacerbate the patient's condition. Shi et al[7] reported that hypertension and diabetes were most common in severe and critical COVID-19 patients. Chen et al[5] reported 50% of patients had underlying diseases including cardiovascular disease, diabetes, and gastrointestinal disease, and such patients were more likely to deteriorate or have poor prognoses. In our study, similar comorbidities (hypertension, diabetes, chronic obstructive pulmonary disease) have observed in both groups of patients. The average time from onset to hospital admission was 7 days, and most patients were be diagnosed within 48 hours. Increased serum level of AST may mean longer hospitalization days.[8] Li et al[6] declared that fever, cough, and myalgia or fatigue were the main symptoms across 41 COVID-19-infected patients. In this study, 72.34% of patients had cough (mainly dry cough). More than half of the patients had fever, which represented as the most common symptom. Other manifestations such as diarrhea, nausea, or vomiting were not significantly diversified between the two groups.

The incidence of fatigue was significantly different between the two groups of patients: Patients in the Group S were more likely to get fatigue than patients in Group R. It might be related to the imbalance of energy metabolism caused by the virus. Using quantitative mass spectrometry, Smallwood et al[9] found that metabolic changes occur after influenza infection in primary human respiratory cells, along with infection-associated increases in c-Myc, glycolysis, and glutaminolysis. Metabolite flux, glucose uptake, and blood amylase levels may limit the replication of the virus. Fatigue may be a clinical feature of patients with persistent positive result in nucleic acid test.

Laboratory tests showed that WBC and lymphocytes counts for most patients had decreased, suggesting that the novel coronavirus may mainly act on lymphocytes, especially the T lymphocytes, just like SARS-CoV.[10] Viral particles spread through the mucous membrane of the respiratory tract and infect other cells, induce cytokine storm, produce a series of immune responses in vivo, and cause changes in peripheral blood leukocytes, lymphocytes, and other immune cells.[11,12] Whether decreased counts of WBC and lymphocytes mean longer turnover time in the NAT did not seem to be ascertained in our research. Chest X-ray or CT scans are of great values in COVID-19 diagnosis, efficacy monitoring, and assessment on recovering and discharge. Imaging on COVID-19 patients is initially characterized as plaque infiltration and then develops into larger ground-glass shadows (often involving both lungs). Chung et al[13] reported that 76% of the patients had bilateral lung affection, and also, 76% had their lower right lobe involved. Zhu et al[14] revealed

that slow absorption of lung lesions in patients may be associated with persistent positive RT-PCR test results. We found in Group S a higher proportion of bilateral lung lobe infections, which implies more serious infections in the lungs. Pan et al[15] evaluated the four stages of the Chest CTs for 21 2019-nCoV-infected patients from early stage to absorption stage. They got the results that initial findings on the chest CTs were small subpleural ground-glass opacities (GGO), which grew larger with crazy-paving pattern and consolidation. Lung involvement increased to consolidation within up to two weeks after the onset of the disease. After two weeks, the lesions were gradually absorbed, leaving extensive GGO and subpleural parenchymal bands.

For mild and common patients, there has been no specific treatment.[16] Since respiratory failure is the most important complication, oxygen therapy is very important in the treatment for COVID-19 patients. Almost all our patients have been applied oxygen therapy and a few of them HFNC. Early oxygen therapy can greatly help to improve the prognosis.[17] Clinical medicines were mainly antibiotics, antiviral, and traditional Chinese medicine. In our study, we found no correlation between the proportion of different treatments used and the duration of the positive NATs. We speculate that drug treatment did not work well on patients in Group S due to other clinical symptoms as vomiting. The use of methylprednisolone is controversial during the treatment of COVID-19. Wu et al[18] reported that treatment with methylprednisolone maybe beneficial for patients who develop ARDS. We also have a small number of patients who use methylprednisolone, but it seemed to be ineffective and had not improved the prognosis. Double-blinded randomized clinical trials to determine the most effective treatments for COVID-19 are still to be done.

This study was conducted under certain limitations. First, medical resources and supplies are limited for mild or common patients during the epidemic of COVID-19. Second, this study was conducted at a single-center hospital with a relatively small sample size, only 47 cases. More clinical samples and controls are needed. Lastly, the electronic medical records did not involve all the biochemical parameters of those patients.

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CONFLICT OF INTEREST

The authors declared that they have no conflicts of interest to this work. We declare that we do not have any commercial or associative interest that represents a conflict of interest in connection with the work submitted.

DATA AVAILABILITY STATEMENT

All the data supporting used in this work were publicly available.

ORCID

Zhongliang Guo https://orcid.org/0000-0003-0414-379X

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