Journal of Community Medicine & Public Health
Zhang Y, et al. J Community Med Public Health 7: 373
www.doi.org/10.29011/2577-2228.100373
www.gavinpublishers.com

OPEN ACCESS

GAVIN PUBLISHERS

Research Article

# Clinical Features of 35 COVID-19 Patients with Hospitalization for More than 20 Days

**Yiling Zhang, Hongmei Yao, Li Zhao, Ying Hu, Xianchun Zeng, Jia Huang, Peibei Zhang, Weijia Liu, Xiangyan Zhang, Xianwei Ye*, Cheng Zhang***

Department of Respiratory Medicine, Guizhou Provincial People's Hospital, Guiyang, Guizhou, China

NHC Key Laboratory of Pulmonary Immunological Diseases (Guizhou Provincial People's Hospital), Guiyang, Guizhou, China

***Corresponding authors:** Cheng Zhang and Xianwei Ye, Department of Respiratory Medicine, Guizhou Provincial People's Hospital, Guiyang, Guizhou, China

**Citation:** Zhang Y, Yao H, Zhao L, Hu Y, Zeng X, et al. (2023) Clinical Features of 35 COVID-19 Patients with Hospitalization for More than 20 Days. J Community Med Public Health 7: 373. DOI: https://doi.org/10.29011/2577-2228.100373

**Received Date:** 19 September, 2023; **Accepted Date:** 02 October, 2023; **Published Date:** 09 October, 2023

## Abstract

**Background**: As we know, some patients with Coronavirus disease 2019 (COVID-19) may stay longer in the hospital, but whether the different hospitalization days are associated with different clinical features is not clear yet. **Methods**: This study is a single-centered, observational and retrospective case series. 97 patients with COVID-19 were divided into two groups: patients with hospitalization for more than 20 days (Group 1, n=35) and those with hospitalization for less than 20 days (Group 2, n=62). Data were collected. **Results**: Acute Respiratory Distress Syndrome (ARDS) and Hospital Acquired Pneumonia (HAP) were more common in Group 1 than in Group 2. There were more patients administered quadruple antiviral therapy in Group 1 than in Group 2. In group 1, 14.3% patients' specimens showed positive again after they were discharged from the hospital. Compared with Group 2, Group 1 had higher percentages of oxygenation index <300mm Hg leucopenia and lymphopenia. In Group 1, 19 patients were treated with chloroquine phosphate, whose nucleic acid tests were negative soon, but 5 patents who hadn't used the medicine had positive testing again. **Conclusions**: COVID-19 patients with longer hospitalization are more severe and need more quadruple antiviral therapy. For patients who don't use chloroquine phosphate, the nucleic acid tests are more likely to return to positive again even if they have no symptoms at that time.

**Keywords:** Antiviral therapy; Clinical feature; COVID-19; SARS-CoV-2; Hospitalization

**Abbreviations:** COVID-19: Coronavirus Disease 2019; SARS-CoV-2: Severe Acute Respiratory Syndrome Coronavirus 2; ARDS: Acute Respiratory Distress Syndrome; HAP: Hospital Acquired Pneumonia; WHO: World Health Organization; CDC: Center for Disease Control; ICU Intensive Care Unit

## Background

Since December 2019, researchers have found SARS-CoV- 2 has strong affinity to human respiratory receptors and that humans are generally susceptible to it, which causes sustained human-to-human transmission and seriously threatens human health [1-4].

The patients infected with SARS-CoV- 2 in Guizhou province are apparently mild in contrast to those originally infected in Wuhan in 2020. However, SARS-CoV-2 was named as severe acute respiratory syndrome coronavirus with a certain mortality rate especially in critically ill patients [5,6], so more attentions should be paid to this kind of disease.

As we know, some of the confirmed patients may stay longer in the hospital for some reasons, but whether the different hospitalization days are associated with different clinical features or different outcomes is not clear yet. In addition, although the conventional antiviral therapy is administered in time, some of patients' nucleic acid tests continuously show positive or return back to positive again, so how to take the next step is still a question. Here, we introduce the clinical features and the antiviral

therapy of 35 patients with hospitalization for more than 20 days to provides important insights into the management of patients with SARS-CoV- 2 infection.

## Methods

This study is a single-centered, observational and retrospective case series. Data of 97 COVID-19 patients were collected in Guizhou Provincial Jiangjun Mountain Hospital between January28, 2020 and March 15, 2020. In Guizhou province, since most of the confirmed patients remained hospitalized for more than 10 days, we divided the cohort into two groups: patients with hospitalization for more than 20 days (Group 1, n=35) and those with hospitalization for less than 20 days (Group 2, n=62). This study was approved by the Ethics Committee of Guizhou Provincial People's Hospital and conducted in accordance with the declaration of Helsinki.

### Data collection

We collected the data from clinical electronic medical documents including nursing records and laboratory tests and imaging reports of 97 COVID-19 patients. The admission data included age, sex, coexisting conditions, exposure history, smoking history, disease severity, signs, symptoms, laboratory findings and the treatment.

### Patient and public involvement

This was a single-centered, retrospective and observational case series study. The patients were not involved in the study design and were not asked to illustrate and explain any question.

### Laboratory confirmation

Sputum or throat swab samples of the patients were immediately collected and tested for SARS-CoV-2 antigens by two real time reverse transcription polymerase chain reaction assay, in Guizhou Province Centers for Disease Control (CDC).

### Statistical analysis

All data were analysed by SPSS software (version 20.0). We described categorical variables as percentages and continuous variables as medians with interquartile ranges, or means and standard deviations.

## Results

As of March 15, 2020, 97 patients infected with SARS-CoV-2 had been admitted to Guizhou Provincial Jiangjun Mountain Hospital between January 28, 2020 and March 15, 2020. Of all the patients, 14 (14.4%) had an exposure history in Wuhan before illness onset; 66(68%) patients had familial cluster and close contact with COVID-19 patients (Table 1); 10 (10.3%) patients had hypertension, 7(7.2%) had diabetes and 5(5.2%) had liver diseases as coexisting conditions (Table 1). The most common symptoms were fever (39.2%), cough (48.5%), sputum production (29.9%) and diarrhea (19.6%, Table 1). 27(27.8%) patients were regarded as mild type, 58(59.8%) as moderate, and 9(9.3%) patients as severe type (Table 1, Figure 1). Some patients had organ function injury, including 1 (2.1%) with ARDS, 1(1%) with acute cardiac injury, 8 (8.2%) with acute liver injury, 12 (12.4%) with hospital-acquired infection and 2 (2.1%) with acute kidney injury (Table 2). 5 (5.2%) patients were treated with single antiviral therapy, 45(46.4%) with dual antiviral therapy, 24(24.7%) with triple antiviral therapy and 23(23.7%)with quadruple antiviral therapy. It was worth mentioning that 83(85.6%) patients were treated with traditional Chinese medicine as important antiviral measures, 26(26.8%) with immune enhancer, 12(12.4%) with antibiotic therapy, 1(1%) with plasma exchange and 2(2.1%) with convalescent plasma therapy. 42(43.3%) patients were treated with nasal cannula, and 2(2.1%) with high- low nasal cannula as oxygen support. Only 4 (4.1%) patients had been admitted to Intensive Care Unit (ICU) (Table 2).

| Characteristics | All Patients (n=97) | ≥20 Days (n=35) | <20 Days (n=62) |
|---|---|---|---|
| **Age, Years** | | | |
| ≤18 | 13(13.4%) | 3(8.6%) | 10(16.1%) |
| 19-40 | 48(49.5%) | 11(31.4%) | 37(59.7%) |
| 41-64 | 29(29.9%) | 16(45.7%) | 13(21%) |
| ≥65 | 7(7.2%) | 5(14.3%) | 2(3.2%) |
| **Sex** | | | |
| Male | 46(47.4%) | 19(5.3%) | 19(5.3%) |
| Female | 51(52.6%) | 16(45.7%) | 34(54.8%) |
| **Coexisting conditions** | | | |
| Chronic obstructive pulmonary disease | 1(1%) | 1(2.9%) | 0 |
| Hypertension | 10(10.3%) | 3(8.6%) | 7(11.3%) |
| Cardiovascular disease | 2(2.1%) | 1(2.9%) | 1(1.61%) |
| Diabetes | 7(7.2%) | 6(17.1%) | 1(1.61%) |
| Renal diseases | 1(1%) | 0 | 1(1.61%) |
| Liver diseases | 5(5.2%) | 2(5.7%) | 3 |
| Obsolete tuberculosis | 4 | 4(11.4%) | 0 |
| Postoperative malignant tumor | 3(3.1%) | 1(2.9%) | 2(3.2%) |
| Exposure history in huh anI2weeks | 14(14.4%) | 8(22.9%) | 6(9.7%) |
| familial cluster | 66(68%) | 24(68.6%) | 42(67.7%) |
| Smoking history | 10(10.3%) | 5(14.3%) | 5(8.1%) |
| Drinking history | 5(5.2%) | 1(2.9%) | 4(6.5%) |
| **Disease severity** | | | |
| Mild type | 27(27.8%) | 8(22.9%) | 20(32.3%) |
| Moderate type | 58(59.8%) | 19(54.3%) | 39(62.9%) |
| Severe type | 9(9.3%) | 6(17.1%) | 3(4.8%) |
| Critically ill | 2(2.1%) | 2(5.7%) | 0 |
| Incubation period (days) | 4 (3-6) | 3 (3-4) | 5 (4-8) |
| Time from illness onset to first hospital admission (days) | 2.5 (1.0-4.5) | 5.5 (5.0-9.5) | 3 (1-4) |
| **Signs and Symptoms** | | | |
| Fever | 38(39.2%) | 16(45.7%) | 22(35.5%) |
| Respiratory rate ≥24 breaths per min | 2(2.1%) | 1(2.9%) | 1(1.61%) |
| Cough | 47(48.5%) | 20(57.1%) | 27(43.5%) |

| | | | |
|---|---|---|---|
| Sputum production | 29(29.9%) | 13(37.1%) | 16(25.8%) |
| Sore throat | 10(10.3%) | 3(8.6%) | 7(11.3%) |
| Fatigue | 14(14.4%) | 3(8.6%) | 11(17.7%) |
| Headache | 5(5.2%) | 1(2.9%) | 4(6.5%) |
| Diarrhea | 19(19.6%) | 9(25.7%) | 10(16.1%) |
| Stomach ache | 2(2.1%) | 1(2.9%) | 1(1.61%) |
| Bloating | 2(2.1%) | 2(5.7%) | 0 |
| Nausea | 8(8.2%) | 2(5.7%) | 6(9.7%) |
| Vomit | 5(5.2%) | 2(5.7%) | 3(4.8%) |
| Palpitations | 2(2.1%) | 1(2.9%) | 1(1.61%) |
| Chest tightness | 13(13.4%) | 6(17.1%) | 7(11.3%) |
| Shortness of breath | 6(6.2%) | 4(11.4%) | 2(3.2%) |
| Nasal congestion | 3(3.1%) | 2(5.7%) | 1(1.61%) |
| Myalgia or arthralgia | 2(2.1%) | 2(5.7%) | 1(1.61%) |

**Table 1:** Personal and clinical characteristics of 97 patients with SARS-CoV-2 infection.

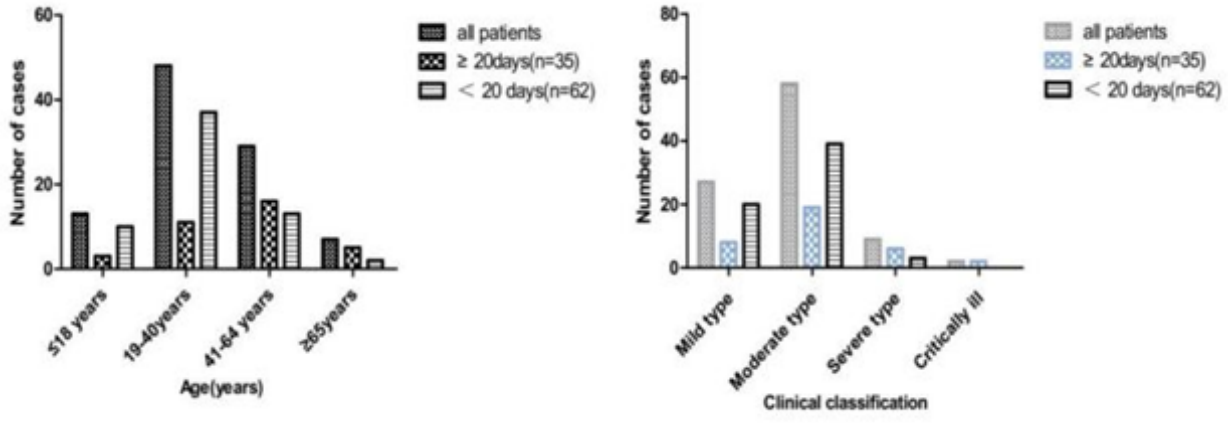


**Figure 1:** Age and clinical classification of the 97 patients with SARS-CoV-2 infection.

97(100%) patients were discharged and no one died. Of all the patients, 6(6.2%) nucleic acid test showed positive again on day 14 of medical isolation after they were discharged from the hospital (Table 2). The laboratory findings of most patients on admission showed that these blood biochemical indicators were in the normal range, but oxygenation index of 85I87.6%I was high, more than 300 mmHg (Table 3).

| Variables | All patients(n=97) | ≥20 days(n=35) | <20 days(n=62) |
|---|---|---|---|
| **Complications** | | | |
| ARDS | 2(2.1%) | 2(5.7%) | 0 |
| Acute cardiac injury | 1(1%) | 1(2.9%) | 0 |
| Acute kidney injury | 2(2.1%) | 1(2.9%) | 1(1.6%) |
| Acute liver injury | 8(8.2%) | 3(8.6%) | 5(8.1%) |
| Secondary infection | 12(12.4%) | 8(22.9%) | 4(6.4%) |
| Shock | 0 | 0 | 0 |
| **Treatment: Antiviral therapy** | | | |
| Single (Interferon alpha inhalation ) | 5(5.2%) | 1(2.9%) | 4(6.4%) |
| Dual (Interferon alpha inhalation; Lopinavir/ritonavir) | 45(46.4%) | 4(11.4%) | 41(66.1%) |
| Triple (Interferon alpha inhalation; Lopinavir/ritonavir;Arbidol) | 24(24.7%) | 10(28.6%) | 14(22.6%) |
| Quadruple(Interferon alpha inhalation;Lopinavir/ritonavir; Arbidol;Chloroquine phosphate) | 23(23.7%) | 19(54.3%) | 4(6.4%) |
| Antibiotic therapy | 12(12.4%) | 8(22.9%) | 4(6.4%) |
| Use of corticosteroid | 1(1%) | 1(2.9%) | 0 |
| Traditional Chinese medicine treatment | 83(85.6%) | 33(94.3%) | 50(80.6%) |
| Chinese patent medicine treatment | 30(30.9%) | 12(34.3%) | 18(29%) |
| Immune enhancer | 26(26.8%) | 23(65.7%) | 3(4.8%) |
| Plasma exchange | 1(1%) | 1(2.9%) | 0 |
| Convalescent plasma therapy | 2(2.1%) | 2(5.7%) | 0 |
| Oxygen support | | | |
| Nasal cannula | 42(43.3%) | 12(34.3%) | 30(48.4%) |
| Non-invasive ventilation or high-flow nasal cannula | 2(2.1%) | 2(5.7%) | 0 |
| Invasive mechanical ventilation | 0 | 0 | 0 |
| Invasive mechanical ventilation and ECMO | 0 | 0 | 0 |
| Admission to intensive care unit | 4(4.1%) | 4(11.4%) | 0 |
| **Prognosis** | | | |
| **Hospital Admission** | | | |
| Discharge | 97(100%) | 35(100%) | 62(100%) |
| Death | 0 | 0 | 0 |
| Nucleic acid test again positive | 6(6.2%) | 5(14.3%) | 1(1.6%) |

**Table 2:** The complications, treatment and prognosis of 97 patients with SARS-Cov-2 infection.

8(22.9%) had an exposure history in Wuhan before illness onset. 24(68.6%) patients had familial cluster and close contact with patients confirmed with SARS-CoV-2 infection. Compared with Group2, Group 1 had more acute respiratory distress syndrome (2 [5.7%] vs 0 [0%]), and hospital-acquired infection (8 [22.9%] vs 4 [6.4%]). Medicine was administered in Group1 and Group 2, such as dual antiviral therapy (4 [11.4%] vs 41 [66.1%]), quadruple antiviral therapy (19 [54.3%] vs4 [6.4%]), antibiotic therapy (8 [22.9%] vs 4[6.4%]) and immune enhancer(23 [65.7%] vs 3 [4.8%], Table 2).

However, it is noteworthy that 19 patients in Group 1 used triple antiviral therapy all the time, whose nucleic acid tests were continuous positive. But, after use of combined chloroquine phosphate, all these patients 'nucleic acid tests became negative for SARS-CoV-2 antigens, so they were discharged within 10 days. 5(14.3%) patients' nucleic acid test turned positive again, even after they were discharged from the hospital for 14 days of medical isolation observation (Table 2).

Compared with Group 2, Group 1 had higher percentage of oxygenation index < 300 mmHg (8 [22.9%] vs 4 [6.5%]), more leucopenia (white blood cell count <4 × $10^9$/L, 5 [14.3%] vs 4 [6.5%]), and more lymphopenia (8 [22.9%] vs 1[1.6%]), lymphocyte count <0.8×$10^9$/L, Table 3).

| Variables | All patients(n=97) | ≥20 days(n=35) | <20 days(n=62) |
|---|---|---|---|
| **Laboratory findings** | | | |
| **OI (Oxygenation Index)** | | | |
| ≥300mmHg | 85 (87.6%) | 27(77.1%) | 58(93.5%) |
| <300mmHg | 12(12.4%) | 8(22.9%) | 4(6.5%) |
| **White blood cell count (4-10 × $10^9$/L)** | | | |
| ≥10×$10^9$/L | 4(4.1%) | 3(8.6%) | 1(1.6%) |
| <4×$10^9$/L | 9(9.3%) | 5(14.3%) | 4(6.5%) |
| **Neutrophil percentage (45-77%)** | | | |
| ≥77% | 12(12.4%) | 10(28.6%) | 2(3.2%) |
| <45% | 8(8.2%) | 2(5.7%) | 6(9.7%) |
| **Lymphocyte count (0.8-4×$10^9$/L)** | | | |
| ≥4×$10^9$ | 2(2.1%) | 2(5.7%) | 0 |
| <0.8×$10^9$ | 9(9.3%) | 8(22.9%) | 1(1.6%) |
| **Eosinophil percentage (0.5-5%)** | | | |
| ≥5% | 5(5.2%) | 2(5.7%) | 3(4.8%) |
| <0.5% | 20(20.6%) | 8(22.9%) | 12(19.4%) |
| **Platelet count (100-300×$10^9$/L)** | | | |
| ≥300×$10^9$/L | 17(17.5%) | 6(17.1%) | 11(17.7%) |
| <100×109/L | 3(3.1%) | 0 | 3(4.8%) |
| **ERS (Erythrocyte sedimentation rate,0-20 mm/h)** | | | |
| ≥20mm/h | 56(57.7%) | 24(68.6%) | 32(51.6%) |
| <20mm/h | 41(42.3%) | 11(31.4%) | 30(48.4%) |
| **C-reactive protein(0-8mg/L)** | | | |
| ≥8mg/L | 31(32%) | 16(45.7%) | 13(21%) |
| <8mg/L | 66(68%) | 19(54.3%) | 49(79%) |
| **Procalcitonin(≤0.5ng/ml)** | | | |
| ≥0.5ng/ml | 11(11.3%) | 6(17.1%) | 5(8.1%) |
| <0.5ng/ml | 86(88.7%) | 29(82.9%) | 57(91.9%) |
| **GLU(3.9-6.1mmol/L)** | | | |
| ≥6.1mmol/L | 23(23.7%) | 11(31.4%) | 12(19.4%) |
| <6.1mmol/L | 74(76.3%) | 24(68.6%) | 50(80.6%) |
| **Alanine aminotransferase (8-40U/L)** | | | |
| ≥40U/L | 12(12.4%) | 8(22.9%) | 4(6.5%) |
| <40U/L | 85(87.6%) | 27(77.1%) | 58(93.5%) |
| **Aspartate aminotransferase (5-40U/L)** | | | |
| ≥40U/L | 8(8.2%) | 3(8.6%) | 5(8.1%) |
| <40U/L | 89(91.8%) | 32(91.4%) | 57(91.9%) |
| **Urea nitrogen(2.9-8.2mmol/L)** | | | |
| ≥8.2mmol/L | 1(1.1%) | 1(2.9%) | 0 |
| <8.2mmol/L | 96(98.9%) | 34(97.1%) | 62(100%) |
| **Creatinine(40-106umol/L)** | | | |
| ≥106umol/L | 2(2.1%) | 1(2.9%) | 1(1.6%) |
| <106umol/L | 95(97.9%) | 34(97.1%) | 61(98.4%) |
| **Glutamyl transpeptidase (8-58U/L)** | | | |
| ≥58U/L | 16(16.5%) | 11(31.4%) | 5(8.1%) |
| <58U/L | 81(83.5%) | 24(68.6%) | 57(91.9%) |
| **Lactate dehydrogenase (115-220U/L)** | | | |
| ≥220U/L | 16(16.5%) | 5(14.3%) | 11(17.7%) |

| | | | |
|---|---|---|---|
| <220U/L | 81(83.5%) | 30(85.7%) | 54(82.3%) |
| **Total bilirubin (5.1-20 umol/L)** | | | |
| ≥20 umol/L | 23(23.7%) | 10(28.6%) | 13(21%) |
| <20umol/L | 74(76.3%) | 25(71.4%) | 49(79%) |
| **Direct bilirubin (0-6.8umol/L)** | | | |
| ≥6.8umol/L | 12(12.4%) | 4(8.6%) | 8(12.9%) |
| <6.8umol/L | 85(77.6%) | 31(91.4%) | 54(87.1%) |
| **Indirect bilirubin (2-17umol/L)** | | | |
| ≥17umol/L | 18(18.6%) | 8(22.9%) | 10(16.1%) |
| <17umol/L | 79(81.4%) | 27(77.1%) | 52(83.9%) |
| **Myoglobin (21ng/ml)** | | | |
| ≥21ng/ml | 30(30.9%) | 16(45.7%) | 14(22.6%) |
| <21ng/ml | 67(69.1%) | 19(54.3%) | 48(77.4%) |
| **Creatine kinase (25-196 U/L )** | | | |
| ≥196 U/L | 1(1%) | 0 | 1(1.6%) |
| <196U/L | 96(99%) | 35(100%) | 61(98.4%) |
| **Creatinase isoenzyme (0-26U/L)** | | | |
| ≥26U/L | 4(4.1%) | 2(5.7%) | 2(3.2%) |
| <26U/L | 93(95.9%) | 33(94.3%) | 60(96.8%) |
| **Troponin (0-0.1 ng/ml)** | | | |
| ≥0.1 ng/ml | 1(1%) | 0 | 1(1.6%) |
| <0.1 ng/ml | 96(99%) | 35(100%) | 61(98.4%) |
| **APTT (26-44sec)** | | | |
| ≥44sec | 2(2.1%) | 0 | 2(3.2%) |
| <44sec | 95(97.9%) | 35(100%) | 60(96.8%) |
| **D-dimer(0-1mg/ml)** | | | |
| ≥1mg/ml | 10(10.3%) | 7(20%) | 3(4.8%) |
| <1mg/ml | 87(89.7%) | 28(80%) | 59(95.2%) |

**Table 3:** The laboratory findings of 97 patients with SARS-Cov-2 infection (on admission).

The percentages of C-reactive protein ≥8mg/L, Procalcitonin ≥0.5ng/ml, D-dimer≥1mg/ml and alanine aminotransferase≥40U/L were higher in Group 1 than in Group 2 (16 [45.7%] vs 13 [21%],6 [17.1%] vs 5 [8.1%], 7[20%] vs3[4.8%],and 8 [22.9%] vs 4 [6.5%],respectively, Table 3).

## Discussion

Since an outbreak of pneumonia caused by SARS-CoV-2 was reported in December 2019, many researchers have found that SARS-CoV-2 can cause sustained human-to-human transmission in other areas, thus resulting in global outbreak with a certain mortality rate, seriously threatening human health [7-11].

This study showed that of the 97 confirmed patients, only 4 had been admitted to the intensive care unit, and no patients died. 6 patients' nucleic acid tests were confirmed to return to positive again after discharge from the hospital, but they had no any symptoms at that time, who continued to receive antiviral therapy and the nucleic acid test turned negative again within 10 days. In this study, only 8 confirmed patients had been to Wuhan city. Most of them were infected by family gathering or close contact with patients confirmed with SARS-CoV-2 infection [12].

Of all the patients, the most common symptoms were fever (39.2%), cough (48.5%), sputum production (29.9%) and diarrhea (19.6%); most of them were regarded as mild and moderate type, but some had organ function injury, including ARDS, acute cardiac injury, and acute liver injury. Only 4.1% patients had been admitted to ICU. All the patients were discharged and no one died. Compared with those initially infected with SARS-CoV-2 in Wuhan, patients in Guizhou province had milder symptoms, better prognosis and lower mortality [13,14] indeed.

In this study, 46.4% of patients were treated with dual antiviral therapy, 24.7% with triple antiviral therapy, and 23.7% with quadruple antiviral therapy. Therefore, combination of antiviral therapy was major choice.

In our province, most of the COVID-19 patients had stayed in hospital for more than 10 days, so we divided the cohort into two groups: patients with hospitalization for more than 20 days (Group 1) and those with hospitalization for less than 20 days (Group 2). To our knowledge, this is the first time we compared the clinical data between the two groups above at home and abroad.

Compared with Group2, Group1 had more acute respiratory distress syndrome, hospital-acquired infection as secondary infection, suggesting that these two complications may lead to longer stay in hospital; more patients received quadruple antiviral therapy, antibiotic therapy and immune enhancer in Group 1, so we think longer hospitalization is usually accompanied by more powerful treatment. In Group1, 2 patients were treated by convalescent plasma therapy and high-flow nasal cannula, with 1 administered plasma exchange [4]. Patients had been admitted to ICU. 14.3% of the patients had the nucleic acid tested after discharged from hospital, which showed positive again. So, we think those repeated positives are common in patients with longer

stays in hospital.

Compared with Group2, Group1 had lower oxygenation index and higher percentages of leucopenia, lymphopenia, C-reactive protein≥8mg/L and procalcitonin≥ 0.5ng/ml, suggesting that higher severity of disease is one of reasons for the longer hospitalization days and that inflammation may be a factor of discharge delays.

In contrast to those of Group2, the percentages of D-dimer and alanine aminotransferase ≥40U/L were higher in Group1, which is consistent with some related studies that higher levels of D-dimer and aminotransferase were associated with severity of disease in critically ill patients [15,16].

It is noteworthy that 19 of the 35 patients in Group1 used triple antiviral therapy all the time, but their nucleic acid tests were continuous positive; after treated with combined chloroquine phosphate, these patients' nucleic acid tests became negative for SARS-CoV-2 antigens again. In addition, 5 patients who hadn't received any treatment with chloroquine phosphate, were confirmed to have positive nucleic acid testing again even after they were discharged from hospital. So, we speculate that chloroquine phosphate as one antiviral therapy against SARS-CoV-2 infection might be superior to other antiviral treatments [17,18]. But due to small sample size of this study, the larger sample size is needed to draw a more accurate conclusion in the near future (Figure 2).

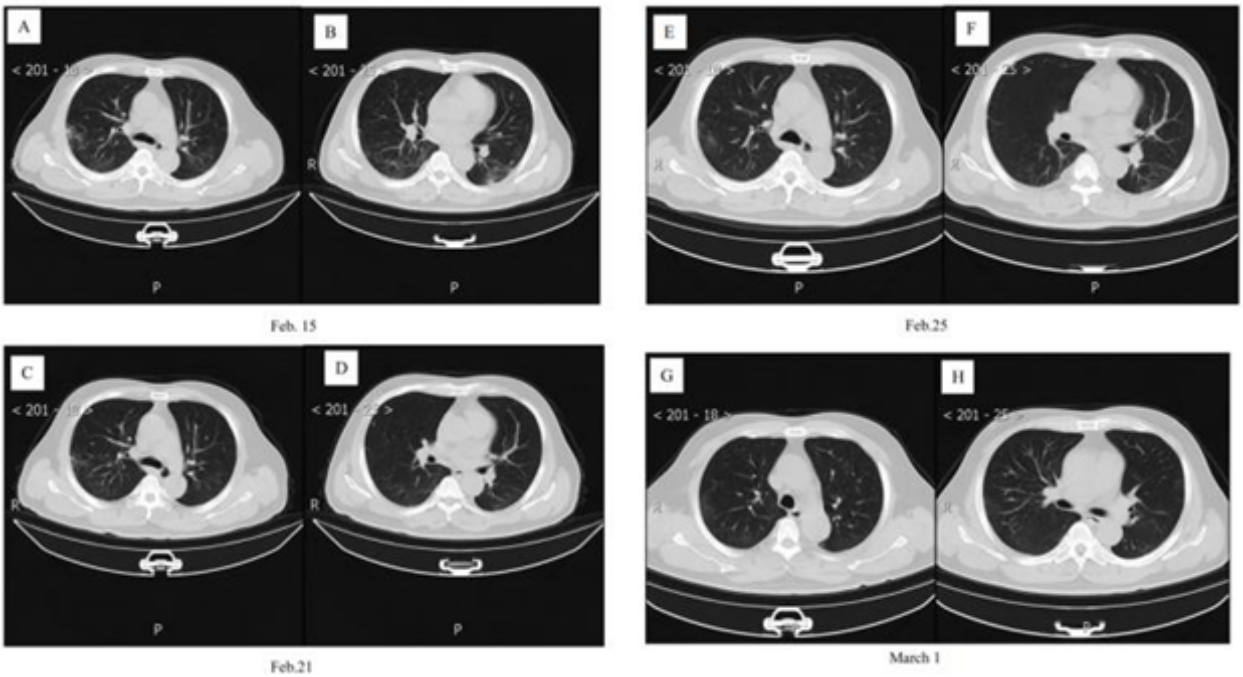


**Figure 2:** Chest CT images of one man with SARS-Cov-2 infection. Transverse chest CT images of one man with SARS-CoV-2 infection revealed bilateral ground-glass opacity in both lungs on admission on February 15, 2020. (Fig. 2 A, B). After antiviral therapy, Transverse chest CT images from the patient with SARS-CoV-2 infection showed bilateral ground glass opacity were obviously absorbed on February 21, February 25, and March 1, 2020 (Fig. 2 C, D, E, F, G, H).

## Conclusions

COVID-19 patients with longer hospitalization are more severe and need more quadruple antiviral therapy; for patients who don't use chloroquine phosphate, the nucleic acid tests may be more likely to return to positive again even if they have no symptoms at that time.

## Declarations

### Authors' Contributions

Xianwei Ye and Xiangyan Zhang conceptualized and designed the research. Yiling Zhang and Cheng Zhang collected the data and wrote the article. Hongmei Yao analysed the data. Li Zhao, Ying Hu and Xianchun Zeng helped to collect the data. All the authors have read and approved the final manuscript.

### Funding

This study was supported by the National Natural Science Foundation of China (Nos. 81860008); Natural Fund of Guizhou Provincial Science and Technology Department (Nos. (2018)1104), and Guizhou Science and Technology Cooperation Support Project (Nos. [2020]4Y002, [2019]5803). The fund is from the national and local Government. They act just as one of supervisors.

### Availability of Data and Materials

All the data and materials are included in the article.

### Ethics Approval and Consent to Participate

This study was approved by Ethics Committee of Guizhou Provincial People's Hospital. Since it is a retrospective study and only data were used, the ethics committee waived the need for written informed consent from the participants.

### Competing Interests

The authors declare that no financial benefits and commercial relationships have been received or will be conducted to this article.

## References

1. Zhu N, Zhang D, Wang W, Li X, Yang B, et al. (2020) A novel coronavirus from patients with pneumonia in China, 2019. N Engl J Med 382: 727-733.
2. Guan WJ, Ni ZY, Hu Y, Liang WH, Ou CQ, et al. (2020) Clinical Characteristics of Coronavirus Disease 2019 in China. N Engl J Med 382: 1708-1720.
3. Wang Z, Yang B, Li Q, Wen L, Zhang R (2020) Clinical Features of 69 Cases with Coronavirus Disease 2019 in Wuhan, China. Clin Infect Dis 71: 769-777.
4. Wang Y, Wang Y, Chen Y, Qin Q (2020) Unique epidemiological and clinical features of the emerging 2019 novel coronavirus pneumonia (COVID-19) implicate special control measures. J Med Virol 92: 568-576.
5. Mo P, Xing Y, Xiao Y, Deng L, Zhao Q, et al. (2021) Clinical characteristics of refractory COVID-19 pneumonia in Wuhan, China. Clin Infect Dis 73: e4208-e4213.
6. Lu R, Zhao X, Li J, Niu P, Yang B, et al. (2020) Genomic characterisation and epidemiology of 2019 novel coronavirus: implications for virus origins and receptor binding. Lancet 395: 565-574.
7. Hoffmann M, Kleine-Weber H, Schroeder S, Kruger N, Herrler T, et al. (2020) SARS-CoV-2 Cell Entry Depends on ACE2 and TMPRSS2 and is Blocked by a Clinically Proven Protease Inhibitor. Cell 181: 271-280. e8.
8. Tai W, He L, Zhang X, Pu J, Voronin D, et al. (2020) Characterization of the receptor-binding domain (RBD) of 2019 novel coronavirus: implication for development of RBD protein as a viral attachment inhibitor and vaccine. Cell Mol Immunol 17: 613-620.
9. Ou X, Liu Y, Lei X, Li P, Mi D, et al. (2020) Characterization of spike glycoprotein of SARS-CoV-2 on virus entry and its immune cross-reactivity with SARS-CoV. Nat Commun 11: 1620.
10. Chen N, Zhou M, Dong X, Qu J, Gong F, et al. (2020) Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study. Lancet 395: 507-513.
11. Chan JFW, Yuan S, Kok KH, To KKW, Chu H, et al. (2020) A familial cluster of pneumonia associated with the 2019 novel coronavirus indicating person-to-person transmission: a study of a family cluster. Lancet 395: 514-523.
12. Zhou F, Yu T, Du R, Fan G, Liu Y, et al. (2020) Clinical course and risk factors for mortality of adult inpatients with COVID- 19 in Wuhan, China: a retrospective cohort study. Lancet 395: 1054-1062.
13. Xu XW, Wu XX, Jiang XG, Xu KJ, Ying LJ, et al. (2020) Clinical findings in a group of patients infected with the 2019 novel coronavirus (SARS-Cov-2) outside of Wuhan, China: retrospective case series. BMJ 368: m606.
14. Huang C, Wang Y, Li X, Ren L, Zhao J,et al. (2020) Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. Lancet 395: 497-506.
15. Yang X, Yu Y, Xu J, Shu H, Xia J, et al. (2020) Clinical course and outcomes of critically ill patients with SARS-CoV-2 pneumonia in Wuhan, China: a single-centered, retrospective, observational study. Lancet Respir Med 8: 475-481.
16. Gautret P, Lagier JC, Parola P, Hoang VT, Meddeb L, et al. (2020) Hydroxychloroquine and azith romycin as a treatment of COVID- 19: results of an open-label non-randomized clinical trial. Int J Antimicrob Agents 56: 105949.
17. Guan WJ, Chen RC, Zhong NS (2020) Strategies for the prevention and management of coronavirus disease 2019. Eur Respir J 55: 2000597.