

## CLINICAL SCIENCE

# Clinical characteristics of 17 patients with COVID-19 and systemic autoimmune diseases: a retrospective study

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## ABSTRACT

**Objectives** Increasing data about COVID-19 have been acquired from the general population. We aim to further evaluate the clinical characteristics of COVID-19 in patients with systemic autoimmune diseases (AIDs).

**Methods** We included all confirmed inpatients with COVID-19 and systemic AIDs in Wuhan Tongji Hospital from 29 January to 8 March 2020. We retrospectively collected and analysed information on epidemiology of 1255 inpatients and additional clinical characteristics of patients with systemic AIDs. Outcomes were followed up until 16 April 2020.

**Results** Of the 1255 patients with COVID-19, the median age was 64.0 years and 53.1% were male. More than half (63.0%) had chronic comorbidities. The proportions of elderly, male and patients with comorbidities were significantly higher in intensive care unit (ICU) than in the general ward ( $p < 0.001$ ). 17 (0.61%) patients with systemic AIDs were further screened and analysed from 2804 inpatients. The median age was 64.0 years and 82.4% were female. All patients were living in Wuhan and two family clusters were found. 1 (5.9%) patient was admitted to ICU and one died. 10 (62.5%) of 16 patients changed or stopped their anti-AIDs treatments during hospitalisation, and 5 of them felt that the disease had worsened after the quarantine.

**Conclusions** Older males with chronic comorbidities are more vulnerable to severe COVID-19. The lower proportion of COVID-19 in patients with systemic AIDs needs more high-quality human clinical trials and in-depth mechanism researches. Of note, the withdrawal of anti-AIDs treatments during hospitalisation can lead to flares of diseases.

## INTRODUCTION

Since December 2019, accumulating pneumonia cases caused by unexplained pathogen emerged in Wuhan City, Hubei Province, China.<sup>1 2</sup> On 8 January, a novel enveloped RNA betacoronavirus was identified by deep sequencing analysis, which was subsequently named as severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) by the Coronaviridae Study Group of the International Committee on Taxonomy of Viruses.<sup>3 4</sup> The WHO named the coronavirus disease as 2019 novel coronavirus disease (COVID-19) and declared it as a global public health emergency of international concern.<sup>5</sup> On 12 March, WHO made a

## Key messages

### What is already known about this subject?

- On 12 March, WHO declared COVID-19 could be characterised as a pandemic. Till 22 April, more than 2.5 million cases of COVID-19 have been reported worldwide.
- Increasing data about COVID-19 based on the general population has been reported. However, little published works were found about COVID-19 in disease-specific groups.

### What does this study add?

- We analysed the epidemiology of 1255 inpatients with COVID-19 who were admitted to Wuhan Tongji Hospital. Additional 17 patients with systemic autoimmune diseases (AIDs) were further screened, the demographic characteristics, epidemiological history, comorbidities, clinical symptoms or signs on admission, chest CT findings, laboratory results on admission, therapies that were prescribed for COVID-19 as well as AIDs, and clinical outcomes were reported. The detailed information of patients with systemic AIDs was investigated.

further assessment that it could be characterised as a pandemic.<sup>5</sup> Till 22 April, more than 2.5 million cases of COVID-19 have been reported worldwide.<sup>6</sup>

Several studies have reported COVID-19 based on data from the general population, but little is known about disease-specific groups.<sup>2 7–9</sup> We retrieved 2804 inpatients who were diagnosed with COVID-19 in two campuses of Tongji Hospital, Tongji Medical College, Huazhong University of Science and Technology (hereinafter referred to as Wuhan Tongji Hospital) and reported the epidemiological and clinical data of 17 inpatients suffering from systemic autoimmune diseases (AIDs), providing more information on this population and relevant therapies.

## METHODS

### Patients

For this retrospective, single-centre study, we obtained the medical records and compiled data for inpatients who were diagnosed with COVID-19 (ordinary, severe and critical cases) and admitted

## Key messages

**How might this impact on clinical practice or future developments?**

- ▶ The pandemic of COVID-19 in multiple countries highlights the demand to develop prophylactic and therapeutic countermeasures. Under such circumstances, hydroxychloroquine (HCQ) and chloroquine, which are widely used in AIDs, have entered the spotlight and aroused much controversy. It is noteworthy that if the application spectrum of HCQ is expanded without enough rationale, it will increase the risk of patients with COVID-19, especially patients who depend on HCQ for their survival. The proportion of COVID-19 in patients with systemic AIDs is low, and whether it is associated with anti-AIDs therapies requires more high-quality human clinical trials and in-depth mechanism researches.
- ▶ The COVID-19 pandemic has taken up substantial medical resources, however, the concern about the underlying diseases of patients with chronic comorbidities cannot be ignored.

to two campuses of Wuhan Tongji Hospital. The data cut-off for the study was 16 April 2020. COVID-19 was diagnosed based on the interim guidance from National Health Commission of the People's Republic of China.<sup>6</sup> Laboratory confirmation of COVID-19 was defined as a positive result by the use of high-throughput sequencing or real-time reverse transcription-polymerase chain reaction (RT-PCR) assay on specimen from the lower respiratory tract. The confirmation of systemic AIDs was through electronic medical records, and by this means eight patients with rheumatoid arthritis (RA), three patients with systemic lupus erythematosus (SLE), two patients with Sjogren's syndrome (SS), two patients with ankylosing spondylitis (AS), one patient with Behcet's disease and one patient with polymyalgia rheumatic were included. Two cases of organ-specific AIDs were excluded, including one patient with Hashimoto's thyroiditis and one patient with pulmonary sarcoidosis. When a ventilator or continuous renal replacement therapy or extracorporeal membrane oxygenation treatment was required, the patient was admitted to the intensive care unit (ICU). This study was approved by the Ethics Commission of Tongji Hospital, Tongji Medical College, Huazhong University of Science and Technology (TJ-IRB20200365). Written informed consent was waived by Tongji Hospital for emerging infectious diseases and the urgent need to collect data.

**Data collection**

We reviewed 2804 electronic clinical records at two campuses of Wuhan Tongji Hospital and extracted demographic characteristics, epidemiological history, comorbidities, clinical symptoms or signs on admission, chest CT findings, laboratory results on admission, therapies that were prescribed for COVID-19 as well as AIDs, and clinical outcomes for all 17 inpatients with systemic AIDs. All radiological assessments and laboratory testing were performed for the clinical care needs of the patients. The radiological abnormality was determined based on description in medical reports. The information about AIDs was collected through telephone follow-up, and one patient was further confirmed as SS with RA. The classification criteria for AIDs were unclear, but they were diagnosed by rheumatologists, and these diseases were consistent with their description of the

symptoms and corresponding elevated antibodies/MRI findings. The information was obtained and collated using a standardised data collection form. Two researchers (YH and ZC) independently reviewed and collated the data collection form to ascertain data accuracy.

**Definitions**

Acute respiratory distress syndrome (ARDS) was defined according to the Berlin Definition.<sup>10</sup> Coagulopathy was defined as prolonged prothrombin time by 3 s or prolonged activated partial thromboplastin time by 5 s.<sup>11</sup> Acute cardiac injury was diagnosed if serum levels of cardiac biomarkers (eg, high-sensitivity cardiac troponin I) were above the 99th percentile upper reference interval, or if new abnormalities were presented in electrocardiography and echocardiography.<sup>2</sup> Hypoproteinaemia was defined as blood albumin below 25 g/L. Acute kidney injury was diagnosed according to the KDIGO clinical practice guidelines.<sup>12</sup> Septic shock was defined according to the 2016 Third International Consensus Definition.<sup>13</sup> The quiescent stage of the disease was roughly defined as no obvious symptoms and signs of inflammatory activity, otherwise it was defined as the active stage. Organ damage was defined as having a medical history, long-term symptoms such as cough and/or corresponding supplementary examination results.

**Statistical analysis**

Continuous variables were expressed as medians and IQRs and compared by the Mann-Whitney U test between two groups; compared by the single sample Wilcoxon test between AID group and the average of Tongji Hospital. Categorical variables were expressed as number (%) or number/total number (%) and compared by  $\chi^2$  test or Fisher's exact test. A p value <0.05 was considered statistically significant. Statistical analysis was done with SPSS, V.21.0. Figures were made with GraphPad Prism V.7.04.

**Patient and public involvement statement**

Patients or the public were not involved in the design, or conduct, or reporting or dissemination plans of our research.

**RESULTS****Distribution of inpatients with COVID-19 in Tongji Hospital**

A total of 1255 inpatients with COVID-19 who were admitted to the two campuses of Tongji Hospital were included in this analysis, and we obtained information regarding sex, age and comorbidities (table 1). The distribution of sex and age is shown in figure 1A. Of the 1255 patients, 236 (18.8%) were admitted to the ICU. The median age of the patients was 64 years (IQR 52.0–70.0); patients in ICU were older than those in the general ward by a median of 6 years ( $p<0.001$ ). About 64.4% of the patients in ICU were older than 65 years and this proportion was significantly higher than that in the general ward. A total of 46.9% were female, and the proportion of male and female was comparable in the general ward, but in ICU, the proportion of male (13.1%) was significantly higher than that of female (5.7%;  $p<0.001$ ). More than half (63.0%) had comorbid conditions with hypertension being the most common (37.5%, figure 1B).

**Demographic and characteristics of patients with COVID-19 and systemic AIDs**

A total of 2804 inpatients were retrieved in two campuses of Tongji Hospital and 17 (0.61%) patients with systemic AIDs were screened and analysed in this study. Among these AIDs,

**Table 1** Demographic characteristics of 1255 inpatients with COVID-19 in Tongji Hospital

Characteristics	All patients (n=1255)	General ward (n=1019)	ICU (n=236)	P value
Age, years				
Median (IQR)	64.0 (52.0–70.0)	62.0 (49.0–70.0)	68.0 (60.0–77.0)	0
<15 years	2 (0.2)	2 (0.2)	0	0.496
15–44 years	210 (16.7)	206 (16.4)	4 (0.3)	0
45–64 years	455 (36.3)	375 (29.9)	80 (6.4)	0.403
≥65 years	588 (46.9)	436 (34.7)	152 (12.1)	0
Sex				0
Female	589 (46.9)	517 (41.2)	72 (5.7)	
Male	666 (53.1)	502 (40.0)	164 (13.1)	
Comorbid conditions				
Any comorbidity	791 (63.0)	594 (47.3)	197 (15.7)	0
Diabetes	224 (17.8)	170 (13.5)	54 (4.3)	0.025
Hypertension	470 (37.5)	358 (28.5)	112 (8.9)	0
Coronary heart disease	110 (8.8)	78 (6.2)	32 (2.5)	0.004
Cerebrovascular disease	63 (5.0)	43 (3.4)	20 (1.6)	0.007
Hematological disease	14 (1.1)	12 (1.0)	2 (0.2)	0.927
Cancer	63 (5.0)	50 (4.0)	13 (1.0)	0.703
AID	10 (0.8)	10 (0.8)	0	0.262

Data are median (IQR) or n (%). P values comparing the general ward and ICU are from  $\chi^2$  test, Fisher's exact test or Mann-Whitney U test. AID, autoimmune disease; ICU, intensive care unit.

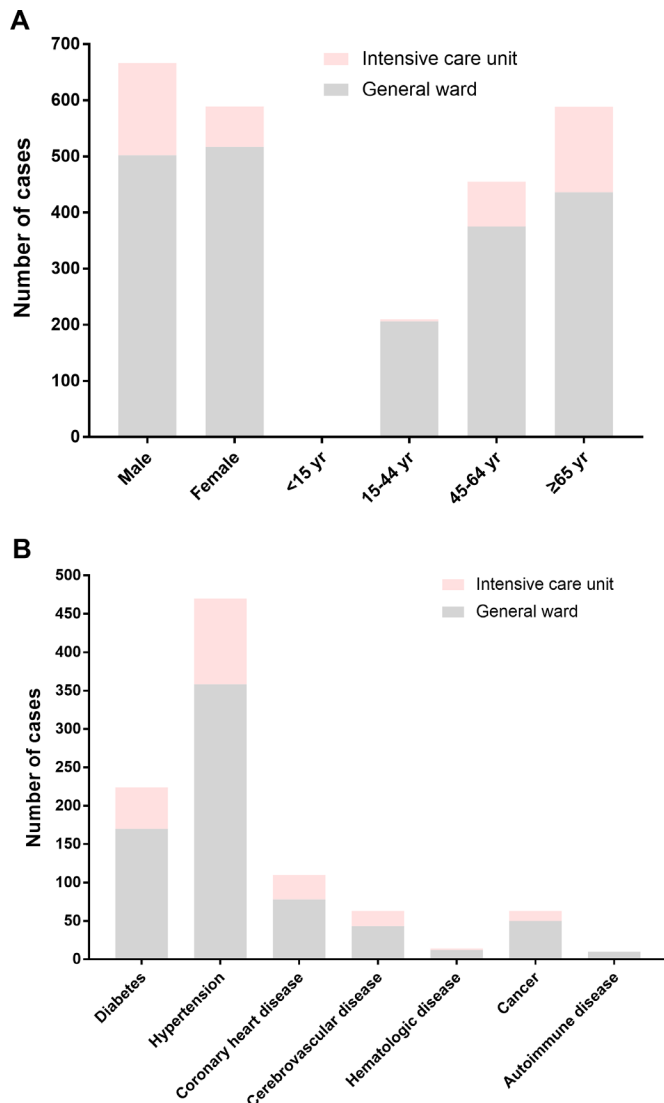
RA was the most common (52.9%), followed by SLE, SS and AS. And one patient had mixed connective tissue disease (RA with SS). The demographic and clinical characteristics of the patients are shown in table 2.

On admission, the degree of severity of COVID-19 was categorised as critical in 1 (5.9%) patient, severe in 3 (17.6%) patients and 5 (29.4%) patients developed into severe disease during hospitalisation. The median age of the AID group (64.0) was the same as the total population, but the proportion of female was significantly higher (82.4%). All patients were living in Wuhan, and two family clusters were found. Comorbid conditions were present in 58.8% of the patients with hypertension being the most common (35.5%). Common symptoms were fever (88.2%), cough (82.4%), shortness of breath (64.7%) and sputum production (58.8%); sore throat, nasal congestion and hemoptysis were uncommon. The median of length of hospital stay (LOHS) was 28.0 days. Most patients received antiviral therapy (94.1%), antibiotic therapy (88.2%) and oxygen support (76.5%). One patient was admitted to ICU for the administration of continuous renal replacement therapy, and she was in the uremic stage of lupus nephritis and underwent dialysis twice a week. Eight (50.0%) of 16 patients received disease-modifying antirheumatic drugs (DMARDs), including methotrexate, leflunomide, thalidomide and hydroxychloroquine (HCQ). Six (37.5%) of 16 patients were treated with methylprednisolone or prednisone acetate, and 4 of them took two tablets per day. Botanicals such as tripterysium glycosides and total glucosides of paeony were prescribed in seven (43.8%) patients. Ten (62.5%) of 16 patients were treated with immunosuppressant (including glucocorticoids, methotrexate, leflunomide, thalidomide, HCQ, tripterysium glycosides and total glucosides of paeony). Ten (62.5%) of 16 patients changed or stopped their anti-AIDs treatments during hospitalisation. Unfortunately, five of them felt that the disease had worsened after the quarantine. Of the 13 patients with severe complications, ARDS was the most common (47.1%). Moreover, the median time from onset of the disease to ARDS was 17.0 days (IQR 11.8–29.3). By the end of 29 March, 16 (94.1%) patients had been discharged from hospital and 1 (5.9%) patient had died. The one death was a 61-year-old female. She had

a history of chronic renal failure for 13 years, SLE for more than 10 years, hypertension for 7–8 years, sciatica for 2 years and a history of chronic gastritis and tuberculosis. She had severe pneumonia with an oxygen saturation of 85% on admission. The subsequent auxiliary examination indicated that she had heart failure, with a progressive increase in high-sensitivity cardiac troponin I and N-terminal pro-brain natriuretic peptide. The chest CT scan showed bilateral patchy shadowing with 'white lung' changes, bilateral pleural effusion, left ventricular enlargement, and pericardial effusion (figure 2J). On the 12th day of admission, the patient developed metabolic acidosis, frequent ventricular premature beats and was declared dead.

Online supplementary table S1 shows the chest CT and laboratory findings of 17 patients with systemic AIDs on admission. Abnormalities in chest CT were found in all patients. Figure 2 shows representative chest CT results of five patients with non-severe disease (figure 2A–E) and five patients with severe disease (figure 2F–J). Among the 17 patients, the most common CT patterns were bilateral patchy shadowing (58.8%) and ground-glass opacity (47.1%). Laboratory tests showed that most patients had decreased levels of lymphocyte counts, haemoglobin and albumin (64.7%, 76.5%, 76.5%). Elevated levels of D-dimer, erythrocyte sedimentation rate and serum ferritin were common (76.5%, 90.0%, 66.7%). Liver and renal function tests showed abnormalities in six patients, of which four were categorised as severe. All 17 patients presented elevated C-reactive protein level. Elevated levels of interleukin (IL) and/or tumour necrosis factor (TNF)- $\alpha$  were presented in 12 (80.0%) of 15 patients; two patients presented a lower level of IL-2 receptor. Patients with severe disease presented higher levels of infection-related biomarkers than those with non-severe disease. Five of 10 patients presented decreased number of helper T (Th) cells; two presented decreased number of both Th cells and suppressor T cells and were categorised as severe. Seven of 10 patients presented decreased number of natural killer cells and all seven were categorised as severe.

Compared with the average LOHS of Tongji Hospital (28.8 days), there were no significant differences ( $p=0.981$ ,  $p=0.799$ ) in that of patients with systemic AIDs (28.0 days, IQR 20.0–39.0)



**Figure 1** Distribution of 1255 inpatients with COVID-19 in Tongji Hospital. (A) Number of hospital admissions by sex and age group. (B) Number of hospital admissions by comorbid conditions.

and immunosuppressive users (28.5 days, IQR 24.3–38.5). Similarly, there were no significant differences in the ventilation rate ( $p=0.120$ ,  $p=0.309$ ), the ICU incidence ( $p=0.291$ ,  $p=0.757$ ) and the case fatality rate ( $p=0.909$ ,  $p=0.970$ ) between patients with systemic AIDs (0/17, 1/17, 1/17) and patients without systemic AIDs (500/2907, 549/2907, 153/2907), and between immunosuppressive users in AIDs (0/10, 1/10, 0/10) and other patients (500/2914, 549/2914, 154/2914). We also stratified patients with systemic AIDs as immunosuppressive users/non-immunosuppressive users (online supplementary table S2), organ damaged/non-organ damaged (online supplementary table S3), those in quiescent stage/those in active stage (online supplementary table S4) and patients with severe COVID-19/patients with non-severe COVID-19 (online supplementary table S5). Nevertheless, there were no significant differences between immunosuppressive users and non-immunosuppressive users regarding laboratory results and LOHS. There were no significant differences between organ damaged and non-organ damaged except for total bilirubin ( $p=0.027$ ). Of note, there were significant differences between patients with active AIDs and patients with quiescent AIDs regarding the levels of IL-2 receptor ( $p=0.022$ ), IL-6 ( $p=0.005$ ), IL-8 ( $p=0.038$ ) and TNF- $\alpha$  ( $p=0.022$ ). In addition, there were significant differences between

**Table 2** Demographic and clinical characteristics of patients with systemic AIDs

Characteristics	Patients (n=17)
<b>Type of AIDs</b>	
RA	9/17 (52.9)
SLE	3/17 (17.6)
SS	2/17 (11.8)
AS	2/17 (11.8)
Behcet's disease	1/17 (5.9)
Polymyalgia rheumatic	1/17 (5.9)
<b>Age, years</b>	
Median (IQR)	64.0 (60.5–71.5)
<15 years	0
15–44 years	1/17 (5.9)
45–64 years	8/17 (47.1)
≥65 years	8/17 (47.1)
<b>Sex</b>	
Female	14/17 (82.4)
Male	3/17 (17.6)
<b>Epidemiological history</b>	
Living in Wuhan	17/17 (100.0)
Family cluster	2/17 (11.8)
Current smoker	0
<b>Comorbid conditions</b>	
Any comorbidity	10/17 (58.8)
Hypertension	6/17 (35.5)
Diabetes	0
Cerebrovascular disease	1/17 (5.9)
Chronic renal disease	2/17 (11.8)
Infectious disease	1/17 (5.9)
Respiratory system disease	2/17 (11.8)
Digestive system disease	2/17 (11.8)
Reproductive system diseases	1/17 (5.9)
<b>Signs and symptoms</b>	
Fever	15/17 (88.2)
Highest temperature, °C	38.8 (38.3–39.0)
<37.3	2/17 (11.8)
37.3–38.0	2/17 (11.8)
38.1–39.0	10/17 (58.8)
>39.0	3/17 (17.6)
Cough	14/17 (82.4)
Fatigue	7/17 (41.2)
Sputum production	10/17 (58.8)
Shortness of breath	11/17 (64.7)
Myalgia or arthralgia	3/17 (17.6)
Sore throat	2/17 (11.8)
Headache	3/17 (17.6)
Chills	3/17 (17.6)
Nausea or vomiting	4/17 (23.5)
Diarrhoea	5/17 (29.4)
Nasal congestion	1/17 (5.9)
Hemoptysis	1/17 (5.9)
More than one sign or symptom	16/17 (94.1)
<b>Disease severity status</b>	
General	13/17 (76.5)
Severe	3/17 (17.6)
Critical	1/17 (5.9)
Time from illness onset to hospital admission, days	10.0 (7.0–21.0)
<b>Treatment</b>	
Antiviral therapy	16/17 (94.1)

Continued

Table 2 Continued

Characteristics	Patients (n=17)
Antibiotic therapy	15/17 (88.2)
Oxygen support	13/17 (76.5)
Glucocorticoids	6/17 (35.3)
Intravenous immunoglobulin therapy	3/17 (17.6)
Mechanical ventilation	0
CRRT	1/17 (5.9)
Admission to ICU	1/17 (5.9)
Length of hospital stay, days	28.0 (20.0–39.0)
Anti-AIDs treatment	
DMARDs	8/16 (50.0)
Hydroxychloroquine	4/16 (25.0)
0.1 g twice daily	2/16 (12.5)
0.2 g twice daily	2/16 (12.5)
Methotrexate	2/16 (12.5)
10 mg once a week	1/16 (6.3)
12.5 mg once a week	1/16 (6.3)
Leflunomide	1/16 (6.3)
10 mg once daily	1/16 (6.3)
Thalidomide	1/16 (6.3)
50 mg once daily	1/16 (6.3)
Glucocorticoids	6/16 (37.5)
Methylprednisolone	2/16 (12.5)
8 mg once daily	2/16 (12.5)
Prednisone acetate	4/16 (25.0)
5 mg once daily	2/16 (12.5)
10 mg once daily	2/16 (12.5)
Botanicals	7/16 (43.8)
Tripterysium glycosides	3/16 (18.8)
20 mg once daily	1/16 (6.3)
20 mg twice daily	2/16 (12.5)
Total glucosides of paeony	3/16 (18.8)
0.3 g twice daily	2/16 (12.5)
0.6 g twice daily	1/16 (6.3)
NSAIDs	5/16 (31.3)
Plasters	2/16 (12.5)
None	1/16 (6.3)
Anti-AIDs treatment during hospitalisation	
Continue	6/16 (37.5)
Change	2/16 (12.5)
Stop	8/16 (50.0)
Activity of AIDs	
In quiescent stage	12/16 (75.0)
In active stage	4/16 (25.0)
Organ damage	6/17 (35.3)
Lung	5/17 (29.4)
Kidney	2/17 (11.8)
Complications	
ARDS	8/17 (47.1)
Coagulopathy	6/17 (35.3)
Acute cardiac injury	3/17 (17.6)
Hypoproteinaemia	3/17 (17.6)
Acidosis	1/17 (5.9)
Acute kidney injury	0
Septic shock	0
Clinical outcome	
Death	1/17 (5.9)
Discharge	16/17 (94.1)

Continued

Table 2 Continued

Characteristics	Patients (n=17)
Data are median (IQR) or n/N (%), and N is the total number of patients with available data. A deceased patient could not be contacted, so her information about AIDs was not obtained. AIDs, autoimmune diseases; ARDS, acute respiratory distress syndrome; AS, ankylosing spondylitis; CRRT, continuous renal replacement therapy; DMARDs, disease-modifying antirheumatic drugs; HCQ, hydroxychloroquine; ICU, intensive care unit; NSAIDs, non-steroidal anti-inflammatory drugs; RA, rheumatoid arthritis; SLE, systemic lupus erythematosus; SS, Sjogren's syndrome.	

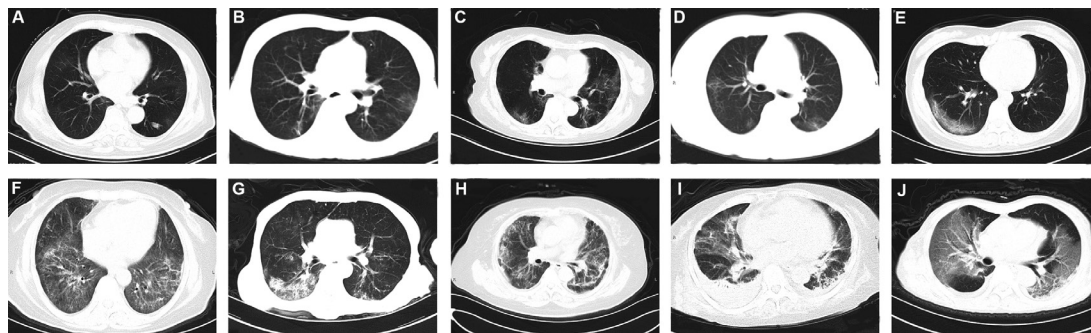
patients with severe COVID-19 and patients with non-severe COVID-19 regarding neutrophil count ( $p=0.036$ ), lymphocyte count ( $p=0.046$ ), haemoglobin ( $p=0.002$ ), D-dimer ( $p=0.011$ ), blood urea nitrogen ( $p=0.008$ ), IL-2 receptor ( $p=0.018$ ) and procalcitonin ( $p=0.016$ ). Given the very limited samples and some equivocal information by telephone follow-up, the results should be interpreted more cautiously.

## DISCUSSION

This is a descriptive study on the epidemiology and clinical characteristics of 17 patients with COVID-19 and systemic AIDs, and an extended report on the epidemiology of 1255 inpatients with COVID-19 in Wuhan Tongji Hospital. The proportion of males was significantly higher in ICU than that of females, and this result may indicate that symptoms are milder in females after SARS-CoV-2 infection. The protective mechanism might be attributed to sex hormones and X chromosome, rendering females stronger antiviral immunity.<sup>14</sup> Notably, more than half (63.0%) of patients with COVID-19 suffered from chronic diseases with 83.5% in the ICU; hypertension (37.5%) and diabetes (17.8%) were the most prominent. This proportion was significantly higher than the study reported on 1099 patients,<sup>7</sup> presumably because more patients with severe COVID-19 were admitted to Tongji Hospital.<sup>15</sup> Altogether, these results suggest that older males with chronic comorbidities are more vulnerable to severe COVID-19, consistent with the finding of 99 patients.<sup>8</sup>

We selected patients with systemic AIDs for further analysis, and 17 cases were eligible from 2804 electronic clinical records. Compared with the data of 1255 cases, a more compact age distribution (IQR 60.5–71.5 vs IQR 52.0–70.0) and more females (82.4% vs 46.9%) were presented in patients with AIDs. This might be because that systemic AIDs generally occur more often in females (table 2). Disease progression in severe cases was extremely rapid and required ICU admission. The time between hospital admission and acute cardiac injury was as short as 1 day; ARDS was 3 days. Furthermore, one death occurred on the 24th day of the onset of COVID-19. Patients with systemic AIDs manifested more gastrointestinal symptoms than the whole COVID-19 population.<sup>2,7,8</sup> Treatment and radiographic and laboratory results were basically consistent with those reported in 1099 patients.<sup>7</sup> Besides, we analysed cytokine and lymphocyte subsets (online supplementary table S1), which were not included in previous studies.<sup>2,7–9</sup> From very limited cases, we did not find any difference in clinical outcomes of COVID-19 between patients with systemic AIDs and other patients, including LOHS, ventilation rate, ICU incidence and the case fatality rate.

Intriguingly, the number of patients with AIDs (0.68%) was far below our expectations, considering that AID might affect approximately 3%–10% of the total population.<sup>16–18</sup> Generally speaking, people with chronic comorbidities are more susceptible to SARS-CoV-2, therefore, we hypothesise whether there are protective factors for patients with AIDs. Therapies that control detrimental immune responses in patients with AIDs have attracted our attention. Chloroquine phosphate, tosituzumab and glucocorticoid



**Figure 2** Chest CT scans (transverse plane) of 10 patients. (A) Case 1: bilateral patchy shadowing. (B) Case 2: bilateral emphysema; bilateral scattered ground-glass opacities and patchy shadowing. (C) Case 3: bilateral scattered ground-glass opacities and patchy shadowing. (D) Case 4: bilateral ground-glass opacities and patchy shadowing. (E) Case 5: light patchy shadowing in the upper left and lower right lobes. (F) Case 6: bilateral blurred shadowing and strip shadowing, and some of them show grid-like changes. (G) Case 7: bilateral scattered ground-glass opacities and consolidation. (H) Case 8: diffuse multiple ground-glass opacities and consolidation bilaterally, showing sign of air bronchus. (I) Case 9: multiple bilateral patchy shadowing with honeycomb-like changes, bilateral pleural effusion and bilateral atelectasis. (J) Case 10: bilateral patchy shadowing with 'white lung' changes, bilateral pleural effusion, left ventricular enlargement and pericardial effusion.

are approved in the Diagnosis and Treatment Plan of Corona Virus Disease 2019 (Tentative Seventh Edition).<sup>6</sup> Among them, chloroquine phosphate is used for conventional antiviral therapy, and the other two are used for severe diseases. It is notable that HCQ, tocilizumab and glucocorticoid are recommended for the management of RA by the European League Against Rheumatism.<sup>19</sup> According to our statistic result, 7 (43.8%) of 16 patients used glucocorticoid and/or HCQ. HCQ has a similar effect to chloroquine phosphate and has higher safety. The recent publications of an *in vitro* and a clinical trial suggested that HCQ might have an anti-SARS-CoV-2 effect.<sup>20,21</sup> Nevertheless, the validity of the clinical findings aroused much controversy because of obvious methodological flaws.<sup>22</sup> Quite unexpectedly, the treatment might be overinterpreted by social media, contributing to great public interest in HCQ. Many clinical trials using HCQ for COVID-19 as postexposure prophylaxis or therapies are under way, and the forthcoming results may shed light on this issue.<sup>23,24</sup> Although high-dose glucocorticoids may delay the resolution of coronavirus, an emergency doctor in Wuhan using inhaled glucocorticoids for asthma has survived exposure to numerous patients confirmed with COVID-19, which enables us to speculate whether patients using low-dose glucocorticoids could prevent coronavirus infection. And certainly, these issues need to be verified by rigorous methodological clinical trials. In our study, however, there is no evidence to show what role immunosuppressants may play in the clinical outcomes of COVID-19.

During the telephone follow-up, we learnt that more than half (62.5%) patients changed or stopped their anti-AIDs treatments during hospitalisation because they were unaware of the consequences of drug withdrawal or were unwilling to trouble doctors. Some patients stopped their anti-AIDs treatments for more than 50 days (hospitalisation +2 weeks hotel quarantine +2 weeks home quarantine), which was more common among elderly people living alone. A landmark clinical study has demonstrated that the withdrawal of HCQ can result in severe and even life-threatening flares of SLE, such as lupus nephritis.<sup>25</sup> Unfortunately, five of them felt the disease had exacerbated after the quarantine, but still dared not go out to see a doctor in this special period. Although the countermeasures towards COVID-19 should be explored with extraordinary vigour and speed, it is noteworthy that if the application spectrum of HCQ is expanded without enough rationale, it will increase the risk of patients with COVID-19, especially patients who depend on HCQ for their survival.

Our study has some limitations. First, only 17 inpatients with COVID-19 and systemic AIDs in a single centre were analysed. It would be more thoroughgoing if eligible patients in more institutions and those who were treated at home could be included. Due to the specificity of Wuhan Tongji Hospital, our analysis might represent more severe outcomes. Second, some patients had incomplete medical records and thus we could not obtain more comprehensive information. Third, most information about AIDs came from telephone follow-up, which might not be comprehensive and objective. Finally, there was insufficient evidence to speculate the effect of immunosuppressants or HCQ on COVID-19; more high-quality human clinical trials and in-depth mechanism researches are urgently needed to explain the relationship between them.

These two decades have seen the global spread of three unprecedented coronavirus diseases: severe acute respiratory syndrome, Middle East respiratory syndrome and COVID-19. The pandemic of COVID-19 in multiple countries emphasises the need to develop prophylactic and therapeutic countermeasures. With such desperate eagerness, the interpretation of the results should be more cautious.

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