





Epidemiological characteristics of COVID-19 patients in convalescence period

B. M. Liu^{1,*} , Q. Q. Yang^{1,*} , L. Y. Zhao¹ , W. Xie²  and X. Y. Si¹¹Department of Nephrology, Zhongnan Hospital of Wuhan University, Wuhan, Hubei, China and ²Department of Laboratory Medicine, Zhongnan Hospital of Wuhan University, Wuhan, Hubei, China

Original Paper

*Bingman Liu and Qingqing Yang contributed equally to this paper.

Cite this article: Liu BM, Yang QQ, Zhao LY, Xie W, Si XY (2020). Epidemiological characteristics of COVID-19 patients in convalescence period. *Epidemiology and Infection* **148**, e108, 1–9. <https://doi.org/10.1017/S0950268820001181>

Received: 15 May 2020

Revised: 26 May 2020

Accepted: 28 May 2020

Key words:

Convalescence period; COVID-19; epidemiological characteristics; SARS-CoV-2

Author for correspondence:

X. Y. Si,

E-mail: lzgj.lxm@163.com**Abstract**

This study aimed to investigate the clinical characteristics and to analyse the epidemiological features of coronavirus disease 2019 (COVID-19) patients during convalescence. In this study, we enrolled 71 confirmed cases of COVID-19 who were discharged from hospital and transferred to isolation wards from 6 February to 26 March 2020. They were all employees of Zhongnan Hospital of Wuhan University or their family members of which three cases were <18 years of age. Clinical data were collected and analysed statistically. Forty-one cases (41/71, 57.7%) comprised medical faculty, young and middle-aged patients (aged ≤60 years) accounted for 81.7% (58/71). The average isolation time period for all adult patients was 13.8 ± 6.1 days. During convalescence, RNA detection results of 35.2% patients (25/71) turned from negative to positive. The longest RNA reversed phase time was 7 days. In all, 52.9% of adult patients (36/68) had no obvious clinical symptoms, and the remaining ones had mild and non-specific clinical symptoms (e.g. cough, sputum, sore throat, disorders of the gastrointestinal tract etc.). Chest CT signs in 89.7% of adult patients (61/68) gradually improved, and in the others, the lesions were eventually absorbed and improved after short-term repeated progression. The main chest CT manifestations of adult patients were normal, GGO or fibre streak shadow, and six patients (8.8%) had extrapulmonary manifestations, but there was no significant correlation with RNA detection results ($r = -0.008$, $P > 0.05$). The drug treatment was mainly symptomatic support therapy, and antibiotics and antiviral drugs were ineffective. It is necessary to re-evaluate the isolation time and standard to terminate isolation for discharged COVID-19 patients.

Introduction

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) belongs to β-coronavirus, and humans may present non-specific clinical manifestations such as fever, cough, fatigue and diarrhoea after infection [1]. Coronavirus disease 2019 (COVID-19) is highly infectious, mainly transmitted by patients infected with SARS-CoV-2. Its incubation period ranges from 1 to 14 days, mostly 3–7 days, and patients in the incubation period were also infectious [2]. According to the ‘Diagnosis and Treatment Protocol for COVID-19 (trial version 7)’ issued by the National Health Commission of the People’s Republic of China (PRC), patients meeting the discharge criteria of COVID-19 should continue to be isolated for 14 days for management and health monitoring [3]. However, the epidemiological characteristics of COVID-19 patients in isolation period have not been clarified. In this study, we retrospectively analysed the clinical characteristics and treatment regimens of COVID-19 convalescent patients.

Methods**General information**

The study was approved by the Medical Ethics Committee of the Zhongnan Hospital of Wuhan University (ethics number: LYL2020056K), and a written informed consent was waived. We enrolled 71 cases of COVID-19 patients in isolation wards from 6 February to 26 March 2020. They were convalescent patients who were transferred to isolation wards after meeting discharge criteria. They were all medical employees of Zhongnan Hospital of Wuhan University or their family members. The admission diagnosis and discharge criteria of COVID-19 patients all met the requirements of COVID-19 diagnosis and treatment protocol issued by the National Health Commission of PRC [3]. The discharged patients must meet the following criteria: (1) the body temperature returns to normal for more than 3 days; (2) respiratory symptoms improve significantly; (3) pulmonary imaging shows that the acute exudative lesions were significantly absorbed and improved; (4) the SARS-CoV-2 ribonucleic acid (RNA) detection results of two consecutive respiratory specimens are negative (sampling interval should be at least 24 h). According to the internal standard for employees of Zhongnan Hospital of Wuhan University to be released from isolation, the convalescent

© The Author(s), 2020. Published by Cambridge University Press. This is an Open Access article, distributed under the terms of the Creative Commons Attribution-NonCommercial-ShareAlike licence (<http://creativecommons.org/licenses/by-nc-sa/4.0/>), which permits non-commercial re-use, distribution, and reproduction in any medium, provided the same Creative Commons licence is included and the original work is properly cited. The written permission of Cambridge University Press must be obtained for commercial re-use.

patients who were consistently negative in five SARS-CoV-2 RNA detections of oropharyngeal swabs (sampling interval should be at least 24 h) could be released. Even though the patients had been released, they should continue to be isolated at home for 14 days, during which the antibodies (IgM + IgG) were detected.

Oropharyngeal swabs sampling

The samples for SARS-CoV-2 nucleic acid detection were taken with oropharyngeal swabs. Two plastic rod swabs with polypropylene fibre heads were used to wipe the bilateral pharyngeal tonsils and posterior pharyngeal wall simultaneously. Then, the heads of the swabs were immersed in a tube containing 3 ml of virus preservation solution (isotonic salt solution, tissue culture solution or phosphate buffer could also be used), the tails were discarded and the tube cap was tightened. This sampling method followed the Laboratory Testing Technical Guidelines for COVID-19 (fourth edition) issued by the National Health Commission of PRC (<http://www.nhc.gov.cn/jkj/s3577/202002/573340613ab243b3a7f61df260551dd4.shtml>).

Observation indicators

General data of patients were collected, including age, gender, underlying disease, medication history, isolation time and frequency of RNA detection. We used real-time reverse transcription polymerase chain reaction (RT-PCR) to detect SARS-CoV-2 in the oropharyngeal swab of respiratory tract specimens. We recorded the clinical manifestations, RNA detection results of oropharyngeal swab specimens, SARS-CoV-2 IgM–IgG antibodies detection results (data were collected on the 28th day after discharge), chest computed tomography (CT) images and medication of these patients. According to patients' age, they were divided into young and middle-aged group (≤ 60 years old) and elderly group (> 60 years old). According to RNA results in isolation period, patients were divided into the re-detectable positive (RP) group and non-RP (NRP) group. The above subgroups were designed to compare their symptoms, RNA detection results, IgM–IgG antibodies detection results, CT results and treatment.

Statistical analysis

All statistical analyses were processed by SPSS 22.0 software. Continuous variables were expressed as means \pm standard deviation (s.d.). The measurement data conforming to normal distribution were compared between groups by *t* test, while those not conforming to normal distribution were compared between groups by Mann–Whitney *U* test. Categorical variables were summarised as frequency and percentage, and chi-square test was used for comparison between groups. The correlation between age, RNA detection results, frequency of positive RNA and symptoms, CT were conducted by Spearman's correlation analysis. All the statistical tests were two-sided, and significant differences were considered at $P < 0.05$.

Results

Clinical characteristics of enrolled adult patients with COVID-19

For all 68 adult patients, the average age was 44.3 ± 16.4 years. In all, 80.9% of patients (55/68) were younger than 60 years of

age, the majority were female (43/68, 63.2%), 41 cases were clinical first-line medical staff (41/68, 60.3%). There were 14 patients (14/68, 20.6%) complicated with underlying diseases ($P < 0.05$), and most of them had a related drug use history. The underlying diseases of elderly patients were mostly hypertension, diabetes, coronary heart disease, lacunar infarction, emphysema and that of young and middle-aged patients were mainly obsolete pulmonary tuberculosis. The shortest isolation time was 4 days, the longest was 38 days and the average isolation time was 13.8 ± 6.1 days (Table 1). In all adult patients, there were 25 patients (25/68, 36.8%) showing RP findings of SARS-CoV-2 RNA in oropharyngeal swab specimens and 43 non-RP (NRP) (43/68, 63.2%). The longest RNA RP time was 7 days (Table 2).

Comparison of clinical indicators of patients in different age groups

Overall, 52.9% of the adult patients (36/68) had no obvious clinical symptoms, and the remaining patients had mild clinical symptoms (one patient was transferred to the ICU because of worsening condition, and eventually improved after therapy), which had no specificity. Adult patients' symptoms included cough in 18 cases (26.5%), diarrhoea in five cases (7.4%), chest distress in four cases (5.9%), expectoration in four cases (5.9%), sore throat in four cases (5.9%), nausea and vomiting in four cases (5.9%), fatigue in three cases (4.4%), eyes discomfort in three cases (4.4%), dizziness in two cases (2.9%), headache in two cases (2.9%) and there was only one case (1.5%) of fever (Table 2). There was no significant relationship between symptoms and age ($r = 0.131$), RNA detection results ($r = 0.230$) and the frequency of RP ($r = 0.223$) (all $P > 0.05$) (Table 5). Compared with the ≤ 60 -year-old group, the diarrhoea symptoms of patients in the > 60 -year-old group were significant (23.1% vs. 3.6%, $\chi^2 = 5.833$, $P < 0.05$), and other symptoms were not significantly different between the two groups. In comparison with patients in ≤ 60 -year-old group, in addition to medication for chronic diseases, the application of drugs for digestive system (46.2% vs. 12.7%, $\chi^2 = 7.598$, $P < 0.01$), sleep improvement (53.8% vs. 9.1%, $\chi^2 = 18.705$, $P < 0.001$) and expectorants (15.4% vs. 0.0%, $\chi^2 = 8.718$, $P < 0.01$) in > 60 -year-old group were significantly different, but antibiotics and antiviral drugs were not statistically significant between the two groups ($P > 0.05$). There was no statistical difference between the two groups in isolation time and frequency of RNA detection, as well as the detection results of IgM (15.4% vs. 16.4%, $\chi^2 = 0.007$, $P > 0.05$) and IgG (46.2% vs. 65.5%, $\chi^2 = 1.659$, $P > 0.05$) antibodies. The results of RNA detection of three COVID-19 convalescent patients aged below 18 years did not turn positive. The symptoms, medication and isolation time (14.3 ± 2.9 days) for them were not significantly different from those of adult patients ($P > 0.05$) (Table 2).

Changes in clinical indicators of RP patients

In all adult patients, there were 25 patients (25/68, 36.8%) showing RP findings of SARS-CoV-2 RNA in oropharyngeal swab specimens and 43 NRP patients (43/68, 63.2%). Compared with NRP adult patients, the isolation time of RP patients increased (15.8 ± 6.0 vs. 12.6 ± 5.9 days, $u = 344$, $P < 0.05$) and frequency of RNA detection increased (10.2 ± 4.2 vs. 5.6 ± 1.4 , $u = 78.5$, $P < 0.001$). Compared with RP patients, the cough symptom in the NRP adult patients was more

Table 1. Clinical characteristics of enrolled adult patients with COVID-19

	All patients (n = 68)	≤60 years (n = 55)	>60 years (n = 13)	P value
Age – years	44.3 ± 16.4	37.7 ± 9.6	71.9 ± 7.8	<0.001
Gender (male/female) – no. (%)	25/43 (36.8/63.2)	17/38 (30.9/69.1)	8/5 (61.5/38.5)	<0.05
Medical staff – no. (%)	41 (60.3)	40 (72.7)	1 (7.7)	<0.001
Underlying disease – no. (%)	14 (20.6)	8 (14.5)	6 (46.2)	<0.05
Hypertension	1 (1.5)	0 (0.0)	1 (7.7)	<0.05
Coronary heart disease	4 (5.9)	2 (3.6)	2 (15.4)	0.11
Diabetes mellitus	3 (4.4)	1 (1.8)	2 (15.4)	<0.05
Lacunar infarction	2 (2.9)	0 (0.0)	2 (15.4)	<0.01
Pulmonary tuberculosis	4 (5.9)	4 (7.3)	0 (0.0)	0.32
Emphysema	3 (4.4)	1 (1.8)	2 (15.4)	<0.05
Asthma	1 (1.5)	1 (1.8)	0 (0.0)	0.62
Myocarditis	1 (1.5)	0 (0.0)	1 (7.7)	<0.05
Medication history – no. (%)				
ACEI/ARB	4 (5.9)	2 (3.6)	2 (15.4)	0.11
β-receptor blocker	2 (2.9)	0 (0.0)	2 (15.4)	<0.01
Calcium channel blocker	1 (1.5)	0 (0.0)	1 (7.7)	<0.05
Bayaspirin	2 (2.9)	0 (0.0)	2 (15.4)	<0.01
Statins	2 (2.9)	0 (0.0)	2 (15.4)	<0.01
Insulin	1 (1.5)	0 (0.0)	1 (7.7)	<0.05
Oral antidiabetic drugs	3 (4.4)	1 (1.8)	2 (15.4)	<0.05
Isolate-time – days	13.8 ± 6.1	13.2 ± 5.8	16.4 ± 7.0	0.09
Frequency of RNA detection – no.	7.3 ± 3.5	6.9 ± 2.7	9.1 ± 5.7	0.45
Frequency of positive RNA – no.	0.8 ± 1.7	0.6 ± 1.1	1.8 ± 3.0	0.54
Maximum time of RP – days	7	7	5	–

ACEI, angiotensin-converting enzyme inhibitors; ARB, angiotensin receptor blocker. Plus-minus values are means ± s.d.

obvious (34.9% vs. 12.0%, $\chi^2 = 4.253$, $P < 0.05$), and the other symptoms were not significantly different (all $P > 0.05$). The detection results of IgM (16.0% vs. 16.3%, $\chi^2 = 0.001$, $P > 0.05$) and IgG (76.0% vs. 53.5%, $\chi^2 = 3.392$, $P > 0.05$) antibodies were not statistically significant between the two groups. There was no significant difference in age and gender between the two groups ($P > 0.05$) (Table 2). Compared with NRP adult patients, CT images showed significantly increased fibre streak shadow in RP patients (28.0% vs. 4.7%, $\chi^2 = 7.505$, $P < 0.01$), but there was no significant difference in other imaging manifestations between the two groups such as ground-glass opacity (GGO), pleural thickening and pleural effusion ($P > 0.05$) (Table 3). All patients used traditional Chinese medicine recovery prescription (Pinellinae Rhizoma Praeparatum 9 g, Citri Reticulatae Pericarpium 10 g, Codonopsis Radix 15 g, Astragali Radix 30 g, Poria 15 g, Pogostemonis Herba 10 g, AmomiFructus (added later) 6 g). Compared with NRP adult patients, there was no significant difference in usage of antiviral drugs (40.0% vs. 25.6%, $\chi^2 = 1.540$, $P = 0.21$), antibiotics (40.0% vs. 32.6%, $\chi^2 = 0.383$, $P = 0.54$), respiratory system drugs (40.0% vs. 37.2%, $\chi^2 = 0.052$, $P = 0.82$) or digestive system drugs (24.0% vs. 16.3%, $\chi^2 = 0.609$, $P = 0.43$) in RP patients ($P > 0.05$) (Table 2).

Clinical characteristics of patients with RNA RP findings >2 times

Of the 25 RP patients, 10 patients (40.0%) were male and 15 patients (60.0%) were female, including seven cases with RP findings >2 times and 18 cases with RP findings ≤2 times, and one patient had eight times of RP findings. Compared with patients with RP findings ≤2 times, the isolation time of patients with RP findings >2 times was prolonged (20.9 ± 6.4 vs. 13.8 ± 4.7 days, $u = 25$, $P < 0.05$), the frequency of RNA detection increased (15.4 ± 4.2 vs. 8.2 ± 1.6, $u = 1.5$, $P < 0.001$) and the age was older (59.6 ± 12.9 vs. 43.0 ± 16.9 yrs, $u = 23.5$, $P < 0.05$). There was no significant difference in gender between the two groups ($P > 0.05$). The detection results of IgM (14.3% vs. 16.7%, $\chi^2 = 0.021$, $P > 0.05$) and IgG (85.7% vs. 72.2%, $\chi^2 = 0.503$, $P > 0.05$) antibodies were not statistically significant between the two groups. In the 25 patients, none of them had fever, and 17 of them had no clinical symptoms. There was no significant difference between the respiratory and cardiovascular symptoms between the two groups ($P > 0.05$), but the symptoms of diarrhoea in patients with RP findings >2 times were worse than in patients with RP findings ≤2 times (28.6% vs. 0.0%, $\chi^2 = 5.590$), and the difference was statistically significant ($P < 0.05$). Among the 25 RP patients,

Table 2. Symptoms and drug application of enrolled adult patients with COVID-19

	All patients (n = 68)	Age groups			RNA detection		
		≤60 years (n = 55)	>60 years (n = 13)	P value	Negative (n = 43)	Positive (n = 25)	P value
Age – years	44.3 ± 16.4	37.7 ± 9.6	71.9 ± 7.8	<0.001	42.3 ± 15.6	47.6 ± 17.4	0.19
Gender (male/female) – no. (%)	25/43 (36.8/63.2)	17/38 (30.9/69.1)	8/5 (61.5/38.5)	<0.05	15/28 (34.9/65.1)	10/15 (40.0/60.0)	0.67
Isolate-time – days	13.8 ± 6.1	13.2 ± 5.8	16.4 ± 7.0	0.09	12.6 ± 5.9	15.8 ± 6.0	<0.05
Frequency of RNA detection – no.	7.3 ± 3.5	6.9 ± 2.7	9.1 ± 5.7	0.45	5.6 ± 1.4	10.2 ± 4.2	<0.001
IgM positive – no. (%)	11 (16.2)	9 (16.4)	2 (15.4)	0.93	7 (16.3)	4 (16.0)	0.98
IgG positive – no. (%)	42 (61.8)	36 (65.5)	6 (46.2)	0.20	23 (53.5)	19 (76.0)	0.07
Symptoms – no. (%)							
Fever	1 (1.5)	1 (1.8)	0 (0.0)	0.62	1 (2.3)	0 (0.0)	0.44
Cough	18 (26.5)	17 (30.9)	1 (7.7)	0.09	15 (34.9)	3 (12.0)	<0.05
Expectoration	4 (5.9)	4 (7.3)	0 (0.0)	0.32	3 (7.0)	1 (4.0)	0.61
Chest distress	4 (5.9)	2 (3.6)	2 (15.4)	0.11	3 (7.0)	1 (4.0)	0.61
Chest pain	1 (1.5)	1 (1.8)	0 (0.0)	0.62	1 (2.3)	0 (0.0)	0.44
Sore throat	4 (5.9)	3 (5.5)	1 (7.7)	0.76	2 (4.7)	2 (8.0)	0.57
Asthma	1 (1.5)	1 (1.8)	0 (0.0)	0.62	1 (2.3)	0 (0.0)	0.44
Fatigue	3 (4.4)	3 (5.5)	0 (0.0)	0.39	1 (2.3)	2 (8.0)	0.27
Muscle soreness	1 (1.5)	1 (1.8)	0 (0.0)	0.62	0 (0.0)	1 (4.0)	0.19
Nausea and vomiting	4 (5.9)	4 (7.3)	0 (0.0)	0.32	3 (7.0)	1 (4.0)	0.61
Diarrhoea	5 (7.4)	2 (3.6)	3 (23.1)	<0.05	3 (7.0)	2 (8.0)	0.88
Dizziness	2 (2.9)	1 (1.8)	1 (7.7)	0.26	2 (4.7)	0 (0.0)	0.27
Headache	2 (2.9)	2 (3.6)	0 (0.0)	0.49	1 (2.3)	1 (4.0)	0.69
Rash	1 (1.5)	1 (1.8)	0 (0.0)	0.62	1 (2.3)	0 (0.0)	0.44
Eye discomfort	3 (4.4)	2 (3.6)	1 (7.7)	0.52	2 (4.7)	1 (4.0)	0.90
Asymptomatic	36 (52.9)	31 (56.4)	5 (38.5)	0.24	19 (44.2)	17 (68.0)	0.06
Drug application – no. (%)							
Antiviral drug	21 (30.9)	18 (32.7)	3 (23.1)	0.50	11 (25.6)	10 (40.0)	0.21
Arbidol	19 (27.9)	16 (29.1)	3 (23.1)	0.66	10 (23.3)	9 (36.0)	0.26
Tamiflu	2 (2.9)	1 (1.8)	1 (7.7)	0.26	2 (4.7)	0 (0.0)	0.27
Antibiotic	24 (35.3)	20 (36.4)	4 (30.8)	0.70	14 (32.6)	10 (40.0)	0.54
Moxifloxacin	21 (30.9)	18 (32.7)	3 (23.1)	0.50	12 (27.9)	9 (36.0)	0.49
Cephalosporin antibiotics	9 (13.2)	6 (10.9)	3 (23.1)	0.24	7 (16.3)	2 (8.0)	0.33
Azithromycin	2 (2.9)	1 (1.8)	1 (7.7)	0.26	2 (4.7)	0 (0.0)	0.27

Amoxicillin	2 (2.9)	2 (3.6)	0 (0.0)	0.49	0 (0.0)	2 (8.0)	0.06
Vitamin C	11 (16.2)	9 (16.4)	2 (15.4)	0.93	6 (14.0)	5 (20.0)	0.51
Centrum	3 (4.4)	1 (1.8)	2 (15.4)	<0.05	2 (4.7)	1 (4.0)	0.90
Immunomodulator	5 (7.4)	2 (3.6)	3 (23.1)	<0.05	3 (7.0)	2 (8.0)	0.88
Diammonium glycyrrhizate	2 (2.9)	2 (3.6)	0 (0.0)	0.49	0 (0.0)	2 (8.0)	0.06
Bronchodilator	2 (2.9)	1 (1.8)	1 (7.7)	0.26	1 (2.3)	1 (4.0)	0.69
Acetylcysteine	24 (35.3)	19 (34.5)	5 (38.5)	0.79	16 (37.2)	8 (32.0)	0.66
Digestive system drugs	13 (19.1)	7 (12.7)	6 (46.2)	<0.01	7 (16.3)	6 (24.0)	0.43
Ophthalmic	7 (10.3)	4 (7.3)	3 (23.1)	0.09	5 (11.6)	2 (8.0)	0.64
Antihypertensive drugs	12 (17.6)	5 (9.1)	7 (53.8)	<0.001	6 (14.0)	6 (24.0)	0.29
Lipid-lowering drugs	5 (7.4)	1 (1.8)	4 (30.8)	<0.001	2 (4.7)	3 (12.0)	0.26
Antidiabetic drugs	3 (4.4)	1 (1.8)	2 (15.4)	<0.05	2 (4.7)	1 (4.0)	0.90
Diazepam	12 (17.6)	5 (9.1)	7 (53.8)	<0.001	5 (11.6)	7 (28.0)	0.09
Deanxit	2 (2.9)	0 (0.0)	2 (15.4)	<0.01	1 (2.3)	1 (4.0)	0.69
Antihistamine	2 (2.9)	1 (1.8)	1 (7.7)	0.26	1 (2.3)	1 (4.0)	0.69
TCM							
Lianhua Qingwen granules and capsules	18 (26.5)	15 (27.3)	3 (23.1)	0.76	10 (23.3)	8 (32.0)	0.43
ELP enteric soft capsules	2 (2.9)	0 (0.0)	2 (15.4)	<0.01	0 (0.0)	2 (8.0)	0.06
Qiangli Pipa syrup	4 (5.9)	4 (7.3)	0 (0.0)	0.32	3 (7.0)	1 (4.0)	0.61
TCM prescriptions	68 (100.0)	55 (100.0)	13 (100.0)	–	43 (100.0)	25 (100.0)	–

ELP, eucalyptol, limonene and pinene; TCM, traditional Chinese medicine.
Plus-minus values are means \pm s.d.

Table 3. Pulmonary CT findings of enrolled adult patients during isolation

CT - no. (%)	All patients (n = 68)	Negative RNA (n = 43)	Positive RNA (n = 25)	P value
Normal	16 (23.5)	10 (23.3)	6 (24.0)	0.61
Light GGO	4 (5.9)	3 (7.0)	1 (4.0)	0.56
Small flaky GGO	3 (4.4)	3 (7.0)	0 (0.0)	0.18
Patchy GGO	24 (35.3)	14 (32.6)	10 (40.0)	0.54
Mixed GGO	1 (1.5)	1 (2.3)	0 (0.0)	0.44
Consolidation shadow	2 (2.9)	0 (0.0)	2 (8.0)	0.06
Fibre streak shadow	9 (13.2)	2 (4.7)	7 (28.0)	<0.01
Nodular shadow	1 (1.5)	0 (0.0)	1 (4.0)	0.19
Patchy shadow	8 (11.8)	4 (9.3)	4 (16.0)	0.41
Fibrosis foci	8 (11.8)	5 (11.6)	3 (12.0)	0.96
Grid-form shadow	2 (2.9)	2 (4.7)	0 (0.0)	0.27
Pleural thickening	2 (2.9)	1 (2.3)	1 (4.0)	0.69
Pleural effusion	3 (4.4)	2 (4.7)	1 (4.0)	0.90
Pneumothorax	1 (1.5)	1 (2.3)	0 (0.0)	0.44
Improved	61 (89.7)	40 (93.0)	21 (84.0)	0.24

CT, computed tomography; GGO, ground-glass opacity.

six showed normal lung imaging (24.0%), 10 patchy GGO (40.0%), seven fibre streak shadow (28.0%) and four patchy shadows (16.0%). There was no statistically significant difference in CT imaging between the two groups ($P > 0.05$). Compared with patients with RP findings ≤ 2 times, the application of drugs for sleep improvement (57.1% vs. 16.7%, $\chi^2 = 4.096$, $P < 0.05$) and expectorants (28.6% vs. 0.0%, $\chi^2 = 5.590$, $P < 0.05$) had statistical differences in patients with RP findings > 2 times, but there was no statistical difference in other systemic drug applications between the two groups ($P > 0.05$) (Table 4).

Discussion

Among the 68 adult patients, the medical staff accounted for 60.3%, of whom after infection, 32 cases (47.1%) entered the convalescence period in February and nine cases (13.2%, $P > 0.05$) in March. It had been previously reported that some medical staff were infected with SARS-CoV-2. Peng *et al.* reported 138 cases of COVID-19 patients (36 cases in ICU and 102 cases in non-ICU) in Zhongnan Hospital of Wuhan University, which included 40 medical staff [4]. Zhong *et al.* found that among 1 099 COVID-19 patients from 552 hospitals in 30 provinces, autonomous regions and municipalities in mainland China, the proportion of medical staff was 3.5% [2]. February was the peak of the COVID-19 outbreak in the urban area of Wuhan, suggesting that in the early stage of the COVID-19 outbreak, an environment with high concentration of virus, insufficient knowledge and inadequate protection may be the main reasons for infection among medical staff. In this study, there were 13 patients in > 60 -year-old group, including eight cases (11.8%) in February

and five cases (7.4%) in March. In all, 46.2% of them had underlying diseases such as hypertension, diabetes, coronary heart disease and emphysema, suggesting that chronic disease-induced decrease of immunity may be a susceptible factor for COVID-19.

The clinical symptoms of COVID-19 convalescent patients who reached the discharge criteria were mostly mild. Asymptomatic patients accounted for more than 50%, and there was only one case of fever. The symptoms were mainly concentrated in the respiratory system and digestive system. It was reported that SARS-CoV-2 infected with respiratory tract host cells through cells expressing angiotensin-converting enzyme 2 (ACE2) receptors [5], but recent studies found that SARS-CoV-2 could also be detected in samples such as anal swabs, blood, urine and faeces [6, 7]. Compared with the respiratory system, the virus remained in the gastrointestinal system for a longer time, and the clearance of viral RNA in faeces was delayed [8–10]. Nasopharyngeal, sputum and faeces were the major shedding routes for SARS-CoV-2, and virus shedding time in sputum was longer and more stable than nasopharyngeal and faeces. The median durations of virus shedding of them in turn were 12 (3–38), 19 (5–37) and 18 (7–26) days. The viral load in sputum was the highest among the three specimens, followed by nasopharyngeal and faeces were the lowest [11, 12]. Another report on three cases of common COVID-19 children showed that all patients had RP findings of SARS-CoV-2 RNA detection in faeces specimens within 10 days after discharge, but no positive results were found in the two RNA detection in throat swab specimens, and there were no clinical symptoms [13]. In this study, the > 60 -year-old group showed obvious symptoms of diarrhoea ($P < 0.05$), but there was no significant correlation between all symptoms with age or RNA detection results (Table 5). It is reasonable to speculate that the virus still persists in some convalescent patients, however, the pathogenicity of the virus is significantly weakened. The symptoms (including fever) cannot be used as the criteria for improvement in COVID-19 patients.

Positive RNA in throat swab is the diagnostic criterion for COVID-19. The seventh edition of the guidelines issued by the National Health Commission of RPC recommended that patients required 14 days isolation and health monitoring after discharge [3], suggesting that the infectivity of patients weakens or disappears. Different companies or detection methods have different sensitivities and specificities for RNA detection in throat swabs. The positive rate is 30–50%, and positive RNA may indicate the persistent existence of the virus. This study showed that after 71 convalescent patients entered isolation wards, 25 patients (35.2%) had RP findings of SARS-CoV-2 RNA in oropharyngeal swab specimens and the longest RNA RP time was 7 days. Some studies found that COVID-19 patients who met the national discharge criteria had RP findings of RNA detection during the follow-up observation outside hospital, and the time for RP findings of RNA detection ranged from 5 to 13 days after discharge [9, 13–16]. A case report of four mild-to-moderate COVID-19 patients (all were medical staff) showed that all convalescent patients without clinical symptoms presented RP findings of RNA detection in throat swab specimens at 5–13 days after discharge [14]. Another study found that among 62 COVID-19 convalescent medical staff, two patients without clinical symptoms showed RP findings of RNA detection in throat swab specimens at 5–6 days after discharge [15]. A case report of seven common COVID-19 patients also showed that three convalescent cases had RP findings of RNA detection in sputum specimens after discharge, without clinical symptoms, and the time interval of RP

Table 4. Symptoms, drug application and CT of patients with RP RNA

	All patients (n = 25)	Positive times ≤twice (n = 18)	Positive times >twice (n = 7)	P value
Age – years	47.6 ± 17.4	43.0 ± 16.9	59.6 ± 12.9	<0.05
Gender (male/female) – no. (%)	10/15 (40.0/60.0)	8/10 (44.4/55.6)	2 /5(28.6/71.4)	0.47
Isolate-time – days	15.8 ± 6.0	13.8 ± 4.7	20.9 ± 6.4	<0.05
Frequency of RNA detection – no.	10.2 ± 4.2	8.2 ± 1.6	15.4 ± 4.2	<0.001
IgM positive – no. (%)	4 (16.0)	3 (16.7)	1 (14.3)	0.88
IgG positive – no. (%)	19 (76.0)	13 (72.2)	6 (85.7)	0.48
Symptoms – no. (%)				
Fever	0 (0.0)	0 (0.0)	0 (0.0)	–
Cough	3 (12.0)	3 (16.7)	0 (0.0)	0.25
Expectoration	1 (4.0)	1 (5.6)	0 (0.0)	0.52
Chest distress	1 (4.0)	1 (5.6)	0 (0.0)	0.52
Chest pain	0 (0.0)	0 (0.0)	0 (0.0)	–
Sore throat	2 (8.0)	2 (11.1)	0 (0.0)	0.36
Asthma	0 (0.0)	0 (0.0)	0 (0.0)	–
Fatigue	2 (8.0)	2 (11.1)	0 (0.0)	0.36
Muscle soreness	1 (4.0)	1 (5.6)	0 (0.0)	0.52
Nausea and vomiting	1 (4.0)	1 (5.6)	0 (0.0)	0.52
Diarrhoea	2 (8.0)	0 (0.0)	2 (28.6)	<0.05
Dizziness	0 (0.0)	0 (0.0)	0 (0.0)	–
Headache	1 (4.0)	1 (5.6)	0 (0.0)	0.52
Rash	0 (0.0)	0 (0.0)	0 (0.0)	–
Eye discomfort	1 (4.0)	1 (5.6)	0 (0.0)	0.52
Asymptomatic	17 (68.0)	12 (66.7)	2 (28.6)	0.82
Drug application – no. (%)				
Antiviral drug	10 (40.0)	6 (33.3)	4 (57.1)	0.28
Arbidol	9 (36.0)	6 (33.3)	3 (42.9)	0.66
Antibiotic	10 (40.0)	6 (33.3)	4 (57.1)	0.28
Moxifloxacin	9 (36.0)	5 (27.8)	4 (57.1)	0.17
Cephalosporin antibiotics	2 (8.0)	1 (5.6)	1 (14.3)	0.47
Amoxicillin	2 (8.0)	2 (11.1)	0 (0.0)	0.36
Vitamin C	5 (20.0)	4 (22.2)	1 (14.3)	0.66
Centrum	1 (4.0)	0 (0.0)	1 (14.3)	0.10
Immunomodulator	2 (8.0)	1 (5.6)	1 (14.3)	0.47
Diammonium glycyrrhizate	2 (8.0)	2 (11.1)	0 (0.0)	0.36
Bronchodilator	1 (4.0)	0 (0.0)	1 (14.3)	0.10
Acetylcysteine	8 (32.0)	6 (33.3)	2 (28.6)	0.82
Digestive system drugs	6 (24.0)	3 (16.7)	3 (42.9)	0.17
Ophthalmic	2 (8.0)	1 (5.6)	1 (14.3)	0.47
Antihypertensive drugs	6 (24.0)	3 (16.7)	3 (42.9)	0.17
Lipid-lowering drugs	3 (12.0)	1 (5.6)	2 (28.6)	0.11
Antidiabetic drugs	1 (4.0)	0 (0.0)	1 (14.3)	0.10
Diazepam	7 (28.0)	3 (16.7)	4 (57.1)	<0.05
Deanxit	1 (4.0)	0 (0.0)	1 (14.3)	0.10

(Continued)

Table 4. (Continued.)

	All patients (n = 25)	Positive times ≤twice (n = 18)	Positive times >twice (n = 7)	P value
Antihistamine	1 (4.0)	1 (5.6)	0 (0.0)	0.52
Traditional Chinese medicine				
Lianhua Qingwen granules and capsules	8 (32.0)	6 (33.3)	2 (28.6)	0.82
ELP enteric soft capsules	2 (8.0)	0 (0.0)	2 (28.6)	<0.05
Qiangli Pipa syrup	1 (4.0)	1 (5.6)	0 (0.0)	0.52
TCM prescriptions	25 (100.0)	18 (100.0)	7 (100.0)	–
CT – no. (%)				
Normal	6 (24.0)	5 (27.8)	1 (14.3)	0.48
Light GGO	1 (4.0)	0 (0.0)	1 (14.3)	0.10
Patchy GGO	10 (40.0)	8 (44.4)	2 (28.6)	0.47
Consolidation shadow	2 (8.0)	2 (11.1)	0 (0.0)	0.36
Fibre streak shadow	7 (28.0)	4 (22.2)	3 (42.9)	0.30
Nodular shadow	1 (4.0)	1 (5.6)	0 (0.0)	0.52
Patchy shadow	4 (16.0)	3 (16.7)	1 (14.3)	0.88
Fibrosis foci	3 (12.0)	3 (16.7)	0 (0.0)	0.25
Pleural thickening	1 (4.0)	0 (0.0)	1 (14.3)	0.10
Pleural effusion	1 (4.0)	1 (5.6)	0 (0.0)	0.52
Improved	21 (84.0)	15 (83.3)	6 (85.7)	0.88

ELP, eucalyptol, limonene and pinene; TCM, traditional Chinese medicine; CT, computed tomography; GGO, ground-glass opacity. Plus-minus values are means ± s.d.

Table 5. Spearman's correlation analysis between age, RNA detection results, frequency of positive RNA and symptoms, CT of enrolled adult patients with COVID-19

	Symptoms		CT	
	r	P value	r	P value
Age	0.131	0.29	0.166	0.18
RNA detection results	0.230	0.06	–0.008	0.95
Frequency of positive RNA	0.223	0.07	0.003	0.98

CT, computed tomography.

findings of RNA was 5–7 days [16]. These research studies indicated that RNA detection and monitoring for asymptomatic discharged patients should be strengthened, such as collect multiple samples (including nasopharyngeal, sputum and faeces samples) from multiple parts of convalescent patients, and adjust isolation time according to the RNA detection results. Antibodies are the products of the humoral immune response after viral infection, and specific antibodies to SARS-CoV-2 were used to determine whether the patient has been recently infected with SARS-CoV-2. The human immune system was able to produce specific IgM and IgG antibodies against virus infection. IgM is the earliest antibody that appears upon the first immune response. IgG is produced later and lasts long. The detection of IgM and IgG antibodies against SARS-CoV-2 might be helpful in the diagnosis and epidemiological survey of COVID-19, and could be used as an effective supplementary indicator for suspected cases of negative viral RNA detection. A combination of RNA and IgM–IgG

antibodies detection could provide a more accurate SARS-CoV-2 infection diagnosis [17]. This study showed that there was no statistically significant difference in the detection results of IgM and IgG antibodies between different age groups, RP or NRP adult patients (all $P > 0.05$). It is speculated that for convalescent patients, RNA antibody detection may have no practical significance.

Chest CT examination is an important indicator to judge the severity of COVID-19 patients. According to this study, chest CT signs in 89.7% of adult patients showed a trend of gradual absorption and improvement, and in 10.3% of patients, the lesions were eventually absorbed and improved after short-term repeated progression. Compared with NRP adult patients, there was no significant increase in GGO, pleural thickening and pleural effusion in RP adult patients, but fibre streak shadow increased significantly. Among the 25 RP patients, those with RNA positive findings ≤2 times and >2 times manifested patchy GGO, fibre streak shadow, patchy shadow etc., but there was no statistically significant difference in CT imaging between the two groups. It had been reported that chest imaging of some COVID-19 convalescent patients with RNA RP findings manifested normal, GGO or fibre streak shadow after discharge [13, 18]. It is speculated that for convalescent patients, CT imaging changes are not affected by whether the RNA turns positive or not, however, persistent virus carriers are likely to leave lung fibrosis. Intermittent CT follow-up may be used to evaluate recovery of COVID-19 patients.

There is no clear standard to decide whether patients need medication or not during convalescence. This study showed that 21 adult patients (21/68, 30.9%) were treated with antiviral drugs such as arbidol and oseltamivir, 24 adult patients (24/68,

35.3%) were treated with antibiotics such as cephalosporins and moxifloxacin, and others were treated with symptomatic drugs. The application of drugs for digestive system, sleep improvement and expectorants in elderly patients increased significantly, however, there was no statistically significant difference in other drugs between different age groups, RP or NRP adult patients, and there was no statistically correlation between drug applications, isolation time and frequency of RP findings. Previous studies showed that the virulence and infectivity of SARS-CoV-2 spontaneously weakened over time, and there were currently no specific antiviral drugs against SARS-CoV-2.

Conclusion

In this study, the RNA detection results of 35.2% of patients (25/71) in the convalescence period turned from negative to positive. RP patients were prone to present pulmonary fibre streak shadow in CT. The convalescent patients were mainly asymptomatic, and the clinical manifestations were not typical, most of which were cough, sputum, sore throat, gastrointestinal symptoms or other untypical manifestations. Most patients' chest CT signs gradually improved, independent of RNA RP or not. The drug treatment was mainly symptomatic support therapy, and antibiotics and antiviral drugs were ineffective. It is necessary to re-evaluate the isolation time and standard to terminate isolation for discharged COVID-19 patients.

Acknowledgements. We thank all the patients and their families involved in this study, as well as all the medical staff who are working together fighting against COVID-19 in Hubei.

Author contributions.

Xiaoyun Si had the idea and designed the study and contributed to critical revision of the report. Qingqing Yang contributed to the statistical analysis. Wen Xie contributed to collect data. Bingman Liu, Qingqing Yang and Liangyu Zhao contributed to collect data and write the report. All authors contributed to data acquisition, data analysis or data interpretation, and reviewed and approved the final version.

Financial support. None.

Conflict of interest. None.

References

1. **Zhang W *et al.*** (2020) Molecular and serological investigation of 2019-nCoV infected patients: implication of multiple shedding routes. *Emerging Microbes & Infections* **9**, 386–389.
2. **Wei-Jie G *et al.*** (2020) Clinical characteristics of coronavirus disease 2019 in China. *The New England Journal of Medicine* **382**, 1708–1720.
3. **National Health Commission of the PRC and National Administration of Traditional Chinese Medicine** (2020) Diagnosis and treatment protocol for COVID-19 (trial version 7). *Jiangsu Journal of Traditional Chinese Medicine* **52**, 1–6.
4. **Wang D *et al.*** (2020) Clinical characteristics of 138 hospitalized patients with 2019 novel coronavirus-infected pneumonia in Wuhan, China. *JAMA* **323**, 1061–1069.
5. **Hoffmann M *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.
6. **Peng L *et al.*** SARS-CoV-2 can be detected in urine, blood, anal swabs, and oropharyngeal swabs specimens. *Journal of Medical Virology*. Published online: 24 April 2020. doi: 10.1002/jmv.25936.
7. **Chen W *et al.*** (2020) Detectable 2019-nCoV viral RNA in blood is a strong indicator for the further clinical severity. *Emerging Microbes & Infections* **9**, 469–473.
8. **Ling Y *et al.*** (2020) Persistence and clearance of viral RNA in 2019 novel coronavirus disease rehabilitation patients. *Chinese Medical Journal* **133**, 1039–1043.
9. **Xing Y *et al.*** (2020) Prolonged viral shedding in feces of pediatric patients with coronavirus disease 2019. *Journal of Microbiology, Immunology and Infection* **53**, 473–480.
10. **Wu Y *et al.*** (2020) Prolonged presence of SARS-CoV-2 viral RNA in faecal samples. *The Lancet Gastroenterology & Hepatology* **5**, 434–435.
11. **Tan W *et al.*** (2020) Viral Kinetics and Antibody Responses in Patients with COVID-19. medRxiv. doi: 10.1101/2020.03.24.20042382.
12. **Yu F *et al.*** Quantitative detection and viral load analysis of SARS-CoV-2 in infected patients. *Clinical Infectious Diseases*. Published online: 28 March 2020. doi: 10.1093/cid/cia345.
13. **Zhang T *et al.*** Detectable SARS-CoV-2 viral RNA in feces of three children during recovery period of COVID-19 pneumonia. *Journal of Medical Virology*. Published online: 29 March 2020. doi: 10.1002/jmv.25795.
14. **Lan L *et al.*** (2020) Positive RT-PCR test results in patients recovered from COVID-19. *JAMA* **323**, 1502–1503.
15. **Xing Y *et al.*** (2020) Post-discharge surveillance and positive virus detection in two medical staff recovered from coronavirus disease 2019 (COVID-19), China, January to February 2020. *Euro Surveillance* **25**, pii=2000191.
16. **Li Y *et al.*** (2020) Follow-up testing of viral nucleic acid in discharged patients with moderate type of COVID-19. *Journal of Zhejiang University (Medical Sciences)* **49**, 270–274.
17. **Gao Y *et al.*** (2020) Evaluation of the auxiliary diagnosis value of antibodies assays for detection of novel coronavirus (SARS-Cov-2) causing an outbreak of pneumonia (COVID-19). medRxiv. doi: 10.1101/2020.03.26.20042044.
18. **Pan F *et al.*** (2020) Time course of lung changes on chest CT during recovery from coronavirus disease 2019 (COVID-19). *Radiology* **295**, 715–721.