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Original Article

Clinical value analysis of IgM and IgG antibodies detected by nucleic acid in patients with COVID-19

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Abstract: Objective: We aimed to analyze the clinical diagnostic value of nucleic acid detection and specific IgM and IgG antibodies in COVID-19 patients. According to the patients' test outcomes of nucleic acid and specific IgM and IgG antibodies, the patients were grouped. Methods: Medical records of 788 COVID-19 patients were collected for retrospective analysis, including demographic data, clinical characteristics, CT outcome and laboratory indicators. According to the patients' nucleic acid detection and the results of specific IgM and IgG antibodies, the patients were grouped, and the clinical application value of COVID-19 nucleic acid detection and specific IgM and IgG antibodies was analyzed. Results: The main clinical manifestations of COVID-19 patients included in this study were fever (431 cases, 54.7%), cough (404 cases, 51.3%), and fatigue (232 cases, 29.4%), and the main comorbidities were hypertension (201 Cases, 25.4%), diabetes (86 cases, 10.9%), coronary heart disease (39 cases, 4.9%), etc. CT abnormalities mainly manifested as ground glass shadows (731 cases, 92.8%), mesh nodules shadows (413 cases, 52.4%), pulmonary fibrosis (118 cases, 15.0%), etc. The majority of patients were positive for IgM and IgG antibodies. There were 50 patients in the qPCR+IgM-IgG- group (only nucleic acid test result was positive), of which 6 patients (12%) were mild in symptoms, and 39 patients (78%) had mild CT findings. There were 321 patients in the qPCR+IgM+IgG+ group (nucleic acid and specific IgM and IgG antibody test results were positive), of which 49 patients (15.5%) were severe or critically ill, and 78 patients (24.8%) had severe CT findings. There were 291 patients in the qPCR-IgM+IgG+ group (specific IgM and IgG antibody test results were positive), of which 22 (7.5%) were severe or critically ill, and 94 (32.3%) patients had severe CT findings. The sensitivity of antibody detection for COVID-19 was higher than that of qPCR (84.9%, 86.4% vs. 53.9%, $P<0.001$). There were significant differences between IgM+ patients and IgM- patients in terms of age distribution, gender, sore throat, clinical classification, and CT findings ($P<0.05$). Conclusion: IgM antibody has a high clinical detection rate, which effectively avoids the missed detection of qPCR and increases the detection rate of COVID-19 patients. There are more severe and critically ill patients with IgM tested positive, which finding has certain guiding significance for clinical diagnosis and treatment.

Keywords: COVID-19, qPCR, IgM, IgG, clinical value

Introduction

According to the latest epidemic data, the number of confirmed cases of new coronavirus pneumonia (COVID-19) worldwide has reached 2,865,938, and the number of deaths has risen to 200,698. COVID-19, a severe acute respiratory syndrome, has many ways of transmission, with rapid speed and wide range [1]. 2019-nCoV (also known as SARS-COV-2) virus is the pathogen, whose key component, the spike protein, causes great harm to human health [2, 3]. Timely control of the spread of 2019-nCoV and accurate detection methods are essential, which are of great significance for patient isolation or treatment as well as epidemic prevention and control [4]. At present, the diagnosis methods of COVID-19 include nucleic acid testing (qPCR) and antibody testing (IgM, IgG antibodies). qPCR is the gold standard for the diagnosis of COVID-19. It is a method that uses fluorescent chemicals to measure the total amount of products after each polymerase chain reaction (PCR) cycle in a DNA amplification reaction. However, it has limitations such as slow aging, complex technology, and high risk of sampling contamination. As serological testing indicators, IgM and IgG antibodies have the advantages of non-invasiveness and simple operation, and can provide auxiliary diagnostic

value for the identification of COVID-19 [5, 6]. Studies have shown that the seropositivity rate of IgM and IgG antibodies is high, while the sensitivity of qPCR detection is low. Antibody detection can be used as an important supplement to qPCR detection [7]. According to reports, as the IgM antibodies appear shortly in early stage, the positive IgM antibodies can indicate early infection, which can contribute to the timely detection and treatment of COVID-19. IgG antibody is produced in the second immune response, later than IgM, and can exist for a long time in the body. The positive IgG indicates that the COVID-19 patient is in the recovery period or belongs to a previous infection [6, 8, 9]. In addition, the combined detection of qPCR-IgM and qPCR-IgM-IgG has been reported to be of great value for improving the positive detection rate, early diagnosis and treatment of COVID-19 patients [10, 11]. The above studies all reflect the importance of antibody testing to fight against the COVID-19 epidemic on the basis of nucleic acid testing. At present, research about the clinical value of COVID-19 diagnostic indicators is rare.

In this study, we analyzed the clinical data related to the diagnosis indicators (qPCR, IgM, IgG) of COVID-19 patients, hoping to provide reference value for the clinical application of the disease, and provide good suggestions for further strengthening the prevention and control of the epidemic.

Materials and methods

Patients

The medical records of 788 COVID-19 patients in our hospital from February 2020 to March 2020 were collected for retrospective analysis, including demographic data, clinical features, CT outcomes and laboratory indicators.

Inclusion criteria: Patients with complete general information; with epidemiological history; patients with positive nucleic acid test or specific IgM and IgG antibody test [12].

Exclusion criteria: Suspected patients and patients with incomplete qPCR or antibody testing.

This study strictly followed the principles of the Declaration of Helsinki and was approved by the ethics committee of our hospital.

Determination of clinical classification

According to the diagnosis and treatment plan for COVID-19, patients with mild clinical symptoms and no pneumonia on imaging were regarded as mild. Patients with symptoms of pneumonia (fever, respiratory symptoms, etc.) and imaging findings were regarded as ordinary. Adults with shortness of breath (respiratory rate ≥30 beats/min), or the oxygen saturation ≤93% in the resting state or the arterial blood oxygen partial pressure/inspired oxygen concentration ≤300 mmHg, were considered as severe. Children 9 years or older with shortness of breath (respiratory rate ≥30 beats/min, except for crying, etc.) or oxygen saturation ≤92% in resting state or groaning, nasal flapping, tri-concave sign, cyanosis, intermittent apnea, drowsiness, convulsions, refusal to eat, or dehydration, were considered as severe. Patients with respiratory failure and requiring mechanical ventilation or shock or other organ failure and requiring ICU treatment were regarded as critical.

Detection methods

2019-nCoV assay kit (fluorescence PCR method, Zhijiang Biotechnology Co., Ltd., Shanghai, China) was used to detect nucleic acid qPCR. 2019-nCoV antibody detection kit (colloidal gold method, Innotek Biotechnology Co., Ltd., Qian'an, China) was adopted for IgM and IgG antibody detection.

Statistical analysis

SPSS 25.0 was used for statistical analysis of the data. Continuous variables were expressed as median and interquartile range, and count data were expressed as n (%). The chi-square test of the R*C table was used for the enumeration data, some outcomes generated from the Fisher's exact probability method, and Kruskal-Wallis H test results of multiple independent samples were adopted for one-way ordered data. When $P<0.05$, the difference was statistically significant.

Results

Analysis of clinical characteristics of COVID-19 patients

In this study, 788 COVID-19 patients with a median age of 59.5 years were included. They

Table 1. Clinical features of the patients with COVID-19

Characteristics	Patients (n=788)
Age	
Median (range)	59.5 yr (9-100 yr)
Distribution (n, %)	
≤17 yr	5 (0.6)
18-44 yr	149 (18.9)
45-64 yr	338 (42.9)
65-74 yr	211 (26.8)
≥75 yr	85 (10.8)
Sex (n, %)	
Male	311 (39.5)
Female	477 (60.5)
Contact information (n, %)	
Unidentified source of infection	673 (85.4)
Contact with suspected case	12 (1.5)
Contact with confirmed case	103 (13.1)
Signs and symptoms (n, %)	
Fever	431 (54.7)
Cough	404 (51.3)
Fatigue	232 (29.4)
Expectaration	49 (6.2)
Asymptomatic	44 (5.6)
Sore throat	13 (1.6)
Shortness of breath	38 (4.8)
Myalgia	11 (1.4)
Chest distress or pectoralgia	84 (10.7)
Headache	9 (1.1)
Dyspnea	7 (0.9)
Nausea and vomiting	3 (0.4)
Diarrhea	5 (0.6)
Rhinorrhea	3 (0.4)
Tachycardia	3 (0.4)
Coexisting disorder (n, %)	
Hypertension	201 (25.4)
Diabetes	86 (10.9)
Coronary heart disease	39 (4.9)
Cancer	20 (2.5)
Cerebrovascular disease	17 (2.2)
Chronic bronchitis	11 (1.4)
Hepatitis B infection	8 (1.0)
Asthma	6 (0.8)
Chronic obstructive pulmonary disease	4 (0.5)
Congestive heart failure	3 (0.4)
Chronic renal disease	3 (0.4)
Cirrhosis	2 (0.3)
Clinical classification (n, %)	
Mild	35 (4.4)
Moderate	656 (83.2)

Severe	84 (10.7)
Critical	13 (1.6)
Highest axilla-temperature during hospitalization (n, %) (normal range <37.3°C)	
Normal	575 (73.0)
Low-grade fever	187 (23.7)
Moderate fever	18 (2.3)
High-grade fever	2 (0.3)
Leucocytes ($\times10^9$/L; normal range 3.5-9.5) (n, %)	
Decrease	27 (3.4)
Normal	716 (90.9)
Increase	25 (3.2)
Neutrophils ($\times10^9$/L; normal range 1.8-6.3) (n, %)	
Decrease	22 (2.8)
Normal	709 (90.0)
Increase	37 (4.7)
Lymphocytes ($\times10^9$/L; normal range 1.1-3.2) (n, %)	
Decrease	119 (15.1)
Normal	640 (81.2)
Increase	9 (1.1)
Monocyte ($\times10^9$/L; normal range 0.1-0.6) (n, %)	
No increase	716 (90.9)
Increase	52 (6.6)
Platelets ($\times10^9$/L; normal range 125.0-350.0) (n, %)	
Decrease	32 (4.1)
Normal	705 (89.5)
Increase	31 (3.9)
Alanine aminotransferase (U/L; normal range 0-55) (n, %)	
No increase	662 (84.0)
Increase	72 (9.1)
Aspartate aminotransferase (U/L; normal range 5-34) (n, %)	
No increase	677 (85.9)
Increase	57 (7.2)
Erythrocyte sedimentation rate (mm/H; normal range 0-15) (n, %)	
No increase	95 (12.1)
Increase	182 (23.1)
Interleukin-6 (pg/mL; normal range 0-10) (n, %)	
No increase	323 (41.0)
Increase	25 (3.2)
C-reactive protein (mg/mL; normal range 0-10) (n, %)	
No increase	669 (84.9)
Increase	73 (9.3)
Procalcitonin (ng/mL; normal range 0.0-0.05) (n, %)	
No increase	371 (47.1)
Increase	121 (15.4)
D-dimer (μg/L; normal range 0.0-1.5) Increased (n, %)	
No increase	451 (57.2)
Increase	43 (5.5)
Abnormalities on chest CT-(n, %)	
Ground glass shadow	731 (92.8)

Reticulated nodule shadow	413 (52.4)
Pulmonary Fibrosis	118 (15.0)
Consolidation	49 (6.2)
Adjacent pleura thickening	16 (2.0)
Pleural effusion	6 (0.8)
Thickening around the bronchus	9 (1.1)
Normal	35 (4.4)
Lesion area (n, %)	
Normal	35 (4.4)
A few lesions	346 (43.9)
Some lesions	188 (23.9)
Many lesions	151 (19.2)
Diffuse lesions	61 (7.7)

Note: yr: year; COVID-19: novel coronavirus pneumonia.

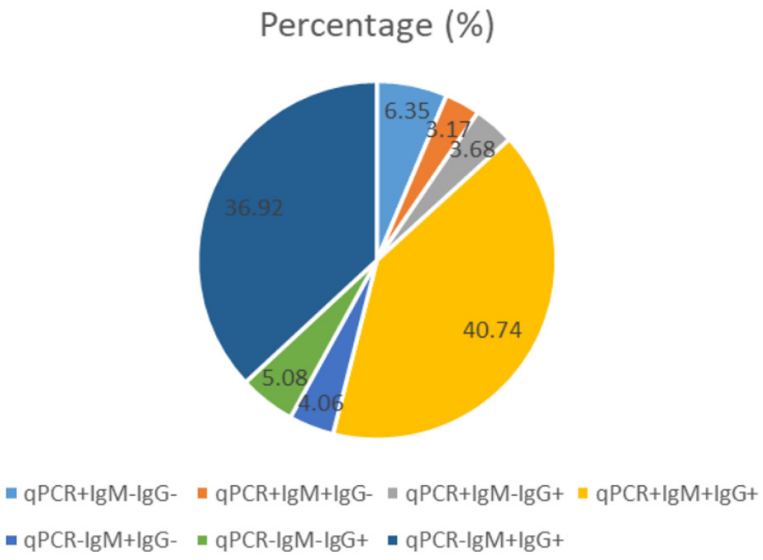

Figure 1. Grouping situation.

were mainly females (477 cases, 60.5%). The main symptoms of the patients were fever (431 cases, 54.7%), cough (404 cases, 51.3%), fatigue (232 cases, 29.4%), etc.; mainly accompanied by hypertension (201 cases, 25.4%), diabetes (86 cases, 10.9%), coronary heart disease (39 cases, 4.9%); the clinical classification was classified as common type (656 cases, 83.2%) and severe type (84 cases, 10.7%). Chest CT abnormalities were mainly ground glass shadows (731 cases, 92.8%), reticular nodules shadows (413 cases, 52.4%), and pulmonary fibrosis (118 cases, 15.0%). See **Table 1**.

Outcomes and characteristics of nucleic acid and specific IgM and IgG antibodies in COVID-19 patients

The patients were divided into seven groups: qPCR+IgM-IgG- (n=50), qPCR+IgM+IgG- (n=25), qPCR+IgM-IgG+ (n=29), qPCR+IgM+IgG+ (n=321), qPCR-IgM+IgG- (n=32), qPCR-IgM-IgG+ (n=40), and qPCR-IgM+IgG+ (n=291), according to different test outcomes. See **Figure 1**.

There were 20 cases of fever (40.0%), 16 cases of combined hypertension (32.0%), 6 cases of mild (12.0%) symptoms and 39 cases of normal/slightly abnormal (78.0%) CT results in qPCR+IgM-IgG- group.

There were 14 cases of cough (56.0%), 8 cases of combined hypertension (32.0%), 7 cases of severe symptoms (28.0%) and 10 cases of normal/slightly abnormal (41.7%) CT results in qPCR+IgM+IgG- group.

There were 20 cases of cough (69.0%), 6 cases of combined hypertension (20.7%), 5 cases of severe symptoms (17.2%) and 16 cases of normal/slightly abnormal (55.1%) CT results in qPCR+IgM-IgG+ group.

There were 165 cases of fever (51.4%), 82 cases of combined hypertension (25.5%), 42 cases of severe symptoms (13.1%) and 165 cases of normal/slightly abnormal (52.4%) CT results in qPCR+IgM+IgG+ group.

There were 17 cases of cough (53.1%), 8 cases of combined hypertension (25.0%), 2 cases of severe symptoms (6.2%) and 12 cases of normal/slightly abnormal (38.7%) CT results in qPCR-IgM+IgG- group.

There were 26 cases of fever (65.0%), 9 cases of combined hypertension (22.5%), 5 cases of mild and severe symptoms (12.5%) and 18 cases of normal/slightly abnormal (45.0%) CT results in qPCR-IgM-IgG+ group.

There were 177 cases of fever (60.8%), 72 cases of combined hypertension (24.7%), 21 cases of severe symptoms (7.2%) and 121 cases of normal/little abnormal (41.6%) CT results in qPCR-IgM+IgG+ group.

Among them, patients with IgM+IgG+ were the majority (612 cases, 77.7%). They showed fever (342 cases, 55.9%), cough (318 cases, 52.0%), and fatigue (181 cases, 29.6%). Besides, there were 4 cases (8.0%) of pharyngalgia in qPCR+ IgM-IgG- group. There were 1-3 cases of headache in the groups except for qPCR+IgM+IgG- group (0 case). There were no cases of tachycardia in the groups except for qPCR-IgM+IgG- group (1 case) and qPCR-IgM+IgG+ group (2 cases). Among the complications, the majority of IgM+ and IgG+ patients were combined with hypertension (154 cases, 25.2%), diabetes (64 cases, 10.5%), and coronary heart disease (29 cases, 4.7%). There were 1 case of congestive heart failure, and 1case of chronic kidney disease in both IgM+ and IgG+ patients. In the clinical classification, there were largest number of severe patients (63 cases, 10.3%) and critical patients (8 cases, 1.3%) in IgM+ and IgG+ groups. See **Table 2**.

Confirmation of nucleic acid antibodies

The sensitivities of qPCR, IgM, and IgG in COVID-19 patients were analyzed, and the results showed that the sensitivities of qPCR, IgM, and IgG were 53.9%, 84.9%, and 86.4%, respectively. Among them, the sensitivity of antibody detection for COVID-19 was higher than that of qPCR (84.9%, 86.4% vs. 53.9%, P<0.001). See **Table 3**.

Comparison of clinical characteristics between IgM+ and IgM- COVID-19 patients

The sensitivity of IgM was significantly higher than that of nucleic acid testing, which played an important role after virus infection. IgM antibodies may have important clinical value in COVID-19 patients, so the relationship between IgM antibody detection and the clinical characteristics of COVID-19 patients was analyzed. The results showed that there were significant differences between IgM+ patients and IgM- patients in terms of age distribution, gender, sore throat, clinical classification, and CT findings (P<0.05). See **Table 4**.

Discussion

COVID-19 is a globally spreading respiratory disease, and its spread has reached the level of pandemic, posing a great threat to the global economy and human health [13]. The total mortality is about 3.46%, and the incubation period is long (0-24 days), which causes certain difficulties in the management of COVID-19 [14]. In this study, the clinical value related to the diagnosis indicators of COVID-19 patients was studied, which is of great significance for the diagnosis and effective management.

In this study, 788 COVID-19 patients with a median age of 59.5 years were included. Majority of patients were in the age group over 45 years (80.5%), while patients under 17 years old were the least (0.6%), suggesting that middle-aged and elderly people over 45 were at high risk of COVID-19. It was pointed out that COVID-19 was mainly concentrated in 30-79 years old patients (86.6%), which was similar to our results [15]. In this study, it was found that the main symptoms of patients were fever, cough, and fatigue, which was similar to the research results of Xu et al. [16]. In this study, the patients included were accompanied with comorbidities such as hypertension, diabetes, and coronary heart disease, which were similar to the study of Zhou et al. [17]. What's more, in this study, ordinary and severe patients accounted for the vast majority (93.9%), while the proportion of mild patients was very small (6.1%).

In addition to analyzing the clinical characteristics of COVID-19 patients, the clinical value related to COVID-19 diagnosis indicators (qPCR

Table 2. Different nucleic acid and antibody detection results and the clinical type in COVID-19 patients

	qPCR+IgM-IgG- n=50	qPCR+IgM+IgG- n=25	qPCR+IgM-IgG+ n=29	qPCR+IgM+IgG+ n=321	qPCR-IgM+IgG- n=32	qPCR-IgM-IgG+ n=40	qPCR-IgM+IgG+ n=291
Age							
Median (IQR)	64.50 (45.75, 79.50)	65.00 (52.50, 74.00)	61.00 (39.50, 68.50)	60.00 (50.00, 68.00)	60.00 (51.25, 66.75)	57.50 (45.25, 67.00)	57.00 (48.00, 66.00)
Distribution no (%)							
≤17 yr	1 (2.0)	0 (0.0)	1 (3.4)	2 (0.6)	0 (0.0)	1 (2.5)	0 (0.0)
18-44 yr	11 (22.0)	4 (16.0)	9 (31.0)	60 (18.7)	6 (18.8)	8 (20.0)	51 (17.5)
45-64 yr	13 (26.0)	8 (32.0)	6 (20.7)	132 (41.1)	14 (43.8)	16 (40.0)	149 (51.2)
65-74 yr	10 (20.0)	8 (32.0)	10 (34.5)	89 (27.7)	11 (34.4)	12 (30.0)	71 (24.4)
≥75 yr	15 (30.0)	5 (20.0)	3 (10.3)	38 (11.8)	1 (3.1)	3 (7.5)	20 (6.9)
Sex (n, %)							
Male	26 (52.0)	12 (48.0)	13 (44.8)	107 (33.3)	14 (43.7)	19 (47.5)	120 (41.2)
Female	24 (48.0)	13 (52.0)	16 (55.2)	214 (66.7)	18 (56.3)	21 (52.5)	171 (58.8)
Signs and symptoms (n, %)							
Fever	20 (40.0)	12 (48.0)	15 (51.7)	165 (51.4)	16 (50.0)	26 (65.0)	177 (60.8)
Cough	17 (34.0)	14 (56.0)	20 (69.0)	164 (51.1)	17 (53.1)	18 (45.0)	154 (52.9)
Fatigue	11 (22.0)	8 (32.0)	7 (24.1)	88 (27.4)	14 (43.8)	11 (27.5)	93 (32.0)
Expectaration	3 (6.0)	2 (8.0)	4 (13.8)	16 (5.0)	3 (9.4)	4 (10.0)	17 (5.8)
Asymptomatic	5 (10.0)	4 (16.0)	1 (3.4)	27 (8.4)	0 (0.0)	0 (0.0)	7 (2.4)
Sore throat	4 (8.0)	1 (4.0)	1 (3.4)	5 (1.6)	0 (0.0)	0 (0.0)	2 (0.7)
Shortness of breath	2 (4.0)	2 (8.0)	1 (3.4)	7 (2.2)	2 (6.3)	0 (0.0)	8 (2.7)
Chest distress or Pectoralgia	5 (10.0)	3 (12.0)	0 (0.0)	30 (9.3)	8 (25.0)	6 (15.0)	37 (12.7)
Dyspnea	1 (2.0)	0 (0.0)	0 (0.0)	2 (0.6)	0 (0.0)	0 (0.0)	4 (1.4)
Myalgia	0 (0.0)	0 (0.0)	0 (0.0)	6 (1.9)	0 (0.0)	0 (0.0)	6 (2.1)
Headache	1 (2.0)	0 (0.0)	1 (3.4)	3 (0.9)	1 (3.1)	1 (2.5)	2 (0.7)
Nausea and vomiting	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.6)	0 (0.0)	0 (0.0)	1 (0.3)
Diarrhea	0 (0.0)	0 (0.0)	0 (0.0)	3 (0.9)	0 (0.0)	0 (0.0)	2 (0.7)
Rhinorrhea	0 (0.0)	0 (0.0)	0 (0.0)	3 (0.9)	0 (0.0)	0 (0.0)	0 (0.0)
Tachycardia	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (3.1)	0 (0.0)	2 (0.7)
Coexisting disorder (n, %)							
Hypertension	16 (32.0)	8 (32.0)	6 (20.7)	82 (25.5)	8 (25.0)	9 (22.5)	72 (24.7)
Diabetes	8 (16.0)	2 (8.0)	2 (6.9)	38 (11.8)	4 (12.5)	5 (12.5)	26 (8.9)
Coronary heart disease	4 (8.0)	1 (4.0)	0 (0.0)	22 (6.9)	2 (0.6)	3 (7.5)	7 (2.4)
Cancer	0 (0.0)	1 (4.0)	1 (3.4)	11 (3.4)	1 (0.3)	0 (0.0)	6 (2.1)
Cerebrovascular disease	3 (6.0)	2 (8.0)	0 (0.0)	8 (2.5)	1 (0.3)	1 (2.5)	2 (0.7)
Chronic bronchitis	1 (2.0)	0 (0.0)	0 (0.0)	5 (1.6)	1 (0.3)	1 (2.5)	3 (1.1)
Hepatitis B infection	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.3)	1 (0.3)	0 (0.0)	6 (2.1)
Asthma	1 (2.0)	0 (0.0)	1 (3.4)	2 (0.6)	0 (0.0)	0 (0.0)	2 (0.7)

Chronic obstructive pulmonary disease	0 (0.0)	0 (0.0)	1 (3.4)	1 (0.3)	0 (0.0)	0 (0.0)	2 (0.7)
Congestive heart failure	2 (4.0)	0 (0.0)	0 (0.0)	1 (0.3)	0 (0.0)	0 (0.0)	0 (0.0)
Chronic renal disease	1 (2.0)	0 (0.0)	0 (0.0)	1 (0.3)	0 (0.0)	0 (0.0)	1 (0.3)
Cirrhosis	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.3)	0 (0.0)	0 (0.0)	1 (0.3)
Clinical classification (n, %)							
Mild	6 (12.0)	0 (0.0)	3 (10.3)	13 (4.0)	0 (0.0)	2 (5.0)	11 (3.8)
Moderate	38 (76.0)	17 (68.0)	20 (69.0)	259 (80.7)	30 (93.8)	34 (85.0)	258 (88.7)
Severe	5 (10.0)	7 (28.0)	5 (17.2)	42 (13.1)	1 (3.1)	3 (7.5)	21 (7.2)
Critical	1 (2.0)	1 (4.0)	1 (3.4)	7 (2.2)	1 (3.1)	1 (2.5)	1 (0.3)
Highest axilla-temperature during hospitalization (n, %)							
Normal	33 (68.8)	11 (44.0)	15 (55.6)	243 (75.9)	24 (75.0)	31 (77.5)	218 (75.2)
Low-grade fever	14 (29.2)	14 (56.0)	10 (37.0)	67 (20.9)	8 (25.0)	8 (20.0)	66 (22.8)
Moderate fever	1 (2.1)	0 (0.0)	1 (3.7)	9 (2.8)	0 (0.0)	1 (2.5)	6 (2.1)
High grade fever	0 (0.0)	0 (0.0)	1 (3.7)	1 (0.3)	0 (0.0)	0 (0.0)	0 (0.0)
Leucocytes ($\times 10^9$/L) (n, %)							
Median (IQR)	6.05 (5.28, 6.63)	5.50 (4.10, 6.70)	6.00 (4.83, 6.80)	5.80 (4.70, 7.00)	5.40 (4.40, 6.50)	6.10 (5.20, 6.80)	5.50 (4.70, 6.60)
Decrease	2 (4.0)	3 (8.6)	1 (3.6)	11 (3.5)	1 (3.2)	1 (2.6)	8 (2.9)
Normal	47 (94.0)	30 (85.7)	26 (92.9)	294 (93.3)	30 (96.8)	36 (92.3)	263 (93.9)
Increase	1 (2.0)	2 (5.7)	1 (3.6)	10 (3.2)	0 (0.0)	2 (5.1)	9 (3.212)
Neutrophils ($\times 10^9$/L) (n, %)							
Median (IQR)	3.83 (2.88, 4.19)	3.34 (2.48, 4.69)	3.76 (2.66, 4.42)	3.49 (2.72, 4.35)	2.98 (2.29, 3.71)	3.59 (2.87, 4.31)	3.31 (2.58, 4.13)
Decrease	0 (0.0)	1 (4.0)	1 (3.6)	12 (3.8)	2 (6.5)	1 (2.6)	5 (1.8)
Normal	47 (94.0)	22 (88.0)	26 (92.9)	287 (91.1)	28 (90.3)	35 (89.7)	264 (94.3)
Increase	3 (6.0)	2 (8.0)	1 (3.6)	16 (5.1)	1 (3.2)	3 (7.7)	11 (3.9)
Lymphocytes ($\times 10^9$/L) (n, %)							
Median (IQR)	1.64 (1.16, 2.08)	1.48 (1.05, 1.68)	1.59 (1.25, 1.83)	1.65 (1.32, 2.07)	1.62 (1.26, 2.14)	1.69 (1.41, 2.02)	1.64 (1.29, 1.96)
Decrease	9 (18.0)	7 (28.0)	5 (17.9)	47 (14.9)	4 (12.9)	3 (7.7)	44 (15.7)
Normal	40 (80.0)	18 (72.0)	23 (82.1)	263 (83.5)	25 (80.6)	36 (92.3)	235 (83.9)
Increase	1 (2.0)	0 (0.0)	0 (0.0)	5 (1.6)	2 (6.5)	0 (0.0)	1 (0.4)
Monocyte ($\times 10^9$/L) (n, %)							
Median (IQR)	0.38 (0.29, 0.43)	0.38 (0.26, 0.45)	0.36 (0.29, 0.48)	0.37 (0.30, 0.45)	0.36 (0.30,0.47)	0.38 (0.32, 0.48)	0.38 (0.29, 0.47)
No increase	47 (94.0)	21 (84.0)	27 (96.4)	299 (94.9)	28 (90.3)	35 (89.7)	258 (92.1)
Increase	3 (6.0)	4 (16.0)	1 (3.6)	16 (5.1)	3 (9.7)	4 (10.3)	22 (7.9)

Platelets (×10^9/L) (n, %)							
Median (IQR)	218.50 (180.75, 259.25)	219.00 (179.00, 246.50)	226.00 (196.25, 287.25)	217.00 (180.00, 255.00)	218.00 (174.00, 282.00)	233.00 (172.00, 261.00)	221.50 (179.50, 254.75)
Decrease	3 (6.0)	3 (12.0)	3 (10.7)	8 (2.5)	2 (6.7)	3 (7.7)	10 (3.6)
Normal	45 (90.0)	21 (84.0)	23 (82.1)	293 (93.0)	27 (90.0)	35 (89.7)	259 (92.5)
Increase	2 (4.0)	1 (4.0)	2 (7.1)	14 (4.4)	2 (3.3)	1 (2.6)	11 (3.9)
Alanine aminotransferase (U/L) (n, %)							
Median (IQR)	16.70 (12.75, 31.70)	22.40 (14.90, 34.5)	15.90 (11.90, 26.75)	18.80 (12.60, 30.38)	18.05 (12.78, 35.75)	17.70 (12.50, 33.80)	23.35 (14.40, 37.53)
No Increase	41 (89.1)	21 (91.3)	25 (100.0)	281 (42.4)	26 (92.9)	36 (92.3)	232 (86.6)
Increase	5 (10.9)	2 (8.7)	0 (0.0)	24 (7.9)	2 (7.1)	3 (7.7)	36 (13.4)
Aspartate aminotransferase (U/L)							
Median (IQR)	16.40 (13.18, 20.45)	18.80 (14.30, 22.70)	14.10 (10.40, 20.70)	15.80 (12.20, 20.95)	16.00 (13.10, 25.78)	17.90 (13.30, 23.50)	16.65 (13.03, 22.45)
No increase	42 (91.3)	23 (100.0)	25 (100.0)	281 (92.1)	26 (92.9)	36 (92.3)	244 (91.0)
Increase	4 (8.7)	0 (0.0)	0 (0.0)	24 (7.9)	2 (7.1)	3 (7.7)	24 (9.0)
Erythrocyte sedimentation rate (mm/H) (n, %)							
Median (IQR)	22.00 (2.25, 69.00)	15.00 (7.00, 93.00)	11.00 (5.00, 26.00)	29.50 (15.04, 62.00)	63.00 (20.50, 102.75)	54.50 (11.50, 77.75)	24.00 (12.00, 57.00)
No increase	8 (40.0)	3 (60.0)	5 (55.6)	34 (28.8)	1 (10.0)	3 (37.5)	41 (38.3)
Increase	12 (40.0)	2 (40.0)	4 (44.4)	84 (71.2)	9 (90.0)	5 (62.5)	66 (61.7)
Interleukin-6 (pg/mL) (n, %)							
Median (IQR)	1.50 (1.50, 2.14)	1.50 (1.50, 4.89)	1.50 (1.50, 10.55)	1.50 (1.50, 1.50)	1.50 (1.50, 1.50)	1.50 (1.50, 1.50)	1.50 (1.50, 1.50)
No increase	16 (100,0)	13 (92.9)	13 (76.5)	138 (92.6)	6 (85.7)	13 (92.9)	124 (94.7)
Increase	0 (0.0)	1 (7.1)	4 (23.5)	11 (7.4)	1 (14.3)	1 (7.1)	7 (5.3)
C-reactive protein (mg/mL) (n, %)							
Median (IQR)	1.24 (0.58, 3.24)	1.61 (5.49)	0.96 (0.53, 2,87)	1.29 (0.40, 3.01)	1.60 (0.42, 3.49)	1.83 (0.65, 5.32)	1.31 (0.60, 2.96)
No increase	44 (93.6)	21 (84.0)	23 (85.2)	278 (90.6)	28 (93.3)	31 (83.8)	244 (90.7)
Increase	3 (6.4)	4 (16.0)	4 (13.8)	29 (9.4)	2 (6.7)	6 (16.2)	25 (9.3)
Procalcitonin (ng/mL) (n, %)							
Median (IQR)	0.40 (0.04, 0.06)	0.04 (0.04, 0.05)	0.04 (0.04, 0.05)	0.40 (0.40, 0.50)	0.40 (0.40, 0.60)	0.40 (0.40, 0.50)	0.40 (0.40, 0.60)
No increase	22 (73.3)	10 (83.3)	17 (81.0)	159 (78.7)	13 (65.0)	23 (79.3)	127 (71.3)
Increase	8 (26.7)	2 (16.7)	4 (19.0)	43 (21.3)	7 (35.0)	6 (20.7)	51 (28.7)
D-dimer (μg/L) (n, %)							
Median (IQR)	0.29 (0.12, 0.58)	0.47 (0.24, 0.99)	0.21 (0.16, 0.83)	0.30 (0.18, 0.56)	0.31 (0.21, 0.46)	0.29 (0.17, 0.60)	0.29 (0.20, 0.68)
No increase	24 (88.9)	8 (88.9)	11 (84.6)	193 (90.6)	16 (88.9)	19 (86.4)	180 (93.8)
Increase	3 (11.1)	1 (11.1)	2 (15.4)	20 (9.4)	2 (11.1)	3 (13.6)	12 (27.9)
Abnormalities on chest CT (n, %)							

Ground glass shadow	40 (80.0)	23 (92.0)	25 (86.2)	298 (92.8)	30 (93.8)	37 (92.5)	278 (95.5)
Reticulated nodule shadow	21 (42.0)	17 (68.0)	15 (51.7)	151 (47.0)	23 (71.9)	28 (70.0)	158 (54.3)
Pulmonary fibrosis	3 (6.0)	6 (24.0)	5 (17.2)	42 (13.1)	8 (25.0)	9 (22.5)	45 (15.5)
Consolidation	1 (2.0)	0 (0.0)	3 (10.3)	18 (5.6)	3 (9.4)	1 (2.5)	23 (7.9)
Adjacent pleura thickening	1 (2.0)	0 (0.0)	1 (3.4)	7 (2.2)	0 (0.0)	0 (0.0)	7 (2.4)
Thickening around the bronchus	0 (0.0)	0 (0.0)	1 (3.4)	4 (1.2)	0 (0.0)	0 (0.0)	4 (1.4)
Pulmonary edema	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.3)	0 (0.0)	0 (0.0)	0 (0.0)
Pleural effusion	2 (4.0)	0 (0.0)	0 (0.0)	4 (1.2)	0 (0.0)	0 (0.0)	0 (0.0)
Normal	6 (12.0)	0 (0.0)	3 (10.3)	13 (4.0)	0 (0.0)	2 (6.3)	11 (3.8)
Lesion area (n, %)							
Normal	6 (12.0)	0 (0.0)	3 (10.3)	13 (4.1)	0 (0.0)	2 (5.0)	11 (3.8)
A few lesions	33 (66.0)	10 (41.7)	13 (44.8)	152 (48.3)	12 (38.7)	16 (40.0)	110 (37.8)
Some lesions	7 (14.0)	5 (20.8)	6 (20.7)	72 (22.9)	8 (25.8)	14 (35.0)	76 (26.1)
Many lesions	3 (6.0)	6 (25.0)	3 (10.3)	55 (17.5)	9 (29.0)	4 (10.0)	70 (24.1)
Diffuse lesions	1 (2.0)	3 (12.5)	4 (13.8)	23 (7.3)	2 (6.5)	4 (10.0)	24 (8.2)

Note: Data are presented as medians (interquartile ranges, IQR), n (%). +: Positive. -: Negative; qPCR: reverse transcriptase polymerase chain reaction; IgM: Immunoglobulin M; IgG: Immunoglobulin G; yr: year; COVID-19: novel coronavirus pneumonia; Highest axilla-temperature during hospitalization: normal range <37.3°C; Leucocytes: normal range 3.5-9.5×10^9/L; Neutrophils: normal range 1.8-6.3× 10^9/L; Lymphocytes: normal range 1.1-3.2×10^9/L; Monocyte: normal range 0.1-0.6×10^9/L; Platelets: normal range 125.0-350.0×10^9/L; Alanine aminotransferase: normal range 0-55 U/L; Aspartate aminotransferase: normal range 5-34 U/L; Erythrocyte sedimentation rate: normal range 0-15 mm/H; Interleukin-6: normal range 0-10 pg/mL; C-reactive protein: normal range 0-10 mg/mL; Procalcitonin: normal range 0-0.05 ng/mL; D-dimer: normal range 0-1.5 μg/L.

Table 3. Comparison of nucleic acid and antibody sensitivity of 788 COVID-19 patients

	qPCR		IgM		IgG	
	+	-	+	-	+	-
Number	425	363	669*	119	681	107
Sensitivity (%)	53.9		84.9		86.4	

Note: Compared with positive qPCR, *P<0.001. Data are presented as n (%). +: Positive; -: Negative; IgM: Immunoglobulin M; IgG: Immunoglobulin G; COVID-19: novel coronavirus pneumonia.

and IgM and IgG antibodies) were also focused on in this study. qPCR testing plays a very important role in the diagnosis of COVID-19, and virus testing is mainly performed through nasopharyngeal swabs [18, 19]. Serum IgM and IgG are specific antibodies produced during the 2019-nCoV infection period, and can be used as auxiliary diagnostic tools when qPCR is negative [20, 21]. Based on the different test results of qPCR and IgM and IgG antibodies, we divided the COVID-19 patients into seven groups for relevant clinical value analysis. The results showed that the qPCR+IgM-IgG- group had more patients with normal appearances and a few lesions in CT results (78.0%), which may be related to the early stage of the disease. Besides, we found that there were as many as 612 (77.7%) patients with both antibodies positive (IgM+IgG+), including 63 (10.3%) severe patients and 8 critically ill patients, which may be related to the acute infection of these patients. There were asymptomatic patients (5.6%) in the double antibody positive group. Asymptomatic patients make the prevention and management of COVID-19 more difficult. The combined detection of qPCR and IgM and IgG antibodies can help avoid the missed detection of asymptomatic COVID-19 [22, 23]. As for the analysis of the sensitivities of qPCR, IgM and IgG antibodies to detect COVID-19, the sensitivity of antibody was higher than that of qPCR (84.9%, 86.4% vs. 53.9%). Although the epidemic situation in China has been clearly controlled, the global COVID-19 cases are still increasing rapidly. With insufficient knowledge of new diseases, the prospect of global anti-epidemic is still unknown. When testing resources are sufficient, it is recommended that nucleic acid antibodies are tested at the same time to reduce the missed diagnosis rate, which is of great significance for epidemic prevention and control.

We finally analyzed the relationship between IgM antibodies and the clinical parameters of COVID-19 patients. The data showed that there were significant differences between IgM+ patients and IgM- patients in terms of age distribution, gender, sore throat, clinical classification, and CT findings, suggesting that IgM antibodies had certain guiding significance in the clinical diagnosis and treatment process. Among them, the proportion of sore throat in IgM+ patients was significantly less than that of IgM- patients. It can be explained that the early colonization of the virus occurred in the upper respiratory tract, while IgM antibodies had not yet been produced at this time. CT results showed that there were 629 ground glass shadows in the IgM+ group, accounting for 94.0%, which was significantly higher than that in the IgM- group. The ground glass shadow is a typical CT feature of COVID-19 patients, which may indicate that COVID-19 patients are in the acute infection stage, and the lesions are mainly manifested as acute inflammatory exudation [24]. In addition, 24 cases of IgM+ group had normal CT, accounting for 3.6%, which was significantly lower than that of IgM- group, suggesting that IgM+ group may be related to severe CT manifestations of COVID-19 patients.

Although this study analyzed the clinical value related to the diagnosis indicators of COVID-19 patients, there are still some limitations. First of all, the medical record data came from patients with confirmed COVID-19, and we could only calculate the sensitivity of nucleic acid and antibody detection, but could not provide specificity results. Second, we did not do the comparison of the data of undiagnosed patients, which further limits the clinical value of the analysis. The latest developments of COVID-19 will be continued to follow up in the future, and we will make improvements and perform new research around the above points when conditions permit.

In summary, we analyzed for the first time the relevant clinical value of the diagnostic indicators of COVID-19 patients, including the clinical value of qPCR, IgM and IgG antibodies in clinical features, laboratory indicators, and CT features. We focused on mining clinical value of IgM antibody in COVID-19 patients. The auxiliary diagnostic value of IgM antibody in COVID-19 patients is beneficial to avoid missed diagnosis

Table 4. Comparison of clinical characteristics of IgM positive and IgM negative patients with COVID-19

	IgM		P
	+ (n=669)	- (n=119)	
Age	59.00 (49.00, 67.00)	62.00 (44.00, 69.00)	
Distribution (n, %)			<0.001
≤17 yr	2 (0.3)	3 (2.5)	
18~44 yr	121 (18.1)	28 (23.5)	
45~64 yr	303 (45.3)	35 (29.4)	
65~74 yr	179 (26.8)	32 (26.9)	
≥75 yr	64 (9.6)	21 (17.6)	
Sex (n, %)			0.025
Male	253 (37.8)	58 (48.7)	
Female	416 (62.2)	61 (51.3)	
Signs and symptoms (n, %)			
Fever	370 (55.3)	61 (51.3)	0.517
Cough	349 (52.2)	55 (46.2)	0.232
Fatigue	203 (30.3)	29 (24.4)	0.188
Expectaration	38 (5.7)	11 (9.2)	0.138
Asymptomatic	38 (5.7)	6 (5.0)	0.780
Sore throat	8 (1.2)	5 (4.2)	0.048
Shortness of breath	34 (5.1)	4 (3.4)	0.419
Myalgia	11 (1.6)	0 (0.0)	0.386
Chest distress or Pectoralgia	74 (11.1)	10 (8.4)	0.387
Headache	6 (0.9)	3 (2.5)	0.285
Dyspnea	6 (0.9)	1 (0.8)	1.000
Nausea and vomiting	3 (0.4)	0 (0.0)	1.000
Diarrhea	5 (0.7)	0 (0.0)	1.000
Rhinorrhea	3 (0.4)	0 (0.0)	1.000
Tachycardia	3 (0.4)	0 (0.0)	1.000
Coexisting disorder (n, %)			
Hypertension	170 (25.4)	31 (26.1)	0.883
Diabetes	71 (10.6)	15 (12.6)	0.521
Coronary heart disease	32 (4.8)	7 (5.9)	0.611
Cancer	19 (2.8)	1 (0.8)	0.336
Cerebrovascular disease	13 (1.9)	4 (3.4)	0.523
Chronic bronchitis	9 (1.3)	2 (1.7)	0.482
Hepatitis B infection	8 (1.2)	0 (0.0)	0.614
Asthma	4 (0.6)	2 (1.7)	0.497
Chronic obstructive pulmonary disease	3 (0.4)	1 (0.8)	1.000
Congestive heart failure	1 (0.1)	2 (1.7)	0.091
Chronic renal disease	2 (0.3)	1 (0.8)	0.940
Cirrhosis	2 (0.3)	0 (0.0)	1.000
Clinical classification (n, %)			0.036
Mild	24 (3.6)	11 (9.2)	
Moderate	564 (84.3)	92 (77.3)	
Severe	71 (10.6)	13 (10.9)	
Critical	10 (1.5)	3 (2.5)	
Highest axilla-temperature during hospitalization (n, %) (normal range <37.3°C)			0.243
Normal	496 (74.4)	79 (68.7)	
Low-grade fever	155 (23.2)	32 (27.8)	
Moderate fever	15 (2.2)	3 (2.6)	
High-grade fever	1 (0.1)	1 (0.9)	
Leucocytes ($\times 10^9$/L; normal range 3.5-9.5) (n, %)			
Median (IQR)	5.60 (4.70, 6.80)	6.00 (5.20, 6.70)	0.869
Decrease	23 (3.5)	4 (3.4)	
Normal	607 (93.2)	109 (94.0)	

Increase	21 (3.2)	4 (3.4)	
Neutrophils (×10^9/L; normal range 1.8-6.3) (n, %)			
Median (IQR)	3.37 (2.65, 4.26)	3.74 (2.83, 4.29)	0.597
Decrease	20 (3.1)	2 (1.7)	
Normal	601 (92.3)	108 (92.3)	
Increase	30 (4.6)	7 (6.0)	
Lymphocytes (×10^9/L; normal range 1.1-3.2) (n, %)			
Median (IQR)	1.63 (1.27, 2.20)	1.64 (1.29, 1.99)	0.892
Decrease	102 (15.7)	17 (14.5)	
Normal	541 (83.1)	99 (84.6)	
Increase	8 (1.2)	1 (0.9)	
Monocyte (×10^9/L; normal range 0.1-0.6) (n, %)			
Median (IQR)	0.37 (0.30, 0.46)	0.38 (0.30, 0.46)	0.713
No Increase	606 (93.1)	110 (94.0)	
Increase	45 (6.9)	7 (6.0)	
Platelets (×10^9/L; normal range 125.0-350.0) (n, %)			
Median (IQR)	220 (180, 255)	225.00 (182.00, 261.50)	0.114
Decrease	23 (3.5)	9 (7.7)	
Normal	602 (92.5)	103 (88.0)	
Increase	26 (4.0)	5 (4.3)	
Alanine aminotransferase (U/L; normal range 0-55) (n, %)			
Median (IQR)	21.00 (13.35, 34.30)	16.90 (12.45, 30.75)	0.332
No Increase	560 (89.7)	102 (92.7)	
Increase	64 (10.3)	8 (7.3)	
Aspartate aminotransferase (U/L; normal range 5-34) (n, %)			
Median (IQR)	16.20 (12.70, 21.68)	16.00 (12.73, 21.60)	0.551
No Increase	574 (92.0)	103 (93.6)	
Increase	50 (8.0)	7 (6.4)	
Erythrocyte sedimentation rate (mm/H; normal range 0-15)			
Median (IQR)	26.00 (12.00, 62.00)	22.00 (8.00, 55.50)	0.218
No Increase	79 (32.9)	16 (43.2)	
Increase	161 (67.1)	21 (56.8)	
Interleukin-6 (pg/mL; normal range 0-10) (n, %)			
Median (IQR)	1.5 (1.5, 1.5)	1.50 (1.50, 2.64)	0.495
No increase	281 (93.4)	42 (89.4)	
Increase	20 (6.6)	5 (10.6)	
C-reactive protein (mg/mL; normal range 0-10) (n, %)			
Median (IQR)	1.31 (0.51, 3.07)	1.22 (0.60, 3.41)	0.472
No increase	571 (90.5)	98 (88.3)	
Increase	60 (9.5)	13 (11.7)	
Procalcitonin (ng/mL; normal range 0.0-0.05) (n, %)			
Median (IQR)	0.04 (0.04, 0.58)	0.40 (0.40, 0.50)	0.635
No increase	309 (75.0)	62 (77.5)	
Increase	103 (25.0)	18 (22.5)	
D-dimer (μg/L; normal range 0.0-1.5) (n, %)			
Median (IQR)	0.30 (0.20, 0.58)	0.27 (0.15, 0.54)	0.210
No increase	397 (91.9)	54 (87.1)	
Increase	35 (8.1)	8 (12.9)	
Abnormalities on chest CT (n, %)			
Ground glass shadow	629 (94.0)	102 (85.7)	0.001
Reticulated nodule shadow	349 (52.2)	64 (53.8)	0.745
Pulmonary Fibrosis	101 (15.1)	17 (14.3)	0.819
Consolidation	44 (6.6)	5 (4.2)	0.323
Adjacent pleura thickening	14 (2.1)	2 (1.7)	1.000
Thickening around the bronchus	8 (1.2)	1 (0.8)	1.000
Pulmonary edema	1 (0.1)	0 (0.0)	1.000
Pleural effusion	4 (0.6)	2 (1.7)	0.229

Normal	24 (3.6)	11 (9.2)	0.006
Lesion area (n, %)			0.001
Normal	24 (3.6)	11 (9.2)	
A few lesions	284 (42.9)	62 (52.1)	
Some lesions	161 (24.3)	27 (22.7)	
Many lesions	141 (21.3)	10 (8.4)	
Diffuse lesions	52 (7.9)	9 (7.6)	

Note: Data are presented as medians (interquartile ranges, IQR), n (%). +: Positive; -: Negative; qPCR: reverse transcriptase polymerase chain reaction; IgM: Immunoglobulin M; IgG: Immunoglobulin G; yr: year; COVID-19: novel coronavirus pneumonia.

of qPCR- patients, and its clinical value in COVID-19 patients is of certain importance for the management of COVID-19 patients.

Disclosure of conflict of interest

None.

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