ORIGINAL RESEARCH PAPER

Relationship between the dynamic changes of serum 2019-nCoV IgM/IgG and patient immunity after 6 month hospital discharge

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Abstract

Objectives To investigate the relationship between the dynamic changes of serum 2019-nCoV IgM/IgG and immunity alteration for patients after 6-month hospital discharge.

Methods One IgM(+) and IgG(−), 32 IgM(+) and IgG(+), 38 IgM(−) and IgG(+), and 40 IgM(−) and IgG(−) patients were included. Demographic data were collected. IgM and IgG antibodies, hypersensitive C-reactive protein (hs-CRP), interleukin-6 (IL-6) and lymphocyte subsets in serum were determined at weeks 0, 2 and 4.

Results The hs-CRP and IL-6 levels of all patients were within the normal ranges. The number of patients with all lymphocyte subset testing items within normal ranges was 12/110 (10.9%) at week 0, 15/110 (13.6%) at week 2 and 18/110 (16.4%) at week 4. The percentages of CD8 + cells, NK cells and B lymphocytes in the IgM(+) and IgG(+) group were quite different from those in the IgM(−) and IgG(+) group and the IgM(−) and IgG(−) group, with much higher percentages of CD8 + cells and much lower percentages of NK cells and B lymphocytes at weeks 0, 2 and 4. Twelve IgM(+) patients in the IgM(+) and IgG(+) group converted to IgM(−), and the percentages of NK cells and B lymphocytes in these patients were significantly increased at week 4.

Conclusions The changes of serum IgM and IgG are closely related to immunity in patients in the recovery stage. However, immunity does not recover when the patients test negative for these antibodies.

Keyword COVID-19 · Antibodies · Immunity · Recovery stage

Introduction

Since December 2019, the 2019 novel coronavirus (2019-nCoV) pneumonia pandemic caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has threatened millions of people worldwide [1]. By March 2020, the coronavirus disease 2019 (COVID-19) epidemic had

been effectively controlled in Wuhan city, China. Infected patients were hospitalized and discharged from the hospital after recovering. Currently, almost all COVID-19 patients in China are in the recovery stage following infection and therapy [2].

Presently, due to the lack of effective antiviral drugs [3] and vaccines [4], convalescent plasma therapy [5] and specific human monoclonal antibodies [6], the treatment of COVID-19 remains the greatest challenge for medical staff and scientific researchers [7]. As a novel coronavirus, the dynamic immunity to and pathogenesis of this disease in the human body are unclear [8–10].

In this study, we focused on COVID-19 patients in the recovery stage after having been discharged 6 months and aimed to evaluate the dynamic changes of the IgM and IgG antibodies, the changes in the plasma levels of hypersensitive C-reactive protein (hs-CRP) and interleukin-6 (IL-6), the alterations in plasma lymphocyte subsets, and potential correlations between the dynamic changes in serum IgM and IgG levels and patient immunity.

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Materials and methods

Patients

From July 1, 2020 to August 31, 2020, consecutive COVID-19 patients in the recovery stage after 6 month hospital discharge who were admitted to the Department of Novel Coronavirus Pneumonia Rehabilitation Clinic at Hubei University of Chinese Medicine Affiliated Hubei Hospital of Chinese Medicine were recruited.

All included patients who were admitted to our department met the criteria of the Diagnosis and Treatment Protocol for Novel Coronavirus Pneumonia (Trial Version 7) proposed by the National Health Commission of China, which were diagnosed based on the most common symptoms of fever, generalized weakness and dry cough, the positive of nucleic acid detection in the nasal and throat swab sampling or other respiratory tract samplings by real-time polymerase chain reaction (PCR), and the multifocal ground glass changes on chest CT scan [11].

The severity in the acute stage was classified as mild, moderate, severe and critical according to the criteria of the National Health Commission of China. Mild was mild clinical symptoms and no pneumonia manifestations on imaging. Moderate was fever, respiratory symptoms and pneumonia manifestations on imaging. Severe was met one of the following: shortness of breath and respiratory rate ≥ 30 time/minute; oxygen saturation of finger $\leq 93\%$ in resting state; arterial partial pressure of oxygen (PaO2)/fraction of inspiration oxygen (FiO2) ≤ 30 mmHg (1 mmHg $= 0.133$ kPa); significant progression of the lesion $> 50\%$ within 24–48 h on pulmonary imaging. Critical was met one of the following: respiratory failure with required mechanical ventilation; shock; combining with other organ failure and required Intensive Care Unit (ICU) monitoring treatment [11].

Inclusion and exclusion criteria

We performed a 4 week clinical study for patients with COVID-19 at our department, which was registered in the Chinese Clinical Trial Registry (ChiCTR2000034794). Inclusion criteria were age between 18 and 70 years old and signed informed consent from the patients (or their families).

The exclusion criteria were as follows: (1) patients discharged less than 6 months prior; (2) patients whose SARS-CoV-2 nucleic acid turned positive again; (3) patients presenting with infection after discharge; (4) patients who underwent surgery during discharge; (5) pregnant or lactating females; (6) patients with cancer; (7) patients with organ dysfunction during discharge; (8) patients with immune system diseases; and (9) patients in other studies.

Treatment

The enrolled patients were treated with standardized management, such as breathing training and daily oral Chinese medicine.

Ethics

Ethical approval was approved by the Research Ethical Committee of Hubei Hospital of Chinese Medicine on April 23, 2020 (grant no. HBZY2020-C26-01).

Data collection

The following data were collected from a consecutive series of 111 patients in the 4-week observation stage: (i) demographic data, including sex, age, severity of hospitalization, and histories of chronic disorder (chronic cardiovascular disease, chronic respiratory disease, chronic cerebrovascular illness, and diabetes); and (ii) serum biochemical data, including antibodies against SARS-CoV-2 (IgM and IgG), hs-CRP, IL-6 and lymphocyte subsets [including the percentage of CD3+/CD8+/CD4+/natural killer (NK) cells/B lymphocytes].

Peripheral venous blood samples were obtained using strict aseptic techniques from patients at weeks 0, 2 and 4. IgM and IgG were detected by the colloidal gold method using a novel coronavirus (2019-nCoV) IgM/IgG antibody detection kit (Livzon Reagent Co., Ltd., Zhuhai, China). Hs-CRP was determined by a Modular PPI automatic biochemical analyser (Roche Diagnostics (Shanghai) Co., Ltd., Shanghai, China). IL-6 was determined by a fully automatic electrochemiluminescence immunoassay system (Cobas e411 analyser series, Roche Diagnostics (Shanghai) Co., Ltd., Shanghai, China). Lymphocyte subsets were detected and counted by a BD FACSCalibur flow cytometer (BD, Bioscience, CA, USA). The following antibodies (BD, Bioscience, CA, USA) were used: FITC anti-human CD14, FITC-conjugated anti-CD4, ECD-conjugated anti-CD3, PC5-conjugated anti-CD8, PE-conjugated anti-CD19, and PC7-conjugated anti-CD16CD45.

Statistical analysis

The software package SPSS 11 (Chicago, IL, USA) was used for all data management and analyses. The descriptive data of continuous variables and the numbers (%) of categorical variables are presented as the mean ± standard deviation (mean ± SD). Multiple groups were compared with one-way analysis of variance. The χ^2 test with Yates correction

was used to compare categorical variables between the two groups. Correlations were evaluated with the Spearman rank test, and $P < 0.05$ was considered statistically significant.

Results

Patients

This study included 111 patients (51 males and 60 females) with COVID-19 in the recovery stage after having been discharged for 6 months. The median age of the patients was 50.3 years (range, 24–70 years). Chronic disorder histories in this population included chronic cardiovascular disease (21 person times), chronic respiratory disease (12 person times), chronic cerebrovascular illness (5 person times), and diabetes (10 person times).

The values of hs-CRP and IL-6 for all patients were within normal ranges (0–3 mg/L and < 7 pg/mL, respectively) at weeks 0, 2 and 4, and the comparisons of groups were meaningless.

A 54-year-old male patent with IgM(+) and IgG(−) was symptomless, had negative nucleic acid, 2019-nCoV open reading frame gene and 2019-nCoV nucleoprotein gene tests, had no infection on chest CT manifestations, and had no chronic respiratory disease. Three antibody tests for IgM and IgG revealed a status of IgM(+) and IgG(−). The lymphocyte subsets of the patient are given in Table 1.

Comparison of patients with different IgM and IgG antibodies

There were 110 patents included in the analysis. Thirty-two (29.1%) of the 110 patients were IgM(+) and IgG(+),38 (34.5%) were IgM(−) and IgG(+), and 40 (36.4%) were IgM(−) and IgG(−).

There were no significant differences in age, sex, clinical classification of hospitalization, or chronic disorders among the IgM(+) and IgG(+), IgM(−) and IgG(+), IgM(−) and IgG(−) groups (Table 2).

The number of patients with all lymphocyte subset testing items within normal ranges was 12/110 (10.9%) at week 0, 15/110 (13.6%) at week 2 and 18/110 (16.4%) at week 4. Specifically, 0 patients (0/32, 0.0%) in the IgM(+) and IgG(+) group, 4 (4/38, 10.5%) in the IgM(−) and IgG(+) group, and 8 (8/40, 20.0%) in the IgM(−) and IgG(−) group

Table 1 Lymphocyte subsets of the IgM(+) and IgG(−) patient

	CD3 + (percentages)	CD8 + (percentages)	CD4 + (percentages)	NK cells (percentages)	B lymphocytes (percentages)
Normal ranges	62.64–76.76	19.17–33.63	30.0–46.0	9.5–23.5	8.48–14.52
0 weeks	79	56	43.0	10.0	7.0
2 weeks	80	45	44	11	9
4 weeks	80	35	45	9	8

Table 2 Characteristics of patients with different IgM and IgG antibodies

	IgM(+) and IgG(+) (n = 32)	IgM(−) and IgG(+) (n = 38)	IgM(−) and IgG(−) (n = 40)	P
Age (years)	50.7 ± 12.7	51.1 ± 13.1	49.9 ± 11.4	0.6773
Sex				
Male	14 (43.8%)	17 (44.7%)	19 (47.5%)	–
Female	18 (56.2%)	21 (55.3%)	21 (52.5%)	0.9451
Clinical classification of hospitalization				
Mild	7 (21.9%)	5 (13.2%)	2 (5.0%)	–
Moderate	21 (65.6%)	28 (73.7%)	31 (77.5%)	–
Severe	4 (12.5%)	5 (13.1%)	7 (17.5%)	0.3172
Chronic disorder				
Chronic cardiovascular disease	7 (21.9%)	8 (21.1%)	6 (15.0%)	–
Chronic respiratory disease	5 (15.6%)	4 (10.5%)	3 (7.5%)	–
Chronic cerebrovascular illness	1 (3.1%)	2 (5.3%)	2 (5.0%)	–
Diabetes	3 (9.4%)	4 (10.5%)	3 (7.5%)	0.8542

at week 0; 1 patient (1/32, 3.1%) in the IgM(+) and IgG(+) group, 5 (5/38, 13.2%) in the IgM(−) and IgG(+) group, and 9 (9/40, 22.5%) in the IgM(−) and IgG(−) group at week 2; and 3 patients (3/32, 9.4%) in the IgM(+) and IgG(+) group, 6 (6/38, 15.8%) in the IgM(−) and IgG(+) group, and 9 (9/40, 22.5%) in the IgM(−) and IgG(−) group at weeks 4 showed values for these items in the normal range (Table 3).

The percentages of CD8 +, NK cells and B lymphocytes in the IgM(+) and IgG(+) group were quite different from the IgM(−) and IgG(+) group and the IgM(−) and IgG(−) group, with much more the percentages of CD8 + and much less the percentages of NK cells and B lymphocytes on weeks 0, 2 and 4 ($P < 0.05$, Table 4). The comparisons of the three groups for the percentages of CD8 + at three time points, the IgM (+) and IgG (+) group was highest, IgM (-) and IgG (-) group was the lowest ($P < 0.05$, Table 4). The comparisons of the three groups for the percentages of NK cells and B lymphocytes at three time points, the IgM(−) and IgG(−) group was highest, IgM (+) and IgG (+) group was the lowest ($P < 0.05$, Table 4).

The percentages of CD8 + cells, NK cells and B lymphocytes in the IgM(+) and IgG(+) group were quite different from those in the IgM(−) and IgG(+) group and the IgM(−) and IgG(−) group, with much higher percentages

Table 3 Characteristics of total lymphocyte subsets in patients with differences in IgM and IgG antibodies

Groups	0 weeks	2 weeks	4 weeks	P
IgM(+) and IgG(+) (n = 32)				
Normality	0 (0.0%)	1 (3.1%)	3 (9.4%)	0.1610
Abnormality	32 (100.0%)	31 (96.9%)	29 (90.6%)	
IgM(−) and IgG(+) (n = 38)				
Normality	4 (10.5%)	5 (13.2%)	6 (15.8%)	0.7493
Abnormality	34 (89.5%)	33 (86.8%)	32 (84.2%)	
IgM(−) and IgG(−) (n = 40)				
Normality	8 (20.0%)	9 (22.5%)	9 (22.5%)	0.9521
Abnormality	32 (80.0%)	31 (77.5%)	31 (77.5%)	
P	0.0257	0.0585	0.3244	

Table 4 Comparison of the dynamic percentage changes in lymphocyte subsets in patients with differences in IgM and IgG antibodies

	Groups	0 weeks	2 weeks	4 weeks	P
	IgM(+) and IgG(+)	67.0 ± 10.8	69.5 ± 8.7	69.7 ± 9.7	0.4712
CD3 +	IgM(−) and IgG(+)	69.4 ± 8.9	69.1 ± 9.3	70.1 ± 9.9	0.8925
	IgM(−) and IgG(−)	70.3 ± 10.7	70.6 ± 10.2	69.1 ± 10.1	0.7903
	P	0.3789	0.7704	0.9044	
	IgM(+) and IgG(+)	48.6 ± 7.3	45.9 ± 10.5	43.7 ± 9.7	0.1117
CD8 +	IgM(−) and IgG(+)	36.5 ± 10.3	30.5 ± 9.3●◎	28.5 ± 10.4◎	0.0020
	IgM(−) and IgG(−)	25.5 ± 9.3	26.1 ± 11.3	25.9 ± 10.1	0.9652
	P	0.0000	0.0000	0.0000	
	IgM(+) and IgG(+)	35.3 ± 4.8	36.5 ± 5.8	35.7 ± 5.2	0.6530
CD4 +	IgM(−) and IgG(+)	34.5 ± 5.3	36.1 ± 6.1	35.6 ± 5.1	0.4359
	IgM(−) and IgG(−)	35.5 ± 4.9	35.9 ± 5.9	35.6 ± 5.4	0.9426
	P	0.6550	0.9120	0.9959	
	IgM(+) and IgG(+)	13.7 ± 7.4	14.9 ± 8.7	15.0 ± 9.6	0.7984
NK cells	IgM(−) and IgG(+)	15.9 ± 6.9	17.4 ± 8.5	19.5 ± 8.9�	0.1585
	IgM(−) and IgG(−)	25.7 ± 6.3▸	26.7 ± 8.1▸	27.1 ± 8.3▸	0.6997
	P	0.0000	0.0000	0.0000	
	IgM(+) and IgG(+)	7.2 ± 3.1	7.4 ± 3.9	7.5 ± 3.8	0.9446
B lymphocytes	IgM(−) and IgG(+)	10.1 ± 3.9*	10.7 ± 4.5*	15.4 ± 5.2★	0.0000
	IgM(−) and IgG(−)	16.1 ± 6.4*	16.4 ± 5.7*	16.7 ± 5.5	0.9012
	P	0.0000	0.0000	0.0000	

*The levels of B lymphocytes between the IgM(−) and IgG(+) group and the IgM(−) and IgG(−) group at weeks 0 and 2 were both significantly different, $P < 0.05$

●In the IgM(−) and IgG(+) group, the values between week 0 and week 2 were significantly different, $P < 0.05$

◎The levels of CD8 + cells between the IgM(+) and IgG(+) group and the IgM(−) and IgG(+) group at week 2 and week 4 were both significantly different, $P < 0.05$

▸The levels of NK cells between the IgM(+) and IgG(+) group and the IgM(−) and IgG(+) group at week 4 and between the IgM(−) and IgG(+) group and the IgM(−) and IgG(−) group at weeks 0, 2 and 4 were all significantly different, $P < 0.05$

★The levels of B lymphocytes between the IgM(+) and IgG(+) group and the IgM(−) and IgG(+) group at week 4 was significantly different, $P < 0.05$

Table 5 Correlation analysis of lymphocyte subsets in patients with differences in IgM and IgG antibodies

Groups	IgM(+) and IgG(+) (n = 32)			IgM(−) and IgG(+) (n = 38)			IgM(−) and IgG(−) (n = 40)		
	r	U	P	r	U	P	r	U	P
IgM(+) and IgG(+)	0.1711	–	–	–	0.0536	0.9572	–	0.0700	0.9442
IgM(−) and IgG(+)	–	0.0536	0.9572	0.1579	–	–	–	0.0165	0.9868
IgM(−) and IgG(−)	–	0.0700	0.9442	–	0.0165	0.9868	0.1541	–	–

of CD8 + cells and much lower percentages of NK cells and B lymphocytes at weeks 0, 2 and 4 ($P < 0.05$, Table 4). The comparisons of the three groups for the percentages of CD8 + cells at the three time points showed that the IgM(+) and IgG(+)group had the highest percentages, and the IgM(−) and IgG(−) group had the lowest percentages ($P < 0.05$, Table 4). The comparisons of the three groups for the percentages of NK cells and B lymphocytes at the three time points showed that the IgM (-) and IgG (-) group had the highest percentages, and the IgM (+) and IgG (+) group had the lowest percentages ($P < 0.05$, Table 4).

Based on the above results, we selected the candidate markers for correlation analysis, which was statistically significant in the analysis. The comparisons of the IgM(+) and IgG(+) group ($r = 0.1711$) versus the IgM(−) and IgG(+) group ($r = 0.1579$) (U = 0.0536, $P = 0.9572$), the IgM(+) and IgG(+) group ($r = 0.1711$) versus the IgM(−) and IgG(−) group ($r = 0.1541$) (U = 0.0700, $P = 0.9442$), and the IgM(−) and IgG(+) group ($r = 0.1579$) versus the IgM(−) and IgG(−) group ($r = 0.1541$) (U = 0.0165, $P = 0.9868$) were relevant, respectively (Table 5).

Comparison of patients within the IgM(+) and IgG(+) antibodies group

During the 4 week observation period, 12 of 32 patients converted from IgM(+) to IgM(−). The 32 patients were divided into the IgM(+) group and the IgM(−) group. There were no significant differences in age, sex, clinical classification of hospitalization or chronic disorders between the two groups (Table 6).

The dynamic percentage changes in CD3 + , CD8 + and CD4 + cells for patients in the IgM(+) group were identical to those in the IgM(−) group ($P > 0.05$, Table 7). Compared with those of the IgM(+) group, the percentages of NK cells and B lymphocytes were significantly increased in the IgM(−) group at week 4 ($P < 0.05$, Table 7). In the IgM(−) group, the percentage of B lymphocytes was significantly greater at week 4 than at week 0 ($P < 0.05$, Table 7). We selected NK cells and B lymphocytes for correlation analysis, which was statistically significant. The comparisons of patients with IgM(+) ($r = 0.2113$) or IgM(−) ($r = 0.2595$) in the IgM(+) and IgG(+) antibodies group were relevant (U = 0.1238, $P = 0.9015$, Table 8).

Table 6 Characteristics of patients in the IgM(+) and IgG(+) antibodies group

	IgM(+) (n = 20)	IgM(−) (n = 12)	P
Age (years)	52.1 ± 13.7	49.3 ± 13.0	0.5728
Sex			
Male	7 (35.0%)	7 (58.3%)	0.1977
Female	13 (65.0%)	5 (41.7%)	
Clinical classification of hospitalization			
Mild	4 (21.9%)	3 (13.2%)	0.7757
Moderate	14 (65.6%)	7 (73.7%)	
Severe	2 (12.5%)	2 (13.1%)	
Chronic disorder			
Chronic cardiovascular disease	3	2	–
Chronic respiratory disease	3	3	–
Chronic cerebrovascular illness	2	1	–
Diabetes	1	1	0.9623

Table 7 Comparison of the dynamic percentages changes in lymphocyte subsets in patients with IgM(+) or IgM(−) in the IgM(+) and IgG(+) antibodies group

	Groups	0 weeks	4 weeks	P
CD3 +	IgM(+)	67.5 ± 10.9	69.1 ± 9.7	0.6267
	IgM(−)	66.7 ± 10.6	69.5 ± 9.9	0.5106
	P	0.8405	0.9115	
CD8 +	IgM(+)	48.8 ± 7.6	43.8 ± 9.8	0.0793
	IgM(−)	48.4 ± 7.2	43.5 ± 9.5	0.1685
	P	0.8842	0.9330	
CD4 +	IgM(+)	35.2 ± 4.9	35.6 ± 5.3	0.8056
	IgM(−)	35.1 ± 4.7	35.9 ± 5.5	0.7054
	P	0.9551	0.8795	
NK cells	IgM(+)	13.9 ± 7.5	13.1 ± 7.3	0.7344
	IgM(−)	13.5 ± 7.3	18.5 ± 7.1	0.1031
	P	0.8837	0.0496	
B lymphocytes	IgM(+)	7.3 ± 3.3	6.5 ± 3.0	0.4274
	IgM(−)	7.0 ± 3.0	10.5 ± 3.4	0.0139
	P	0.7987	0.0016	

Table 8 Correlation analysis of lymphocyte subsets in patients with IgM(+) or IgM(−) in the IgM(+) and IgG(+) antibodies group

Groups	IgM(+) ($n=20$)			IgM(−) ($n=12$)		
	r	U	P	r	U	P
IgM(+)	0.2113	–	–	–	0.1238	0.9015
IgM(−)	–	0.1238	0.9015	0.2595	–	–

Discussion

Mortality from COVID-19, which is high in Wuhan city, China, mainly occurs during hospitalization in the acute stage, during which the patient is at risk for lung and/or systemic complications [12]. SARS-CoV-2 is a very strange virus that can lead to cellular immune deficiency and an excessive immune response in the acute stage [13, 14].

The production of antibodies is the host's immune response to viral infection; in the case of COVID-19, serum 2019-nCoV IgM/IgG are detectable as early as 4 days and reached a peak in the second week after symptom onset [15, 16]. Serological antibody testing may be helpful for the identification of suspected patients who show negative results from nucleic acid tests and in the diagnosis of asymptomatic infections [17].

The importance of antibody detection in convalescent patients seems to be completely different from that in infected patients [18, 19]. In this report, we enrolled 111 COVID-19 patients in the recovery stage after having been discharged for six months: 1 IgM(+) and IgG(−), 32 IgM(+) and IgG(+), 38 IgM(−) and IgG(+), and 40 IgM(−) and IgG(−) patients.

The important pro-inflammatory cytokines of hs-CRP and IL-6 cause cascade and amplify cytokine storm [20]. Hs-CRP is a nonspecific inflammatory marker that is widely used in the prediction of COVID-19 pneumonia [21] and is not affected by radiotherapy, chemotherapy, or corticosteroids. IL-6 is the key proinflammatory cytokine in the excessive immune response to SAP and is a potential, reliable and easy-to-use predictor of COVID-19 prognosis [22]. However, our results indicate that the values of hs-CRP and IL-6 for all patients were within the normal ranges 6 months after discharge.

The lymphocyte subsets in peripheral blood play an important role in preserving immune function, in which the immune cells restrict and regulate each other. Previous studies revealed that T cell subset counts were significantly decreased for COVID-19 patients during hospitalization [23–25]. Our findings suggest that serum lymphocyte subset counts are correlated with dynamic changes in serum IgM and IgG and are not related to inflammatory cytokines or the severity of the disease during hospitalization. The number of patients with all lymphocyte subset testing items within normal ranges was 12/110 (10.9%) at week 0, 15/110 (13.6%) at week 2 and 18/110 (16.4%) at week 4. The percentages of CD8+, NK cells and B lymphocytes in the IgM(+) and IgG(+) group were quite different from those in the IgM(−) and IgG(+) group and the IgM(−) and IgG(−) group, with much higher percentages of CD8+ cells and much lower percentages of NK cells and B lymphocytes at weeks 0, 2 and 4. The correlation analysis among the three groups for the percentages for CD8+, NK cells and B lymphocytes were relevant.

Recent studies have reported that plasma levels of lymphocyte subsets and inflammatory cytokines are associated with the severity of COVID-19 [26, 27]. Liu et al. [26] found that the degrees of lymphopenia and the levels of pro-inflammatory cytokines in severe COVID-19 patients were higher than those in mild cases and were associated with the severity of disease. Jiang et al. [27] reported that the counts of CD8+ and CD4+ cells in COVID-19 patients could be used as predictors of disease severity. Our results indicate that the immune status of patients (lymphocyte subsets and inflammatory cytokines) in the recovery stage is completely different from that in the acute stage.

We found that on conversion from IgM(+) to IgM(−), the patient's immunity gradually improved, mainly manifested by the compensation in NK cells and B lymphocytes. In our study, we analyzed 12 patients with IgM(+) who converted to IgM(−) in the IgM(+) and IgG(+) group. Compared with those in the IgM(+) group, the percentages of NK cells and B lymphocytes were significantly increased in the IgM(−) group at week 4. The correlation analysis of NK cells and B lymphocytes for patients with IgM(+) or IgM(−) in the IgM(+) and IgG(+) antibodies group was relevant.

In conclusion, the dynamic changes in serum IgM and IgG are closely related to immunity for patients in the recovery stage, which is dominated by CD8+ for IgM(+) patients and gradually improves by the compensation of NK cells and B lymphocytes when IgM(+) converts to IgM(−). However, immunity does not recover when the patients test negative for SARS-CoV-2 antibodies. Future large-scale studies are required to clarify the dynamic changes in antibodies and immunity throughout the course of COVID-19.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

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