SARS-CoV-2 Neutralizing Antibody has Better Diagnostic Sensitivity than IgM and IgG

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Abstract

COVID-19 has spread worldwide. However, SARS-CoV-2 serological markers, which usually important indicators of disease progression, remains to be studied. To determine serological patterns during infection and their corresponding influencing factors, we conducted a cohort study including 115 patients with COVID-19 from 41 hospitals. The study included measuring IgM, IgG, and neutralizing antibodies (NAb) in serum, conducting epidemiological survey of the subjects, and retrieving clinical indicators from electronic medical records. We found NAb had the highest seroconversion rate (79.61%), followed by IgG (60.42%), and IgM (26.56%). Seroconversion rate peaked 20–40 d post-infection with NAb reaching 100%. The Geometric mean of NAb ID₅₀ is 201 (30 to 6271). The NAb titer was positively correlated with duration of infection ($p = 0$), IgM ($p = 0.016$), and IgG ($p = 0$). Compared with IgM or IgG, NAb has better diagnostic sensitivity and serological patterns are valuable for clinical diagnosis and disease monitoring.

Introduction

Severe acute respiratory syndrome coronavirus 2 (SARS-Cov-2), is a newly emerging virus first isolated and identified from a patient with unexplained pneumonia in early December 2019¹. The geographic spread and transmissibility of SARS-CoV-2 has grown to be an immediate crisis and now a once-in-a-century worldwide pandemic². SARS-CoV-2 belongs to the Coronaviridae family. It is an enveloped, positive-stranded RNA virus with a ~ 30 kb genome³. The main transmission routes of SARS-CoV-2 among humans including respiratory droplets and direct contact^{4–8}, causing coronavirus disease 2019 (COVID-19).

COVID-19 exhibits varying degrees of clinical features, including atypical symptoms like fever, dry cough, fatigue, as well as pneumonia symptoms such as inflammation and abnormal radiological findings in the lungs^{9,10}. As the pandemic continues, screening is promoted among the population, asymptomatic infected people are gradually being discovered and becoming the focus of intense screening and control of infection sources^{11,12}. The potential clinical progression and outcome of COVID-19 include self-healing, influenza-like illnesses, pneumonia, severe pneumonia with acute respiratory distress syndrome (ARDS), or even death. The incubation period of COVID-19 is still unclear; it may be 14 d in most patients, but it can be as long as 24 d in a few patients¹⁰. There are still a few efficient antiviral drugs or prophylactic vaccines against the virus approved for widespread use; effective clinical indications for the diagnosis and treatment are still urgent¹³.

Specific serological markers including IgG, IgM, and neutralizing antibodies (NAb) are important signs of pathogen infection and related host humoral immune responses^{14,15}. Antibody response patterns and kinetics provide a basis for diagnosis, treatment, and prognosis¹⁶. Due to the suddenness of the new coronavirus pandemic, serological patterns require further and immediate study. Here, an observational cohort consisting of laboratory-confirmed patients in Beijing was employed to study the patterns and kinetics of COVID-19 serological markers and the factors which potentially influencing them.

Materials And Methods

This study was approved and the informed consent is waived by the Ethics Committee of the Beijing Center for Disease Prevention and Control. All methods were carried out in accordance with relevant guidelines and regulations.

Clinical and epidemiology data sources

Patient enrolment were performed in 41 hospitals in Beijing. The timeline ranges from the first diagnosis report in Wuhan to March 15, 2020. Patients who tested positive for SARS-CoV-2 RNA were included. Clinical features were obtained from medical records including virus-related epidemiological history. Data extraction was carried out independently by two technicians; the extracted content contained a) demographic data including age and gender, b) epidemiological data

including exposure history, date of infection, date of onset, and possible transmission chain, and c) baseline clinical manifestations including date of sampling, white blood cell counts (WBC), lymphocyte (LYMPH) and neutrophil (NEUT) percentages, and body temperature (temp).

Collection of serum specimens

Serum collection was carried out using standard, approved operating procedures. Briefly, specimens were collected using additive-free vacuum blood collection tubes and kept at room temperature for 30–60 min to allow for blood coagulation. Subsequently, the serum was separated by centrifugation at 3600 g for 15 min, and the supernatant was frozen at -20°C until tested. Then, samples were pasteurized in a 56°C water bath for 30 min to inactivate viruses and complement.

SARS-CoV-2 IgM and IgG testing

IgG and IgM antibodies were tested using a commercial kit named the new coronavirus (2019-nCoV) antibody detection kit (Innovita Co., Tangshan, China). The nitrocellulose membranes were coated with murine anti-human IgM (μ chain) monoclonal antibody, murine anti-human IgG monoclonal antibody and goat anti-mouse IgG antibody. Recombinant SARS-CoV-2 antigens/mouse IgG labeled with colloidal gold were used as tracers. Serum testing followed the manufacturer's instructions. If there are SARS-CoV-2 antibodies, they will complex with the colloidal-gold-labeled SARS-CoV-2 antigen and the complex can be captured by mouse anti-human IgM/mouse anti-human IgG monoclonal antibodies. One can determine whether the antibody is SARS-CoV-2 IgM or IgG according to the position of the band as stated by the manufacturer. Results were subjectively divided into negative (-), and positive which are further classified by reaction intensity, including weakly reactive (+), moderately reactive (++), strongly reactive (+++) and extremely reactive (++++)

SARS-CoV-2 pseudovirus-based neutralizing antibodies quantification

NAb was tested using a pseudovirus-based neutralizing assay (PBNA) established and validated by our laboratory as previously described¹⁷. Briefly, the Spike gene (GenBank MN908947) was subcloned into pcDNA3.1 vector. For pseudovirus packaging, HEK293T cells (ATCC, cat. no. CRL–3216) were first transfected with the spike-pcDNA3.1 plasmid, and 24 h later they were infected with G*ΔG-VSV. Culture supernatants containing the pseudovirus were harvested, purified, and stored at -70°C in 2-mL aliquots for later use. Huh–7 cells (Japanese Collection of Research Bioresources, cat. no. 0403) were cultured at 37°C in 96-well plates at a density of 1.5×10^4 cells per well for 6 h. Serum samples were diluted 3-fold in duplicate and the pseudovirus was diluted to 1.3×10^4 TCID₅₀/mL. Equal volumes of the serially diluted serum and pseudovirus diluent were mixed and incubated with cell and virus at 37°C for 1 h before freshly trypsinized Huh7 cells were added. Mixtures were then cultured in 5% CO₂ at 37°C for 24 h. Then, culture supernatant was dropped gently with 100 μ L left in each well. 100 μ L luciferase substrate (PerkinElmer, 6066769) was then added for 2 min. Luminescence was detected using 150 μ L of lysate transferred to a white, solid 96-well plate and a microplate luminometer (PerkinElmer, Ensign). The neutralization titers were interpreted as ID₅₀, which were calculated by non-linear regression (four parameters), i.e. log (inhibitor) divided by response.

Data manipulation and statistical analysis

Statistical analysis was performed using Stata 13.0 (StataCorp LP, College Station, TX, USA) and GraphPad Prism 9.0 (GraphPad Software, Inc., San Diego, CA, USA). Continuous variables are summarized as means $\pm$ standard deviation (SD) or ranges. Categorical variables are represented as counting data or rates. Since multiple measurements were included in this study, a mixed regression model was applied to analyze the neutralizing antibody titer kinetics and their potential influencing factors. A P value < 0.05 represents the validity of the mixed model and the statistical significance of specific explanatory variables. Interactive analyses of mixed-effect models were further applied between the factors of interest. Also, group analysis of serological indicators and factors of interest was conducted using a Student's t-test or F-test with a P-value < 0.05 considered statistically significant.

Results

Demographic and epidemiological characteristics of SARS-Cov-2-infected cases

As of March 15, 2020, there are 115 patients (60 males and 55 females) diagnosed with COVID-19 (Table 1). Approximately 90% of the patients were middle-aged or elderly(> 40 years), which was consistent with previous reports^{18,19}. During the 70-d follow-up, 205 visits were conducted. The visits interval ranged from 2–41 d. Exposure explanations were grouped into eight categories, among which, more than 40% of the cases were related to Wuhan or Hubei Province and more than 35% of the cases reported contact history with diagnosed or suspected infected individuals. Meanwhile, transmission chains were analyzed and converted to generations of infection. Among 83 enrolled patients within a known transmission chain, those considered to be second-generation infections (48.19%) accounted for the greatest percentage, followed by mixed generation (30.12%), first-generation (15.66%), and finally third-generation infections (6.02%).

Table 1
Demographic and epidemiology characteristics of COVID-19 patients.

Factors	Characteristic values
Cases enrolled	
Male	n = 60 (52.17%)
Female	n = 55 (47.83%)
Total	115
Age distribution (years)	
Range	2–89
Mean	45.5 (SD = 15.69)
< 18	2 (1.73%)
19–29	10 (8.69%)
30–39	39 (33.91%)
40–59	34 (29.57%)
≥ 60	30 (26.09%)
Follow-up situations	
Observations	205
Visits per case	1–7 ($\bar{x}$ = 1.8)
Time range (d)	0–70 ($\bar{x}$ = 17.7)
Interval (d)	2–41 ($\bar{x}$ = 10.7)
Generation of infection	
Observations	83
First generation	13 (15.66%)
Second generation	40 (48.19%)
Third generation	5 (6.02%)
Mixed generation	25 (30.12%)
Exposure explanation	
Observations	94
Wuhan or Hubei Province related	38 (40.43%)
Contact with diagnosed individual	30 (31.91%)
Other provinces related	10 (10.64%)
Contact with suspected infected individuals	8 (8.51%)
Iatrogenic	6 (6.38%)
No specific exposure history	4 (4.26%)
Foreign travel history	2 (2.12%)

Baseline clinical manifestations

Baseline clinical manifestations were quantified and classified according to the clinically acceptable range (Table 2). Of the 115 patients, observations of TEMP, WBC, NEUT, LYMPH, CRP were 109 (94.78%), 100 (86.96%), 84 (73.04%), 71 (61.74%), 23 (20%) and 86 (74.78%), respectively. Of the 109 subjects observed for temp, 94.49% (CI 88.4–98%) had a temp higher than 37 °C. For the 23 subjects with CRP observations, 56.52% (CI 34.49–76.81%) were defined abnormal.

Table 2
Baseline data of clinical manifestations of SARS-CoV-2-infected patients.

Clinical manifestations	Obs. ^a	Range	Mean	SD	Normal ^c	%	95% CI	Abnormal ^c	%	95% CI
Temp ^b (°C)	109	35.9–39.2	38	0.65	6	5.5	0.02–0.12%	103	94.49	88.4–98%
WBC ^b (10 ⁹ /L)	100	1.31–19	5.24	2.25	83	83	74.18–89.77%	17	17	10.23–25.83%
NEUT ^b (%)	84	27.62–88.7	63.49	12.58	47	55.95	44.7–66.78%	37	44.05	33.22–55.3%
LYMPH ^b (%)	71	11.5–92	33.29	16.8	48	67.61	55.45–78.24%	23	32.39	21.76–44.55%
CRP ^b (mg/L)	23	0.25–96	14.61	22.87	10	43.48	23.19–66.51%	13	56.52	34.49–76.81%

^aObs., observations; SD, standard deviation;

^bTemp, body temperature; WBC, white blood cell count; NEUT, neutrophils; LYMPH, lymphocytes; CRP, C-reactive protein;

^c Normal = Within the clinical reference range of specific indicators(Temp: ≤37 °C; WBC: 4.0–10.0×10⁹/L, NEUT: 50–70%; LYMPH: 20–40%; CRP ≤ 10mg/L);

Abnormal = Not within the clinical reference range of specific indicators.

For WBC-related indicators, we take 4.0–10.0 (10⁹/L), 50–70%, and 20–40% as the clinical reference intervals of WBC count, NEUT, and LYMPH, respectively. Individuals whose detection value falls within the clinical reference range are defined as normal, and those exceeding the clinical reference value are set as abnormal. The setting above the upper limit of the reference range is above normal, and the setting below the lower limit of the reference range is below normal. For WBC counts, 18 of 100 subjects (18%) exhibited abnormal results, including 13 below normal and 5 above normal. All baseline clinical data were quantified and classified according to the clinically acceptable range.

Diagnostic roles of COVID-19 specific serological markers

NAb, IgM, and IgG were tested in all 115 cases; observations of NAb, IgM, and IgG were 206, 192, and 192, respectively (Table 3). Since all cases were diagnosed with SARS-CoV-2 RNA positive, the positive coincidence rate or seroconversion rate with SARS-CoV-2 RNA was used as an indicator of the sensitivity of the serological assay. As shown in Table 3, NAb had the highest (79.61%) positive coincidence rate, followed by IgG (60.42%), while IgM had the lowest (26.56%).

Table 3
Consistency of serological marker and RNA testing for SARS-Cov-2

Antibody type	Obs. ^a	Positive coincidence rate ^b	95% CI	Reactive ^d						Nonreactive ^c		
				+	%	++	%	+++	%	++++	-	%
NAb	206	79.61%	73.46–84.89%								42	20.39%
IgM	192	26.56%	20.46–33.4%	4	2.08%	33	17.19%	10	5.21%	4	141	73.44%
IgG	192	60.42%	53.12–67.38%	8	4.17%	17	8.85%	84	43.75%	7	76	39.58%

^aObs., observations; NAb, neutralizing antibody; reactive,

^bPositive coincidence rate = cases tested positive/ cases tested

^c- Nonreactive, cases tested negative

^dReactive, cases tested positive; +, ++, +++, +++++: positive cases classified according to the reaction intensity, weakly positive, moderately reactive, strongly reactive and extremely reactive.

According to the qualitative results of antibodies, there were six different serological patterns. Among which, 56 (29.02%) observations were NAb positive alone, accounting for the largest proportion of all serological models, followed by 53 (27.46%) observations of both IgG and NAb positive, 43 (22.28%) were all-positive, 20 (10.36%) were all negative, 12 (6.22%) were IgG positive alone, and 8 observations (4.15%) were both IgM and IgG positive. No cases of IgM positive alone were found.

To characterize the dynamic changes in IgM, IgG, and NAb in the SARS-CoV-2-infected population, the 5-d mean seroconversion rates of the antibodies were plotted over the 70-d duration of infection (Fig. 1a, Supplementary table 1). The seroconversion rates of IgM, IgG, and NAb gradually increased from the estimated initiation of infection until about day 15, and peaking around day 20. The high positive rate persisted from day 20 to day 40; the NAb seroconversion rate was as high as 100%. After the 40th day, the positive rates of IgM, IgG, and NAb showed a slow decline with time and IgM decreased to 0% by day 70.

NAb titers and influencing factors

205 observations of NAb ID₅₀ were obtained, NAb titers ranged from less than 30 (detection limit; cases with titers < 30 were regarded as 15) to 6271, with a geometric mean of 201. For the 163 cases above the NAb detection limit, the geometric mean was 393 (Fig. 1b). Figure 2 showed the dynamic changes of NAb quantitative individual follow-up observations/the overall 5-d geometric mean over time. The NAb titer distributions of different individuals and different sampling time points were diverse (Fig. 2a). Regardless of the majority of the individual observation curves or the overall geometric mean curve (Fig. 2b), the NAb titer of the initial stage of infection increased with time, reaching a peak in about 30–40 days, and then slowly declined.

127 observations of 71 patients were included in a mixed model. Log-transformed NAb ID50 values with a base of 10 were taken as dependent variables. Potential influencing factors including gender, age, duration of infection, generation of infection, onset interval, and IgM and IgG intensity were taken as independent variables. According to the results, the establishment of the model was statistically effective ($P = 0$). As detailed in Table 4, the correlation coefficients for gender, age, generation of infection, and onset interval were $P > 0.05$; thus, there was insufficient evidence to infer that they were the

influencing factors of NAb. Three other independent variables including duration of infection, IgG antibody response intensity, and IgM antibody response intensity had regression coefficients of $P < 0.05$, among which, both the duration of infection and IgG antibody response had a value of $P < 0.01$. These results indicated a statistically significant correlation between NAb and the three factors. All regression coefficients of the three factors were greater than 0, reflecting that the NAb titers were positively correlated with IgG, IgM, and duration of infection. On the premise that the other independent variables in the model remain constant, IgG had the greatest influence on NAb titers. For each grade of IgG intensity increase, the NAb titer increased $\text{Log}_{10}(0.2274)$. The inferior influential factor is IgM and duration of infection, which increases by $\text{Log}_{10}(0.1276)$ and $\text{Log}_{10}(0.0186)$, respectively. We also established interaction terms of gender and age with the duration of infection, respectively. Interaction terms were then re-integrated into the model, to explore whether the influence of infection days on the NAb titer is influenced by genders and ages. We found the regression coefficients of the interaction terms are not statistically significant ($P > 0.05$), which showed that age and gender do not interfere with the correlation.

Table 4
COVID-19 neutralizing antibody (NAb) titers and potentially related factors^a

Potential factors	Correlation coefficient	z values	P values	95% CI	
Gender	-0.0455	-0.42	0.671	-0.2556	0.1645
Age	0.0042	1.19	0.236	-0.0028	0.0112
Duration of infection	0.0186	3.90	0	0.0092	0.0279
Generation of infection	0.0595	0.56	0.577	-0.1495	0.2686
Onset interval	-0.0167	-1.67	0.094	-0.0363	0.0029
IgG	0.2274	5.01	0	0.1384	0.3165
IgM	0.1276	2.42	0.016	0.0242	0.2311
Duration of infection _ age ^b	0.0002	1.00	0.315	-0.0002	0.0006
Duration of infection _ gender ^b	-0.0071	-0.89	0.371	-0.0228	0.0085
Intercept	1.3876	6.93	0	0.9954	1.7799

^aNon-neutralizing serum was assigned an ID50 value of 15, i.e. one-half of the detection limit.

^bInteractive variable formed between the duration of infection and age or gender.

Serological patterns and clinical manifestations

Cases with clinical manifestations data were grouped into five different serological patterns. among which, 28 cases were all negative, 1 case was IgM and IgG positive, 15 were IgG and NAb positive, 31 were NAb positive alone, and 25 were all-positive. WBC count, NEUT, LYMPH, and CRP were calculated and analyzed. Scatter diagrams are shown in Fig. 3. No significant difference was found between different serological patterns for WBC count, NEUT, or LYMPH. While for CRP, there was a significant difference between the all negative group and the all-positive group, and a higher significant difference (0.0031) between the NAb positive group and the all-positive group. Except for the 'IgG and IgM' group (because the observation less than 3), groups showing differences in CRP included all-positive, all negative, and 'IgG and Nab'. Further, we grouped CRP data based on the reactivity of IgM, a highly significant difference ($P < 0.0001$) was found between IgM positive and negative group.

In Fig. 4, we grouped NAb IC_{50} according to the clinically acceptable range of clinical indicators. NAb observations were log-transformed to ensure that all data are normally distributed and they were divided into three groups according to the clinical

reference value range, including normal group, below normal group, and above normal group. No significant differences were observed among different groups. Although no statistically significant differences were observed, we characterized the NAb titer distribution by standardizing the shape of the violin schematic. For all indicators in the normal group within clinically acceptable ranges compared with that of abnormal group, the NAb violins schematic exhibits a wider base. In other words, the negative rate of NAb was generally higher. The upper end of the NAb violins was thinner, indicating that for the observation of NAb positive, no matter what the titer was, the proportion was less than that of the abnormal group. For NEUT and LYMPH, the shapes of the violins of the below normal group and the above normal group were similar, but in the opposite position, which is consistent with the complementary calculation method of these two indicators. For WBCs, the prominent position of the violin was in the below normal group around Log10 (2), which may indicate that there are more relatively low concentrations of NAb detection values in this group.

Discussion

A key to SARS-CoV-2 epidemic control is the diagnosis and screening of infected people as early as possible, and to effectively determine the progression of the disease during treatment. Viral infections trigger humoral immunity and generated antibodies. IgM is usually produced first, which is a sign of early infection. Subsequently, IgG is produced. In our study, both IgG and IgM were found at the early stage of infection, and no single IgM positive pattern was found, which is consistent with previous reports²⁰. However, there have also been reports of SARS-CoV-2 infected cases with IgM and IgG seroconversion times of 18 and 20 days or 10 and 12 days after onset, respectively²⁰. One possible reason is that the IgG antibody triggered by the SARS-CoV-2 virus is produced relatively quickly. That is, IgG can be detected at an early stage, and the short interval between IgG and IgM was not captured by sampling. Another reason may be that our infection date estimation is based on epidemiological investigations, and there may be errors resulting in missing the very early infection period. Besides, we also found that the early positive rate of IgG was higher than that of IgM²¹, which is consistent with previous studies. However, other studies have reported that the detection of IgM is earlier than IgG²⁰, which may be due to the sensitivity differences between methods.

In the early stage of infection, the NAb positive rate was similar to that of IgG, and both were higher than that of IgM. However, the subsequent continuous increase resulted in the NAb having the highest positive rate among the three indicators, up to 100%. The good sensitivity of NAb detection may have two aspects. First, NAb is a type of mixed polyclonal antibody, covering a variety of antibody isotypes, including not only IgG but also IgM. Second, PBNA uses the natural conformation of Spike proteins as antigens, which may be more effective in capturing polyclonal antibodies against natural viral antigens during infection. The antigens including our IgG and IgM colloidal gold method and other commercial kits are all synthesized by the manufacturers themselves. In the establishment of their methods, there are differences in the selection of antigenic determinants, coating amount, and composition. Therefore, the characterization of antibodies against different epitopes during infection requires further research. Moreover, compared with nucleic acid detection sampling using nasopharyngeal swabs^{22,23}, blood specimens used in serological testing are easier to obtain, the quality of specimens is more assured, and the risk of exposure by medical staff during specimen collection and testing is reduced. Moreover, serological markers may also help to trace the transmission chain of patients in disease control and prevention.

For individual and group perspectives, the NAb titers changes dynamically with time, rising first and peaking at 30–40 days, which is consistent with our mixed effect analysis. However, only one case was followed up to the 70th day, the mixed effect analysis may have limited analytical power in the later stage of infection. Interestingly, the NAb titer of this case increased firstly and then fell below the detection limit at the last visit. We conservatively deduce that in the late stage of infection in some patients, the titer of SARS-CoV-2 NAb may gradually decrease or even vanish. Previous research is still controversial about the protection of SARS-CoV-2 NAb. Some studies believe that neutralizing antibodies are an important indicator of disease outcomes^{24,25}, while for other studies, compared with patients with mild infections, the progression to severe disease of patients present with higher titers of neutralizing antibodies²⁶. Moreover, whether SARS-CoV-2 NAb is a

protective factor for disease progression, its protective duration, and whether previous infections have acquired continuous immunity remains to be further studied.

CRP rises sharply when overcome infection or tissue damaging²⁷. The increase in CRP is an important indicator of disease progression and mediating inflammation^{8,28,29}. In our results, different concentrations of CRP were seen in the all-positive group, and IgM positive groups. Therefore, we have reason to speculate that SARS-CoV-2 IgM may be related to the acute stage of disease progression and mediate inflammation. The WBC count is an important clinical indicator of disease status²⁸. Elevated WBCs are usually associated with bacterial inflammation, while reduction is usually associated with the viral infection. WBCs can also be subdivided into the proportion of NEUT and LYMPH. Increased LYMPH and decreased NEUT are mainly seen in viral infections, while increased NEUT with decreased LYMPH is mainly seen in bacterial infection. According to our study, no statistical differences were found in WBC-related indicators among different serological patterns. Also, we found that lower levels of NAb may be associated with WBC-related signs of viral infection, while high concentrations of NAb may be associated with WBC-related signs of bacterial infection. Therefore, we conservatively speculate that there may be bacterial co-infection after SARS-CoV-2 infection, which together leads to disease, and increased NAb titer may be used as a potential risk factor to evaluate bacterial co-infection.

There are some limitations. First, we failed to obtain information on which patients eventually developed severe pneumonia or even died. We could not study the relationship between the severity of disease progression and the serological response pattern. Second, because many hospitals were involved, not all samples had been tested for all of the clinical indicators, and we only obtained baseline data and failed to study the relationship between clinical indicators and serological response patterns at other time points. Third, because the infection time point was mainly inferred through epidemiological investigation, there may have been some dates that are not accurate. Fourth, we did not include people with negative nucleic acid tests as controls to study the specificity of serological tests.

Conclusions

SARS-CoV-2 IgM, IgG, and NAb could all be detected as the infection progressed. The positive rate of NAb in diagnosed patients was significantly higher than that of IgG followed by IgM. The NAb titers were positively correlated with the duration of infection, IgG, and IgM. The three antibodies exhibited a variety of serological patterns in the body, among which simultaneously positive IgM, IgG, and NAb results may be related to the acute stage of the disease and inflammation. Therefore, antibody detection can be used as a meaningful supplementary index for clinical diagnosis, tracing of the transmission chain, and the progression of COVID-19.

Declarations

Declaration of Competing Interest

None.

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Figures

Figure 1

Specific serological markers against SARS-CoV-2. Seroconversion rates of SARS-CoV-2 infection change dynamically with the duration of infection.

Figure 2

The kinetic of SARS-CoV-2 neutralizing antibody (NAb) ID₅₀ with time. A. Curves of different colors represent different individuals being followed up to indicate the dynamics of neutralizing antibody (NAb) titers of infected cases in different visits. B. The curve represents the 5-d geometric mean value of neutralizing antibody (Nab) at different time points to represent the dynamic change of Nab in the enrolled population.

Figure 3

Serological patterns and clinical features. Scatter plots of white blood cell counts (WBC), C-reactive protein (CRP), neutrophil (NEUT) and lymphocyte (LYMPH) grouped by different serum patterns. Statistical analysis was performed using the Student's t-test/F-test (*P < 0.05, **P < 0.01).

Figure 4

Titers of COVID-19 neutralizing antibody (NAb) in white blood cell counts (WBC), neutrophil (NEUT), and lymphocyte (LYMPH). The y-axis corresponds to the NAb ID50 with logarithmic conversion, and different violins represent the distribution of standardized NAb concentration levels. Grey, green, and orange violins represent the group below the clinical reference range, the group within the clinically acceptable range, and the group above the acceptable range, respectively. The dotted lines show medians (middle line) and third and first quartiles of the NAb concentration.

Supplementary Files

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- [Supplementarytable1.docx](#)