

Distribution characteristics of SARS-CoV-2 IgM and IgG in false-positive results detected by Chemiluminescent immunoassay

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Abstract

There have been several false-positive results in the antibody detection of the COVID-19. This study aims to analyze the distribution characteristics of SARS-CoV-2 IgM and IgG in false-positive results detected using chemiluminescent immunoassay. The characteristics of the false-positive results in SARS-CoV-2 IgM and IgG testing were retrospectively analyzed. The dynamic changes in the results of SARS-CoV-2 IgM and IgG antibodies were observed. The false-positive proportion of the single SARS-CoV-2 IgM positive results was 95.88%, which was significantly higher than those of the single SARS-CoV-2 IgG positive results (67.50%) ($P < 0.001$) and SARS-CoV-2 IgM & IgG positive results (29.55%) ($P < 0.001$). The S/CO of the SARS-CoV-2 IgM and IgG in false-positive results ranged from 1.0 to 50.0. The false-positive probability of SARS-CoV-2 IgM in the S/CO range (1.0 ~ 3.0) was 91.73% (77/84), and the probability of false-positive of SARS-CoV-2 IgG in the S/CO range (1.0 ~ 2.0) was 85.71% (24/28). Dynamic monitoring showed that the S/CO values of IgM in false-positive results decreased or remained unchanged, whereas the S/CO values of IgG in false-positive results only decreased. The possibility of false-positive of the single SARS-CoV-2 IgM positive and single SARS-CoV-2 IgG positive results was high. As the value of S/CO decreased, the probability of false-positive consequently increased, especially among the single SARS-CoV-2 IgM positive results.

Introduction

The coronavirus disease 2019 (COVID-19) pandemic, caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), has had a catastrophic effect on the world's demographics, becoming the most consequential global health crisis since the influenza pandemic of 1918¹⁻⁴. Since the onset of the pandemic, rapid and accurate diagnoses have helped in epidemiologic monitoring, effective preventive measures, and appropriate antiviral therapies. Nucleic acid tests (N.A.T.s) have been widely used to detect viral infections as confirmed etiological evidence for suspected COVID-19 patients⁵. However, a significant limitation in N.A.T.s is the high false-negative rate, owing to various factors, including improper sampling, sample types, viral mutation, and patient viral load⁶⁻¹¹. Moreover, N.A.T.s require high-quality environmental conditions and equipment, and its detection procedure is time-consuming and labor-intensive, in addition to its already limited sensitivity⁸⁻¹¹.

Aside from nucleic acid detection, assay kits for detecting IgM and IgG antibodies against SARS-CoV-2 proteins have expanded our measures for COVID-19 detection. Compared with N.A.T.s, serological tests have a faster turnaround time, significantly reducing the risk of infection among medical staff during pharyngeal swab sampling. Some studies have reported that almost all COVID-19 patients develop detectable IgG and IgM antibodies within several weeks of symptom onset¹²⁻¹⁵. Studies have also shown that serology-based diagnosis methods can be used with N.A.T.s to improve detection accuracy and exclude false-negative results¹⁴⁻¹⁸. Furthermore, the detection of specific antibodies has been proven to show public health and clinical utility for pandemic monitoring and response and managing affected patients¹⁸.

Currently, serological testing products for COVID-19 include chemiluminescent immunoassay (C.I.A.), gold immunochromatography assay (GICA), and enzyme-linked immunosorbent assay (ELISA), all of which detect SARS-CoV-2 specific antibodies^{19–22}. C.I.A. was clinical laboratory-based methods amendable to high throughput testing using serum or plasma. Chemiluminescence detection of SARS-CoV-2 IgM and IgG antibodies has high sensitivity and specificity, but false-positive results also occur regularly¹⁵. However, it should be noted that overdiagnosis in false-positive results can lead to an incorrect conclusion that an individual has been infected, thereby causing psychological damage and unnecessary financial losses for community isolation and contact tracing²³. Given antibodies detection's role in the pandemic response, clinicians and technicians must practice vigilance in possible false-positive results. Furthermore, our previously published work²⁴ showed that false-positive SARS-CoV-2 IgM results could be caused by a moderate to a high concentration of rheumatoid factor IgM (RF-IgM) in the patient's serum. Thus, from a practical perspective and to combat the increasing number of COVID-19 cases, a timely and effective way to check the authenticity of screening positive results is needed.

We retrospectively analyzed the cases with false-positive results in SARS-CoV-2 IgM and IgG testing using the C.I.A. method. We analyzed the characteristics of false-positive results to distinguish false-positive results from true-positive ones. Moreover, a reference for strategizing and guidance may be provided for other researchers.

Materials And Methods

Subjects and case definition. This was a retrospective study involving the data of patients who tested for SARS-CoV-2 infection in the outpatient and inpatient departments of the Affiliated Hospital of North Sichuan Medical College and Nanchong Central Hospital, Nanchong, China.

For this study, clinical classification, clinical manifestations, personal demographics, and laboratory findings were obtained from the electronic medical records. When the initial test of the SARS-CoV-2 specific antibody was positive, patient records regarding SARS-CoV-2 infection were retrospectively reviewed in duplicates by two or more physicians independently to determine whether each case did have a SARS-CoV-2 infection. A confirmed COVID-19 case was defined based on the Diagnosis and Treatment Protocol for COVID-19 (7th edition), released by the National Health Commission of the People's Republic of China⁵. When the diagnostic criteria were fulfilled, the case was true SARS-CoV-2 infection, including a case of current SARS-CoV-2 infection or resolved SARS-CoV-2 infection. On the other hand, a case that was clinically excluded for COVID-19 or was vaccinated against COVID-19 was no evidence of SARS-CoV-2 infection. Moreover, a false-positive case was defined as a positive antibody result with no evidence of SARS-CoV-2 infection.

Measurement of SARS-CoV-2 IgM and IgG. Serum levels of the SARS-CoV-2 IgM and IgG were determined using the automatic C.I.A. system (Bioscience Biotechnology Co., Ltd) with reagents, including the SARS-CoV-2 antibodies (IgM and IgG) detection kits (Bioscience Biotechnology Co., Ltd, lot number of IgM: G202002415, IgG: G202002414). Briefly, IgG and IgM antibody detection was developed based on

magnetic particle chemiluminescence immunoassay (MCLIA), which uses recombinant antigens containing the receptor-binding domain (RBD) of the SARS-CoV-2 spike protein, acting as the conjugated antigen. The tests were conducted on an automated magnetic chemiluminescence analyzer, and antibody levels were expressed by the chemiluminescence signal. The commercially available assay used in this study has been evaluated to be sufficiently sensitive and specific for detecting SARS-CoV-2 IgM and IgG in clinical specimens²⁵. According to the manufacturer's instructions and standard operating procedures, the daily maintenance was operated before sample testing, and both internal quality control and sample testing were carried out afterward.

Samples showing initial positive antibody test results were retested when there was no apparent history of SARS-CoV-2 infection or when the case had no previous laboratory test results, including SARS-CoV-2 IgM and IgG detection and SARS-CoV-2 R.N.A. testing.

Result judgment. SARS-CoV-2 IgM and IgG results detected via chemiluminescent immunoassay were given in the form of the ratios of specimen signals to the cut-off values (S/CO), which were considered to be negative if $S/CO < 1.0$ and positive if $S/CO \geq 1.0$.

Statistical Analysis. Data were classified and counted using the Excel 2007 software. Measurement data were expressed as means \pm S.E.M.s, whereas count data were expressed as percentages. The Chi-square test was used to compare the enumeration data. All statistical analyses were performed using the SPSS version 23.0 program (SPSS Co., Inc., Chicago, IL), and statistical significance was defined at $p < 0.05$, as determined by two-tailed tests.

Ethical approval and informed consent. The study protocol was approved by the Ethics Committee of the Affiliated Hospital of North Sichuan Medical College. All experimental protocols and methods were carried out by the relevant guidelines and regulations, and they complied with the principles of the Declaration of Helsinki. Since the samples included in the study were conducted anonymously, the ethics committee of the Affiliated Hospital of North Sichuan Medical College waived the need for written informed consent.

Results

A total of 14,708 patients were tested with IgM and IgG against SARS-CoV-2 from March 2020 to January 2021, excluding cases with duplicated patients. 181(1.23%) patients with positive results ($S/CO \geq 1.0$) were included in this study. Among these 181 cases, 48(26.52%) were defined as "true positive," the remaining 133(73.48%) were defined as "false positive."

Ninety-seven of 181 (53.59%) cases were single SARS-CoV-2 IgM positive results: 4/97 (4.12%) were true positives, and 93/97(95.88%) were false positives. Forty of 181 (22.10%) cases were single SARS-CoV-2 IgG positive results: 13/40 (32.5%) were true positives, and 27/40 (67.50%) were false positives. Forty-four of 181 (24.31%) cases were SARS-CoV-2 IgM & IgG positive results: 31/44 (70.45%) were true positives, and 13/44 (29.55%) were false positives. The false-positive proportion of the single SARS-CoV-

2 IgM positive results (95.88%) was significantly higher than those of the single SARS-CoV-2 IgG positive results (67.50%) ($p < 0.001$) and SARS-CoV-2 IgM & IgG positive results (29.55%) ($p < 0.001$) (Table 1).

Table 1
Comparison of true-positive and false-positive proportion of cases among the single SARS-CoV-2 IgM positive, single SARS-CoV-2 IgG positive, and SARS-CoV-2 IgM & IgG positive results. n, number; * Pearson Chi-Square.

	n	SARS-CoV-2	
		True-Positive [n (%)]	False-positive [n (%)]
Single IgM (+)	97	4 (4.12%)	93 (95.88%)
Single IgG (+)	40	13 (32.50%)	27 (67.50%)
IgM & IgG (+)	44	31 (70.45%)	13 (29.55%)
p-value		< 0.0001*	

In this study, 69 of 133 (51.88%) false positives were male: 43/69 (62.32%) with a single SARS-CoV-2 IgM positive result, 18/69 (26.09%) with a single SARS-CoV-2 IgG positive result, and 8 /69 (11.59%) with SARS-CoV-2 IgM & IgG positive results. Meanwhile, 64 of 133 (48.12%) false positives were female: 50/64 (78.13%) with a single SARS-CoV-2 IgM positive result, 9 /64 (14.06%) with a single SARS-CoV-2 IgG positive result, and 5 /64 (7.81%) with SARS-CoV-2 IgM & IgG positive results. Based on these results, no significant difference was found in the false-positive proportion of the three result patterns between different sexes ($p > 0.05$) (Table 2). Similarly, no significant difference was also found in the false-positive rates of the three result patterns in different age groups ($p > 0.05$) (Table 3).

Table 2
Comparison of the false-positive proportion of the three patterns in different sexes

	Single IgM (+)	Single IgG (+)	IgM & IgG (+)
Male	62.32% (43/69)	26.09% (18/69)	11.59% (8/69)
Female	78.13% (50/64)	14.06% (9/64)	7.81% (5/64)
p-value	0.072	0.085	0.463

Table 3
Comparison of the false-positive proportion of the three patterns in different ages

Age(years)	Single IgM (+)	Single IgG (+)	IgM & IgG (+)
≤ 20	54.55% (12/22)	40.91% (9/22)	4.55% (1/22)
21~	69.23% (9/13)	15.38% (2/13)	15.38% (2/13)
31~	72.00% (18/25)	20.00% (5/25)	8.00% (2/25)
41~	68.42% (13/19)	10.53% (2/19)	21.05% (4/19)
51~	65.22% (15/23)	17.39% (4/23)	17.39% (4/23)
61~	90.91% (10/11)	9.09% (1/11)	0.00% (0/11)
> 70	80.00% (16/20)	20.00% (4/20)	0.00% (0/20)
p-value	0.436	0.327	0.169

Among the cases in our study, 141 had the S/CO values of SARS-CoV-2 IgM greater than or equal to 1.0. 97/141(68.79%) cases had the single SARS-CoV-2 IgM positive results. Figure 1 shows the distribution of SARS-CoV-2 IgM S/CO values in the false-positive and true-positive results. The S/CO values of IgM false positives ranged from 1.0 to 32.0, with most of them concentrated between 1.0 and 3.0 (Fig. 1A, Fig. 1B). The S/CO values of the SARS-CoV-2 IgM true-positive cases ranged from 1.0 to 180.0, with most of them between 3.0 and 10.0 (Fig. 1A), whereas the S/CO values of single SARS-CoV-2 IgM true-positive cases all were more than 100.0 (Fig. 1B). The overlapping range of S/CO values for SARS-CoV-2 IgM false-positive and true-positive cases was mainly from 1.0 to 50.0 (Fig. 1A). Notably, neither SARS-CoV-2 IgM nor single SARS-CoV-2 IgM in false-positive cases showed S/CO values greater than 40.0 (Fig. 1A, Fig. 1B).

As shown in Table 4, when the S/CO values of the SARS-CoV-2 IgM were in the ranges of 1.0 ~ 3.0, 3.0 ~ 5.0, 5.0 ~ 10.0, 10.0 ~ 50.0, and greater than 50.0, the probability of SARS-CoV-2 IgM false-positive was 91.73%, 52.63%, 38.89%, 75.00%, and 0.00%, respectively. Meanwhile, when the S/CO values of the single SARS-CoV-2 IgM were in the ranges of 1.0 ~ 50.0 and greater than 50.0, the probability of the single SARS-CoV-2 IgM false-positive was 100.00% and 0.00%, respectively.

Table 4

The probability of the false-positive results in SARS-CoV-2 IgM and single SARS-CoV-2 IgM S/CO = ratios of specimen signals to the cut-off values

S/CO	The false-positive rates	
	SARS-CoV-2 IgM	Single SARS-CoV-2 IgM
1.0 ~ 3.0	91.73% (77/84)	100.00% (70/70)
3.0 ~ 5.0	52.63% (10/19)	100.00% (8/8)
5.0 ~ 10.0	38.89% (7/18)	100.00% (5/5)
10.0 ~ 50.0	75.00% (12/16)	100.00% (10/10)
> 50.0	0.00% (0/4)	0.00% (0/4)

Of the 84 cases that had the S/CO values of SARS-CoV-2 IgG greater than or equal to 1.0, 40/84 (47.62%) cases had the single SARS-CoV-2 IgG positive results. Figure 2 shows the distribution of SARS-CoV-2 IgG S/CO values in false-positive and true-positive results. The S/CO values of false positives ranged from 1.0 to 40.0, with most of them concentrated between 1.0 and 2.0, whereas the S/CO values of true positives ranged from 1.0 to 360.0, with most above 10.0. Moreover, the overlapping range of S/CO values for SARS-CoV-2 IgG positive and false-positive cases was mainly from 1.0 to 50.0 (Fig. 2A, Fig. 2B). Interestingly, S/CO values above 40.0 indicated no SARS-CoV-2 IgG false-positive results (Fig. 2A, Fig. 2B).

When the S/CO values of the SARS-CoV-2 IgG were in the ranges of 1.0 ~ 2.0, 2.0 ~ 5.0, 5.0 ~ 10.0, 10.0 ~ 50.0, and greater than 50.0, the probability of SARS-CoV-2 IgG false-positive were 85.71%, 40.00%, 50.00%, 18.75%, and 0.00%, respectively. When the S/CO values of the single SARS-CoV-2 IgG were in the ranges of 1.0 ~ 2.0, 2.0 ~ 5.0, 5.0 ~ 10.0, 10.0 ~ 50.0, the probability of false-positive of single SARS-CoV-2 IgG results were 94.74%, 50.00%, 75.00%, and 22.22%, respectively (Table 5).

Table 5

The probability of the false-positive results in SARS-CoV-2 IgG and single SARS-CoV-2 IgG S/CO = ratios of specimen signals to the cut-off values

S/CO	The false-positive rates	
	SARS-CoV-2 IgG	Single SARS-CoV-2 IgG
1.0 ~ 2.0	85.71% (24/28)	94.74% (18/19)
2.0 ~ 5.0	40.00% (8/20)	50.00% (4/8)
5.0 ~ 10.0	50.00% (5/10)	75.00% (3/4)
10.0 ~ 50.0	18.75% (3/16)	22.22% (2/9)
> 50.0	0.00% (0/10)	-

Eighteen SARS-CoV-2 IgM false-positive cases and four true-positive cases were dynamically monitored at different time points. Of the 18 false-positive cases, 10 cases turned negative, and the remaining eight cases did not. The median time of conversion to seronegative of the 10 cases was nine days. Compared with the dynamic change trend of true-positive cases, the dynamic change trend in SARS-CoV-2 IgM false-positive cases was significantly lower. On the other hand, among the eight false-positive cases that were not monitored to seronegative, three cases showed a decreasing trend, whereas five remained unchanged (Fig. 3A).

Seven SARS-CoV-2 IgG false-positive cases and four true-positive cases were dynamically monitored at different time points. Of the seven false-positive cases, six turned seronegative, while only one case did not. The median time of conversion to seronegative of the six cases was five days. Compared with the dynamic change trend of SARS-CoV-2 IgG in true-positive cases, the dynamic change trend in false-positive cases was significantly lower. Notably, the only one false-positive case which was not monitored to seronegative showed a decreasing trend (Fig. 3B).

Discussion

Generally, coronavirus genomes encode four major structural proteins, namely spike (S), envelope (E), membrane (M), and nucleocapsid (N). Current serologic tests have been developed to target antibodies directed against these antigens, showing that spike protein-based detection was more sensitive than nucleocapsid protein-based detection^{26,27}. In our study, we used the C.I.A. method, which was based on the recombinant SARS-CoV-2 S-RBD protein to detect serum IgG and IgM, and its analytical performance was successfully evaluated by Wan Y et al. They reported the performance verification of the SARS-CoV-2 IgM (82% sensitivity and 93.85% specificity) and SARS-CoV-2 IgG (86% sensitivity and 96.92% specificity) detection kits among COVID-19 patients²⁵.

However, due to the problems of immunological detection methods, there have been interferences attributed to certain pathological factors, biological factors, and cross-reactions, resulting in false-positive results that were inconsistent with clinical manifestations and epidemiological characteristics. Some of these factors identified by previous studies included inadequacy during any step of the testing process, presence of cross-reactive antibodies, other endogenous interference factors, and other viral infections^{24,28-29}. Additionally, some false-positive cases likely did not result from problems with the sample, procedure, or other random factors, which was supported by obtaining repeated positive results with similar S/CO values on repeat testing (data was not shown) in our study, making a transient response to antigen less likely. Furthermore, this phenomenon regarding endogenous interference factors in SARS-CoV-2 antibody testing was also reported in our previous study²⁴. Although we can use the electronic medical records and laboratory results, including N.A.T.s, as a source to determine true anti-SARS-CoV-2 status, the procedure is labor-intensive and time-consuming. Therefore, we attempted to seek an effective strategy to solve such problems when confronted with false-positive results in the SARS-CoV-2 antibody screening test.

To elucidate these issues, we retrospectively analyzed the false-positive cases of SARS-CoV-2 IgM, and IgG detected using C.I.A. This study showed that the false-positive rate of the single SARS-CoV-2 IgM positive results was 95.88%, which was significantly higher than those of the single SARS-CoV-2 IgG positive results (67.50%) and SARS-CoV-2 IgM & IgG positive results (29.55%). Therefore we concluded that the possibility of false-positive of the single SARS-CoV-2 IgM positive and single SARS-CoV-2 IgG positive results was high, and the combined detection of SARS-CoV-2 IgM and IgG antibody was better than the single detection in terms of a positive detection. Previous investigations have shown that SARS-CoV-2 IgM and IgG antibodies could be detected as early as the 4th day following symptom onset³⁰. The positive rates of the single SARS-CoV-2 IgM, single SARS-CoV-2 IgG, and SARS-CoV-2 IgM and IgG positive results among COVID-19 patients were 1.72%, 3.45%, and 94.83%, respectively, concluding that the combined detection of IgM and IgG had better practicability and sensitivity than IgM or IgG alone³¹. Interestingly, most false-positive signals were detected in the SARS-CoV-2 IgM assays, which other studies have also noted^{28,32}. Thus, the combined detection of SARS-CoV-2 IgM and IgG should be given high priority in its implementation as the standard serological test in clinical and public health practice during the pandemic.

In this study, we found that the S/CO values of the IgM false-positive results were mainly between 1.0 and 3.0, whereas the S/CO values of the IgG false-positive results were mainly between 1.0 and 2.0. These results indicated that the SARS-CoV-2 IgM and IgG false-positive results detected by C.I.A. mainly existed in the low-value area. The false-positive results, which were low positive or low-value, needed to be confirmed further. Therefore, the S/CO ratio may be a helpful indicator in differentiating false positives from true positives. Aside from the S/CO values, we also compared the false-positive proportions of the single SARS-CoV-2 IgM, single SARS-CoV-2 IgG, and SARS-CoV-2 IgM & IgG positive results in different sexes and ages. Our study showed no significant differences for the false-positive proportion in different sexes and ages.

After SARS-CoV-2 invades the human body, the time and duration of producing IgM and IgG antibodies are different. Due to the dynamic change of specific antibodies, cases with a single positive SARS-CoV-2 IgM/IgG antibody test can be determined by dynamically monitoring them over some time⁵. Despite this, the question of how long the supposed "antibody" level could last in the false-positive cases remains unknown. To investigate this, we reviewed the subsequent results of four true-positive cases and 25 false-positive cases, including 18 cases with a SARS-CoV-2 IgM positive result and seven cases with a SARS-CoV-2 IgG positive result, and dynamic monitoring of the serum "antibody" levels after the first test. It was found that the time of conversion to seronegativity in IgM false-positive cases was 4 to 19 days, with a median seroconversion time of 9 days. Moreover, the "antibody" duration in the IgM false-positive cases was significantly shorter than that in COVID-19 patients with a duration of 2 to 6 months, as reported in other studies^{13,30}. Meanwhile, the conversion time to seronegativity in IgG false-positive cases was 2 to 8 days, with a median seroconversion time of 5 days. Compared with previous studies, the "antibody" duration in the IgG false-positive cases was also significantly shorter than the duration of serum IgG antibodies in COVID-19 patients (6 months)^{13,30}. For other cases observed during the monitoring period and those that did not turn seronegative, "IgM antibody" levels showed a downward trend or remained unchanged. Similarly, "IgG antibody" levels in those same cases also showed a downward trend. Due to the lack of blood samples collected from the false-positive cases in the later stage, the time of conversion in their "antibodies" remained unknown.

In this study, the results suggest that the dynamic monitoring of serum antibody level was also of practical value in distinguishing between true-positive and false-positive results. When confronted with positive results in SARS-CoV-2 specific antibody testing, these findings should be comprehensively judged. First, it is crucial to observe the antibody pattern. If it is a single SARS-CoV-2 IgM positive pattern, the probability of a false-positive is higher than that of a single SARS-CoV-2 IgG positive pattern. Meanwhile, if it is a SARS-CoV-2 IgM & IgG positive pattern, the probability of a true-positive is higher than that of a single positive antibody result. Second, one must observe the S/CO value distribution of the antibody results as follows: (1) if the S/CO value of a single SARS-CoV-2 IgG positive result was between 1.0 and 2.0, the probability of a false-positive is approximately 94.74% (Table 5); (2) if the S/CO value of a single SARS-CoV-2 IgM positive result was between 1.0 and 3.0, the probability of a false-positive is approximately 100.0% (Table 4); (3) if a single SARS-CoV-2 IgM has a positive result, and the S/CO value is very high (>20.0), the result needs to be judged in combination with the S/CO value of the SARS-CoV-2 IgG result; (3a) if the S/CO value of the SARS-CoV-2 IgG result approaches 0, there is a high possibility of a false-positive result; (3b) if the S/CO value of SARS-CoV-2 IgG result is close to 1.0, it is more likely to be a true-positive result. Lastly, antibody level changes should be observed dynamically. In cases of a single SARS-CoV-2 IgM positive status, IgM antibody increases and IgG antibody turns positive (i.e., IgM and IgG positive status), with which we can judge if the patient truly has a SARS-CoV-2 infection. Otherwise, it is a false-positive result. On the other hand, in the dynamic monitoring of SARS-CoV-2 positive IgM and positive IgG status, the IgM antibody is the first to increase and subsequently decrease, whereas the IgG antibody titer has a 4-fold increase, with which we can judge if the patient truly has a SARS-CoV-2 infection⁵. Otherwise, these are false-positive results. Furthermore, the single SARS-CoV-2 IgG positive

status shows a rapidly decreasing trend in dynamic monitoring, which may indicate a false-positive result.

Despite the findings of our study, several limitations were noted. First, due to the insufficient conditions of our laboratory, we failed to determine the interferences or factors causing false-positive results. Second, the number of samples included in this study was limited, leading to some deviation in the analysis results. More cases should be included in further studies of the same topic. Third, since the majority of the SARS-COV-2 specific antibody detection was performed using the C.I.A. platform due to its high throughput, our research analysis was only focused on the C.I.A. Methods and molecules used for generating and detecting signals. The epitopes and specificities of antigens and antibodies are different between the assays. Thus, the characteristics of the false-positive results analyzed in this study may not apply to other SARS-COV-2 antibody detection methods. Regardless, this study can still provide a reference strategy for other researchers.

Conclusion

We proposed that the possible usage of the SARS-COV-2IgM and IgG antibody patterns, S/CO values or ranges, and dynamic changes in antibody levels is of great significance in screening positive antibody results. This study aimed to assist clinicians or technicians in developing timely and effective diagnostic strategies to distinguish false-positive results from true-positive ones. Thus, if the number of false positives can be reduced with these suggested adjustments, this would have implications for other COVID-19 screening tests.

Declarations

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Author contributions statement

Lei.Y.Data curation, Writing-original draft. Lu X.L. Data curation, Writing-original draft. Mou D.Y.Figures, Tables. Du Q. Software, Validation. Guo B.Data curation, Investigation. Guo X.L. Supervision, Writing - review & editing. Wang G.R.Conceptualization, Methodology, Project administration. Wang Q.Conceptualization, Methodology, Project administration. All authors reviewed the manuscript.

Competing interests

The authors declare no competing interests.

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Figures

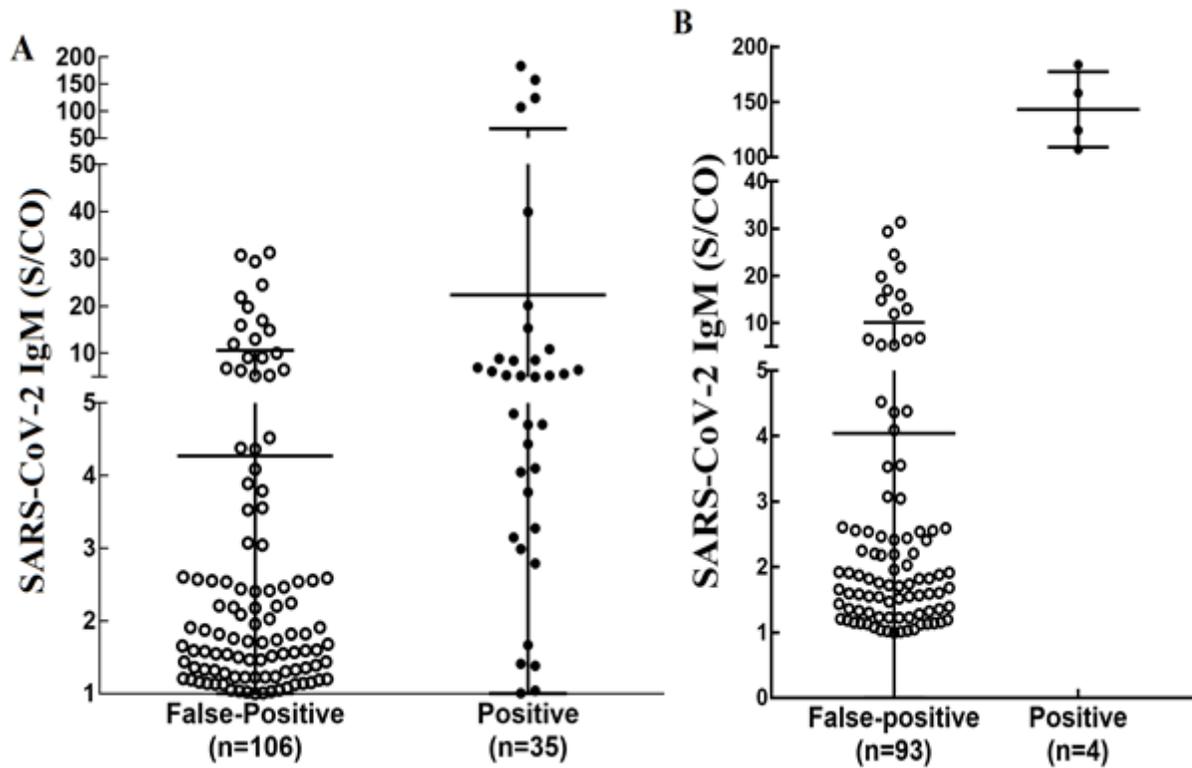


Figure 1

Distribution of SARS-CoV-2 IgM S/CO results greater than or equal to 1.0. (A). Distribution of S/CO values of SARS-CoV-2 IgM in false-positive and positive results. (B). Distribution of S/CO values of single SARS-CoV-2 IgM in false-positive and positive results.

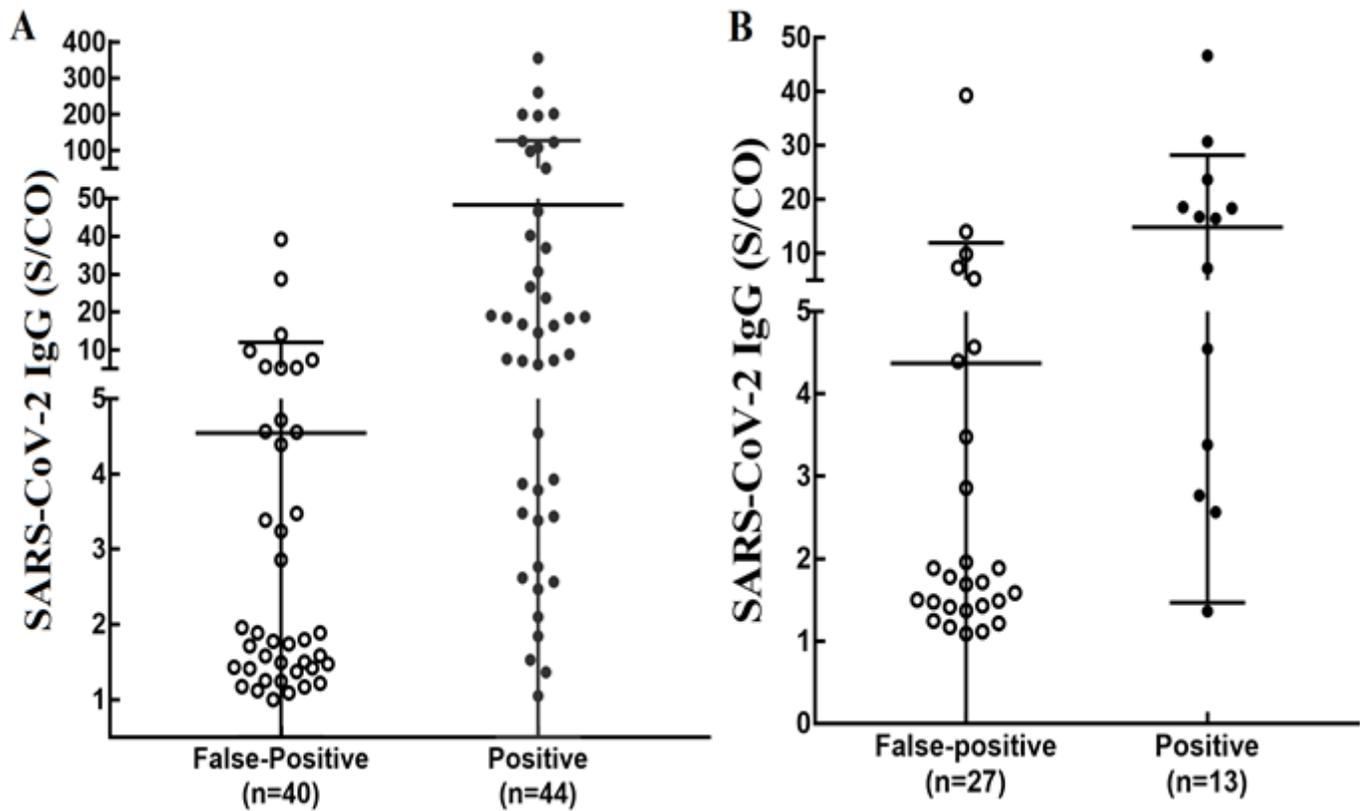


Figure 2

Distribution of SARS-CoV-2 IgG S/CO values greater than or equal to 1.0. (A) Distribution of S/CO values of SARS-CoV-2 IgG in false-positive and positive results. (B). Distribution of S/CO values of single SARS-CoV-2 IgG in false-positive and positive results.

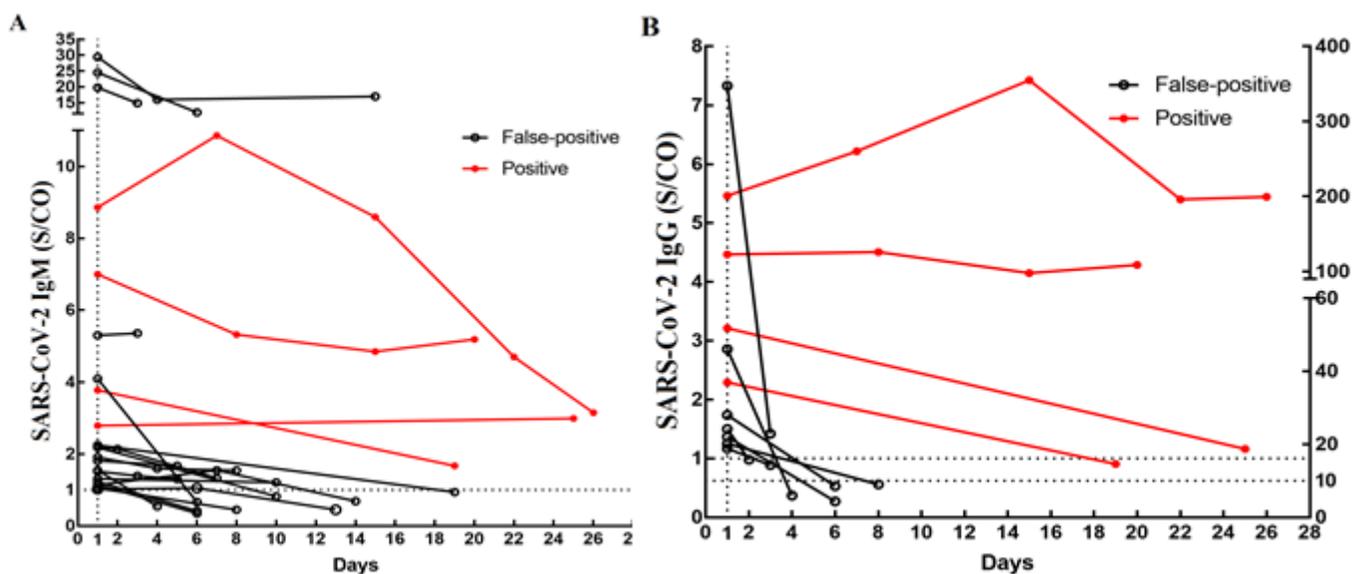


Figure 3

Dynamic changes of SARS-CoV-2 specific antibody in patients with false-positive or positive results. (A). Dynamic changes of SARS-CoV-2 IgM in false-positive results. (B). Dynamic changes of SARS-CoV-2 IgG in false-positive results. The left vertical axis was suitable for the false-positive results, and the right vertical axis was suitable for the positive results. The axis "Days" represents the days after the first test.