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MINI REVIEW

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Serological tests for COVID-19: Potential opportunities

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Abstract

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is a novel betacoronavirus, caused a pandemic leading to a standstill of nearly all global activities. There are some controversies on the production of specific immunoglobulin M (IgM) and IgG antibodies after the infection with SARS-CoV-2. This paper seeks to elaborate on the potential application of IgM and IgG antibodies and the viral antigens for the diagnosis and the course of the disease as well as the recurrence of positive nucleic acid tests after discharge.

KEYWORDS

antibody, coronavirus, diagnosis, IgG, IgM, SARS-CoV-2

1 | INTRODUCTION

In December 2019, the world was hit by a novel virus, known as severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), which later developed in a pandemic causing the coronavirus disease 2019 (COVID-19). It has since then infected over 30 million people all over the world with over 24 million recoveries and over a million deaths (end of September 2020). Real-time reverse-transcriptase polymerase chain reaction (rRT-PCR) continues to be a test technique that is widely used to validate the results of both symptomatic and asymptomatic patients of COVID-19. Though there have been improvements in this technique, parts of the world like the United States still have a limited track record of rRT-PCR testing. In other places like China, this method was used for clinical COVID-19 patients and it produced suboptimal sensitivity results with 72 out of 104 sputa being positive, 5 out of 8 nasal swabs, and 126 out of 392 pharyngeal swabs being positive (Huang et al., 2020). These results conform with barriers that have already been seen in the molecular diagnosis of this novel coronavirus, SARS-CoV-2. Some of these challenges include but not limited to low viral count during the onset of the disease, lack of a gold standard to confirm various tests, and also, the wide genetical variations in the strains that have been identified. To augment the rRT-PCR technique, some serological tests of various forms were created that can probe immunoglobulins (Ig) like IgG and IgM for viral proteins of SARS-CoV-2. However, just like the rRT-PCR, these tests also have their barriers. So far, the challenges that have been seen across different regions include delayed positivity, response and function of the host immune system, and interference of other coronaviruses in detecting SARS-CoV-2 (Ozturk et al., 2020).

Abbreviations: ACE2, angiotensin-converting enzyme 2; COVID-19, coronavirus disease; nAbs, neutralizing antibodies; NLR, neutrophil-to-lymphocyte ratio; rRT-PCR, real-time reverse-transcriptase polymerase chain reaction; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.

2 | ANTIBODY PRODUCTION

The human immune system produces antibodies which are mainly blood proteins that serve the function of protecting the body from the attack of both external and internal substances or organisms that are recognized as foreign to the body like viruses. These antibodies can avert future attacks from similar or the same foreign bodies and are mainly found in the bloodstream and body secretions, such as saliva. The immune systems' response to SARS-CoV-2 through the antibodies produced against it is important to determine the progress of the disease and also in providing the best available supportive care (Saghazadeh & Rezaei, 2020b). Antibodies like IgG and neutralizing antibodies (nAbs) are specific for their function, and, therefore, are very important for preventing an individual's immune system from attack and averting pathogens into the cells after a viral attack leading to an infection. The antibody detection gives vital clinical information of a viral attack just like in patients with COVID-19. A study reports that researchers at Chongqing Medical University found out that almost all 285 COVID-19 patients in their study produced IgM, as it is the foremost antibody that is produced during an infection to protect the body. Only 40% of the patients produced IgM in their first week when they got infected with the SARS-CoV-2 but this percentage of patients saw a drastic rise to about 95% in the following 2 weeks, that is, 12–14 days. All the subjects in this study also produce IgG antibodies. So far, the antibodies that are most important in SARS-CoV-2 are the IgG antibodies. Antibodies to SARS-CoV-2 can be found in the middle and later stages of the disease. Antibody detection can play an important role in the COVID-19 diagnosis as a complementary approach to assays with viral nucleic acids (Qu et al., 2020; Nasab et al., 2020). Antibody tests of the blood (and in some cases saliva) detect whether the antibody is present or absent. Although their production in patients with COVID-19 occurs later as compared to IgM, IgGs have the noumenon to confer sustained immunity to patients with COVID-19 (Jahanshahlu & Rezaei, 2020). Using evidence from other coronaviruses such as human endemic coronaviruses, SARS-CoV-1 and Middle East respiratory syndrome (MERS)-CoV can provide clues and guide future prediction and research on sustained immunity on SARS-CoV-2. Table 1 shows the main antibodies involve in SARS-CoV-2 disease clinical response.

3 | VIRAL ANTIGENS

SARS-CoV-2 continues to spread worldwide with the concomitant urgency of developing effective nAbs as prophylactic and therapeutic agents to prevent, treat, and monitor its spread (Jiang et al., 2020). Four structural proteins belong to the coronavirus family: spike (S), membrane (M), envelope (E), and nucleocapside (N) proteins. Two of those proteins tend to be important antigenic sites for the production of COVID-19 serological assays. Most serological approaches have focused on identifying the coronavirus spike of serum antibodies against S proteins and N proteins. SARS-CoV and SARS-CoV-2 bind to human angiotensin-converting enzyme 2 (ACE2), which can be found in human respiratory cells, renal cells, oral epithelial cells, and gastrointestinal cells (Tang et al., 2020). The protein S1 binds on the surface of human cells to the protein ACE2 and plays a crucial role in infection with viruses (R. Zhao et al., 2020). Most serological assays are using the S and N proteins as antigens since these are the two antigens that showed the highest sensitivity within the community of commercially available assays so far tested (Kohmer et al., 2020). In SARS-CoV-2 infection, it induces IgG development against N protein which can be detected by serum as early as Day 4 after the onset of disease and with most patients being seroconverted by Day 14 (Rokni et al., 2020) but studies using an antigen S are more sensitive than tests based on antigen N with IgG tests performing better than IgM tests. After symptom onset, N and S specific IgM and IgG steadily increases and can be used for the identification of SARS-CoV-2 infection (Sun et al., 2020). S-IgG dynamics analysis can aid in predicting prognosis. An increase in S-IgG positively associated with a decrease in C-reactive protein. It has been recognized that S-specific antibodies can block the binding of S protein to the cellular human ACE2 receptor, which mediates the binding and entry of SARS-CoV-2 into target cells. There is no evidence that the N-specific antibodies could prevent infection with the virus. Due to its high immunogenicity and intracellular aggregation before virus packaging, N protein is a suitable candidate for the early diagnosis of infection. Therefore, a continuous rise in N-IgG can indicate the progression of disease towards a more serious disease (Sun et al., 2020). SARS-CoV and MERS-CoV studies have shown that various fragments (S1-N-terminal domain, receptor-binding domain [RBD], S2) in S proteins can be used as targets for the

TABLE 1 A summary of main SARS-CoV-2 antibodies and their clinical observations are shown below (Iyer et al., 2020; Peeling et al., 2020; Ravi et al., 2020)

SARS-CoV-2 antibodies	Days since symptom onset	Clinical observations
IgG	Detectable at least 14 days	Associated with the presence of protective neutralizing antibodies, remained detectable for at least 4 months but have the severe clinical outcome of the disease
IgA	Detectable at least 5 days	Relatively short-lived, declining to low levels within two and a half months or less, averagely, clinically associated with mild-to-moderate disease outcome
IgM	Detectable at least 5 days	Declined faster, thus less than two and half months averagely, and correlates with mild-to-moderate clinical course of the disease

Abbreviations: IgA, immunoglobulin A; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.

TABLE 2 A summary of SARS-CoV-2 structural proteins, binding sites, and their roles (Ravi et al., 2020)

Protein name	Binding mechanism	Role
Spike (S) protein	Utilizes an N-terminal signal sequence to gain access to the endoplasmic reticulum	Mediates attachment to host receptors
Nucleocapsid protein	Binds the viral genome in a beads-on-a-string type conformation	Tethers the viral genome to replicase-transcriptase complex, packages the encapsulated genome into viral particles
Envelope protein	A transmembrane protein with ion channel activity	Facilitates assembly and release of the virus; involved in ion channel activity
Membrane protein	Binds to nucleocapsid	Promotes membrane curvature
Hemagglutinin-esterase dimer protein	Binds sialic acids on surface glycoproteins	Thought to enhance S protein-mediated cell entry and virus spread through the mucosa

Abbreviation: SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.

production of nAbs. RBD-based antibodies have a greater potential to neutralize diver-gentle virus strain infection, indicating that SARS-CoV-2 RBD may also serve as a significant target for the production of potent and sensitive nAbs (Jiang et al., 2020). Table 2 gives an overview of the structural viral proteins (antigens) associated with SARS-COV-2.

4 | SEROLOGICAL TESTS

Serological testing is traditionally defined as a diagnostic technique used to determine immune response to an infectious agent (Lippi et al., 2020). Inherent in this description is the basis of many misunderstandings and wrong perception about the use of serological testing in COVID-19, through which this method of testing is not intended to replace the detection of viral RNA for COVID-19 etiological diagnosis, but rather to assess if individuals have been infected with the virus and/or developed an immune response. If the test shows positive for the antibodies, this is interpreted as a previously infected person of the virus and can also be potentially immune to the virus. To put this in the sense of COVID-19, serology testing involves the identification (by qualitative tests) and/or measurement (using quantitative tests) of different groups of Igs (typically IgA, IgM, and IgG) against SARS-CoV-2 to determine if a person has been infected with SARS-CoV-2 and has developed antibodies that, if they have neutralizing effects, can protect them from reinfection (Lippi et al., 2020). Serological assays to detect SARS-CoV-2 antibodies from patient serum or plasma samples have been developed by a variety of commercial companies and research institutes to date. Closely related to another pathogen, SARS-CoV, these serological assays primarily target immunogenic coronavirus proteins: S protein, which is the most exposed viral protein, and N protein, which is abundantly expressed during infection (C. Y.-P. Lee et al., 2020). These tests, specifically for detection of IgM and IgG antibodies, SARS-CoV-2 S protein antigen, and N protein antigen-based enzyme-linked immunosorbent assay (ELISA) test, evaluated in different studies showed that antibody detection is more sensitive using the ELISA than detecting viral nucleic acid using the rRT-PCR for diagnosis of the disease (Kohmer et al., 2020; Liu et al., 2020; W. Zhang et al., 2020). Serology testing is one of the two methods used in testing for SARS-CoV-2, for antibodies produced against the virus, notably IgM and IgG antibodies but with questions around immunity-based protection like delayed and weak antibody responses linked to severe outcomes, many carriers of the virus having only mild symptoms of COVID-19 or not showing any symptoms at all, known as asymptomatic carriers, a positive molecular test does not give automatic protective antibody IgG still remains a scientific setback.

Serological tests are also important to evaluate the susceptibility or resistance to subsequent reinfection (Padoan et al., 2020). Other methods like rRT-PCR exist which are efficient and specific but serological test kits are significantly helpful in determining and ascertaining the antibody production against the virus and the chance of sustained immunity leading to herd immunity for individuals. A study evaluated the efficiency of a commercially available test kit, designed and produced for fast (in <15 min) confirmation of SARS-CoV-2-specific IgG and IgM by 29 PCR-confirmed COVID-19 cases and 124 negative controls. Results from this particular study showed a sensitivity of 69% and 93.1% for IgM and IgG, respectively. This was exclusively based on PCR positivity since there is no serological gold standard for detecting the virus. Specificities for this test were obtained at 100% for IgM and 99.2% for IgG (Krüttgen et al., 2020; Pan et al., 2020). It gives a hint that this test is good to determine past infection in an individual, although negative test results cannot be trusted especially in the early stages after exposure to the virus (Hoffman et al., 2020). Acute antibody response was detected in a study that involved 285 COVID-19 patients. The antibodies reacted to SARS-CoV-2 in the space of 19 days after the start of symptoms with 100% of the study subjects testing positive for antiviral IgG. There was a seroconversion for both IgM and IgG at the same time or concurrently. There was a comparatively stable level of IgM and IgG antibodies titer in the space of 6 days after seroconversion. Those study subjects (patients) with positive virus-specific IgG attained 100% in about 17–19 days after the start of symptoms, while those study subjects with virus-specific IgM positive attained a stable level of 94.1% in about 20–22 days after the start of COVID-19 symptoms. However, there was no association between stable IgG numbers and the clinical outcome and severity of the disease (J. Zhao et al., 2020). In contrast, a different study reported a link between the severity of COVID-19 and high levels of IgG in response

to the infection as the disease progressed. An immune response phenotyping relying on late IgG activity and neutrophil-to-lymphocyte ratio (NLR) (Lotfi & Rezaei, 2020) could be an added and useful method to segregate severe patients from nonsevere individuals, and could also forecast the clinical outcome of patients with COVID-19. Immune response phenotyping based on late IgG levels and NLR was profiled to group patients showing various degrees of severity and outcome of the disease. The antibody response phenotypes with the degree of infection were profiled in study subjects using laboratory parameters. This particular study reported increased IgM numbers during the early stage, and increasing numbers were mostly associated with severely diseased patients. IgG numbers rose during the later stage, whereas a significant rise of IgG numbers was frequently noticed among study subjects with high disease severity. The results showed that besides the antiviral efficacy, the immune response might be linked to secondary antibody-mediated organ damage. The levels of NLR and IgG that are seen at a later stage in sera of the disease were used to produce a combined immune response phenotype that can forecast the course of disease progression in patients with COVID-19 (B. Zhang et al., 2020). IgG/IgM test technique was used in a study of 14 confirmed individuals with SARS-CoV-2. This particular study included 28 negative controls and this time around the results showed a variation of antibody reaction per the degree of infection and clinical presentation of the disease in these patients. Those with clinical symptoms produced IgM antibodies and had a faster rRT-PCR positive result with no change in the severity of the disease than those that had no IgM antibodies against the virus (Y. L. Lee et al., 2020). As seen previously in other studies, this one records rising values of IgM in the first-week infection with the virus, this rise was stable after 2 weeks before it went back to very low amounts in most of the patients. However, IgG was noticed a week later and remained at increased levels for a significant duration (Saghazadeh & Rezaei, 2020a). Among the different groups of cases, thus, mild, severe, and critical, there was no prominent variation in the positive diagnosis of these two antibodies. It was observed that a rise in IgM values seems to cut across both critical and severe cases but the IgG number was lower specifically for critically ill patients than the other groups of cases. It is speculated that these results may be due to a weakened immune reaction or a strong attack from the SARS-CoV-2 virus in critically ill patients. Deceased individuals from the virus had a little higher IgM numbers as compared to individuals who survived the virus though IgG levels in both situations looked similar. However, in a longitudinal study, dead patients had a rise in IgM levels or both antibodies could not be measured in the progress of the disease. Individuals who survived had reduced amounts of IgM (Hou et al., 2020). It is stipulated that accurate serological assays can improve the early diagnosis of the coronavirus, just a very limited number of investigations have juxtaposed the efficiencies of these immunological assays for both symptomatic patients and those that have recovered from the viral attack. The levels of both IgM and IgG are affected by the pedigree of the disease as well as the duration of the infection. IgG offers a good option for rapid diagnosis of severe cases while IgM suits the rapid diagnosis of less severe cases (Ozturk et al., 2020). The production of IgM, IgA, and IgG antibodies against the virus (SARS-CoV-2) was positive from the first day of the manifestation of clinical symptoms as reported by Guo et al. (2020). The current method of diagnosis by quantitative PCR or deep sequencing-based technologies rely on the presence of replicating virus in sufficient amount to ensure sufficient quantitates of the virus is collected. This method often fails to detect the viral infection if the collection procedure is not optimal, or if the patient has low viral load due to the early stage of the disease or suppressed by host immunity, or if the samples were obtained at a late stage in the course of infection (Guo et al., 2020). Reinfection of patients also emerged and raises doubts about sustained immunity to the virus, which is in contrast to predictions of other studies. In assessing the possibility of SARS-CoV-2 reinfection (Bao et al., 2020), in their recent study with a group of *Rhesus macaques* monkeys saw that reinfection did not happen a month post first viral infection, which implies a little and weak immunity in the rhesus monkeys. Patients can be tested positive again, the IgG antibody level rises to four times or more in the plasma, against short and mild period. A cohort of patients who were reinfected and hospitalized had one study subject showing positive outcomes for both rRT-PCR and IgM-IgG tests, another five tested positive for both IgM and IgG but negative for the rRT-PCR test, another three tested positive for rRT-PCR and serum IgG but tested negative for serum IgM (Chen et al., 2020). To increase the sensitivity of SARS-CoV-2 detection, an IgM–IgG combined assay was developed and used to diagnose suspected cases of COVID-19 by Xie et al. (2020). Fifty-six study subjects were recruited and the virus diagnosed with both the rRT-PCR and IgM–IgG antibody tests methods. The study investigated both clinical and laboratory samples and data. The results indicated a link between the duration of virus exposure and subsequently developing a severe form of the disease with a strong immune response (Xie et al., 2020). A high serum IgM numbers were linked to poor results of study subjects with COVID-19 pneumonia (Mózo, 2017).

Young individuals infected with SARS-CoV-2 are seen not to be presenting classical symptoms (Lotfi, Hamblin, et al., 2020) with a fast-viral clearance and decreased IgM with an increased total antibodies, IgG and IgA (Xiao et al., 2020). Xiao et al. (2020) suggest that their study results give a strong basis for viral clearance and antibody kinetics of patients without classical symptoms of COVID-19. Table 3 summarizes some of the major serological tests, comparing them on various parameters.

5 | DISCUSSION

COVID-19 has evolved swiftly from just a cluster of pneumonia-like cases to a pandemic that is still spreading daily. In both clinical and research findings, it has been seen that the serological tests for antibodies are very significant especially when combined with RNA tests like rRT-PCR. There are several drawbacks to the real-time PCR test kits. Initial studies indicated that they recorded high false-negative rates. RT-PCR used for pharyngeal swaps gave different results which shows that they are potentially unstable (Y. Li et al., 2020; Z. Li et al., 2020). These research results serve as a strong basis for the use of various

TABLE 3 An overview comparing major serological assays for COVID-19 with FDA-EUA approval (Espejo et al., 2020)

Serological test	Manufacturer	Test type	Time to result	SARS-CoV-2 biomarkers	Sensitivity and specificity	References
Atellica IM SARS-CoV-2 Total (COV2T)	Siemens Healthcare	Chemiluminescent microparticle immunoassay	~10 min	Total antibody against RBD of S1 protein	100% (42/42) 14 days postsymptom onset/ 99.8% (1089/1091)	https://www.siemens-healthineers.com/en-us/laboratory-diagnostics/assays-by-diseases-conditions/infectious-disease-assays/cov2t-assay
Anti-SARS-CoV-2 Rapid Test	Autobio Diagnostics Anti-SARS-CoV-2	Lateral flow immunoassay	~15 min	IgG and IgM only against S proteinTime	99.0% (299/302)/ 99.04% (309/312) 93.8%	https://www.cardinalhealth.com/en/cmp/ext/med/med-lab/hardy-diagnostics-autobio-anti-sars-cov-2-rapid-test.html
SARS-CoV-2 IgG Assay	Abbott Laboratories	Chemiluminescent microparticle immunoassay	~30 min	IgG only against N protein	100% (88/88) ≥14 days postsymptom onset/ 99.63% (1066/1070)	https://www.corelaboratory.abbott/us/en/offerings/segments/infectious-disease/sars-cov-2
qSARS-CoV-2 IgG/IgM Rapid Test	Cellex	Lateral flow immunoassay	~15–20 min	IgG and IgM only against S and N proteins	93.8% (120/128)/96% (240/250)	https://cellexcovid.com/
LIAISON SARS-CoV-2 S1/S2 IgG	DiaSorin	Chemiluminescent immunoassay	~35 min	IgG against S1/S2 protein	97.56% (40/41) ≥15 days postsymptom onset/99.3% (1082/1090)	https://www.diasorin.com/en/node/11756/
Elecsys Anti-SARS-CoV-2 Atellica	Roche	Electrochemiluminescence immunoassay	~18 min	Total antibody against N protein ~100	100% (29/29) ≥14 days post-symptom onset/ 99.81% (5262/5272)	https://diagnostics.roche.com/us/en/products/params/elecsys-anti-sars-cov-2.html
Platelia SARS-CoV-2 Total Ab assay	Bio-Rad Laboratories	ELISA	~100 min	Total antibody against N protein	92.2% (47/51)/99.6% (684/687) 100%	https://www.bio-rad.com/en-us/sku/72710-platelia-sars-cov-2-total-ab-assay?ID¼72710
VITROS Immunodiagnostic Products Anti-SARS-CoV-2 Total Reagent Pack	Ortho Clinical Diagnostics	Chemiluminescent immunoassay	~50 min	Total antibody against S1 protein	100% (49/49)/100% (400/400)	https://www.orthoclinicaldiagnostics.com/en-us/home/ortho-covid-19-answer

Abbreviations: COVID-19, coronavirus disease; ELISA, enzyme-linked immunosorbent assay; FAD-EAU, Food and Drug Administration-emergency use authorization; IgA, immunoglobulin A; RBD, receptor-binding domain; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.

serological tests that have been approved to diagnose SARS-CoV-2 and consequently in providing clinical supportive care to patients with COVID-19 (Saghazadeh & Rezaei, 2020b; J. Zhao et al., 2020). Excellent results were obtained from other serological tests like the Abbott Architect SARS-CoV-2 IgG assay (Bryan et al., 2020). Immunological assays are capable of compensating effectively for false-negative limitations of rRT-PCR (Qu et al., 2020). Some assays sensitivities were, however, poor in asymptomatic and symptomatic patients during the early phase and may not be recommended for COVID-19 initial diagnostic testing (Imai et al., 2020). Nevertheless, it is unknown which antibodies are optimally successful in the COVID-19 scenario and which of these neutralize and it is still unclear as to the antibody isotype (IgM, IgG, or IgA) (single or combined) is the best option in these different contexts. Table 4 summarizes diagnostic considerations between rt-PCR and serological assays.

5.1 | Producing a vaccine

A high-level selection of IgG antibodies could be helpful in the production of vaccines and in the treatment of SARS-CoV-2 by convalescent plasma therapy (Infantino et al., 2020). In the future, this detailed collation of the latest immunoassays against SARS-CoV-2 will provide insights into the detection and characterization of monoclonal antibodies for developing a SARS-CoV-2 vaccine (C. Y.-P. Lee et al., 2020).

5.2 | Immunity to COVID-19

Humoral immune response, in particular, the production of nAb, plays a protective function by restricting infection at a later stage and preventing reinfection in the future (Z. Li et al., 2020). Currently, SARS-CoV-2-infected polyclonal antibodies have been used to treat SARS-CoV-2 infection but no SARS-CoV-2-specific neutralizing nAbs have been reported (Jiang et al., 2020), but there is a clear association between antibody titers for neutralization and the numbers of virus-specific T cells (Ni et al., 2020). The strength and length of immunity following infection are the main challenges for herd immunity. Past studies have shown that circulating antibodies to SARS-CoV or MERS-CoV last for at least 1 year while maintained IgG levels have been kept for more than 2 years post-SARS-CoV infection. Presently, several studies that characterize adaptive immune responses to SARS-CoV-2 infection have shown that most COVID-19 convalescent individuals have detectable nAbs that correlate with SARS-CoV-2 infection (Long et al., 2020). It is seen that patients that are positively responding to treatment and have redetectable viral RNA showed lesser IgG amounts proposing that the reduction in the amount of IgG as the patient recovers gives a hint that a sustained immunity from IgG is not likely and this should be thoroughly assessed to ascertain a conclusive result since pertinent issues concerning herd immunity against SARS-CoV-2 relies on the ability of IgG to confer sustained and life-long immunity to people previously infected by the virus (Randolph & Barreiro, 2020).

5.3 | Way forward

Viral serological testing is an important diagnostic tool for infection with SARS-CoV-2. IgG's positive levels and titer variance are greater than IgM's in COVID-19 (Jin et al., 2020). With the state of COVID-19 science, a combined IgG/IgM test tends to be a safer option in terms of sensitivity than testing a single antibody (Kontou et al., 2020). Compared with a single IgM or IgG test, the IgM–IgG combined assay has greater utility and sensitivity. It can be used in hospitals, clinics, and research laboratories for the rapid screening of SARS-CoV-2 carriers, symptomatic or asymptomatic (Z. Li et al., 2020). Serological testing for SARS-CoV-2 could play a significant role in prescribing individuals before admission to vaccine clinical trials and tracking vaccine recipients' temporal immune responses and eventually helping

TABLE 4 Practical diagnostic considerations of RT-PCR test and serological immunoassay (Ravi et al., 2020)

	Antibody test	RT-PCR test
Primary utility	Screening test for stratifying newly infected patients, remotely infected patients, and asymptomatic patients; surveillance assay for seroprevalence, immunity, and vaccination efficacy	Standard of care diagnosis of newly infected and/or active COVID-19 patients
Merit	Easy to use serological sample	Highly specific
Limitation	Generally, not as accurate as of the RT-PCR test, with false positives and false negatives. False positives in a low prevalence population can give an exaggeration of exposure and immunity. (e.g., a specificity of 99% in a population of 1% prevalence can lead to ~50% of positive results being false)	Sensitivity can suffer due to sampling errors or insufficient viral load (false negatives). Inactive virus and viral fragments could also test positive (false positives)
Remedy	Assay validation with sufficient positive and negative sample cohorts; cannot be used to diagnose newly infected patients, but can be used as a screening test (optimizing antibody test sensitivity for rule-out, optimizing specificity for rule-in)	Testing twice sequentially to improve sensitivity (e.g., a single test sensitivity of 70% would result in a two-test sensitivity of 91%) and/or combination with chest CT scan and clinical factors

Abbreviations: COVID-19, coronavirus disease; CT, computed tomography; RT-PCR, reverse-transcriptase polymerase chain reaction.

to determine vaccine effectiveness and very important to remember that serological assays capable of detecting a response to the nAb will be crucial to producing the most reliable results for immunogenicity studies. In particular, whether such antibodies may mediate antibody-dependent enhancement leading to adverse effects is an important issue to be addressed through efficacy studies and postvaccine surveillance (Theel et al., 2020). Though there has been considerable progress with COVID-19 science, some findings indicate that none of the serological tests tested early in the course of infection allowed the detection of SARS-CoV-2-specific antibodies and were only reliably positive longer than 4 weeks after the onset of the disease. Suggesting that, the use of serology for acute disease diagnosis must be treated with caution and rRT-PCR for virus detection remains the method of choice (Bastos et al., 2020; Perera et al., 2020).

Overall, researching on SARS-CoV- and MERS-CoV-specific nAbs should, therefore, provide valuable guidance for the rapid design and production of SARS-CoV-2-specific nAbs. So far, the development of serological tests targeting a wide range of viral antigens has certainly helped to diagnose COVID-19 patients accurately. Contact tracing, viral reservoir recognition, and epidemiological studies are some aspects of COVID-19 validated by serological assays. These are assays will be instrumental in tracking patient contacts, serosurveillance studies, and assessment of vaccines (Okba et al., 2020).

6 | CONCLUSION

Antibodies detection, thus, IgM and IgG, in patients with COVID-19 is a rapid and easy technique. Using the serological method of detecting SARS-CoV-2 in addition to RNA testing is very important in our quest to unravel the course of disease progression in patients with COVID-19, right from the onset to end of disease in an individual. The serological test for IgG and IgM antibodies is a technique that can be relied on since this method proves to be accurate and also sensitive in detecting the virus (Krüttgen et al., 2020; Pan et al., 2020). However, it is recommended that this technique should be performed together with rRT-PCR or RNA test to give more certainty to the results in terms of sensitivity and accuracy. This approach will give room for rapid diagnosis and timely intervention to COVID-19 patients and suspected carriers from contact tracing especially when they are tested negative using the rRT-PCR method. Moving forward, there is an urgent need for medical research to determine and ascertain the number of antibodies against SARS-CoV-2 for the prediction of the outcome of COVID-19, as suggested by (Du et al., 2020; Yazdanpanah et al., 2020) knowing that there exists a rather complex relationship in the number of antibodies, the prognosis of COVID-19, and the start of symptoms. There is also the need to probe into ways of detecting the antibody levels of a patient which can aid in correct forecasting of disease progress and severity in a patient if it is ascertained accurately at the start of the disease (Fathi & Rezaei, 2020). S-IgG developed steadily in severe cases. It was significantly lower in severe patients by 2 weeks after the onset than nonsevere patients, which may explain the longer hospital stays and positive days of nucleic acid in severe patients. Therefore, tracking S-IgG's kinetics can help predict prognosis (Sun et al., 2020).

CONFLICT OF INTERESTS

The authors declare that there are no conflict of interests.

DATA AVAILABILITY STATEMENT

Data sharing is not applicable to this article as no new data were created or analyzed in this study.

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