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Covid-19 Detection Methods: A Review

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Abstract

Coronavirus infection 2019 (COVID-19) diagnosis is crucial for prompt isolation of infected individuals and treatment of infected patients. Numerous methods exist for detecting COVID-19, including molecular testing or nucleic acid amplification tests (NAATs) and serological or antibody-based tests. NAAT detects the pathogen's genetic material, while serological tests detect antibodies. For the purpose of detecting COVID-19, radiological imaging of the lungs and viral antigen detection in vitro can also be used. This review article compares and contrasts several methods used to identify COVID-19 and discusses their respective merits and drawbacks.

Keywords: Coronavirus Disease, Covid-19 diagnosis, NAAT, Serological tests, Antibody based tests

Introduction

The novel human coronavirus disease 2019 (COVID-19) was first reported in Wuhan, China, in 2019, and subsequently spread globally to become the fifth documented pandemic since the 1918 flu pandemic. The first official cases of COVID-19 were recorded on the 31st of December, 2019, when the World Health Organization (WHO) was informed of cases of pneumonia in Wuhan, China, with no known cause. On the 7th of January, the Chinese authorities identified a novel coronavirus, temporarily named 2019-nCoV, as the cause of these cases.

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Weeks later, the WHO declared the rapidly spreading COVID-19 outbreak as a Public Health Emergency of International Concern on the 30th of January 2020. It wasn't until the following month, however, on the 11th of February that the novel coronavirus got its official name - COVID-19.

A coronavirus is a large group of viruses that includes the Middle East respiratory syndrome coronavirus (MERS-CoV), the severe acute respiratory syndrome coronavirus (SARS-CoV), and the most recent one, SARS-CoV-2, also known as coronavirus disease 2019 (COVID-19). In early December 2019, SARS-CoV-2 occurred and eventually affected more than 585 million people globally. According to a recent figure by the World Health Organization (WHO), more than 6.4 million deaths from SARS-CoV-2 have been reported [1]. The distinct variants of COVID-19 are targeting lungs, consequently resulting severe damage towards breathing [2-3]. The virus spreads through human-to-human or human-to-surface interactions and mainly triggers flu, fever, cough, ageusia, and respiratory problems [4-5]. The clinical symptoms of COVID-19 are nonspecific and range from asymptomatic to fatal pneumonia. Common symptoms include fever, myalgia (muscle pain), cough, shortness of breath, and sudden appearance of olfaction and taste disturbances [6]. Headaches, nausea, dizziness, diarrhea, and abdominal pain are less common in patients infected with SARS-CoV-2 [6]. Infected individuals may develop symptoms 2e14 days after infection, depending on the age and immune system of the patient [7].

COVID-19 is highly contagious, and the speed and extent to which it spreads are not merely due to transmission from symptomatic persons. Several reports have shown that the transmission of COVID-19 can occur in individuals who are pre-symptomatic (when the virus is detected before the onset of symptoms) [8] or asymptomatic (when the virus is detectable with no symptoms) [9]. In addition, vaccinated individuals can be carriers of SARS-CoV-2 while remaining asymptomatic [10], which makes the containment of the virus more challenging. Therefore, early detection of the disease and isolation of infected individuals from the healthy population are imperative to addressing the COVID-19 pandemic.

Current COVID-19 testing techniques are classified into two general groups: nucleic acid amplification tests (NAAT) or molecular tests, and serological tests, also known as antibody-based tests. Molecular tests detect the genetic material of the virus in respiratory secretions, oropharyngeal and nasopharyngeal swab samples, as well as saliva by targeting one or more parts of the SARS-CoV-2 genome. Some of these targets include spike (S), which is composed of two subunits (S1 + S2), nucleocapsid (N), envelope (E) gene, and regions in the first open reading frame of the RNA-dependent RNA polymerase (RdRp) gene. Currently, reverse transcription quantitative polymerase chain reaction (RT-qPCR) is considered as the “gold standard” and is consistently used to diagnose COVID-19. Alternative amplification techniques include recombinase polymerase amplification (RPA) and loop-mediated isothermal amplification (LAMP), which have been developed in the past decade, and are timely, simpler, and less expensive than RT-qPCR.

In addition to NAAT, COVID-19 diagnostic tests that detect viral proteins (antigens) and antiviral antibodies have been developed. Serological tests measure seroconversion in plasma/serum via different types of assays such as enzyme-linked immunosorbent assay (ELISA), chemiluminescent immunoassay (CLIA), colloidal gold immunochromatographic assay (GICA), and lateral flow immunoassay (LFIA). However, because seroconversion of infected individuals depends on the stage of infection, serological tests may not detect antibodies in those with active infection and are more appropriate for individuals who have been pre-exposed to SARSCoV-2. In some instances, imaging of the lungs can be used to diagnose patients with COVID-19, which is also appropriate for assessing the severity of the disease. Computed tomography (CT), chest radiography (CXR), and lung ultrasound (LUS) are common imaging modalities for diagnosis of COVID-19. Tests based on imaging of the lungs have some shortcomings, such as being limited to healthcare settings and requiring professional radiologists to assess the results. Moreover, the results are time dependent and can vary depending on the stage of infection. Thus, imaging of the lungs cannot always rule out the probability of SARS-CoV-2 infection. In this review, various testing techniques currently available for the diagnosis of COVID-19 are described by outlining their merits and demerits as well as suitable indications for a more accurate diagnosis. The COVID-19 pandemic may not be the last

pandemic of the century. Therefore, a review that highlights different diagnostic methods for monitoring SARS-CoV-2 infection may be useful for selecting appropriate diagnostic techniques.

Nucleic Acid Amplification Tests (NAAT)

In this article following methods have been discussed:

- RT-qPCR
- Isothermal amplification (LAMP and RPA)
- Clustered regularly interspersed short palindromic repeats (CRISPR)
- Sequencing-based detection method

RT-qPCR

Quantitative reverse transcription PCR (RT-qPCR) is used when the starting material is RNA. In this method, RNA is first transcribed into complementary DNA (cDNA) by reverse transcriptase from total RNA or messenger RNA (mRNA). The cDNA is then used as the template for the qPCR reaction. COVID-19 can be confirmed by the identification of SARS-CoV- 2 genome using RT-qPCR. The process involves respiratory sample collection, RNA extraction and purification, followed by RT-qPCR. RT-qPCR can be used as a qualitative or quantitative test. The quantitative test claims to provide information regarding viral load, whereas when applied qualitatively, the presence or absence of a particular pathogen is reported. A qualitative test is usually an end-point determination although when used with target-specific fluorescent probes, the real-time amplification plots are helpful to ascertain the quality of the reaction. However, the widespread use of RT-qPCR as a quantitative research tool has resulted in its extension to quantitative diagnostic usage, where results are interpreted in terms of viral load and infectiousness.

Since the identification of SARS-CoV-2, numerous RT-qPCR assays that target different regions of the SARS-CoV-2 genome with different limits of detection (LOD) have been developed and used worldwide which are presented in below table. [11-18] LOD is defined as the smallest amount of analyte (RNA copies in the case of SARS-CoV-2

molecular tests) detected in a sample, and the lower the LOD, the higher the analytical sensitivity of the test.

Table 1: RT-qPCR tests targeting different regions of the SARS-CoV-2 genome

Test	**Target**	**Sample source**	**LOD**
RT-qPCR (RdRp, E, and N assay)	RdRp, E, and N genes	Throat, sputum, and nose swabs	RdRp: 3.6 RNA copies/reaction E: 3.9 RNA copies/reaction N: 8.3 RNA copies/reaction
RT-qPCR (RdRp-P2 assay)	RdRp gene	Respiratory specimens, saliva, sputum, plasma, urine samples and stool/rectal swabs	18 TCID50/mL RNA from culture lysate, 3.6 RNA copies/reaction (in vitro viral RNA transcripts)
RT-qPCR (RdRp/Hel assay)	RdRp/Hel	Respiratory specimens, saliva, sputum, plasma, urine specimens and stool/rectal swabs	1.8 TCID50/mL with genomic RNA from culture lysate, 11.2 RNA copies/reaction (in vitro viral RNA transcripts)
RT-qPCR (pan-CoV assay)	RdRp gene	Nasopharyngeal swabs, saliva specimens, and rectal swab	4 to 400 RNA copies/reaction, depending on the coronavirus
Multiplex RT-qPCR	N gene (N1 and N2)	Nasopharyngeal swabs	<5 RNA copies/reaction
Multiplex RT-qPCR	N and E genes	Nasopharyngeal and sputum swabs	<25 RNA copies/reaction
OSN-qRT-PCR	ORF1ab and N genes	Respiratory specimens	1 RNA copy/reaction
RT-qPCR (nsp1 assay)	nsp1 gene	Nasopharyngeal and saliva samples	18 TCID50/mL viral RNA
RT-qPCR (nsp2 assay)	nsp2 gene	Respiratory specimens, saliva, plasma, urine samples, and stool/rectal swabs	1.8 TCID50/mL viral RNA

Although RT-qPCR is commonly used to diagnose COVID-19, the turnaround time is long and requires expensive tools, trained personnel, and a stable power supply. In addition, the results may be affected by human errors, incorrect sample collection, and technical issues, which can give rise to false-negative or false positive results. Consequently, individuals suspected of having COVID-19 may not be diagnosed in time and create a risk for the unaffected population. Therefore, RT-qPCR tests should not be the only means of diagnosing patients with COVID-19.

Isothermal Amplification- LAMP

Loop-mediated isothermal amplification (LAMP) is a nucleic acid amplification technique that is primarily used for diagnosis and detection of diseases. It is a powerful amplification method that is carried out in an isothermal setting, therefore changes in the temperature typically required by conventional PCR is not necessary. Amplification and detection of the nucleic acid could be completed at the same time, in a single step, by incubating the nucleic acid sample, 4 (or 6) specifically designed primers, and Bst DNA polymerase in the same test tube at about 60 to 65 °C, depending on the optimal LAMP temperature [19].

Recently, Lamb et al. [20] reported to develop a rapid screening LAMP test for COVID-19 with an assay time under 30 min. However, the assay was validated using simulated patient samples, where the samples were spiked with viral RNA. Similarly, Zhang et al. [21] detected SARS-CoV-2 from purified RNA or patient cell lysis samples using a colorimetric LAMP-based assay. The results were further analyzed and approved using RNA samples extracted from the respiratory swabs of patients with COVID-19. The performance of this test was reported to be comparable to that of commercial RT-qPCR tests. However, the test performance was validated on only 7 patients.

To develop a fast and simple-to-use COVID-19 test kit, Huang et al. designed 4 sets of LAMP primers that targeted different gene regions of SARS-CoV-2 [22]. Two primer sets (N1 and N15) target the N gene of the virus, while the other two (S17 and O117) target the S gene and ORF1ab gene of SARS-CoV-2, respectively. The ORF1ab gene targeted is close to the 5-end of the virial RNA, while the N gene is close to the 3-end.

The specificity of all primers for COVID-19 detection was confirmed to be high, as they do not cross react with human DNA, indicating that these primers can be used in the detection of clinical samples. The accuracy of the tests is acceptable, as the test results are in good agreement with the conventional RT-qPCR. In detecting virial RNA, the N1 primer set performed the best with a sensitivity of 2 RNA copies per reaction of 25μL in 20 min of reaction time. The N15 and S17 primers have the same detection limit of 2 RNA

copies per reaction, but in 30 min of reaction time. The O117 primer set could only detect 20 RNA copies per reaction in 30 min. An additional one-step test using stem cells was administered, in order to investigate if RNA extraction can be omitted from the RT-LAMP based nucleic acid amplification. As observed, 40 min of the RT-LAMP process caused a color change visible to naked eye, indicating that it is possible and feasible to run RT-LAMP without the RNA extraction step. Impressively, both the N15 and O117 primer sets accurately detected all 8 positive and all 8 negative clinical samples, indicating that this developed test can be used to replace the classic RT-PCR tests for COVID-19 detection.

Recently,Yu et al. [23, 24] have developed an iLACO assay (isothermal LAMP based method for COVID-19) to target on ORF1ab gene for molecular diagnosis of the novel coronavirus. The iLACO is vastly faster than the conventional PCR method due to its high amplification efficiency. The iLACO detection process takes15-40 min, depending on the virial load in the sample. In this experiment, the optimal primer set was determined from testing as well as software-enabled comparison between the sequences of designed primers and other viruses' genome. In read out of the amplification step, SYBR green dye was first used for the enhanced fluorescence resulted from the intercalation of dyes in dsDNA. However, in order to increase the sensitivity of fluorescence detection at lower dilutions of viral RNA, GeneFinder dye with blue light was also used.

Using synthesized RNA equivalent to COVID-19, the limit of detection of iLACO assay is about 10 copies of the ORF1ab gene, which is on par with Taqman based qPCR assay. In addition, the as developed iLACO was subject to the challenge of testing 43 positive clinical samples con-firmed by RT-qPCR in Shenyang, China. The sensitivity of this diagnostic test is reasonable with 97.6% (42/43) of 43 positive samples being correctly detected except a singular negative. A low viral RNA load may result in the false negative result, which may be attributed to the viral RNA loading below the limit of detection. How the sample amount affected the assay was also investigated. When the sample volume increased from 1μL to 5μL, variable results were observed, which may be attributed to the presence of either Tris or EDTA used in the RNA dilution buffer. Therefore, concentration of the RNA buffer would have to be optimized to improve the accuracy.

Overall, this study demonstrated that well-designed RT-LAMP primer set possess high specificity and can generate high sensitivity and high accuracy in COVID-19 clinical sample test.

Isothermal Amplification- RPA

RPA is the latest and faster LAMP approach. Reverse transcriptase can be incorporated into RPA (RTRPA) to amplify RNA targets. Optimal temperature range (37-42ºC) and short experimentation time (approximately 10 min) are the benefits of RPA. PCR primers could also be used for the RPA assays. Kim et al. [25] employed the single-strand RPA (ssRPA) method for the detection of SARS-CoV-2. The ssRPA method includes amplification of double-stranded DNA, conversion to ssDNA, and sequence specific hybridization-based readout. ssRPA showed 100% specificity and sensitivity in all types of samples, such as buffer-spiked samples, nasopharyngeal swabs in water, and saliva samples. RPA and LAMP can be combined into a two-stage amplification procedure referred to as RAMP. The COVID-19 University of Pennsylvania rapid amplification assay designed by El-Tholoth et al. [26] is a nested nucleic acid amplification method that can be performed with minimal sample processing in closed tubes and is compatible with colorimetric or fluorescence readout. This assay takes advantage of two stages of isothermal amplification, thereby eliminating false-negative results and increasing sensitivity. The first stage is the RPA carried out in the cap of the tube at 38ºC, and the second stage is the LAMP which takes place inside the tube at 63ºC. The LOD of this assay has been reported to be 7 copies of viral RNA/reaction and is more sensitive than conventional RT-qPCR assays that use purified targets or LAMP assays without RPA.

Clustered regularly interspersed short palindromic repeats (CRISPR)

CRISPR is a different method for detecting SARS-CoV-2 in addition to RT-qPCR and isothermal amplification methods. Foreign RNA or DNA is recognized and cut by (Cas) proteins linked to CRISPR. Due to these technologies' excellent accuracy and precision, they are frequently used in genome editing applications. Due to their nuclease activity, the Cas proteins Cas12a and Cas13a have been utilized to diagnose illnesses. Cas13a is employed for RNA or DNA detection in a technique known as specialized high

sensitivity enzymatic reporter unlocking (SHERLOCK). This approach does not require specialized PCR equipment because the target sequence is amplified using RT-RPA and T7 transcription. DNA detection is achievable when reverse transcriptase is used to convert RNA into DNA. Following binding to the target sequence, Cas13a is activated. An RNase called active Cas13a randomly cuts a reporter RNA, generating a fluorescence signal that may indicate the presence of viral RNA.

One of the first teams to employ the SHERLOCK technique to pinpoint the ORF1ab and S genes of SARS-CoV-2 was Zhang et al. [27]. The LOD of this test has been reported to be 10-100 copies of RNA/mL of input, and lateral flow dipstick findings can be achieved in one hour. Similar to this, Joung et al. [28] developed the SHERLOCK testing in one pot diagnostic platform, which is a one-step reaction with a LOD of 100 copies of SARS-CoV-2 per sample that runs for an hour. Additionally, this assay's sensitivity and specificity were also reported to be 97% and 100%, respectively.

Sequencing-based detection method

The use of sequencing platforms is an additional option that can be considered for the diagnostic process of COVID-19. Identification of pathogens and monitoring of viral mutations that may increase transmissibility are made possible by the sequencing-based detection method. Metagenomic next-generation sequencing was used to discover SARS-CoV-2 for the first time [29]. Reverse transcription to create cDNA from respiratory specimen RNA was followed by PCR amplification. By utilizing tagged nucleotides to sequence the amplified DNA, the target sequence was found during polymerase elongation by keeping an eye on the fluorescence signal. To examine overlapping DNA regions, the sequences were next aligned with databases [29]. To find SARS-CoV-2 and other respiratory viruses, sequencing procedures based on nanopore target sequencing (NTS) have been created. NTS has a better sensitivity for the detection of SARS-CoV-2 than conventional RT-qPCR. NTS was used by Wang et al. [30] to target the SARS-CoV-2 genome as well as other respiratory viruses. 10 RNA copies/mL was recorded as the LOD. Additionally, this approach allows for the simultaneous detection of mutations. The procedure does, however, require 6–10 hours, and the turnaround time is longer than RT-

qPCR. NTS can therefore not be utilized for COVID-19 mass screening, but it can be used to supplement RT-qPCR and find viral mutations.

Antibody-based (serological) assays

Innate and adaptive immune systems are crucial in reducing the severity of disease. B and T cells are both a part of adaptive immunity. Following virus entrance, a strong B cell response occurs, resulting in the release of antiviral antibodies. T cell receptors (TCRs) on T cells allow them to recognize viral antigens and destroy virus-infected cells, hastening the generation of virus-specific antibodies. Clonal expansion caused by T cell activation allows for the proliferation of T cells with consistent TCRs and identical antigen-recognition capacities [31]. Next-generation sequencing technologies can be used to assess TCR repertoires. There is currently minimal information available regarding variations in TCR repertoires among COVID-19 patients. The TCR repertoire profiles of COVID-19 cases range from mild to severe, according to reports [32].

As a supplement to NAAT, serological or antibody testing can be utilized to find antibodies against viral proteins that are present in the host. The N protein, S1 and S2 subunits, as well as the receptor-binding domain (RBD) of the S protein are all targets of the current COVID-19 serological assays. The virus can enter the host cells when RBD binds to the angiotensin-converting enzyme 2 receptor. As a result, the S protein is one of the most researched targets and is crucial in initiating immunological responses. According to reports, the SARS-CoV-2 N protein is more immunogenic than the S protein and causes the development of antibodies sooner. Additionally, compared to experiments targeting the N protein, a study demonstrating the S protein of SARS-CoV-2 has greater cross-reactivity with antibodies generated against other related coronaviruses. Which antigen is superior in terms of the generation of related antibodies is still up for debate. Antiviral IgM and IgG antibodies were revealed to be a sign of viral infection in the SARS pandemic of 2002–2003. The diagnosis of COVID-19 can be aided by identifying IgM and IgG because SARS-CoV-2 and SARS are closely related. Antibodies against COVID-19 have unpredictable kinetics. IgM is frequently the first antibody made when an infection occurs and is connected to a basic immune response. In order to identify recent infections, IgM

antibody detection is used. The production of IgG antibodies, on the other hand, is known to occur at a later stage of infection and is essential for the development of long-term immunity and immunological memory. According to one study, patients with COVID-19 can detect both IgM and IgG as early as day 4 after the onset of symptoms [33]. IgG antibody levels remained constant and began to fall at day 28 after the onset of symptoms, but IgM antibody levels started to decline at week 3 of illness. Even sooner than IgM and IgG antibodies, IgA antibodies can be identified. IgA, however, cannot be a reliable marker for the detection of SARS-CoV-2 because it reacts with other similar viruses [34]. In general, the IgG antibody has a higher level of specificity than the IgM antibody, and its levels are higher in severe COVID-19 cases compared to moderate cases. As a result, IgG levels and disease severity are related. Depending on the degree of the disease, patients with COVID-19 have different antibody titers. Acute cases of COVID-19 have been shown to have earlier seroconversion and greater IgM, IgG, and IgA titers than mild to moderate cases. It's interesting to note that a study found that people pre-exposed to SARS-CoV-2 who received one dose of the messenger RNA vaccine had higher antibody titers and comparable immunogenicity than a naive person who received two doses of the same vaccine [35]. For the assessment and quantification of SARS-CoV-2 IgG and IgM antibodies, established techniques include CLIA, LFIA, ELISA, and GICA (Table 2) [36–40].

Table 2: Different serological assays available for SARS-CoV-2 detection

Test	**Sample source**	**Target**	**Sensitivity (%)**
ELISA	Serum samples	IgM, IgG or IgA	IgM: 77.94 IgG: 82.35 IgA: 94.12
Gold-ICG assay	Serum samples	IgM and/or IgG	IgM: 57.1 IgG:81.3 Combined detection: 82.4
Peptide-based magnetic CLIA	Serum samples	IgM and/or IgG	IgM: 57.2 IgG: 71.4 Combined detection: 81.52
LFIA	Finger prick blood, serum, and blood plasma samples	IgM and IgG	Combined detection: 88.66-94.83
Colloidal gold-based ICG strip assay	Blood plasma	IgM and/or IgG	IgM: 11.1e74.2 IgG: 3.6-96.8

Test	Sample source	Target	Sensitivity (%)
			Combined detection: 11.1-96.8
ELISA: enzyme linked immunosorbent; ICG: immunochromatographic; CLIA: chemiluminescent immunoassay; LFIA: latera flow immunoassay.			

The sensitivity of this antibody assay was evaluated across all three stages of the infection: early, intermediate, and late. The positive rates for IgG and IgM were quite modest during the early stages of infection and began to rise as the illness progressively worsened. As a result, the sensitivity of antibody tests rises in relation to the infection stage. In comparison to molecular tests, antibody tests are less complicated, involve less equipment, and can be completed more quickly. The latter, however, provides the most accurate diagnosis for COVID-19 patient diagnosis. Additionally, antibody testing are more useful for diagnosing COVID-19 in those who have already been exposed to the disease or in severe forms of the disease. They can therefore be used in conjunction with molecular tests.

Alternative methods:

- Antigen tests
- Electrochemical approach
- Imaging of the lungs

Antigen tests

Instead of the viral genome, antigen assays identify viral antigens or bits of viral proteins. These tests have been made available in the commercial market for a number of years. Antigen assays are more precise than antibody tests in the diagnosis of COVID-19 because they are target-specific. The fluorescent immunochromatographic (FIA) assay is the antigen test for SARS-CoV-2 detection that is most widely employed. Using nasopharyngeal swabs and urine samples, the FIA assay created by Diao et al. [41] identified the N antigen of SARSCoV-2 in 10 minutes. By using RT-qPCR, this assay's sensitivity was confirmed, and it was found to be 68% sensitive and 100% specific. Even though antigen tests are easy and the results are ready in just a few minutes, they are not accurate enough because they may not be able to find active SARS-CoV-2 infections

and are more likely to give false-negative results. This can be caused by insufficient or inconsistent viral loads in the patients. Testing symptomatic and acute patients with sufficient virus loads is better suited to antigen tests [42].

Electrochemical approach

Electrochemical biosensors have a lot of untapped promise when it comes to the development of COVID-19 diagnostic tests that are both fast and sensitive. A graphene-based field-effect transistor (FET) biosensor has been made to detect SARS-CoV-2. Graphene sheets coated with antibodies against SARS-CoV-2 S protein act as a sensor to detect signal production in clinical samples when SARSCoV-2 binds [43]. Without sample pretreatment or labeling, the FET biosensor differentiated the SARS-CoV-2 S protein from that of MERS in clinical samples with a LOD of 242 copies/mL. The assay developed by Mavrikou et al. [44] is another biosensor-based test. It looks for the S1 protein of SARS-CoV-2 and is connected to a portable readout device that can be controlled by a smartphone or tablet. With a semilinear response range between 10 fg and 1 g/mL and a LOD of 1 fg/mL, the results can be acquired in as little as 3 minutes. This biosensor can be used for extensive COVID-19 patient screening because to its quick sample-to-result time and lack of pre-sample processing.

Imaging of the lungs

Background Chest CT is a crucial addition to RT-qPCR tests because it is quicker and easier to do than molecular tests and gives details on the severity of the disease that molecular tests cannot. However, depending on the infection stage, CT readings can vary. Bilateral ground-glass opacities on the CT scan are frequently observed in COVID-19 patients, mostly in the lower and peripheral lobes, and are comparable to those in SARS patients [45]. Ground-glass opacities and vascular thickening are more likely to be found in COVID-19 CT scans than tree-in-bud sign, nodules, and peripheral effusion are, according to studies comparing patients with COVID-19 and those with viral pneumonia that is not COVID-19, such as influenza [46].

It has been shown that patients with negative RT-qPCR results occasionally have chest CT results that exhibit anomalies similar to those of COVID-19 [47]. As a result of the CT signs improving 6–12 days after the onset of symptoms, a chest CT performed on patients with COVID-19 may be negative at the time of initial presentation, and this limits the accuracy of the test. The usage of CXR and LUS in COVID-19 patients is quite rare. Patients with COVID-19 have similar CXR and CT features, with both displaying ground-glass opacities and/or bilateral peripheral consolidation. Similar to CT, CXR signals appear 10–12 days after the onset of symptoms, during the later stages of infection. Patients with COVID-19 present with uneven or interrupted pleural line thickening, minor subpleural consolidations, and B lines as LUS characteristics. Lung imaging is essential for the treatment of SARS-CoV-2 infection. To determine the effectiveness of LUS and CXR in the diagnosis of COVID-19 patients, more research is necessary.

Conclusion

The rapid global spread of COVID-19 calls for sustained investment of diagnostic testing. There is a rapidly expanding pool of testbeds designed to identify SARS-CoV-2. There are pros and cons to every type of testing method. Therefore, it is essential to use a set of tests, rather than depending on a single detection method, to diagnose patients with COVID-19. Since its inception, RT-qPCR has become the gold standard for COVID-19 testing. However, due to sampling error, timing of sample collection, and technical faults, RT-qPCR tests take a long time and can sometimes yield false-negative or false-positive results. For this reason, it is important to employ both molecular tests and additional methods of testing, such as antibody or antigen-based testing, to confirm suspected instances and take the necessary medical treatments. In spite of the fact that vaccines are the only surefire way to put an end to the COVID-19 pandemic, effective, affordable, and reliable diagnostic tests for the virus are urgently needed to save lives in the meantime.

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