Abstract: The emergence of SARS-CoV-2, responsible for COVID-19 disease, has caused a substantial worldwide pandemic and has become a significant public health problem. World Health Organization (WHO) has declared COVID-19 as a devastating health emergency for all countries. Public health officials continue to monitor the situation closely to control this new virus-related outbreak. In order to continue to manage this pandemic, a fast and sensitive diagnosis of COVID-19 is attempted. Emerging tests have become an essential part of the management of the COVID-19 crisis. This review article aims to provide a detailed explanation of ongoing and new diagnostic technologies for SARS-CoV-2 and a summary of method principles. Examples of new diagnostic methods for providing efficient and rapid diagnostic tests for managing the SARS-CoV-2 outbreak are also mentioned.

Keywords: COVID-19; diagnosis; performance; SARS-CoV-2.

Introduction

Respiratory viruses threaten human life throughout centuries. The pandemic outcomes of RNA viruses generally occur because of changes in their molecular mechanisms. Emerging health threats of these viruses are originating from animals, with a 70% rate. After several mutations, pathogens become human viruses with subsequent spread in human populations [1].

Such a novel coronavirus (SARS-CoV-2) observed with acute respiratory illness emerged in Wuhan, China, in December 2019. By the end of March 2020, the virus has spread all over the world and caused the most prominent global outbreak [2]. This unpredictable pandemia indicated the necessity to develop readily available, accurate, fast, and reliable diagnostic test methods for the detection of viral pathogens [3].

In vitro diagnostic methods for human pathogens have changed significantly with the development of novel tests and the availability of updated methods. After the revelation of pandemia, these new tests are started to use in hospitals that facilitate to identify and treat the patients [3].

Currently, the tests used for COVID-19 can be divided into two groups. The first group contains tests for the detection of the presence of the virus RNA, antigen and antibody detection tests. They are used for the screening of infections in key target groups such a person who is infectious or recovering from COVID-19. The second group of tests detects the antibodies that occurred against SARS-CoV-2. The immunity gained by the antibodies is a very complex system and yet full of many unknowns. Once clarified, such antibody tests are going to be an essential

*Corresponding author: Assist. Prof. Ebru Saatçı, Biology Department, Faculty of Science, Erciyes University, Kayseri, Turkey, E-mail: saatci@erciyes.edu.tr
tool in developing emerging strategies along with direct virus detection [4].

**Laboratory tests for COVID-19**

**Test materials**

Different types of specimens are taken from suspected COVID-19 patients. Mostly these specimens are obtained with inevitable inaccuracy. Therefore, standardization of diagnostic accuracy of additional specimen types has crucial importance for laboratory diagnosis and monitoring of SARS-CoV-2 pandemic. Also, the clinical picture varied in various cases, and some patients only show asymptomatic infection, which is acutely endangering for control strategies [5, 6].

According to various available tests, urine, blood, stool, oropharyngeal swab, nasopharyngeal swap [6], sputum, bronchoalveolar lavage fluid [5], and saliva [7, 8] samples are collected from the COVID-19 patients.

**Hematological laboratory testing**

In the early stages of COVID-19, it is given that the total count of leukocytes decreased or remained as usual, with a reduced number of lymphocytes and with an increased or regular amount of monocytes. The number of CD4 and CD8 T cells is significantly reduced [9], and due to these changes, cytokine monitoring is getting crucial in the management of patients with severe symptoms. Cytokine Release Syndrome (CRS or Cytokine Storm) [10] activation in patients’ immune system causes an increase of inflammatory cytokines and chemokines in the circulation system, such as Granulocyte macrophage-colony stimulating factor (GM-CSF), Interferon-gamma (IFN-γ), macrophage inflammatory protein-1alpha (MIP-1α), tumor necrosis factor-alpha (TNF-α), Interleukin-2 (IL-2), IL-4, IL-6, IL-8, IL-10, IL-13, IL-22, and IL-17A [11]. In order to control the release of cytokines, the whole cytokine panel is investigated by researchers for COVID-19 patients.

Besides cytokine storm, macrophage activation syndrome (MAS) or secondary haemophagocytic lymphohistiocytosis (sHLH) is also seen in COVID-19 patients [12]. Inflammatory factors (IL-1, IL-6, IL-10, IL-18, IFNγ, and TNF-α) are monitored for the presence of MAS/sHLH syndrome [9, 12].

COVID-19 may cause severe adult respiratory distress syndrome (ARDS) with consequent release of pro-inflammatory cytokines IL-1β and IL-6. Due to their importance, IL-1β and IL-6 become the most studied cytokines in the panel [12, 13]. Also, monitoring of the suppression of IL-1β and IL-6 shows the therapeutic effect of treatments in COVID-19 disease [13].

**Biochemical and other laboratory testings**

Classical laboratory tests for SARS-CoV-2 infection, including blood gas analysis, liver and kidney function, myocardial enzyme, myoglobin, erythrocyte sedimentation rate (ESR), procalcitonin (PCT), lactate, D-dimer, CRP, ferritin amount, and others are performed in the hospital laboratories [9]. Especially highly elevated CRP and hyperferritinemia is found as the key to diagnosing MAS/HLH [12].

**Emerging diagnostic tests for COVID-19**

According to WHO, the first approach should be to develop and detect nucleic acid and protein tests at on-site for COVID-19 diagnostic research. In addition to nucleic acid tests, serological tests with proteins are required to improve monitoring efficiency. In contrast to nucleic acid tests, serological tests have the advantage of the detection of antibodies after recovery. These enable clinicians to follow both infected and cured patients and get a better prediction of the total SARS-CoV-2 infections. Point-of-care tests (POCT) are inexpensive portable devices for diagnosing patients. In order to increase the viability of diagnosis, the priority is to develop multiplex, fast, and portable test panels by designing novel methods, such as biosensors [14] (Figure 1).

**Molecular diagnostic tests**

SARS-CoV-2 is a single-stranded (+) RNA virus, which belongs to the genus Betacoronavirus. Phylogenetic analysis showed that SARS-CoV-2 is closely related to bat-derived SARS-like coronaviruses, namely Bat-SL-CoVZC45 and Bat-SL-CoVZXC21 with 88–89% similarity [15], and 96% identity with Bat-RaTG13-2013, suggesting that the virus spillover could come from a bat or through an animal secondary host [16]. Accurate RNA detection of SARS-CoV-2 is the “gold standard” test for the diagnosis of COVID-19, which is done by fluorescence-based quantitative PCR (qPCR) method [9].
Real-time detection of reverse transcriptase-PCR (RT-PCR) is the first preferred test for the Coronavirus, because of its better advantages, like being a specific quantitative assay. Besides, real-time RT-PCR is more sensitive than traditional qPCR assays, which is extremely helpful in diagnosing early infection. Therefore, RT-PCR assay is the most used method for the detection of SARS-CoV-2 [17–19].

Moreover, several non-PCR based molecular tests are developed for the detection of coronavirus RNA, such as isothermal nucleic acid amplification (loop-mediated isothermal amplification (LAMP) and nucleic acid sequence-based amplification) to improve both the specificity and sensitivity [17]. The LAMP is a novel isothermal nucleic acid (DNA and RNA) amplification method with high efficiency, sensitivity, and specificity [20, 21].

Specific High Sensitivity Enzymatic Reporter UnLOCKing (SHERLOCK) is a diagnostic platform that uses Cas13a ribonuclease for RNA sensing [22]. It is based on CRISPR (clustered regularly interspaced short palindromic repeats) technology. SHERLOCK is composed of nucleic acid pre-amplification with CRISPR-Cas enzymology to identify desired DNA or RNA sequences [23] accurately. It affords multiplexed, portable, and highly sensitive detection of RNA from COVID-19 patients samples [24]. Now, the technique is started to use in SARS-CoV-2 detection [25, 26].

A modified method of SHERLOCK technique was recently developed by Broughton et al., (2020) for the detection of SARS-CoV-2. The method is based on CRISPR–Cas12 detection, which can distinguish SARS-CoV-2 by using the N and E gene of the guide RNAs of the virus. Method includes RNA extraction, which can be used as an input to DETECTR (LAMP preamplification for E and N gene, RNase P, and Cas12 based detection) and visualized by LFIA [27].

Newly developed a single-step, ligation-dependent isothermal reaction cascade, called SENSitive Splint-based single-stage isothermal RNA detection (SENSR) is used to detect SARS-CoV-2 guideRNAs (gRNA). This method enables the fast detection of highly specific RNAs. SENSR is based on two simple enzymatic reactions. The first one is the ligation reaction of the SplintR ligase and is continued with the transcription by T7 RNA polymerase. The transcript produces an RNA aptamer, which is going to label with fluorogenic dye and gives fluorescence with the target RNA present in the sample [28].

Nucleic acid tests for viral RNA measures the current infection with SARS-CoV-2, and protein-based tests show the past exposure to SARS-CoV-2 [29].

Serological diagnostic tests

SARS-CoV-2 is a β family coronavirus, with a spike surface glycoprotein (S), a small envelope protein (E), matrix (membrane) protein (M), and nucleocapsid protein (N). Among these, N-protein is the mostly found and relatively conserved protein in coronaviruses. Therefore, it is the most used diagnostic antigen for the detection of neutralization antibodies [14, 30] (Figure 2). In coronaviruses, the S gene encodes the receptor binding spike protein, which ensures the virus infection. This spike protein ensures receptor binding and membrane fusion,
which determines the tropism. S protein is essential for binding to host cells, which is present on the surface of virus particles and highly immunogenic. Receptor-binding domain (RBD) of the S protein ensures the binding with angiotensin converting enzyme 2 (ACE2) and the virus itself [31, 32] (Figure 3).

In SARS-CoV-2, the S gene differs by <75% similarity of the nucleotide sequences compared to other SARS-related coronaviruses [14]. Other structural proteins are genetically more conserved than S protein and crucial for other essential functions [33].

M and E proteins are compulsory for virus assembly. N protein is related to transcription and replication of SARS-CoV-2 RNA, packaging of the encapsulated genome in virions. Besides, the N-protein has the most intense immunogenic activity during infection. Both S and N proteins are potential antigens for the serodiagnosis of COVID-19, and most of the diagnostic methods for SARS-CoV-2 immunoglobulin detection are based on S and/or N [30, 31].

**Immuoassay-based diagnostic tests**

Testing specific antibodies for SARS-CoV-2 present in a patient’s blood is the right choice to detect seroconversion of COVID-19 [34]. As it is known, IgM is the first released antibody against viral infections before high-affinity adaptive IgG responses are produced. IgG is essential for long-term immunity and immunological memory. It is seen that after SARS infection, IgM antibodies are detected in the patient’s blood after six days and IgG after 10 days, and persists for 2–3 years [35, 36]. The detection of IgM antibodies indicates recent exposure to SARS-CoV-2, while the detection of COVID-19 IgG antibodies allows to determine contact tracing and surveillance. Rapid detection of IgM and IgG antibodies is valuable for the diagnosis and treatment of COVID-19 disease [37].

Detection of IgA in SARS-CoV infected patients serum is another way to provide information on the virus infection status over time [37]. IgM and IgG antibodies are mostly produced against N protein of SARS and SARS-CoV-2 [38, 39], and IgA is also produced against S1 protein of the virus [40]. When the immune response of the patients against SARS coronaviruses is compared to produce the immunoglobulins, it is shown that IgA response starts earlier than IgG response. On the other hand, the presence of IgG in serum continues during the infection time and shows past infections [41].

**Point-of-care tests: POCT**

POCT devices, based on lateral flow immunoassays (LFIA), are the most used techniques for qualitative and semi-quantitative analysis. LFIA is carried out over a strip, of which various parts are mounted on a plastic carrier. Strip parts are composed of conjugate adsorption and sample application pads, and nitrocellulose membrane. By immobilizing biorecognition elements on nitrocellulose membrane, the test strip is divided into test and control lines. When liquid samples put on the cassette and flow through the membrane, the analyte of interest binds to the
test line, and the line becomes visible. LFIA combines the unique advantages of biorecognition elements and liquid chromatography [41]. For labeling detection antibodies, several types of materials are used in LFIA systems, including gold nanoparticles, colored latex beads, magnetic particles, carbon nanoparticles, quantum dots, and others. Different materials can be used as a label to detect the analyte concentration and retain their properties when conjugated with bioreceptor molecules [41].

Usage of POC tests are common in the clinical field, where the purpose of the test is to develop a portable, integrated system for testing biomarkers using for different samples. It is used as a rapid medical test at the patient’s location. Another advantage is no need for sample pretreatment or the need for trained personnel and a fully designed laboratory. The user only needs a drop of sample, and the capillary force controls the process for dispensing without fluid power and/or external energy [42].

The same as the other coronavirus immunoglobulin release timeline, IgM is the first antibody, synthesized by the patient against the virus infection. When both IgM and IgG tests are positive for SARS-CoV-2, this means that the patient is infected with SARS-CoV-2 recently, or he/she is at the early stage of infection. If only the IgG line is positive, this means that the patient had an infection in the past, or he/she is at the late stage of a viral infection. The combined detection of IgG and IgM antibodies is recommended to monitor different stages of COVID-19 [43].

SARS-CoV-2 rapid POC tests generally are based on commercial applications of colloidal gold-based LFIA [44–46]. Mainly, IgM, IgG, and IgA are detected by the indirect LFIA strip method, which means that N-protein of SARS-CoV-2 is used as an antigen on the surface of the strip membrane. In this way, the presence of neutralizer antibodies in the patient’s blood sample is visualized on the strips, and positive and negative results could be detected. [40, 45]. Test durations are changing in 5–15 min [30, 40]. Although strip assays are rapid and sensitive detection methods against SARS-CoV-2, there are some disadvantages of these tests. The specificity analysis of the tests shows that the sensitivity is lower than other methods. This disadvantage will affect the accurate evaluation of SARS-CoV-2 infection [44]. After a certain time of the onset of the infection, RT-PCR tests for SARS-CoV-2 may become negative, but the antibodies can still be detected in the serum of COVID-19 patients [44].

For a colloidal gold LFIA system, a COVID-19 Quick Touch Point CE-IVD test can be given as an example for the visualization of COVID-109 IgG and an IgM. The anti-human IgG is located the G test line region and the anti-human IgM is located the M test line region. During the test, the sample reacts with SARS-CoV-2 antigen-coated gold nanoparticles (AuNP) on the conjugation pad. Any antibody that recognizes the SARS-CoV-2 antigen in the patient sample binds to the Antigen-AuNP complex. As these human antibody / antigen / AuNP complexes move along the test lines, they are captured in the anti-human IgM ‘M’ Line, the anti-human IgG ‘G’ Line, or both, depending on the antibody content. If the sample contains IgM antibodies against SARS-CoV-2, a colored line will appear in the M test line region. If a sample contains IgG antibodies to SARS-CoV-2, the conjugate sample complex reacts with anti-human IgG. As a result, a colored line appears in the G test line region. Rabbit IgG-AuNP complexes are captured by the control line (containing anti-rabbit-IgG) [47].

**Enzyme-linked immunosorbent assay (ELISA)**

ELISA-based antibody detection tests with recombinant antigens are mostly used tests in indirect point-of-care assays. These tests offer high reproducibility and user-friendly detection protocols [48]. Also, serological analysis is crucial to understand the epidemiology of SARS-CoV-2, including the role of asymptomatic infections [3]. Recently, researchers have used the recombinant SARS-CoV-2 nucleocapsid and spike protein for designing ELISA-based IgM and IgG antibody tests [30, 49].

Diagnosis of COVID-19 can be based on the combination of the patient’s medical history, laboratory, and CT images. However, the final decision mainly depends on the detection of nucleic acids. However, there is a remarkable point that many new patients cannot be diagnosed due to negative nucleic acid tests. For example, qPCR test may give false-negative results if the sample is taken from the throat. Because the viral load in the upper respiratory tract samples is generally lower than in the lower respiratory tract samples, and the viral load of patients varies at different stages of the disease [46]. A combination of the IgM-IgG ELISA test with nucleic acid qPCR can give a more precise diagnosis of SARS-CoV-2 infection. [3]. Although ELISA tests also provide quantitative analysis for SARS-CoV-2 load, the similarity between SARS-CoV-2 and the other virus infection might cause cross-reactivity [50].

In the literature, in addition to the SARS IgG and IgMs direct measurement ELISA methods, various screening kits are also available. They are called inhibitor screening ELISA kits. These tests are designed to facilitate the identification and characterization of SARS-CoV-2 inhibitors. The assay stands on a simple colorimetric ELISA platform, which measures the binding between immobilized SARS-CoV-2 S protein RBD (receptor binding domain) and Human ACE2 protein [51]. The tests can be used in the
screening of inhibitors in SARS-CoV-2 binding tests or drug development against spike glycoprotein of SARS-CoV-2 [52], and a potential to develop a screening kit for the SARS-CoV-2 main protein (M protein) exists [53].

Electrochemiluminescence methods are also known to be used in COVID-19 IgG and IgM detection. Rosch SARS-CoV-2 Elecsys immunoassay system is a valuable example of this kind of method. In this system, the patient sample is incubated with a mix of biotinylated and ruthenylated nucleocapsid (N) antigen. Double-antigen sandwich immune complexes (DAGS) are formed in the presence of related antibodies. After the addition of streptavidin-coated magnetic-microparticles, the DAGS complexes bind to the particles via interaction of biotin and streptavidin. The mixture is transferred to the measuring cell, and magnetically captured onto the surface of the electrode. Electrochemiluminescence is then induced by applying a voltage and measured with a photomultiplier. The signal yield increases with the antibody titer [54].

**Biosensors and other novel methods for SARS-CoV-2 testing**

The popularization of POCT is getting an increase of interest in healthcare diagnostics. However, there are significant challenges that exist in the development of simple, fast, easy to use, highly specific, and sensitive biosensors for POC testing [55]. Therefore, more attention should be given to developing analytical devices as well as biosensors.

Devices or kits containing various material-based electrochemical (EC) sensors (such as paper- and screen-printed electrode-based) are in high demand for analysis because of their ease of use, portability, and higher sensitivity with short analysis times. In recent years, EC sensors have been widely applied to POCT in various fields, including healthcare monitoring [56].

In the last 25 years, for the detection of pathogens, biosensors, competed with PCR and ELISA, have appeared in the market. Biosensors are based on several selective and sensitive biological recognition elements and various transformation elements, and via this way, they became a complementary system to PCR and ELISA for the identification and quantification of pathogens [57].

A biosensor provides quantitative or semi-quantitative analytical performance. While a biosensor can be integrated into a portable device, the measurement method can change into a drop to continuous flow types. By using biosensors, precise and selective real-time detection of pathogens can be achieved on-site without the need for sample pretreatment [57]. Currently, biosensor systems are in the process of development for SARS-CoV-2 detection.

Nunez-Bajo and his co-workers (2020) developed a silicon-based integrated Point-of-Need (PoN) transducer (TriSilix) that can detect SARS-CoV-2-specific sequences of nucleic acids quantitatively in real-time [58].

A new LAMP-based test for simple, fast, and reliable diagnosis of COVID-19 is reported as COVID-19 RT-LAMP-NBS. The technique is a combination of LAMP amplification, reverse transcription, and multiplex analysis with a nanoparticle-based biosensor, which is done in a one-step single-tube reaction and finished with LFIA strip measurement. Rabbit anti-fluorescein antibody (anti-FITC), sheep anti-digoxigenin antibody (Anti-Dig), and biotinylated bovine serum albumin (biotin-BSA) are immobilized as test line 1 (TL1), test line 2 (TL2) and control line (CL), respectively. Dyed streptavidin-coated polymer nanoparticles (SA-DNPs) are immobilized in the conjugated regions. In the detection phase, the working buffer with the sample moves through the strip with the capillary action and re-hydrates the SA-DNPs fixed on the conjugate pad. F1ab-RT-LAMP products labeled with FITC are captured by the anti-FITC antibody in the TL1 region, and np-RT-LAMP products with Dig are captured by the anti-Dig antibody in the TL2 region. The other ends of the F1ab and np-RT-LAMP products, labeled with biotin, bind streptavidin-conjugated colored nanoparticles for imaging. Colored nanoparticles conjugated with streptavidin remaining unbound are captured by biotinylated bovine serum albumin immobilized in CL (Control line) [59].

For detecting SARS-CoV-2, various other technologies are also used. A luminescent immunoassay for the detection of the SARS-CoV-2 antibody, based on using synthetic peptide antigens as the immunosorbent, is developed for IgM and IgG detections. Researchers synthesized different peptides as antigens from the S and N proteins and purified them with streptavidin-coated magnetic beads, and perform luminescent immunoassay for the detection of SARS-CoV-2 IgG and IgM antibodies [60].

On the other hand, an engineered cell-based portable biosensor is developed for the direct detection of SARS-CoV-2. The biosensor is based on membrane engineered fibroblast cells with the human spike S1 antibody. Signal (Volts) is received with a membrane potential difference, measured by binding of the viral protein to the membrane-bound antibodies with a detection limit of 1 fg/mL. It can be used with a ready-to-use platform, including a portable reading device powered by smartphone/tablet [61].

SARS-CoV-2 proteome microarray is also performed to analyze antibody interactions at amino acid residues on the virus. Such biomarkers can also give information about
Table 1: Company and method examples of molecular and serological tests used in the detection of SARS-CoV-2 [65, 66].

| Company/test name | Target | Specimen | Test method | Test time | Clinical performance | Authorization |
|-------------------|--------|----------|-------------|-----------|----------------------|--------------|
| Abbott diagnostics Scarborough, Inc./ID NOW COVID-19 | RdRP gene | Nasopharyngeal, nasal and throat swaps | Isothermal nucleic acid amplification | 15 min | LoD: 125 copies/mL Sensitivity: ≥95% No significant cross-reactivity | US (FDA) |
| Cepheid/Xpert xpress SARS-CoV-2 test | N1 and E genes | Nasopharyngeal and throat swaps | RT-PCR | 45 min | LoD: 250 copies/mL Sensitivity: ≥95% No potential unintended cross-reactivity | US (FDA) |
| Cepheid Sherlock Biosciences/Sherlock™ CRISPR SARS-CoV-2 DETECTR | ORF1ab and nucleocapsid (N) genes | Respiratory samples | Sherlock’s Cas12 and Cas13 enzymes for nucleic acid detection | 1 h | LoD: 6.75 copies/µL Sensitivity: 100% No significant cross-reactivity | US (FDA) |
| Mammoth biosciences/SARS-CoV-2 DETECTR | N and E genes | Respiratory samples | CRISPR-based lateral flow assay isothermal amplification | 40 min | LoD: 10–50 copies/µL Sensitivity: 100% No significant cross-reactivity | US (FDA) |
| Abbott core Laboratory/m2000 SARS-CoV-2 assay | IgG | Serum, plasma, whole blood (heparin, EDTA, citrate) | Chemiluminescent microparticle immunoassay | 470 patient samples /24 h 2–10 min | Sensitivity: 99.6% Specificity: 99% Cross-reactivity: Cytomegalovirus (CMV) IgG IgG sensitivity 96.7% IgM sensitivity 86.7% IgG specificity 98.0% IgM specificity 99.0% | USA, Australia |
| Aytu biosciences/COVID-19 IgG/IgM point of care rapid tests | IgG/IgM | Serum, plasma, whole blood | Lateral flow immunoassay | – | – | China, USA |
| Bioscience diagnostic technology co., Ltd./IgG antibody test kit for novel coronavirus 2019-nCoV | IgG | Serum | Magnetic particle-based chemiluminescence immunoassay | – | – | China |
| Cellex Inc./qSARS-CoV-2 IgG/IgM rapid test | IgG/IgM (specific for N protein) | Serum, plasma, whole blood | Lateral flow immunoassay | 15–20 min | Sensitivity: 93.8% Specificity: 96% Cross-reactivity: none reported Sensitivity: 93.3% Specificity: 100% | Australia, US, Belgium |
| Creative diagnostics/DEI-ASL019/020 SARS-CoV-2 IgG ELISA kit | IgG (specific for N protein) | Serum, plasma | ELISA | 1 h | Sensitivity: 93.3% Specificity: 100% | Australia, US |
| Rosche/Elecsys anti-SARS-CoV-2 | Total ab | Serum, plasma | Electrochemiluminescence immunoassay | 18 min | Sensitivity: 100% Specificity: 99.8% Cross-reactivity: none reported Sensitivity: 60% Specificity: 100% Cross-reactivity: none reported | US (FDA) |
| Coris biocconcept/COVID-19 Ag Respi-strip | Viral antigen | Nasal mucus swaps | Lateral flow immunoassay (dipstick) | 15 min | – | Belgium |
potential targets for diagnosis and vaccine development [62]. Another newly developed surface plasmon resonance (SPR)-based biosensor and artificial intelligence (AI) assisted is also used for the diagnosis of COVID-19 [63].

Comparison of SARS-CoV-2 test methods

Among all tests, qPCR shows a lower limit of detection, high sensitivity, and accuracy. In PCR tests, CRISPR is tested only on plasmid-positive controls or spiked human samples. LAMP is often used for point-of-care testing (POCT) due to its high sensitivity, fast response, and ease of use. It is a highly specific technique with the combined detection of three coronavirus genes [4].

For comparison of quick strip and ELISA tests, it seems that ELISA tests give better results than LFIA tests. While the latter is faster and more suitable for POC tests, the first seems more sensitive and reliable. The sensitivity and specificity of the serology tests are variable in the range of 81–98% [4]. Although there is not enough study about biosensors to make a comparison between the others, biosensors should be more sensitive, selective, and specific to anti-viral antibodies and virus itself, because of their analytical performance criteria for other viral tests [64]. The comparison of the analytical performance criteria of some companies commercial tests is given in Table 1.

Table 1: (continued)

| Company/test name | Target | Specimen | Test method | Test time | Clinical performance | Authorization |
|-------------------|--------|----------|-------------|-----------|----------------------|--------------|
| SD biosensor/Standard Q COVID-19 Ag | Viral antigen | Nasopharyngeal swaps | Chromatographic immunoassay | 30 min | Sensitivity: 84.38%, Specificity: 100% | South Korea |

* Emergency Use Authorization by US FDA and other authorities.
** PFU: plaques in semisolid media; CRISPR (clustered regularly interspaced short palindromic repeats); DETECTR (DNA Endonuclease-Targeted CRISPR Trans Reporter).

Identification and improvement of SARS-CoV-2 outbreak. On the other hand, for sufficient and fast identification and treatment of SARS-CoV-2 infections, new tests containing recent technologies and approaches should be developed and provided to health care workers.

Remarkably, data on COVID-19 is developing rapidly. Some of the information in this review may change as further studies emerge. Some of the referenced articles are pre-printed and have not been reviewed by experts.

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