Emerging diagnostic tools for detection of COVID-19 and perspective

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Abstract
The COVID-19 caused by a novel coronavirus, named Severe Acute Respiratory Syndrome Corona Virus 2 (SARS-CoV-2) has taken a great toll of life affecting lakhs of people around the globe. It was detected initially in Wuhan, China and has spread rapidly to more than 208 countries to date. A range of molecular and immunoassay-based techniques ranging from central laboratory testing to point-of-care tests is urgently needed for the diagnosis and management of COVID-19 patients. Intensive research is going on for the rapid and highly sensitive detection of COVID 19 using varied approach. Hence, this review will focus on the structure of SARS-CoV-2 and recent progress of different detection tool for the detection of COVID-19. This review will also stimulate academics and researcher to update their current technology. Additionally, we also state about the future revolving around the detection of the novel coronavirus. Lately, the way ahead for better management are also put forward.

Keywords SARS-CoV-2 · Point of care · RT-PCR · CRISPR · Isothermal amplification · Biosensors

1 Introduction
The year 2019 ended with a fatal outbreak of a novel coronavirus, Severe Acute Respiratory Syndrome Corona Virus 2 (SARS-CoV-2), preliminarily identified as a causative agent of a series of unusual pneumonia cases in Wuhan City, Hubei Province, China. The International Committee on Taxonomy of Viruses (ICTV) permanently named the pathogen SARS-CoV-2 and the disease it caused coronavirus disease 2019 (COVID-19) and declared the crisis a pandemic (Enserink 2020). As per the World Health Organisation (WHO), latest situation report (Sep 14, 2020) at the time of this writing, more than 28.9 million confirmed cases with more than millions of deaths have been reported in 208 countries (Organisation 2020). The first reported case of COVID-19 was in Wuhan, Hubei province with symptoms such as fever, cold, shortness in breath very similar to the common cold in few cases and within a week had a reported cluster cases of acute pneumonia (Nishiura et al. 2020). The Computerized Tomography (CT) scan of the patients revealed slight opacity and difference from the healthy scan of the lungs (Ai et al. 2020). It was concluded as a possible case of pneumonia but the speculation was rejected as soon as PCR results revealed it belongs to coronavirus family using the bronchoalveolar lavage samples of the patients (Ai et al. 2020). It was speculated that the viral disease caused had a zoonotic source. Genome sequencing of SARS-CoV-2 has revealed that it is 96.2% identical to the bat coronavirus and 79.6% identical to SARS-CoV, while 50% similarity to MERS-CoV (Zhou et al. 2020; Ai et al. 2020). The USA can be regarded as the new epicenter of the diseases more than 6.7 million reported cases with 198,520 death followed by India and Brazil having more than 450,000 cases as of Sep 14, 2020. The infection spread is increasing at an alarming rate all around the globe as no great breakthrough has been made in vaccine development to treat the virus. Although, structural analysis and molecular characterization has illuminated a lot of advancement to fight the COVID-19 outbreak even though there is a lot to be uncovered for better disease detection and prevention.

SARS-CoV-2 belongs to beta lineage of subgenus Sarbecovirus, genus Betacoronavirus, the Coronaviridae family, and the Orthocoronavirinae subfamily (Huids et al. 2020; Weiss and Leibowitz 2011). It is an enveloped single-stranded RNA virus (+ve ssRNA) with a genome size of 29.9 kb that spreads widely among humans and other mammals, causing a wide range of symptoms from those of the common cold to fatal diseases such as SARS (Zhu et al. 2020; Zhou et al. 2020). Based on their antigenic properties, they were classified into three main groups (Schoeman and Fielding 2019): i) alpha-CoVs, responsible for gastrointestinal disorders; ii) beta-CoVs,
which includes: (a) Bat coronavirus (BCoV), and mammals (b) the human Severe Acute Respiratory Syndrome (SARS) virus, (c) Middle Eastern Respiratory Syndrome (MERS) virus; and iii) gamma-CoVs, that mainly infect avian species (iv) delta-CoVs mostly in pigs. Severe disease has been caused previously to humans by corona family of viruses like MERS-CoV, SARS-CoV and very recent SARS-CoV-2 being the leading cause of death around the globe falls in beta type of coronavirus (Schoeman and Fielding 2019). The four major structural proteins of the Coronaviridae family consists of the spike surface glycoprotein (S), a small envelope protein (E), matrix protein (M), and nucleocapsid protein (N) as shown in Fig. 1.

The spike protein has great importance for entry into the host and can greatly act as a major point to focus for therapeutics and vaccine development as it has better binding as compared to SARS-CoV (Wrapp et al. 2020; Yuan et al. 2017). The M protein has two conformations elongated and compact hence aids in viral assembly (Neuman et al. 2011). The E protein act as an ion-channeling viroporin and interacts with host cell protein (Schoeman and Fielding 2019). The transmission from animal to human lead to the occurrence of the diseases while the spread of the disease is attributed mostly to human transmission making it impossible to constrain the spread of the diseases without distancing (Li et al. 2020a; Chan et al. 2020b). The symptoms for SARS-CoV-2 vary from patient to patient. The symptoms are highly influenced by factors such as sex, age and the attributed diseases underlying a person like hypertension, cardiovascular diseases or even diabetes. The symptoms can range from mild fever, cough, fatigue in certain cases symptoms like diarrhea, hemoptysis and even headache are also reported. In certain cases, complications like acute respiratory distress syndrome, anemia, acute cardiac injury and other secondary infection are also reported (Huang et al. 2020). The case-fatality rate of COVID-19 ranges from 0.6% to 7.2% by region and seem to be substantially higher than the 0.1% mortality rate of seasonal influenza (Onder et al. 2020; Dong et al. 2020; Centers For Disease Control and Prevention 2020a). Few medications are highlighted to treat the COVID-19 which includes of Lopinavir /Ritonavir (Yao et al. 2020; Lu 2020). Chloroquine has also been described to be effective in the treatment of the novel virus (Gao et al. 2020). Vaccine development for treatment is under extensive research and is under rigorous screening before that it can be made available for human use. Currently, the vaccine is in the developmental stages but research is progressing rapidly to find a cure. To constrain the further spread until a vaccine is available for treatment constant efforts also needs to be made in the direction of accurate and point of care detection technique. Point of care testing is a bed side testing which helps to take quick medical decisions by the individuals based on the proximate result. In recent scenario, point of care testing can act as an armor by mass screening the population as it provides result in minutes. The virus can be the next great pandemic in the history of diseases caused by viruses if not managed appropriately. The death toll is increasing day by day with no potential vaccine in hand. Although the field of disease detection has revolutionized in a short time like never before.

The prospect related to COVID-19 detection is reforming at great pace. In regard to the amount of people screened as of

![Fig. 1 Structure of COVID-19](image)
Sep 14, 2020 for detection with highest testing been done by China having a count of one hundred sixty million followed by USA and India having ninety-two million and fifty seven million testing done respectively (Elflein 2020). Pertaining to the number of test performed per 1000 people is highest in countries like Australia, Canada, USA, Russia, Saudi Arabia and Spain. Whereas relatively fewer tests are performed per 1000 people in countries like Brazil, Peru, Colombia and South Africa to name a few (Hannah Ritchie et al. 2020). Case Fatality Rate (CFR) is high in countries like Mexico, Italy, UK and Yemen (Hannah Ritchie et al. 2020). This review is a holistic resource of all the information currently necessary to be considered for COVID-19 diagnosis. The review will act as an aid in field of COVID-19 detection and diagnosis. In a systemic way it also put forward various efforts across the globe taken to tackle the deadly virus. Moreover, it provides information in what way nanotechnology interventions could possibly be linked in a better and more accurate detection apart from the available technology. Initially it sheds lights on the current scenario and rate at which the virus has affected the globe followed by the structure of the virus and later the detection of the virus. Finally, it also states various pioneering commercial names at present in the field of detection. The goal of this review is to present an overall idea pertaining to SARS-CoV-2 detection.

2 Current diagnostic tests for COVID-19

COVID-19 has spread massively all over the world since its breakthrough making the field of disease detection and testing to revolutionize (Udugama et al. 2020). Enormous biological examination is done attributed to the structure of virus this is help in development of both the vaccine and the diagnostics measures further to constrain the spread of virus. Here in we elaborate specifically on Nucleic acid and protein based diagnostic techniques developed over time for detection of COVID-19.

2.1 Nucleic acid based detection

With increasing in several cases each day there is a constant need for the diagnosis of the diseases. Currently, the diagnosis of the COVID-19 is done using nucleic acid-based testing method. In nucleic acid-based testing usually, RT-PCR is used for detection (Corman et al. 2020). A nasopharyngeal samples taken from the respiratory tract to assess the presence of one or several Nucleic Acid (NA) targets specific to SARS–CoV-2 is preferred choice at the moment, but samples from oropharyngeal, mid-turbinate, or anterior nares are also acceptable (Centers for Disease Control and Prevention 2020b; Zou et al. 2020). For better sensitivity than upper respiratory tract samples, sputum, endotracheal aspirates, and bronchoalveolar lavage are also preferred after microbiological processing (Zhu et al. 2020). Inadequate or improper sample collection may result in a false-negative test. For setting up the reaction initially a reverse transcription of SARS-CoV-2 virus RNA is done which converts the RNA into complementary DNA (cDNA) strand which is then followed by amplification of specific regions of the cDNA (Fig. 2). Three regions that are usually targeted to carry out the detections using RT-PCR are (a) the RDRP gene (RNA-dependent RNA polymerase gene) in the open reading frame ORF1ab region, (b) the E gene (envelope protein gene), and (c) the N gene (nucleocapsid protein gene) (Corman et al. 2012a, b). Two types of RT-PCR formats are currently available in the market one known as the singleplex format and other the multiplexed format. In both the format one primer and probe set is used to detect human RNase P (RP) to ensure the RNA extraction was successful. Singleplex format uses three primers whereas the multiplexed make use of only two primers (Authorization 2020). Basic steps for setting up the RT-PCR for detection of COVID-19 are simple although needs trained personnel to carry it out. The major drawback in using lone RT-PCR test for detection is the occurrence of false-negative detection of the specimens making it difficult to take the necessary steps for taking the right measures for the treatment of the patient. In the case of asymptomatic patients if becomes difficult to identify such individuals on the bases of RT-PCR results and take the necessary actions to stop the further spread of the disease (Lee et al. 2020). Hence it was reported that it was beneficial to make use of CT scans to complement the RT-PCR results for enhanced and better diagnosis of the diseases (Ai et al. 2020; Feng et al. 2020; Fang et al. 2020). Leo L M Poon et al. reported making of RT-PCR based test for detection of COVID-19 which specifically used two different regions (ORF1b and N) of the virus (CHU et al. 2020). Another group reported the development of RT-PCR based testing targeting RNA-dependent RNA polymerase (RdRp)/helicase (Hel), spike (S), and nucleocapsid (N) genes of SARS-CoV-2 and compared it with RdRp-P2 assay, and concluded that COVID-19-RdRp/Hel assay was reported as the most effective test for detection of the COVID-19 as it did not cross-react with other coronavirus species (Chan et al. 2020a). The major downfall in diagnosis using the traditional RT-PCR in the testing of COVID-19 includes of unavailability of enough test reagent for testing, requirement of trained personnel for carrying out the testing, availability of developed and well-equipped lab for the entire process to occur in a critical manner. Lastly, the time required for completion of the test is too large to produce results. The ability of RT-PCR assays to rule out COVID-19 on the basis of upper respiratory tract samples obtained at a single time point remains unclear. To overcome some of the problems encountered efforts are made around the globe to transverse this problem at the earliest.

Recently the development of straightforward detection technique which made use of mini PCR and well plate reader
was reported which can be possibly used in a remote area as well provide early results after the detection. Samples were combined with a DNA intercalating reagent (Evagreen Dye) which was then detected after amplification using the fluorescence indicator in a 96 well plate format (Gonzalez-Gonzalez 2020). Another progress in the field is the development of direct rapid extraction-free PCR (DIRECT-PCR). The single-tube homogeneous reaction was developed which included all Viral lysis, reverse transcription, amplification and detection within 36 min in just a tube for regions where laboratory competency is a major constrain. It would be helpful for early screening of mass population (Wee et al. 2020). To overcome the problem faced by using nucleic acid-based detection using RT-PCR technique which included of laborious system, a large amount of time required to process the sample, necessity of developed facilities to carry out the detection, trained personnel to carry out the test and occurrence of false-positive results (Gallagher 2020). Lastly, the test is not point of care hence there is a need to find some alternatives that are easy to use and provides accurate results instantaneously.

2.1.1 Aptamer based testing

Aptamer are single stranded nucleic acid molecule which can be readily used for detection of specific disease in an accurate manner as they have property to be modified at random position and could act as a great advantage to tackle the COVID-19 crisis at hand. Exploiting aptamers as they are small oligonucleotide which can be used for detection of COVID-19 as they are stable and easy to modify (Chen and Yang 2015). Again, synthesis of aptamers is easy in large quantity and at a lower price when compared to RT-PCR based nucleic acid testing. As many strategies are already put forward in line for commending the use of aptamers one such strategy was used was put forward by Ahn et al. in 2009 for detection of SARS-CoV by finding application in the preparation of nanoaptamer chip in detection by making use of the nucleocapsid protein which acted as a selective marker for detection a chemiluminescence based immunosorbent assay was developed and a detection limit of 2 pg/ml was achieved (Ahn et al. 2009). Another possibility can be making use of aptamers to develop anti-corona virus agent (Jang et al. 2008). Group of scientist from Aptamer Group Ltd. are working extensively to develop aptamers based point of care test for COVID-19 using spike protein of the SARS-CoV2 (Group2020). Selex (systemic evolution of ligands through exponential enrichment) process is another potential way of creating aptamers and finding its application in virus detection in conjugation with the microfluidics system (Liebich 2020; Lai et al. 2012). COVID-19 being an RNA virus recently reported MANGO a fluorogenic dye tactic in the detection of the virus as the dye has background-free technology for live-cell RNA imaging upon ligand binding (Cawte et al. 2020). The group of scientists from Simon Fraser University (SFU) proposed making use of MANGO system which consists of an RNA Mango aptamer bounded by fluorescent dye and glows brightly when bounded by the target. The team has proposed developing Mango

![Fig. 2 Traditional RT-PCR based nucleic acid testing](image-url)
NABSA (nucleic acid sequence-based amplification) kit for detection of the COVID-19 (News 2020).

2.2 CRISPR-Cas based testing

Another aspect to be explored for detecting COVID-19 is making use of CRISPR-Cas gene editing tool which can create wonders in the field of detection (Chekani-Azar et al. 2020). Making use of CRISPR-Cas has been reported for use in medicine and diagnostics over the years. Success in making use of the CRISPR-Cas has enabled to ascertain new systems for targeting and manipulating nucleic acids including those from Cas9, Cas12, Cascade and Cas13 orthologues (Pickar-Oliver and Gersbach 2019; Li et al. 2019). Possibilities of developing a diagnostic tool for detection of TB is already known using CRISP-Cas technology which lay the foundation for making its use in COVID-19 detection as well (Ai et al. 2019). Very recently, developed SARS-CoV-2 DNA Endonuclease-Targeted CRISPR Trans Reporter (DETECTR) for detection of COVID-19 using CRISPR-Cas12. This developed lateral flow strip could decrease the detection time required by the ongoing RT-PCR testing and aid in better disease management in this crucial time (Broughton et al. 2020). Exploiting the potential of CRISPR-Cas technology fluorescence and colorimetric based detection of COVID-19 was made possible. The technology is named as specific high-sensitivity enzymatic reporter unlocking (SHERLOCK) by making use of recombinase-mediated polymerase pre-amplification of DNA or RNA for detection. The reported technology takes less than an hour to provide results making it one of the potent applicants in the field of diagnosis of COVID-19 (Kellner et al. 2019). An improved version of SHERLOCK was put forward which overcome major challenges of SHERLOCK and is named as STOP (SHERLOCK testing in one pot). The mentioned assay is capable of solely performing extraction, amplification and CRISPR-mediated detection of the viral RNA in a go on a single temperature. Two version are presented as STOP covid version 1 and 2 respectively. STOP covid version 1 is compatible with lateral-flow and fluorescence readouts whereas STOP covid version 2 makes use of magnetic beads concentrated SARS-CoV-2 RNA for detection (Joung et al. 2020). CREST is another pioneering discovery in the field of diagnosis for detection of COVID-19. The CREST stands for (Cas13-based, Rugged, Equitable, Scalable Testing) and has overcome major drawbacks associated with the current diagnostic system of COVID-19. The Cas13 can be used in point of care setting and it would be low cost when compared to traditional lateral flow assay as it doesn’t require antibody conjugates for the detection (Rauch et al. 2020). Another effective use of CRISPR Cas 12 was seen by integrating into a lateral flow system named as iSCAN having potential to be used as effective management system for point of care detection(Ali et al. 2020). AIOD CRISPR assay, made use of a pair of crRNAs to initiate the detection using CRISPR-Cas12a for improved sensitivity. The assay have potential in detecting nucleic acids (DNA and RNA) of SARS-CoV-2 and HIV (Ding and Yin 2020). Integration of lateral flow system along with nucleic acid as a substrate for quick and point of care results can prove to be fruitful amid this pandemic as shown in Fig. 3a. Another perspective to be explored is pairing CRISPR-Cas with electrochemical based sensing as it can help in achieving even lower limit of detection. Can Dincer et.al, reported (CRISPR)/Cas13a-powered microfluidic based electrochemical sensor for detection of cancer reaching a limit of 10 pM on site (Bruch et al. 2019). Such a system should be made available at this crucial time in detection of COVID-19. Development of CRISPR-Cas based on-chip electrical detection of nucleic acid could be the future of detection in COVID-19 screening as it can detect even in femto Molar levels (Hajian et al. 2019).

2.3 Protein based testing

Along with the on-going nucleic acid-based testing for detection of COVID-19 protein-based detection can also act as an excellent supplement alongside for better mass screening for early measures in a point of care setting. Although nucleic acid, CRISPR-Cas and aptamer-based testing are currently being employed for detection protein-based avenues needs to be explored. Antigen and antibody are the among the major protein-based entities which are already used for detection of several diseases over a long time. Protein-based detection system mostly includes ELISA, chromogenic based or fluorescence-based detection using dye, lateral flow-based detection. Not much was developed until recently since the viral load has reported fluctuating with weeks after detection providing results which are not possibly reproducible when test was made using saliva sample from infected patients. Viral load was highest at the start and subsequently declined at the end (To et al. 2020). Although it can be speculated that antibody-based test can provide more time since antibody can be detected even after a long time in the patient.

2.3.1 Antigen based testing

An antigen test has ability to reveals if a person is presently infected with a pathogen such as the SARS-CoV-2 virus. Antigen tests mostly detect proteins or glycans, such as the spike proteins found on the surface of the SARS-CoV-2 virus. Sona nanotech is one of the pioneers in the filed leading the way of COVID-19 testing by developing antigen-based test kit for detection. The gold nanorod particles used are CTAB (cetyltrimethylammonium) free hence limiting the toxic risks associated with the use of other gold nanorod technologies in medical applications. It was reported recently that the test
attained a positive response to a recombinant whole spike protein control reagent specific to SARS-CoV2 and neither had false positives (Nanotech 2020). Another milestone is reached by E25Bio’s rapid diagnostic which provide results in 15 min by detecting the presence of the virus in the patient sample (Misra 2020). Iceni Diagnostics run by Prof Rob Field, has developed a diagnostic technique that make use of an artificial glycan receptor to detect the novel virus (Iceni Diagnostics Ltd 2020). OraSure envisions is another established name being working on developing antigen based testing kit (OraSure Technologies 2020). Roche has reported of developing test having sensitivity of 96.52% and a specificity of 99.68%, based on 426 samples from two independent study centers the test helps in identifying both symptomatic and asymptomatic people with in 15 min (Roche Ltd 2020a). Lately special consideration is being given to point of care antigen testing in order to detect infected person at the earliest and decreasing the chances of mass transfer of the virus (Dinnes et al. 2020). However, it was reported that antigen based detection alone cannot be effective in detection of SARS-CoV-2 (Mak et al. 2020).

2.3.2 Antibody based detection

Major class of immunoglobins includes of IgG, IgM, IgA, IgE and IgD which can contribute in detection of diseases. IgG been the first line of defense initiated as part of the immune response when infected by a pathogen and creates immunological memory to further fight the infection is mostly targeted in detection of COVID-19. Also reported is that IgM appears in the blood of the patient when infected by SARS after 3 to 6 days and IgG can be detected 8 days after the infection occurred (Racine and Winslow 2009; Wan et al. 2003).

IgG and IgA ELISAs in conjunction with the EURO Lab workstation (Euroimmun, Lübeck, Germany). EUROIMMUN enzyme-linked immunosorbent assay (ELISA) for semi-quantitative detection of IgA and IgG antibodies in serum and plasma samples using recombinant S1 domain of the SARS-CoV-2 spike protein as antigen is report-ed demonstrates excellent sensitivity for detection of IgA and IgG antibodies from samples collected ≥3 days and ≥4 days, respectively, after COVID-19 diagnosis by PCR (Beavis et al. 2020). Other ELISA based IgG and IgA showed specificity of 91.9% and 73.0% 12 and 11 days after symptom onset (Jääskeläinen et al. 2020). Many industries as well have developed ELISA based detection kit for COVID-19 like Epitope diagnostic, Inc. and Eagle bioscience although tests are yet to be approved by FDA for use. Eagle bioscience test kits are now available for use in the US for detection (Epitope Diagnostics 2020; Bioscience 2020). Making use of protein for detection is known and adopted for development over decades but recently making use of neutralizing antibody had been adopted to fight against the novel coronavirus. The antibody targets the spike protein of the virus which is made up of two subunits the S1 and S2. The S1 subunit is necessary for entry into the host cell while S2 subunit helps in fusion of the cellular and viral membrane. SARS-CoV-2 binds the receptor human angiotensin-converting enzyme 2 (ACE2) (Wang et al. 2020a). Considering the fact that neutralizing antibodies have great potential to fight the diseases making its use in disease diagnosis could be the near future. On evaluation of IgM/IgG based detection kit the highest specificity was reported for the Wantai SARS-CoV-2 Total Antibody ELISA followed by 93% for the Euroimmun IgA ELISA and 96% for the Euroimmun IgG ELISA with sensitivities of 90%, 90%, and 65%, respectively (Lassaunière et al. 2020).

Development of lateral flow strip for detection makes use of antigen-antibody reaction. Here the reaction occurs on the nitrocellulose membrane. Once the sample is added into the strip the antigen interacts with the already loaded capture antibody for detection through capillary action. The gold nanoparticle-conjugated antibody is present near the sample port to interact with the sample for the formation of the visible color change after formation of the immunocomplex. Making use of lateral flow assay for diseases detection which makes use of antigen-antibody for detection can be a better
alternative for COVID-19 diseases management. Lateral flow assay (LFA) is well established in terms of diseases detection and been used for more than a decade as shown in Fig. 3b (Bahadir and Sezgintürk 2016).

Building on this concept various lateral flow strip has been developed lately (Li et al. 2020b). Development of a rapid and simple point-of-care lateral flow immunoassay that can detect immunoglobulin M (IgM) and IgG antibodies simultaneously against SARS-CoV-2 virus in human blood within 15 min having an overall testing sensitivity of 88.66% and specificity of 90.63%. This IgM-IgG combined assay would result in better utility and sensitivity on contrary to single IgM or IgG test. (Li et al. 2020b). Lateral flow immunoassay strip with various optimizing parameters such as concentration of coating antigen, BSA blocking concentration and pH value for conjugation was also developed (Wen et al. 2020). IgG based NG-Test® based lateral flow immunoassay strip showed sensitivity (around 80%) for CLIA, ELISA and LFIA (Nicol et al. 2020). IgG and IgA ELISAs in conjunction with the EURO Lab workstation (Euroimmun, Lübeck, Germany).

Many companies have developed LFA which is ready to use and provide results within minutes. Roche diagnostic reported making a serological test for COVID-19 named as Elecsys which make use of cobas-e analyser for analysis of the results and provides results in 18 min with detection at a rate of 300 test/h can by targeting the nucleocapsid (N) antigen for the determination of antibodies against SARS-CoV-2 (Roche Ltd 2020b). Abbott’s, on the other hand, developed another platform knowns as ARCHITECT i1000SR and i2000SR laboratory-based instruments which run 100–200 tests an hour for effective detection using antibodies (Abbott 2020). Although IgG and IgM based test strip are claimed to provide results which are not accurate and reliable hence now are having limited use in the field of diagnosis of COVID-19 due to the drawbacks (Burog et al. 2020). Milenia Biotec a Germany based company has already intervened in the development of dipstick based COVID-19 detection system named as HybriDetect which uses gene amplification system or protein for detection of the novel virus (Biotec 2020). Although a lot has developed within a short time in testing related to COVID-19 multiple detection of close related biomarker or multiple analyte could be the next step in early and timely detection of the virus (Dincer et al. 2017). Concurrently, it was reported recently that alone RT-PCR had few limitation which could be overcome by making simultaneous use of antibody based tests resulting in an overall sensitivity and specificity of 95.7% and 98.7% respectively (Wang 2020). Concluding, we represent the current tool of diagnosis for COVID-19 Diagnosis as shown in Fig. 4.

### 2.3.3 Chemiluminescence based COVID-19 detection

Chemiluminescent based immunoassay is one is the effective modification to overcome traditional immunoassay drawbacks which can be used in order to detect COVID-19 effectively. Peptide-based luminescent immunoassay to detect IgG and IgM is been proposed for COVID-19. Cut-off value of this assay was determined by the detection of 200 healthy sera and 167 sera from patients infected with other pathogens than SARS-CoV-2. To evaluate the performance of this assay, detection of IgG and IgM in the 276 sera from confirmed patients were done. The positive rate of IgG and IgM were 71.4% (197/276) and 57.2% (158/276) respectively. By combining with real time RT-PCR detection, this assay might help to enhance the accuracy of diagnosis of SARS-CoV-2 infection (Cai et al. 2020). Highly purified receptor-binding domain (RBD) of the SARS-CoV-2 spike protein was expressed in human 293F cells and used to make a set of chemical luminescence kits for detecting the presence of RBD-specific IgA, IgM, and IgG, respectively. The RBD-specific IgA, IgM, and IgG kits showed diagnostic sensitivities of 98.6%, 96.8%, and 96.8%, and specificities of 98.1%, 92.3%, and 99.8%, respectively (Ma et al. 2020).

### 3 Nanotechnology interventions

Nanotechnology intervention is disease detection, vaccine development and therapeutics is known for a long time. Advanced research has been done for hand in hand application of nanotechnology along with disease management. The recent pandemic can put forward more ways to tackle the pandemic by making use of nanotechnology. Few advancements already are done in a field of COVID-19 diagnosis using nanotechnology (Weiss et al. 2020; Mujawar et al. 2020). In recent time, the field-effect transistor (FET)-based biosensing device for detecting SARS-CoV-2 was developed. The developed biosensing platform made use of graphene-coated FET against specific spike protein against COVID-19. One major advantage of the biosensing platform is that does not require any pre-treatment of the sample for detection (Seo et al. 2020). Another use of nanotechnology-based COVID-19 detection is in making use of innovative nanoparticles to simplify the existing available technologies for efficient results. One such developed nanoparticle is of poly (amino ester) with carboxyl groups (PC)-coated magnetic nanoparticles (pcMNPs) which aided in viral RNA extraction. pcMNPs-RNA complex can directly integrate into the RT-PCR reactions and help in detection. The proposed pcMNPs can be a great help in this decisive time to reduce the turnaround time which is obligatory to take early measure as fast as possible (Zhao et al. 2020). Recent improvement and novel strategy were integrated in making LFA for detection benefiting the advantage of glyconanoparticles. It was accomplished by exploiting the sialic acids affinity with SARS-CoV-2 spike protein by using glyconanoparticle platform rather than the traditional IgG and
IgM based testing. A novel strategy helped in having a detection limit of $5 \mu\text{g}\cdot\text{mL}^{-1}$ (Baker et al. 2020).

Another report is in development of naked eye detection test for SARS-CoV-2 by making use of AuNPs capped with thiol-modified antisense oligonucleotides (ASOs) specific for N-gene (nucleocapsid phosphoprotein). Results appear in 10 min from the isolated RNA samples showing agglomeration in the presence of its target RNA sequence of SARS-CoV-2, moreover RNaseH helps in cleaving the RNA strand from the RNA–DNA hybrid aiding in visually detectable precipitate. The limit of detection is 0.18 ng/μL of RNA having SARS-CoV-2 viral load (Moitra et al. 2020). Development of lanthanide-doped polysterene nanoparticles (LNPs) used as a fluorescent reporter to detect anti-SARV-CoV-2 IgG in human serum using Lateral flow immunoassay. The developed assay can be of great benefit in positive identification in doubtful cases and evaluating patients response to treatment (Chen et al. 2020). Wuhan Dgensee Clinical Laboratory Co., Ltd. reportedly developed nanopore target sequencing (NTS) to detect SARS-CoV-2 and other respiratory viruses simultaneously within 6–10 h. The NTS is not constrained to detect only COVID-19 but can be used in the application of diseases detection of other pathogenic viruses as well for improved results (Wang et al. 2020b).

Lately, smart electronics has emerged as a potential field in the development and detection of pathogenic infections. Diseases like cancer, H1N1, HIV and many more have been detected by making use of biosensors. Point-of-care based biosensors are reported to have high selectivity and sensitivity and works on bio affinity receptors (Morales-Narváez and Dincer 2020). All kinds of biomolecules like aptamers, antibody nucleic acid and lipids are reported to be detected by making use of biosensors (Tu et al. 2019). TriSilix is a recent advancement in the field of detection which makes use of silicon and have three modes of working on a single chip starting from electrical heater followed by temperature sensor and lastly electrochemical sensor when tested using cDNA from SARS-CoV-2 the system could detected up to 1 pg (Nunez-Bajo et al. 2020). Further, development of exhaled breathe analyzer based on nanomaterial hybrid array was developed and showed an accuracy of 90% and 95% in differentiating COVID-19 patients or other related lung infection if any, such an analyzer will help in better screening of patient in point of care setting (Shan et al. 2020). Integration of biosensors into a mobile technology can be the future of disease management and detection which can also be adapted for detection of COVID-19 (Zhang and Liu 2016). Multiplexing using smart and flexible electronics can also be adopted at this crucial time for detection of the novel virus as it has been reported for accurate and timely detection of many diseases (Konstantinov et al. 2009). Microfluidics can be used in detection as they have the capability of been point of care also been small in size it becomes user friendly in diseases management (Myers and Lee 2008; (Chin et al. 2011; Martinez et al. 2008). Table 1 represents the available list of commercial SARS-CoV-2 in-vitro diagnostic assays.

4 Conclusion and future prospect

The development and research have ramped up at a greater speed than ever in the field of diseases diagnosis due to COVID-19 outbreak leading to an increase in the mortality rate each day in an unpredictable manner. Still countries are struggling to speed up testing due to the laborious and expensive
| No. | Manufacturer                                                                 | Diagnostic test name                        | Technology/Platform | Description                                                                                                                                                                                                 |
|-----|------------------------------------------------------------------------------|---------------------------------------------|---------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| 1   | Rutgers Clinical Genomics Laboratory at RUCDR Infinite Biologics - Rutgers University | Rutgers Clinical Genomics Laboratory TaqPath SARS-CoV-2-Assay | rRT-PCR             | Real-time Reverse Transcription Polymerase Chain Reaction (rRT-PCR) test intended for the qualitative detection of nucleic acid from SARS-CoV-2 in oropharyngeal (throat) swab, nasopharyngeal swab, anterior nasal swab, mid-turbinate nasal swab, and bronchoalveolar lavage (BAL) fluid from individuals suspected of COVID-19. |
| 2   | Zymo Research Corporation                                                   | Quick SARS-CoV-2-rRT-PCR Kit                | rRT-PCR             | The kit works by programming a CRISPR molecule to detect the presence of a specific genetic signature – in this case, the genetic signature for SARS-CoV-2 – in a nasal swab, nasopharyngeal swab, oropharyngeal swab or bronchoalveolar lavage (BAL) specimen. When the signature is found, the CRISPR enzyme is activated and releases a detectable signal. |
| 3   | OPTI Medical Systems, Inc.                                                    | OPTI SARS-CoV-2 RT PCR Test                 | rRT-PCR             | The kit is a real-time RT-PCR test intended for the qualitative detection of nucleic acid from SARS-CoV-2 in oropharyngeal swabs, anterior nasal swabs, nasopharyngeal swabs, and lower respiratory specimens (such as sputum, tracheal aspirates, and bronchoalveolar lavage) from patients suspected of COVID-19. |
| 4   | Sherlock BioSciences, Inc.                                                    | Sherlock CRISPR SARS-CoV-2 Kit              | CRISPR/RT-LAMP      | The kit works by programming a CRISPR molecule to detect the presence of a specific genetic signature – in this case, the genetic signature for SARS-CoV-2 – in a nasal swab, nasopharyngeal swab, oropharyngeal swab or bronchoalveolar lavage (BAL) specimen. When the signature is found, the CRISPR enzyme is activated and releases a detectable signal. |
| 5   | BioMérieux SA                                                                | SARS-COV-2 R-GENE                          | rRT-PCR             | The kit works by programming a CRISPR molecule to detect the presence of a specific genetic signature – in this case, the genetic signature for SARS-CoV-2 – in a nasal swab, nasopharyngeal swab, oropharyngeal swab or bronchoalveolar lavage (BAL) specimen. When the signature is found, the CRISPR enzyme is activated and releases a detectable signal. |
| 6   | Fast Track Diagnostics Luxembourg S.à.r.l. (a Siemens Healthineers Company) | FTD SARS-CoV-2                            | rRT-PCR             | The kit is a real-time RT-PCR test intended for the qualitative detection of nucleic acid from SARS-CoV-2 in oropharyngeal swabs, anterior nasal swabs, nasopharyngeal swabs, and lower respiratory specimens (such as sputum, tracheal aspirates, and bronchoalveolar lavage) from patients suspected of COVID-19. |
| 7   | Sansure BioTech Inc.                                                          | Novel Coronavirus (2019-nCoV) Nucleic Acid Diagnostic Kit (PCR-Fluorescence Probing) | rRT-PCR             | The kit is a real-time RT-PCR test intended for the qualitative detection of RNA from SARS CoV-2 in nasopharyngeal swabs, oropharyngeal (throat) swabs, anterior nasal swabs, mid-turbinate swabs, nasal washes and nasal aspirates from individuals who are suspected of COVID-19. |
| 8   | Bio-Rad Laboratories, Inc                                                    | Bio-Rad SARS-CoV-2 ddPCR Test               | digital droplet rRT-PCR | The kit is a real-time RT-PCR test intended for the qualitative detection of nucleic acid from SARS-CoV-2 in nasopharyngeal anterior nasal and mid-turbinate nasal swab specimens, as well as nasopharyngeal wash/aspirate and nasal aspirate specimens from patients suspected of having COVID-19. |
| 9   | BioFire Diagnostics, LLC                                                      | BioFire Respiratory Panel 2.1 (RP2.1)       | rRT-PCR             | The kit is a real-time RT-PCR test intended for the qualitative detection of nucleic acid from SARS-CoV-2 in nasopharyngeal anterior nasal and mid-turbinate nasal swab specimens, as well as nasopharyngeal wash/aspirate and nasal aspirate specimens from patients suspected of having COVID-19. |
| 10  | LabGenomics Co., Ltd.                                                        | LabGun COVID-19 RT-PCR Kit                  | rRT-PCR             | The kit is a real-time RT-PCR test intended for the qualitative detection of nucleic acid from SARS-CoV-2 in nasopharyngeal, or oropharyngeal, anterior nasal and mid-turbinate nasal swabs, as well as nasopharyngeal wash/aspirate or nasal aspirate specimens and sputum, from individuals who are suspected of COVID-19. |
| 11  | Rheonix, Inc.                                                                | Rheonix COVID-19 MDx Assay                  | rRT-PCR             | The kit is an in-vitro diagnostic product intended for Real-time PCR based detection of new Coronavirus (COVID-19) infection via.                                                                                                                                 |
| 12  | SEASUN BIOMATERIALS                                                          | U-TOP COVID-19 Detection Kit                | rRT-PCR             | The kit is an in-vitro diagnostic product intended for Real-time PCR based detection of new Coronavirus (COVID-19) infection via.                                                                                                                                 |
| No. | Manufacturer                        | Diagnostic test name                          | Technology/Platform | Description                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |
|-----|-------------------------------------|-----------------------------------------------|---------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| 13  | SD Biosensor, Inc.                  | STANDARD \text{M} nCoV Real-Time Detection Kit | rRT-PCR             | Real-Time Detection kit is used for rapid identification and detection of novel coronavirus (2019-nCoV) nucleic acids in human nasopharyngeal swabs and throat swab samples targeting ORF1ab (RdRp) gene and E gene.                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |
| 14  | altona Diagnostics GmbH              | RealStar SARS-CoV02 RT-PCR Kits U.S.          | rRT-PCR             | The kit is a reagent system, based on real time PCR technology, for the qualitative detection and differentiation of lineage B-betacoronavirus (B-\beta CoV) and severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) specific RNA (targets E and S gene).                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |
| 15  | Covance/Seegene, Inc.               | Allplex 2019-nCoV Assay                       | rRT-PCR             | Assay is multiplex Real-time PCR assay for simultaneous detection of 3 target genes of SARS-CoV-2 in a single tube. The assay is designed to detect RdRP and N genes specific for SARS-CoV-2, and E gene for all of Sarbecovirus including SARS-CoV-2.                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |
| 16  | Trax Management Services Inc.       | PhoenixDx 2019-CoV                             | rRT-PCR             | The test should be run on the BIO-RAD CFX96-IVD platform, with RNA extracted using a separate kit. Sensitivity was determined using 30 positive samples, and specificity from 10 negative samples.                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |
| 17  | OSANG Healthcare                    | GeneFinder COVID-19 Plus RealAmp Kit          | rRT-PCR             | This is a one-step RT-PCR test, with each kit having reagents for 100 tests.                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |
| 18  | Fosun Pharma USA Inc.               | Fosun COVID-19 RT-PCR Detection Kit           | rRT-PCR             | This test uses TaqMan chemistry. Sensitivity was determined from 50 positive samples, and specificity from 100 negative samples. Their results were compared to the CDC RT-PCR protocol.                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |
| 19  | KorvaLabs Inc.                      | Curative-Korva SARS-Cov-2 Assay               | rRT-PCR             | The test should be run on the BioRad CFX 96 Touch, BioRad CFX Connect Real-Time PCR systems and Roche LightCycler 480 II Real-Time PCR systems. Sensitivity was determined from 34 positive samples, and specificity from 18 samples.                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |
| 20  | GenoSensor, LLC                     | GS\textsuperscript{TM} COVID-19 RT-PCR KIT    | rRT-PCR             | The test should be run on the Applied Biosystems 7500 Fast Dx Real-Time PCR system, and can be run in a 96-well or 384-well format. The test takes about 1.5 h. Sensitivity and specificity were determined using 32 positive and negative samples.                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |
| 21  | Maccura Biotechnology (USA) LLC     | SARS-CoV-2 Fluorescent PCR Kit                | rRT-PCR             | The kit includes reagents for RNA extraction and for PCR. The test takes about 2 h, and requires the Applied Biosystems 7500 Real-Time PCR Systems with v2.3 software. Sensitivity and specificity were determined from 30 positive and negative samples. There was a false positive rate of 3.3% in the N gene.                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |
| 22  | Atila BioSystems, Inc.              | iAMP COVID-19 Detection Kit                   | Isothermal amplification (OMEGA), patented | There is no extraction process necessary for this kit, and the amplification is isothermal. The test takes about 1 h, and 94 samples can be processed in a single run.                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |
| 23  | DiaCarta, Inc                       | QuantiVirus SARS-CoV-2 Test kit               | rRT-PCR             | This is a multiple rRT-PCR diagnostic, called the QuantiVirus SARS-CoV-2 Multiplex Test. The test can be run in under 2 h. The test should be run on the Thermo Fisher (ABI) QuantStudio 5, Thermo Fisher (ABI) 7500 Fast Dx, and Bio-Rad CFX 384 platforms. Sensitivity was determined from 41 positive clinical samples, and specificity from 52 negative clinical samples.                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |
| 24  | Becton, Dickinson & Company         | BD SARS-CoV-2 Reagents for BD MAX System      | Antigen (chromatographic digital immunoassay) | The nasal swab specimen is directly placed in the extraction reagent tube, during which time virus particles present in the specimen are disrupted, exposing internal viral nucleoproteins. After processing the swab in the extraction reagent, the specimen is added to the BD Veritor System test device. SARS-CoV-2 antigens present in the specimen then bind to antibodies conjugated to detector particles in the test strip. The antigen-conjugate complexes migrate across the test strip to the reaction area and are captured by a line of antibodies bound on the membrane. Test results of the BD Veritor System test
Table 1 (continued)

| No. | Manufacturer                           | Diagnostic test name                     | Technology/Platform | Description                                                                                                                                 |
|-----|----------------------------------------|------------------------------------------|---------------------|--------------------------------------------------------------------------------------------------------------------------------------------|
| 25  | InBios International, Inc              | Smart Detect SARS-CoV-2 rRT-PCR Kit       | rRT-PCR             | device are read using the BD Veritor Plus Analyzer Instrument, or other authorized instrument, when the 15-min assay development time is complete. |
| 26  | Gnomegen LLC                           | Gnomegen COVID-19 RT-Digital PCR Detection Kit | rRT-PCR             | RNA extraction should be performed before using this kit. The test should be run with the 7500 Fast Dx Real-Time PCR Instrument (Applied Biosystems) or the CFX96 Touch Real-Time PCR Detection System (Bio-Rad) with CFX Maestro Software (Bio-Rad). The oligonucleotide primers and probes for detection of SARS-CoV-2 were selected CV03030005 R01 Gnomegen 4 from regions of the virus nucleocapsid (N) gene. The panel is designed for specific detection of the 2019-nCoV (two primer/probe sets). An additional primer/probe set to detect the human RNase P gene (RP) in control samples and clinical specimens is also included in the panel. RNA isolated and purified from upper and lower respiratory specimens is reverse transcribed to cDNA and subsequently amplified in the Applied Biosystems 7500 Fast Dx Real-Time PCR Instrument with SDx version 1.4 software. |
| 27  | Co-Diagnostics, Inc                    | Logix Smart Coronavirus Disease 2019 (COVID-19) Kit | rRT-PCR             | The test is a one-step, RT-PCR with CoPrimer technology. The test takes 1–1.5 h, for use with CoDx Box, MiC qPCR Cycler, and Ecor8 cycler. The test must be performed on the AB 7500 Fast DX system, and extraction of RNA is required before use of this kit. |
| 28  | ScienCell Research Laboratories        | ScienCell SARS-CoV-2 Coronavirus Real-time RT-PCR (RT-qPCR) Detection Kit | rRT-PCR             | The test should be performed on the AB 7500 Fast DX system, and extraction of RNA is required before use of this kit. |
| 29  | Luminex Corporation                    | ARIES SARS-CoV-2 Assay                   | rRT-PCR             | A combination of lytic and extraction reagents is used to perform cell lysis and DNA/RNA extraction. Nucleic acids released from the target organisms are captured on magnetic affinity beads. The beads, together with the bound nucleic acids, are washed and the nucleic acids are eluted by a combination of heat and pH variation. The final chate is used to rehydrate BioGX SARS-CoV-2 Reagents, which contains all reagents necessary for RT-PCR including primers and probes. After reconstitution, the BD MAX System dispenses a fixed volume of RT-PCR-ready solution containing extracted nucleic acids into the PCR Cartridge. Microvalves on the cartridge are sealed by the system prior to initiating PCR in order to contain the amplification mixture and thus prevent evaporation and contamination. The test should be used with Applied Biosystems QuantStudio12 Flex (QS12) instrument with software version 1.2.2. Clinical sensitivity and specificity were determined using 36 and 30 samples, respectively. |
| 30  | Becton, Dickinson & Company (BD)       | BioGX SARS-CoV-2 Reagents for BD MAX System | RT-PCR              | The Bio-Speeedy Direct RT-qPCR SARS-CoV-2 is a one-step molecular test. The test should be run on the Roche LightCycler 96, Bio-Rad CFX96 Touch, or Qiagen Rotor-Gene 5 Plex platforms. They did a very extensive study of the limit of detection using various sample types and collection methods. Sensitivity was determined from 347 positive clinical samples, and negativity from 94 negative samples. |
| 31  | Ipsum Diagnostics, LLC                 | COV-19 IDx assay                         | rRT-PCR             | The test relies on a one-step RT-qPCR with Taqman chemistry. The kit should be used with the NeuMoDx Molecular System, and swabs should be collected with the Copan UTM-RT® System or BD UVT System. For sensitivity and specificity, they used 87 and 82 samples, respectively. |
| 32  | QIAGEN GmbH                            | QIAstat-Dx Respiratory SARS-CoV-2 Panel   | rRT-PCR             | The test incorporates multiplex Reverse Transcriptase Polymerase Chain Reaction (RT-PCR) with the Luminex® proprietary universal target sorting system on the Luminex platform to easily detect SARS-CoV-2 s. Extracted total nucleic acid is added to pre-plated, |
| No. | Manufacturer | Diagnostic test name | Technology/Platform |
|-----|--------------|----------------------|---------------------|
| 35  | Abbott Diagnostics, Inc. | ID NOW COVID-19 | RT-PCR |
| 36  | BGI Genomics Co. Ltd | Real-Time Fluorescent RT-PCR Kit for Detecting SARS-CoV-2 | RT-PCR |
| 37  | Avellino Lab USA, Inc. | Test for SARS-CoV-2 | RT-PCR |
| 38  | Mesa Biotech Inc. | Accula SARS-CoV-2 Test | RT-PCR and lateral flow |
| 39  | BioFire Defense, LLC | BioFire COVID-19 Test | RT-PCR |
| 40  | Cepheid | Xpert Xpress SARS-CoV-2 Test | RT-PCR |
| 41  | Primerdesign Ltd. | COVID-19 genesig | Real-Time PCR assay |
| 42  | GenMark Diagnostics, Inc. | ePlex SARS-CoV-2 Test | RT-PCR |
| 43  | DiaSorin Molecular LLC | Simplex COVID-19 Direct assay | RT-PCR |
| 44  | Abbott Molecular | Abbott RealTime SARS-CoV-2 assay | RT-PCR |

The selected target sequences are highly conserved and also specific to this strain of coronavirus. The IC

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Table 1 (continued)

| No. | Manufacturer | Diagnostic test name | Technology/Platform |
|-----|--------------|----------------------|---------------------|
| 35  | Abbott Diagnostics, Inc. | ID NOW COVID-19 | RT-PCR |
| 36  | BGI Genomics Co. Ltd | Real-Time Fluorescent RT-PCR Kit for Detecting SARS-CoV-2 | RT-PCR |
| 37  | Avellino Lab USA, Inc. | Test for SARS-CoV-2 | RT-PCR |
| 38  | Mesa Biotech Inc. | Accula SARS-CoV-2 Test | RT-PCR and lateral flow |
| 39  | BioFire Defense, LLC | BioFire COVID-19 Test | RT-PCR |
| 40  | Cepheid | Xpert Xpress SARS-CoV-2 Test | RT-PCR |
| 41  | Primerdesign Ltd. | COVID-19 genesig | Real-Time PCR assay |
| 42  | GenMark Diagnostics, Inc. | ePlex SARS-CoV-2 Test | RT-PCR |
| 43  | DiaSorin Molecular LLC | Simplex COVID-19 Direct assay | RT-PCR |
| 44  | Abbott Molecular | Abbott RealTime SARS-CoV-2 assay | RT-PCR |

The selected target sequences are highly conserved and also specific to this strain of coronavirus. The IC
| No. | Manufacturer | Diagnostic test name | Technology/Platform | Description |
|-----|--------------|----------------------|---------------------|-------------|
| 46  | Quest Diagnostics | Quest SARS-CoV-2 rRT-PCR | rRT-PCR | The test is a real-time RT-PCR test intended for the qualitative detection of nucleic acid from the SARS-CoV-2 in upper respiratory specimens (for example, nasopharyngeal swabs, oropharyngeal swabs, sputum, BAL, and tracheal aspirates). The assay is composed of two principal steps: (1) extraction of RNA from patient specimens, (2) one-step reverse transcription and PCR amplification with SARS-CoV-2 specific primers and real-time detection with 2019-nCoV specific probes. The assay targets regions of the virus nucleocapsid gene (N1 & N3) and is designed for the detection of SARS-CoV-2. Amplification and detection are accomplished using TaqMan chemistry on the ABI 7500. |
| 47  | Quidel Corporation | Lyra SARS-CoV-2 Assay | rRT-PCR | This test procedure received EUA status on 3/17/2020, but this revised EUA replaces the RNA extraction step with a single-step heat extraction in order to decrease reagent bottlenecks. The kit now contains a "process buffer" and there are some differences in volumes of positive and negative controls. The rest of the procedure is approximately the same as the entry on 3/17/2020, with changes made to incorporate the new RNA extraction procedure. |
| 48  | Laboratory Corporation of America (LabCorp) | COVID-19 RT-PCR Test | rRT-PCR | The test is an rRT-qPCR test, and therefore detects viral RNA. LabCorp does not collect specimens, only running the samples. Samples may be collected by the healthcare provider, or at home using the Pixel by LabCorp COVID-19 test home collection kit. |
| 49  | Hologic, Inc. | Panther Fusion SARS-CoV-2 Assay | rRT-PCR | The Assay amplifies and detects two conserved regions of the ORF1ab gene in the same fluorescence channel. The two regions are not differentiated and amplification of either or both regions leads to a fluorescence signal. The Panther Fusion system compares the fluorescence signal to a predetermined cut-off to produce a qualitative result for the presence or absence of the analyte. Performed using TaqPath COVID-19 Combo Kit on the Applied Biosystems 7500 Fast Dx Real-Time PCR instrument, or other authorized instruments. The cobas SARS-CoV-2 test is based on fully automated sample preparation (nucleic acid extraction and purification) followed by reverse transcription, PCR amplification and detection on the cobas 6800/8800 system, or other authorized instruments. Designed to be a single-well, dual target qualitative assay. |
| 50  | Thermo Fisher Scientific, Inc. | TaqPath COVID-19 Combo Kit | rRT-PCR | |
| 51  | Roche Molecular Systems, Inc. (RMS) | cobas SARS-CoV-2 | rRT-PCR | |
| 52  | Wadsworth Center, New York State Department of Public Health's (CDC) | New York SARS-CoV-2 Real-time Reverse Transcriptase (RT-PCR) Diagnostic Panel | RT-PCR | |
| 53  | Centers for Disease Control and Prevention’s (CDC) | CDC 2019-nCoV Real-Time RT-PCR Diagnostic Panel (CDC) | RT-PCR | |

**Serological**

| No. | Manufacturer | Diagnostic test name | Technology/Platform | Description |
|-----|--------------|----------------------|---------------------|-------------|
| 1   | EUROIMMUN US Inc. | Anti-SARS-CoV-2 ELISA (IgG) | Serology IgG | The test kit contains microplate strips each with 8 break-off reagent wells coated with recombinant structural protein of SARS-CoV-2. In the first reaction step, diluted patient samples are incubated in the wells. In the case of positive samples, specific IgG (also IgA and IgM) antibodies will bind to the antigens. To detect the bound antibodies, a second incubation is carried out using an enzyme-labelled anti-human IgG (enzyme conjugate) catalyzing a color reaction. It is an immunoassay based test for the in vitro qualitative detection of antibodies (including IgG) to SARS-CoV-2 in human serum and plasma. The test is |
| 2   | Roche Diagnostics | Elecsys Anti-SARS-CoV-2 | Serology Antibody | |
| No. | Manufacturer                                      | Diagnostic test name                                      | Technology/Platform | Description                                                                                                                                                                                                                                                                                                                                 |
|-----|---------------------------------------------------|-----------------------------------------------------------|--------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| 3   | Wadsworth Center, New York State Department of Health | New York SARS-CoV Microsphere Immunoassay for Antibody Detection | Serology Total Antibody | Intended as an aid in the determination of the immune reaction to SARS-CoV-2. It is to be used as an aid in identifying individuals who may have high levels of SARS-CoV-2-reactive antibodies in their blood that reflect an adaptive immune response to SARS-CoV-2 indicating recent or prior infection.                                                                                             |
| 4   | Bio-Rad Laboratories, Inc                         | Platelia SARS-CoV-2 Total Ab assay                        | Serology Total Antibody | The Platelia SARS-CoV-2 Total Ab is a one-step antigen capture format, enzyme-linked immunosorbent assay (ELISA), intended for the qualitative detection of total antibodies (IgM/IgG/IgA) to SARS-CoV-2 in human serum and plasma (dipotassium EDTA, tripotassium EDTA, lithium heparin, ACD, or sodium citrate). |
| 5   | Abbott Laboratories Inc.                          | SARS-CoV-2 IgG assay                                      | Serology IgG only    | The SARS-CoV-2 IgG assay is a chemiluminescent microparticle immunoassay (CMIA) used for the qualitative detection of IgG antibodies to SARS-CoV-2 in human serum and plasma on the Alinity i and ARCHITECT i Systems.                                                                                                                 |
| 6   | DiaSorin Inc.                                     | LIAISON SARS-CoV-2 S1/S2 IgG                               | Serology IgG only    | Qualitative detection of IgG antibodies to SARS-CoV-2 in human serum. Intended for use as an aid in identifying individuals with an adaptive immune response to SARS-CoV-2, indicating recent or prior infection.                                                                                                                                                                   |
| 7   | Ortho-Clinical Diagnostics, Inc.                  | VITROS Immunodiagnostic Products Anti-SARS-CoV-2 IgG Reagent Pack | Serology IgG only    | Qualitative detection and differentiation of IgM and IgG antibodies to SARS-CoV-2 in human plasma from anticoagulated blood (Heparin/ EDTA/ sodium citrate) or serum. Intended for use as an aid in identifying individuals with an adaptive immune response to SARS-CoV-2, indicating recent or prior infection.                                                                 |
| 8   | Autobio Diagnostics Co. Ltd.                      | Anti-SARS-CoV-2 Rapid Test                                | Serology IgM and IgG | A lateral flow immunoassay intended for the qualitative detection and differentiation of IgM and IgG antibodies to SARS-CoV-2 in serum, plasma (EDTA, citrate) or venipuncture whole blood specimens from patients suspected of COVID-19 infection by a healthcare provider                                                                                       |
| 9   | Cellex Inc.                                       | qSARS-CoV-2 IgG/IgM Rapid Test                            | Serology IgM and IgG | A lateral flow immunoassay intended for the qualitative detection and differentiation of IgM and IgG antibodies to SARS-CoV-2 in serum, plasma (EDTA, citrate) or venipuncture whole blood specimens from patients suspected of COVID-19 infection by a healthcare provider.                                                                 |
| 10  | Mount Sinai Laboratory                            | COVID-19 ELISA IgG Antibody Test                          | Serology IgG         | ELISA IgG Antibody Test consists of two serial direct Enzyme-Linked Immunosorbent Assays (ELISA) for the qualitative detection of human IgG antibodies in serum and plasma specimens collected from individuals suspected of prior infection with the virus that causes COVID-19 by their healthcare provider. An initial ELISA is performed against recombinant Receptor Binding Domain of SARS-CoV-2 in serum and plasma, followed for positive specimen by a confirmatory ELISA against full length SARS-CoV-2 Spike protein in serum and plasma. |
| 11  | Chembio Diagnostic System, Inc                    | DPP COVID-19 IgM/IgG System                               | Serology IgM and IgG | A single-use rapid immunochromatographic test for the qualitative detection and differentiation of Immunoglobulin M (IgM) and Immunoglobulin G (IgG) antibodies to SARS-CoV-2 in fingerstick whole blood, venous whole blood, serum, or plasma (lithium heparin or EDTA) samples from patients suspected of COVID-19 infection by a healthcare provider                                                                 |

*EUA Emergency Use Authorization, FDA U.S. Food and Drug Administration*
RT-PCR lab technique, which often require centralized services. Few RT-PCR based innovative diagnostic methods are in the developmental stage which detect viral materials in different ways such as gene editing tool CRISPR. But, need of the hour in this pandemic is the development and establishing innovative diagnostic tool which would be easy to use, accurate, sensitive and point of care. Although point of care serological tests (lateral flow immunoassay based) is readily available in the market for COVID-19 detection but still the quality of commercial kits needs to be re-evaluated due to occurrence of false positive results. The lateral flow-based immunoassay has advantages over RT-PCR in developing nations were the facilities for RT-PCR set up is scare. However, the lateral flow immunoassay does not give an explicit picture of the severity of the disease but can help as an aid the detection alongside with RT-PCR technique.

With the available technology, the diagnosing of the disease could be a menace shortly. Although the process of technology development is hurting up day by day integrating them for a better output is essential. In our view, following developments can make an advanced COVID-19 detection tools (Fig. 5): 1) Making isothermal amplification-based LFA could be one of the alternatives in hand to overcome the problem with current lateral flow assay of giving false negative results. 2) Paper-based device with real-time simultaneous detection of multiple DNA targets can be developed for highly sensitive and specific detection, 3) Nanotechnology intervention in the pipeline of disease detection can be potentially fruitful, 4) Development needs to be made in making use of microfluidic devices for development of new prototype for early point of care detection of the novel virus. Even screening of close biomarkers for development of accurate and precise diagnostics kit is necessary, 5) Efforts need to be made for technology forward approach by integrating it to smartphone mobile devices which are omnipresent in nature, 6) Making CRISPR-Chip based electrical detection can help us to detect the analyte even at lower concentration, 7) Development of novel face mask which in turn is integrated with an sensor can help in detecting even lower limit of virus 8) Making use of electrochemical based device as it can detect even narrow antigenic load. There is also possibility to explore the development of point-of-care tests with multiplex assays and breathe analyzer. With integration with technology it will be easy not only to identify the people suffering and also take measure as early as possible for better diseases management.

Research in the field of COVID-19 is evolving quickly and new data are generated each day. Some referenced manuscripts are preprints and have not been peer-reviewed.

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