



COVID-19 detection: Comparison and accuracy of several diagnostic tests

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Abstract

The emergence of coronavirus disease 2019 (COVID-19) pandemic caused by the severe acute respiratory syndrome coronavirus (SARS-CoV-2) has created a global alarming situation. Initially, diagnosis of the virus was conducted by a combination of different assays including; electron microscopy (EM), computed tomography (CT) scan and whole-genome sequencing. However, such time-consuming diagnosis has critically highlighted the need for a fast and specific testing approach for earlier detection. It is expected that the ongoing research advances and the continuing efforts for the fight against COVID-19 will soon bring a fruitful discovery in *in vitro* diagnostics techniques. Meanwhile, the efficiency and performance of any novel diagnostic approach should be censoriously analyzed before it comes into practice. The aims of this study were to evaluate and compare the different diagnostic tests recommended by the World Health Organization (WHO) for earlier detection of the novel SARS-CoV-2. We found that the Clustered regularly interspaced short palindromic sequence (CRISPR/Cas) detection has relatively higher efficiency, compared to all the other tests. Therefore from this report, we concluded that the discovery of CRISPR/Cas based *in vitro* diagnostics will minimize the time limit as well as the cost for COVID-19 detection.

Keywords: SARS-CoV-2, Pandemic, *In vitro* diagnostics, COVID-19, CRISPR/Cas

1. Introduction

The coronavirus disease 19 (COVID-19) has emerged at the end of December, 2019 in Wuhan city, China, which has created a panic situation all over the world ([Lin et al., 2020](#); [Wu et al., 2020](#)). In the initial stages of the outbreak its impact was greatly on China, as Wuhan province was the epicenter, subsequently it spread to the other provinces of China, as reported by

[Lin et al., \(2020\)](#); [Wang et al., \(2020a\)](#). Furthermore, [Cucinotta and Vanelli, \(2020\)](#); [WHO. \(2020a\)](#) added that since then the COVID-19 was spreading at an alarming rate, and effected many continents that led the situation to a worldwide pandemic, which has created a new challenge for human beings. The WHO reported that, since the 10th of May, 2020, the infection

caused by SARS-CoV-2 has spread in about 215 countries and territories, affecting nearly four million peoples with more than 265,862 confirmed deaths. The highest number of positive cases ($\geq 10^6$), have been reported in the United States of America (USA), followed by Spain, Italy and the United Kingdom (UK). Correspondingly, the highest numbers of death reports ($\geq 69 \times 10^3$) have been received from the USA with an accelerated number of deaths in Italy, Spain, and France (WHO, 2020b). It is to be mentioned that the number of new cases in the Wuhan epicenter was greatly reduced at the end of March, while South Korea also have successfully controlled the spread of COVID-19 and succeeded in stopping the epidemic by taking several essential measures.

2. Structure of COVID-19

Recent studies of Gorbalenya *et al.*, (2020); Pal *et al.*, (2020) reported that the novel coronavirus (SARS-CoV-2), which causes severe acute respiratory syndrome have a crown-like structure, and it belong to a family of coronaviruses known as *Coronaviridae*, which comes in the order of Nidovirales. Wrapp *et al.*, (2020) reported that the spike proteins are responsible for the attachment of the virus to the host cell receptors causing pneumonia, and may lead to other respiratory illness with symptom ranging from mild to severe state. Cui *et al.*, (2019); Andersen *et al.*, (2020) added that the genome sequence of the SARS-CoV-2 show homology with the previously reported coronaviruses, which have been seen in 2002 as they were the sources of pneumonia infections in case of severe acute respiratory syndrome (SARS), and in 2012 during the middle east respiratory syndrome (MERS). Due to high homology with SARS-CoV, the virus is coined as coronavirus (2019-nCoV) after the genome sequencing (Zhang and Holmes, 2020). Several recent studies of Khan *et al.*, (2020); Shereen *et al.*, (2020); Wang *et al.*, (2020a) revealed that the SARS-CoV-2 is a positive sense, single-stranded RNA virus with a genome of 26-32 kb, and size of around 60-200 nm in length. Its genetic characteristic features are determined by the open reading frame (ORF) genes, responsible for expression of envelope (E)

proteins, spikes (S) proteins, nucleocapsid (N) proteins and membrane (M) proteins, as shown in Fig. (1).

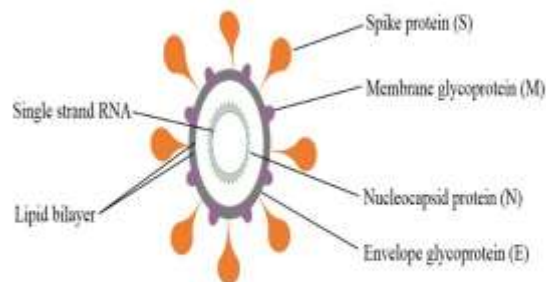


Fig. 1. Structural features of SARS-CoV-2: The outer surface contains bounded envelope proteins (E) with protruding spike proteins (S), membrane proteins (M) are found embedded in the lipid bilayer of the SARS-CoV-2, while nucleocapsid proteins (N) are present inside along with single-strand RNA

According to Shereen *et al.*, (2020); Sun *et al.*, (2020); Wang *et al.*, (2020b), the receptor-binding domain (RBD) of spike subunit 1 (S1) is known to be crucial for causing the viral infection as it recognizes and binds with the angiotensin-converting enzyme two receptors (ACE2), which is usually present in the host lower respiratory tract. Lu *et al.*, (2020); Zhang and Holmes, (2020) are claiming that all types of human coronaviruses may share a common origin, the reservoir of which are considered to be the bats.

3. Symptoms of SARS-CoV-2 infection

Instead of the low fatality rate of SARS-CoV-2, it is highly contagious as compared to SARS and MERS, due its rapid transmission rate (Chan *et al.*, 2020a; Liu *et al.*, 2020a). Peoples infected with COVID-19 may express symptoms within 14 days' time period after being exposed or come in close contact with an infected person and/or an object carrying the virus

particle. Recent studies conducted by [Chen *et al.*, \(2020a\)](#); [Huang *et al.*, \(2020a\)](#); [Singhal, \(2020\)](#) revealed that symptoms of COVID-19 may be mild to severe depending on the host immune response and his/her age, they include fever, dry cough, body ache, muscle fatigue, runny nose and shortness of breath. Old age and immune-compromised peoples are highly prone to COVID-19 with a much higher fatality rate; however, it may be completely asymptomatic in some cases. In the young population, about 80% of them experience mild symptom only ([Singhal, 2020](#); [Udugama *et al.*, 2020](#)). Moreover, [Chan *et al.*, \(2020a\)](#) added that in higher severe cases of the disease, it may also lead to diarrhea, acute respiratory distress syndrome (ARDS), and even to renal failure.

4. Treatment of COVID-19

There is no specific treatments or vaccines discovered for COVID-19; however, several studies conducted by [Colson *et al.*, \(2020\)](#); [Hu *et al.*, \(2020a\)](#) reported that symptomatic use of antibiotics and certain antiviral drugs along with a combination of chloroquine and hydroxychloroquine showed a little satisfactory results.

Accordingly, as there is a lack of *in vivo* studies for the current drugs related to COVID-19, experts recently reported the possible adverse effects of the anti-malarial drugs, thus there might be a potential threat to the underlying peoples having secondary disorders ([Juurink, 2020](#); [Owens, 2020](#)). For finding the effective drug, the latest study on cell lines with a pre-human trial, claimed the use of Atazanavir as an antiviral drug for inhibiting the SARS-CoV-2.

On the other hand, the Food and drug administration (FDA) approved the anti-parasitic drug named Ivermectin, which showed slight inhibitory effects in a lab trial, and was reported as being effective when its activity was checked *in vivo* on cell culture ([Caly *et al.*, 2020](#)). Since at present there is no highly effective drug or vaccine available to combat the COVID-19, thus the primary tactic to fight the current pandemic is the early detection and diagnosis

of infected peoples on time to isolate them, and avoid further spread of the disease. In the current study, we are going to discuss certain promising and rapid diagnostic tests that can be used for early detection of COVID-19.

5. Diagnostic tests for detection of SARS-CoV2

5.1. Real-time reverse transcription-polymerase chain reaction (RT-PCR)

The RT-PCR is one of the highly sensitive and specific methods used for COVID-19 detection ([East *et al.*, 2020](#); [Feigelman *et al.*, 2020](#)). The genome sequences of SARS-CoV-2 revealed by the National Center for Biotechnology Information (NCBI) made detection of COVID-19 easier through RT-PCR assay ([NCBI, 2020](#)). The RT-PCR phenomenon for detection of COVID-19 is based on reverse transcription; for this reason, the RNA extracted from patient's samples (may be lower or upper respiratory specimens such as nasopharyngeal or oropharyngeal swabs, sputum etc.) is initially reversed transcribed to complementary DNA (cDNA). After amplification, the RNA is finally detected through the real-time quantitative PCR, with primers and probes specifically designed for COVID-19 ([Won *et al.*, 2020](#)). For this purpose, the particular primer sets and specific guideline for detection of COVID-19 through RT-PCR were made available by the Center for Disease Control (CDC) USA, according to [CDC, \(2020b\)](#).

The design of COVID-19-RT-PCR process may be one step, thus providing a rapid and reproducible result, or it may be normally performed in a two-step process which includes; 1) sequence alignment with designing primers and probes, and 2) assay optimization, as reported recently by [Corman *et al.*, \(2020\)](#). Different institutes and departments have their own designed system of RT-PCR for COVID-19 detection, targeting either nucleocapsid gene (N), RNA dependent RNA polymerase/helicase (RdRp/Hel) spike (S), or envelope gene (E) ([Chan *et al.*, 2020a](#); [Udugama *et al.*, 2020](#)). The main steps involved in RT-PCR are presented in Fig. (2).

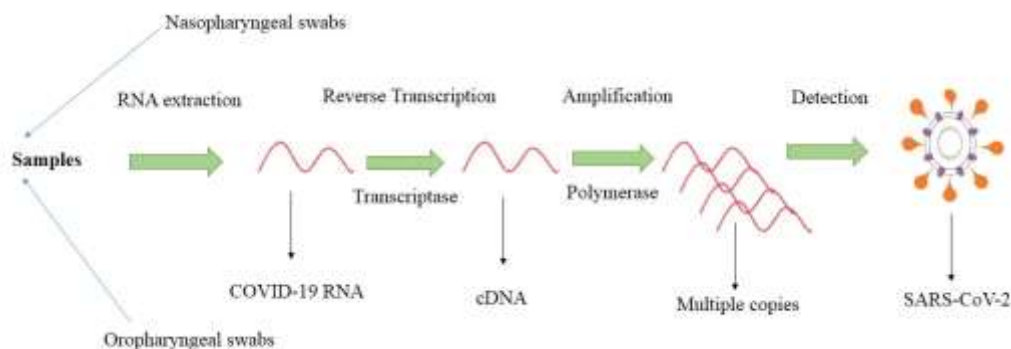


Fig. 2. RT-PCR steps for SARS-CoV-2 detection: Nasopharyngeal/oropharyngeal swab samples taken from patients are processed for RNA extraction. The extracted RNA is reverse transcribed to complementary DNA (cDNA) through reverse transcriptase enzyme. After that, the cDNA is amplified through polymerase enzyme forming multiple copies, which is finally detected as SARS-CoV2 nucleic acid

Recently, [CDC. \(2020a\)](#); [Chan, *et al.*, \(2020a\)](#) highlighted that for detection of SARS-CoV-2, the US Centers for Disease Control and Prevention uses a single RT-PCR assay, in which the extracted RNA is added to a master mixture. This master mixture primarily contains a DNA polymerase enzyme, a set of primers and a probe; containing a single oligonucleotide chain complementary to the targeted COVID-19 DNA, with a reporter and a quencher at each end. According to [Wong and Medrano, \(2005\)](#), during DNA amplification, the probe is cleaved and degraded on the base of 5'- 3' exonuclease activity of the polymerase enzyme, which in turn will release the reporter from the quencher thus permitting fluorescence.

This means that the intensity of fluorescence is highly proportional to the magnitude of the freshly synthesized DNA strands; on this basis the COVID-19 complementary DNA in any patient specimen can be quantified. [Chan *et al.*, \(2020a\)](#) revealed that among

all RT-PCR assays, the COVID-19-RdRp/Hel (RNA dependent RNA polymerase/helicase) is considered to be highly sensitive and exceptionally specific for COVID-19 diagnosis, as there is minimum reported cross-reactivity with other human coronaviruses. [Holshue *et al.*, \(2020\)](#) reported that in order to avoid any potential cross-reactivity and increase the assay performance, researchers in several countries have used more than one molecular target at a time, such as two targets loci from the nucleocapsid gene that were used in the US.

A recent study conducted by [Won *et al.*, \(2020\)](#) reported that for early detection of SARS-CoV-2, an alternative low cost rapid diagnostic RT-PCR kit for COVID-19 using Trizol-based RNA purification and SYBR Green-based RT-PCR with a newly developed protocol has also been proposed, which can be practiced at any conventional Biosafety Level II laboratories (BSL II). Several studies have also revealed that the RNA-extraction step can be omitted

by the direct detection of SARS-CoV-2 through TaqMan™ 2019-nCoV Assay Kit v1 obtained from Thermo Fisher Scientific ([Beltrán-Pavez *et al.*, \(2020\)](#)). In spite of the high sensitivity and specificity of RT-PCR, certain inadequacies with this technique also do exist, such as the required PCR testing kits that are costly, thus reduced the availability of these kits in the community hospitals ([Giri and Rana, \(2020\)](#)).

Moreover, [Corman *et al.*, \(2020\)](#) added that the experimental inaccuracy or improper handling may sometimes lead to false positive or false negative results in initial PCR testing; accordingly such mismanagement may prolong the detection process. Moreover, rural areas have no possible PCR infrastructure to handle such heavy samples for COVID-19 screening.

5.2. Computed tomography (CT) scanning

A computed tomography scan acts as a supplementary analytic and diagnostic tool, which is highly effective when there is no available setting for PCR during emergency concerns. In addition, sometimes the RT-PCR fails to detect the gene responsible for COVID-19 due to low viral load, as it is observed in the case of patients being at the early stages of infection. Recently, [Bai *et al.*, \(2020\)](#); [Chan *et al.*, \(2020b\)](#); [Huang *et al.*, \(2020b\)](#) reported that CT imaging enables the physician to detect COVID-19 patients with significant abnormalities in the lungs on the basis of certain ground-glass opacities.

[Caruso *et al.*, \(2020\)](#); [Hani *et al.*, \(2020\)](#); [Zhang *et al.*, \(2020\)](#) added that although CT scan findings for COVID-19 depends on the disease severity, some common features of the chest CT which may help the radiologist in detecting COVID-19 include; multiple lobes involvement, bilateral and sub-pleural distribution, linear or peripheral consolidations, segmental vessel enlargement and showing a crazy-paving pattern. Studies of [Caruso *et al.*, \(2020\)](#); [Fang *et al.*, \(2020\)](#) revealed that although RT-PCR is a specific method which is used as a standard reference for COVID-19 detection; however, several studies

reported that the sensitivity of CT scan in many cases was high as compared to PCR. Accordingly, during this COVID-19 pandemic, the CT scan played an important role in the early diagnosis of SARS-CoV-2 pneumonia. Recently, a deep learning-based model for COVID-19 detection through the high resolution computed tomography, showed 100% sensitivity with improved specificity ([Chen *et al.*, \(2020b\)](#)). Moreover, [Long *et al.*, \(2020\)](#) added that severe cases of COVID-19 suspects with false-negative RT-PCR results can be diagnosed using the high-resolution CT scan.

Recent findings of [Fan *et al.*, \(2020\)](#) study highlighted that apart from the positive role of CT scan, sometimes differential analysis between COVID-19 and other pulmonary syndromes/diseases is exceptionally difficult due to the overlap imaging features. However, several recent studies of [Hu *et al.*, \(2020b\)](#); [Mungmunpantipantip and Wiwanitkit, \(2020\)](#) demonstrated that certain asymptomatic cases of COVID-19 showed no any particular findings in the chest CT, so it can't be trusted as a standard assay for COVID-19 diagnosis, but it will provide complementary information's in severe cases only.

5.3. Immuno-assays/serological assays

The human adaptive immune system gets activated after entering of SAR-CoV-2 into the host cell, and then induces the production of various immune molecules, including cytokines TNF α and interleukins. Along with its different immunoglobulin proteins, the production of IgM and IgG also takes place. [Haveri *et al.*, \(2020\)](#) demonstrated that IgM production starts within the first 3-4 days, whereas IgG antibodies are produced on the 6-8 days post-infection. The study of [Xiang *et al.*, \(2020a\)](#) revealed that the detection of these antibodies may indicate the exposure of patients to SARS-CoV-2. According to [Guo *et al.*, \(2020a\)](#), the existence of IgM antibody indicates a recent infection, while IgG indicates an earlier exposure to the virus, this could be determined on the basis of the highly specific antigen-antibody interaction. However, [Zhao *et al.*, \(2020\)](#) highlighted that the current antibody tests can only provide

supplementary information's to confirm COVID-19 infection.

5.3.1. Enzyme-linked immunosorbent assay (ELISA)

Various recombinant antigens such as envelop protein (E), spike protein (S), nucleocapsid protein (N) and membrane protein (M) for COVID-19, are now available on GeneMedi, and they made the antigen detection possible through the different serological assays.

As a result, different ELISA kits based on specific antibodies (i.e. IgG and IgM) can also be used for detecting COVID-19. [Zhong *et al.*, \(2020\)](#) demonstrated that as ELISA is being rationally pronounced throughout its capacity, this technique is considered as one of the efficient tools for detection of the SARS-CoV-2 antigen. The principle of ELISA assay is based on double sandwich of the antigen and antibodies complex. The assay plate is coated with a primary capture antibody that on the addition of a specimen interacts with the antigen, and then a secondary antibody conjugated with biotin acts as a detecting antibody ([Zhao *et al.*, 2020](#)), as expressed in Fig. (3).

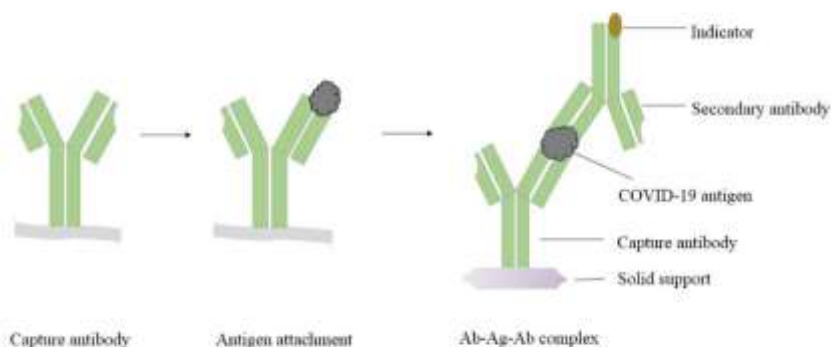


Fig. 3. Mechanism of ELISA Detection: The capture antibody is fixed on a solid support, the antigen recognizes and then binds with the capture antibody. After that, binding of a secondary antibody along with biotin Ab-Ag-Ab complex is formed. The biotin attached with secondary antibody act as a detector

[Liu *et al.*, \(2020b\)](#) reported that the SARS-CoV-2 ELISA kits are highly based on recombinant nucleocapsid (rN-based) or it may be based on the recombinant spike (rS-based) proteins, which will detect the IgM and IgG antibodies. [Liu *et al.*, \(2020b\)](#) study reported that on detecting the IgM antibodies, the rS-based ELISA kits are considered to be highly

sensitive compared to the rN-based ELISA; however, on detecting the IgG antibodies, there is no significant difference observed. In spite of ELISA being a simple, safe and rapid process with maximum specificity, but is effective in late diagnosis only, and no sufficient data is available on the precise serological diagnosis of COVID-19.

5.3.2. Point-of-Care (POC) and other rapid testing's

A number of POC testing, including lateral flow assays and Loop-mediated isothermal amplification (LAMP) are made available by the different diagnostic test manufacturers, but the WHO recommended its use only in research settings ([WHO. 2020a](#)).

However, recent studies of [FDA. \(2020a\)](#); [Li *et al.*, \(2020\)](#) reported that under emergency use authorization (EUA) approval by the FDA, a variety of newly developed combined IgM-IgG antibody-based tests have attained remarkable attention for fast screening of COVID-19 (Fig. 4).

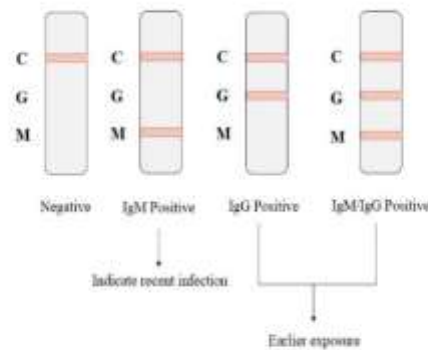


Fig. 4. Demonstration of different testing results through lateral flow assay, including a control line (C), IgM line (M) showing recent infection, and IgG band indicating early exposure to the virus

Another recent breakthrough in the *in vitro* diagnostic (IVD) assays is the development of ID Now™ COVID-19 test by [Abbott, \(2020a\)](#), which targeted the RdRp gene of the SARS-CoV-2, thus provided a leading molecular POC platform in the US. Recently, [Abbott, \(2020a\)](#), [\(2020b\)](#); [FDA. \(2020b\)](#) reported that this POC assay utilizes an isothermal amplification technology for quantitative detection of the viral RNA in a time limit of 5 minutes.

Due to the competition of speedy testing discovery by different manufacturers, Colloidal Gold- Immunochromatographic Assay (GICA) is another conventional serological assay that developed for rapid diagnosis, and showed maximum sensitivity with 100% specificity for COVID-19. A study conducted

by [Xiang *et al.*, \(2020b\)](#) revealed that kits for this GICA assay were commercialized for the 1st time by Zhu Hai Liv Zon Diagnostics Inc. Moreover, [Padoan *et al.*, \(2020\)](#) highlighted that the Chemi luminescence immunoassay (CLIA) is a new alternative IgM and IgG based supplementary serological assay, which uses the antigens from the N and S proteins of the SARS-CoV-2 that are coated on the magnetic bead of the assay.

Further development in the CLIA assay is made by the Diazyme laboratory, USA, which used an automated DZ-Lite 3000 Plus chemi-luminescence analyzer. In addition, they received the FDA emergency approval for the DZ-Lite SARS-CoV-2 CLIA discovery, as recorded by [San Diego, \(2020\)](#).

5.4. CRISPR/Cas detection system

The clustered regularly interspaced short palindromic repeats (CRISPR) is known to be a well-established biotechnological gene-editing technique, recently used in the *in vitro* detection of nucleotides sequences, hence it may play a dynamic role as an emerging and precise tool for viral diagnosis in

molecular biology ([Aman *et al.*, 2020](#)). Although the CRISPR/Cas system is a gene-editing tool, it has been reported that apart from the well-known CRISPR/Cas9 system, two other types of CRISPR systems can play significant roles in the detection of SARS-CoV-2 ([Guo *et al.*, 2020a](#)). The main components of such CRISPR/Cas diagnostic systems are shown in Fig. (5).

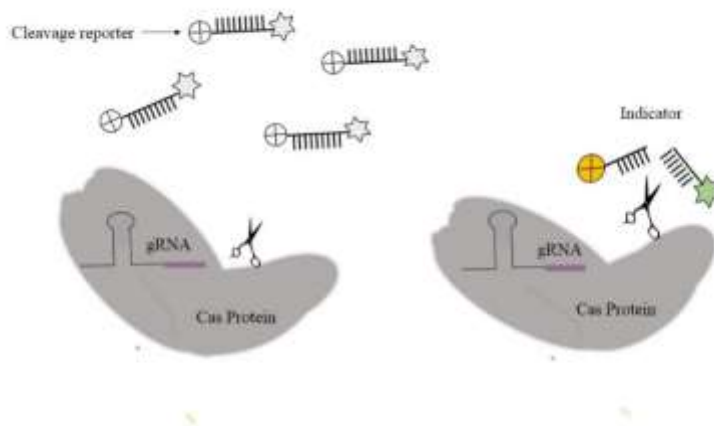


Fig. 5. CRISPR/Cas diagnostics is based on specific nucleic acid recognition and its cleavage along with non-specified reporter molecule. The gRNA recognizes the target nucleic acid sequence while the activated Cas protein cleaves it. This CRISPR/Cas complex cut the reporter molecules, which in turn emit visual signals acting as a detector for a specified nucleic acid

5.4.1. CRISPR/Cas13a (SHERLOCK)

The combination of the collateral effect of Specific high sensitivity enzymatic reporter unlocking (SHERLOCK) technology with the isothermal amplification led to the discovery of a CRISPR based diagnostic tool, having high sensitivity and single-base specificity, which may provide rapid detection of the nucleic acid ([Gootenberg *et al.*, 2017](#); [Kellner *et al.*, 2019](#)). Moreover, [Li *et al.*, \(2018\)](#); [Metsky and Freije, \(2020\)](#) revealed that as SHERLOCK uses RNA based detection system, thus through using the CRISPR-Cas13a based technology, it is now possible to do real-time *in vitro* detection of the target RNAs. In such case, the phenomenon of signal amplification is based

on a non-specific collateral cleavage of adjacent non-targeted reporter RNA ([Jia *et al.*, 2020](#)). The mechanism of SHERLOCK CRISPR/Cas model for detection of SARS-CoV-2 as demonstrated in Fig. (6), is based on the use of two particular gRNAs targeting S gene and Orf1ab. In the proposed design, isothermal amplification of the extracted RNA takes place using recombinase polymerase amplification (RPA) kit, which requires 25 minutes of incubation. The pre-amplified RNA sequence is then determined through 30 minutes of incubation with Cas protein. After a final incubation of two minutes, the result can be detected visually using a commercially available dipstick ([Guo *et al.*, 2020b](#)).

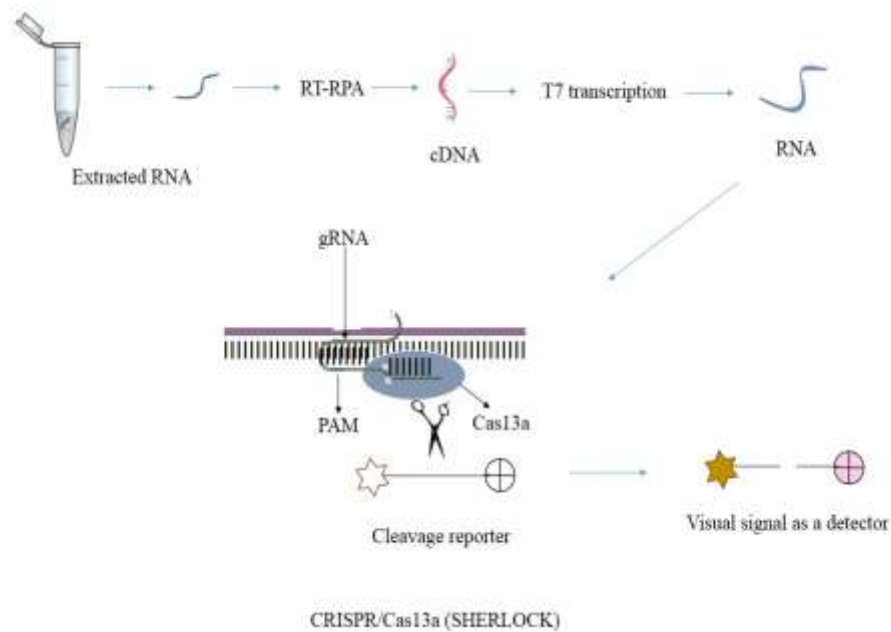


Fig. 6. Illustration of SHERLOCK model (CRISPR/Cas13a system) for SARS-CoV-2 detection: The RNA extracted from a patient sample is initially processed through reverse transcriptase, recombinase polymerase amplification (RT-RPA). The isothermally amplified cDNA is again transcribed through T7 RNA polymerase forming ssRNA. gRNA of Cas13a is based on targeted recognition of ssRNA sequence; after cleaving of specific RNA sequence by Cas13, it also does non-specific cleavage of the RNA probe. The Cas13a mediated collateral cleavage of reporter RNA can be visualized with an available paper dipstick, acting as a detector

5.4.2. CRISPR/Cas12a based detector

Recent studies of [Broughton *et al.*, \(2020\)](#); [Lucia *et al.*, \(2020\)](#) proposed another CRISPR/Cas12a based detector, which can be used as a virtuous alternative to the RT-PCR assay for the rapid diagnosis of SARS-CoV-2. The whole mechanism of CRISPR/Cas12a detection is presented in Fig. (7). [Guo *et al.*, \(2020b\)](#) proposed a design for this CRISPR CAS detection through using a combination of CRISPR and nucleic acid amplification methods along with other detection protocols, with reduced cross-reactivity. Since the CRISPR/Cas strategy is less resource-intensive and will take comparatively less time than RT-PCR, therefore it would be highly sensitive and could be more specific for detection of SARS-COV-2, according to [LeMieux, \(2020\)](#); [Morales-Narváez and](#)

[Dincer, \(2020\)](#). However, the major possible downside of CRISPR/Cas technology will be its off-target effects. Moreover, it is expected that CRISPR/Cas will need a high load for viral detection; hence it may produce slightly more false-negative results than RT-PCR ([Jia *et al.*, 2020](#)).

Various other in vitro diagnostic (IVD) companies have developed a large number of rapid testing systems. Being highly sensitive and specific, there is no need for advanced-level equipment for these tests and they can be operated on a large scale. However, related to its accuracy and evaluation, there is very little peer-reviewed data available for such rapid testing assays. As a result, many methods are not recommended by WHO as reliable tools for COVID-19 detection ([Mallapaty, 2020](#); [WHO, 2020a, b](#)).

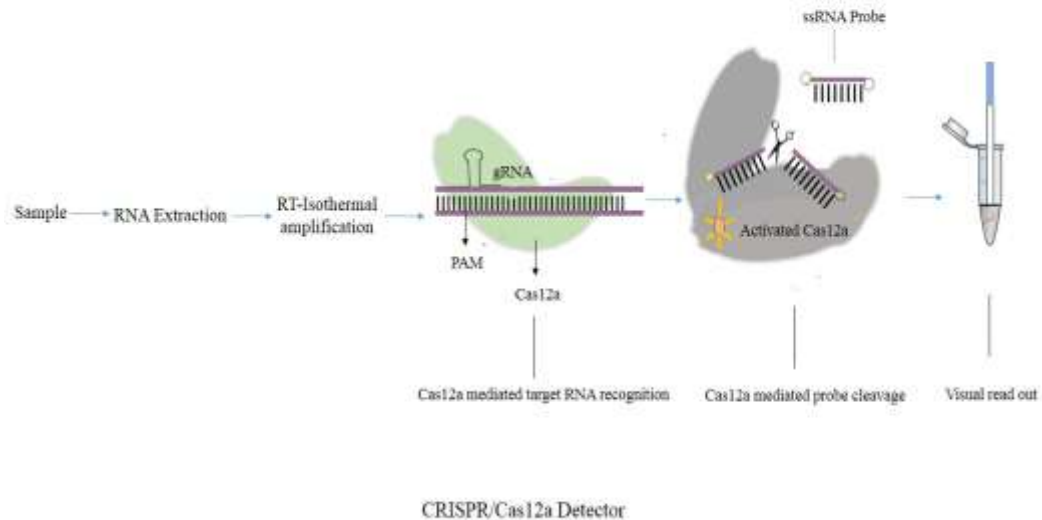


Fig. 7. Schematic flow of CRISPR/Cas12a detection system for SARS-CoV-2: RNA extraction from the patient's sample takes place, after which reverse transcription isothermal amplification of the extracted RNA occurs. The gRNA recognizes the single strand targeted complementary DNA sequence specifically and is degraded by Cas12a, whereas the single-strand DNA probe is cleaved nonspecifically by the Cas12a nucleases. This Cas12a mediated collateral cleavage of the ssDNA probe can be visualized through a color change thus acting as a detector

Conclusion

The present study reviewed the various possible diagnostic tools and compared the significances and limitations of each assay used for COVID-19 detection. Although the most precise and highly specific method for detection of COVID-19 is RT-PCR; however, the current situations also demand new and rapid diagnostic approaches. Therefore, by reviewing the different available detection technologies, and the recent application of CRISPR/Cas based detection in in vitro diagnostics, we concluded that this quick and accurate diagnostic strategy might play a complementary role in the detection of COVID-19. However, the evaluation of each diagnostic technique and approval from the FDA are necessary before practical application.

Conflict of interest

The authors declare that there is no conflict of interest.

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Ethical Approval

Non-applicable.

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