Review Article

REVIEW ON CORONAVIRUS DISEASE 2019 TRANSMISSION, DIAGNOSIS AND TREATMENT.

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ABSTRACT:

COVID-19 is caused by SARS-CoV-2, which first appeared in Wuhan, Hubei Prvince, Central China, in December 2019 and has spread rapidly since then. Coronavirus Disease 2019 (COVID-19) is caused by an infection with the Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) and has caused one of the largest global outbreaks in recent years, posing a serious threat to global public health. World Health Organization (WHO) declared a global health emergency on January 30, 2020. Despite global efforts to prevent SARS-CoV-2 transmission by quarantining infected people and their family members, social distancing, and school closures, the spread of infection could not be stopped. The case fatality rate is estimated to range from 2 to 3%. Diagnosis is by demonstration of the virus in respiratory secretions by special molecular tests. Common laboratory findings include normal/ low white cell counts with elevated C-reactive protein (CRP). The computerized tomographic chest scan is usually abnormal even in those with no symptoms or mild disease. Treatment is essentially supportive; role of antiviral agents is yet to be established'

Key Words: SARS-CoV-2, COVID-19.

INTRODUCTION

The coronavirus disease 2019 (COVID-19) pandemic has caused a sudden significant increase in hospitalizations for pneumonia with multiorgan disease. COVID-19 is caused by the novel severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). SARS-CoV-2 infection may be asymptomatic or it may cause a wide spectrum of symptoms, such as mild symptoms of upper respiratory tract infection and life-threatening sepsis. COVID-19 first emerged in December 2019, when a cluster of patients with pneumonia of unknown cause was recognized in Wuhan, China. As of July 1, 2020, SARS-CoV-2 has affected more than 200 countries, resulting in more than 10 million identified cases with 508 000 confirmed deaths. This review summarizes current evidence regarding pathophysiology, transmission, diagnosis, and management of COVID-19.

PATHOPHYSIOLOGY

Coronaviruses are single-stranded RNA viruses that are large, enveloped, and found in humans and other mammals such as dogs, cats, chickens, cattle, pigs, and bSARS-CoV-2 virions have a diameter of 60 nm to 140 nm and distinct spikes ranging from 9 nm to 12 nm, giving the virions the appearance of a solar corona. Through the process of genetic recombination Coronaviruses can adapt to and infect new environments due to their diversity.hosts. Bats are thought to be a natural reservoir for SARS-CoV-2, but this is not proven. It's possible that humans became infected with SARSCoV.2 through an intermediary host, such as a pangolin.

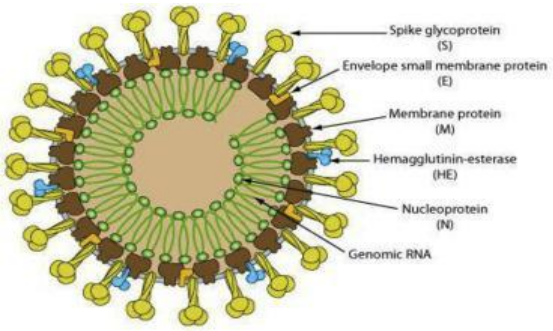

Figure 1 structure of covid 19

SARS-genomic CoV-2's component encodes four major structural proteins: spike (S), membrane (M), envelope (E), and nucleocapsid (N). It also encodes a slew of non-structural and accessory proteins. The pathogenicity of this virus is primarily determined by the virus-host interaction between the virus S protein and the host membrane receptor angiotensin-converting enzyme 2. (ACE2) The binding affinity of SARS-CoV-2 with ACE2 is greater than that of other CoV species, resulting in a higher rate of transmission,

MECHANISM OF SARS-COV-2 INVASION INTO HOST CELLS

SARS-CoV-2 is classified within the genus Betacoronavirus (subgenus Sarbecovirus) of the family Coronaviridae. Coronaviruses are 30 kb enveloped, positive-sense, single-stranded RNA viruses. They infect a wide range of hosts. Based on their genomic structure, they are classified into four genera α, β, γ, and δ. coronaviruses only infect mammals. Human coronaviruses such as 229E and NL63, which cause the common cold and croup, are coronaviruses. SARS-CoV, Middle East respiratory syndrome coronavirus (MERS-CoV), and SARS-CoV-2, on the other hand, are coronaviruses. The virus is transmitted via respiratory droplets and aerosols from person to person. Once inside the body, the virus binds to host receptors and enters host cells through endocytosis or membrane fusion. The virus's life cycle with the host consists of five steps: attachment, penetration, biosynthesis, maturation, and release. When viruses bind to host receptors (attachment) they enter host cells through endocytosis or membrane fusion (penetration). Once viral contents are released inside the host cells, viral RNA enters the nucleus for replication. Viral mRNA is used to make viral proteins (biosynthesis). Then, new viral particles are made (maturation) and released. Spike is a transmembrane trimetric glycoprotein that protrudes from the viral surface and determines coronavirus diversity and host tropism.

Spike is made up of two functional subunits: the S1 subunit is in charge of binding to the host cell receptor, and the S2 subunit is in charge of the viral and cellular membranes.

Angiotensin converting enzyme 2 (ACE2) was discovered to be a functioning SARS-CoV receptor. The spike for SARS-CoV-2 linked to ACE2 according to structural and functional analyses. The lung, heart, ileum, kidney, and bladder all had significant levels of ACE2 expression. On lung epithelial cells, ACE2 was strongly expressed. Further research is needed to see if SARS-CoV-2 attaches to another target.

The spike protein is cleaved by proteases after SARS-CoV-2 binds to the host protein. A two-step sequential protease cleavage model for activating SARS-CoV and MERS-CoV spike protein was proposed as a model, consisting of priming cleavage at the S1/S2 cleavage site and activation cleavage at the S′2 location, which is proximal to a fusion peptide .S1 and S2 subunits remain non-covalently linked after cleavage at the S1/S2 cleavage site, and the distal S1 subunit assists in the prefusion stabilisation of the membrane-anchored S2 subunit. The spike is apparently activated for membrane fusion by irreversible conformational changes caused by subsequent cleavage at the S′2 location. Because it may be cleaved and activated by a variety of proteases, the coronavirus spike is uncommon among viruses. The presence of a furin cleavage site (the "RPPA" sequence) at the S1/S2 site distinguishes SARS-CoV-2 from other coronaviruses. During biosynthesis, the S1/S2 site of SARS-CoV-2 was completely cleaved the S2 subunit. Patients infected with SARS-CoV-2 have symptoms that vary from mild to severe respiratory failure with multiple organ failure. Even in asymptomatic patients, the typical pulmonary ground glass opacification can be visible on a computerised tomography (CT) scan. Because ACE2 is strongly expressed on the apical side of lung epithelial cells in the alveolar area, this virus has a good chance of infecting and killing them. This is consistent with the fact that early lung injury frequently manifested in the distal airway.

HOST RESPONSE TO SARS-COV-2

1. **Cytokine response**

COVID-19 produces cytokines in one of two ways: directly through pattern-recognition receptors, particularly virus-specific Toll-like receptors (TLR3, TLR7, TLR8, and TLR9), and indirectly through the mediation of damage-associated Non-cytokine inflammatory mediators have been understudied in COVID-19

2. Non-cytokine mediators

Non-cytokine inflammatory mediators have been understudied in COVID-19, with the exception of ferritin and C-reactive protein (CRP; both acute-phase proteins). In critically unwell individuals, circulating ferritin is a detectable indication of secondary haemophagocytic lymphohistiocytosis (HLH) and macrophage activation syndrome (MAS-HLH)

Hormones and endocrine factors

COVID-19 problems and mortality are linked to comorbidities such hypertension, type 2 diabetes, and obesity. Circulating hyperglycaemia and diabetes were found to be independent predictors of morbidity and mortality in SARS patients. The thyroid, endocrine pancreas, testes, ovaries, and adrenal and pituitary glands, among other metabolic organs, express ACE2. Infection of pancreatic cells with SARS-CoV-2 resulted in glycaemic dysregulation, implying that coronavirus-dependent -cell dysfunction can occur in people who do not have diabetes. COVID-19 severity and mortality were found to be linked to glucose control in a retrospective analysis of 952 individuals with type 2 diabetes. Patients with well-controlled glycaemia (variability between 3•9–10•0 mmol/L) had lower mortality than those with high glycaemic variability (>10•0 mmol/L). A higher frequency of cardiovascular illness, increased ACE2 expression, lower viral clearance, and metabolic derangements may all contribute to increased COVID-19 severity in diabetic patients

In patients with severe COVID-19 the renin–angiotensin–aldosterone system (RAAS) is significantly active. Although the effect of therapeutic RAAS blocking (ACE inhibitors and angiotensin receptor blockers) is unknown, existing research does not justify stopping the medications. Through the type 1 angiotensin II receptor (AT1), angiotensin II may cause hyper inflammation by inducing IL-6 in endothelial and vascular smooth muscle cells. Furthermore, angiotensin II causes vasoconstriction and water reabsorption by increasing aldosterone levels

Cellular immune response Mild neutrophilia and T-cell lymphopenia are common in COVID-19 patients, leading in an elevated neutrophil-to-lymphocyte ratio, which is a helpful predictive marker for COVID-19 severity. Other leukocyte subsets exhibit similar fluctuations and trajectories, however they are more diverse Granulocytes.

Despite inconsistent findings on eosinophil count, the majority of investigations have found mild peripheral neutrophilia in individuals with COVID-19, regardless of disease severity. Highly active CD38+, CD11b+, and HLA-DR+ neutrophils, as well as myeloid-derived suppressor cells, make up peripheral neutrophils (MDSCs). The increase in MDSCs is suggestive of an inflammation-related, emergency haematopoiesis.

1) Monocytes and macrophages
COVID-19, studies on monocyte–macrophage composition differ, despite the fact that monocyte numbers are not significantly altered. Some research has found a shift from CD16+ monocytes to conventional CD14+ monocytes, while others have found very minor changes. . In severe COVID-19, circulating monocytes display indications of activation, such as enhanced CD and increased IL-1 and IL-6 production. Activated monocytes have been shown to migrate to the lungs in patients with COVID-19 and in mouse models of SARS-CoV-2 infection.

2) Dendritic cells
Patients with COVID-19 have a decrease of myeloid and plasmacytoid dendritic cells in their blood, according to limited data. In one study, patients with severe COVID-19 had lower dendritic cell numbers in their lungs. The key function of dendritic cells in pathogen sensing and adaptive immune responses, dendritic cell depletion might compromise the development of a protective anti-viral T-cell response.

3) T cells
For virus eradication, the cytotoxic T-cell response, a complicated process involving antigen-activated CD4+ helper T cells, is critical. Excessive T-cell activation can cause host cell death, whereas insufficient activation can aid viral propagation. The development of perivascular T lymphocytes has been linked to the deterioration of the lungs' epithelium and endothelium in severe COVID-19. Notably, in children with mild-to-moderate COVID-19, lymphopenia is rare and mild, whereas in severe paediatric cases with multisystem inflammatory syndrome, Evidence suggests that a higher proportion of T cells from patients with COVID-19 express markers characteristic of activation and exhaustion than do those from healthy participants. Lung infection by respiratory viruses typically results in recruitment and local accumulation of distinct T-cell populations mediated by various chemoattractants.

4) Natural killer cells
Natural killer cells are commonly enriched in the lungs and respond rapidly to a broad collection of viral infections. Consequently, patients with moderate-to-severe COVID-19 feature an accumulation of natural killer cells in the infected lungs, whereas natural killer cells counts in the periphery decline

TRANSMISSION OF COVID 19 BETWEEN PEOPLE

The SARS-CoV-2 virus, which can travel between humans in a variety of ways, is known to be the cause of the disease.
Coughing, sneezing, speaking, singing, and breathing can spread the virus from an infected person's mouth or nose in microscopic liquid particles. • Current data suggests that the virus transmits mostly amongst people who are in close proximity to one another, often within 1 metre (short-range). When the virus is breathed or comes into direct contact with the eyes, nose, or mouth, a person might become infected

- According to current evidence, the virus transmits primarily amongst people who are in close proximity to one another, often within 1 metre (short-range). When virus-containing aerosols or droplets are breathed or come into direct contact with the eyes, nose, or mouth, a person can get infected.
- The virus can also spread in cramped and/or poorly ventilated interior environments, where people tend to spend longer periods of time. This is due to the fact that aerosols remain suspended in the air or reach a distance of more than one metre (long-range).

SYMPTOMS OF COVID-19

The most common symptoms of COVID-19 are

- Fever, Dry cough, Fatigue

Other symptoms that are less common and may affect some patients include:

- Loss of taste or smell, Nasal congestion, Conjunctivitis (also known as red eyes), Sore throat, Headache, Muscle or joint pain, Different types of skin rash, Nausea or vomiting, Diarrhoea, Chills or dizziness.

Symptoms of severe COVID-19 disease include:

- Shortness of breath, Loss of appetite, Confusion, Persistent pain or pressure in the chest, High Temperature

Other less common symptoms are

- Irritability, Confusion, Reduced consciousness (sometimes associated with seizures),

Anxiety, Depression, Sleep disorders,

CORONAVIRUS DISEASE 2019 (COVID-19) TREATMENT & MANAGEMENT

COVID-19 is usually treated with supportive care, depending on the organ systems that are involved. Considering the high mortality rate among hospitalised patients and the facilities available for infection control, the setting of patient treatment, i.e., intensive care unit or high dependency unit versus general wards, should be selected early in the course of the disease. Patients that required hospitalisation were treated with broad-spectrum antibacterial antibiotics and glucocorticoids, according to published evidence from preliminary therapeutic experiences Non-invasive ventilation, mechanical ventilation, and extracorporeal ventilation may be used to treat respiratory failure depending on the treatment plan.

1.Antiviral drugs

Remdesivir (CIPREMI/COVIFOR)

Remdesivir has in vitro efficacy against several RNA viruses (including Ebola) and may be useful for both prophylactic and therapy of coronavirus infections, according to some preclinical investigations. Remdesivir is a broad-spectrum antiviral drug that works by inhibiting viralRNA. Although Remdesivir was found to be superior to placebo in reducing lower respiratory tract infection rates and shortening hospital stays in two different studies, there was no meaningful difference between a 5-day and a 10-day course of remdesivir. In comparison, therapeutic doses of lopinavir (LPV)/ritonavir (RTV) improved pulmonary function, albeit only marginally.

Lopinavir/ritonavir (KALETRA)

In vitro and in animal tests, LPV has been demonstrated to suppress coronavirus protease activity and to reduce mortality rates, as seen in a cohort study. The effective dose of LPV is 400 mg orally every 12 hours, and it was first thought to be a treatment option for COVID-19 based on its efficacy during prior SARS and Middle East respiratory syndrome virus epidemics. A recent randomised controlled trial, however, found no conclusive benefit of LPV/RTV therapy when compared to standard management.

Favipiravir

Favipiravir is active against RNA viruses because it is converted into the ribofuranosyl triphosphate derivative by host enzymes and then inhibits the viral RNA-dependent RNA polymerase selectively. Toyama Chemical Company in Japan was the first to discover it for use as a treatment for resistant influenza infections. The medicine has also been demonstrated to be successful in the treatment of avian influenza and could be used to treat illnesses caused by viruses such as the Ebola virus and COVID-19. Glenmark Pharmaceuticals has launched Favipiravir under the brand name ‘FabiFlu' in June 2020 for patients with mild-to-moderate COVID-19, making it the first drug of its kind. In vitro, Favipiravir has shown to be effective against the SARS CoV2 virus, and COVID-19 demonstrates a considerable improvement in mild to moderate cases. It's linked to a rapid drop in viral load and early symptom relief.

2.Immunomodulatory drugs (tocilizumab, chloroquine and hydroxychloroquine)

Tocilizumab

Tocilizumab is a humanised IgG1 monoclonal antibody that targets the IL-6 receptor and is used to treat rheumatoid arthritis, juvenile arthritis, and giant cell arteritis. It may be considered in patients with mild disease who have elevated inflammatory markers (IL-6) and a gradually higher oxygen demand, as well as mechanically ventilated patients who are recalcitrant to therapy. In patients with severe COVID-19 pneumonia, tocilizumab treatment, whether given intravenously or subcutaneously, may reduce the need for invasive mechanical ventilation or death.

Chloroquine and hydroxychloroquine

Chloroquine is a frequently used antimalarial medication with antiviral action throughout a broad spectrum.76 Chloroquine (500 mg every 12 hours) prevents SARS-CoV receptor glycosylation and so limits virus infection by raising the endosomal pH necessary for virus/cell fusion. Its demonstrated Efficacy in reducing COVID-19 pneumonia exacerbations as well as accelerating viral and symptomatic clearance. The chloroquine analogue HCQS (200 mg every 12 hours) has a better safety profile and anti-SARS-CoV efficacy in vitro. In

SARSCoV-2-infected Vero cells, HCQS was found to be more effective than chloroquine. Both chloroquine and HCQS have been observed to have Immunomodulatory effects and have the capacity to suppress the massive immune response in COVID-19 (cytokine storm) induced by mediators such as IL-1, IL-6 and IL-10.

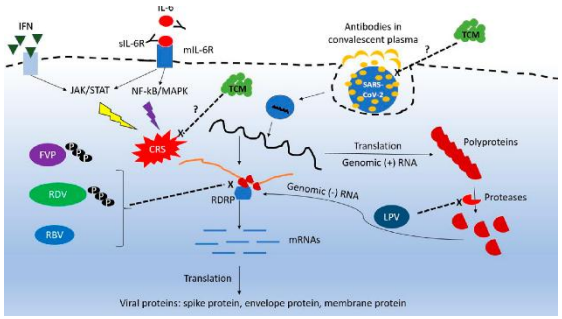

Figure 2 Conceptual diagram of mechanism of repurposing antiviral agents against SARS-CoV-2

3. Antibiotics

Although an optimal and effective antibiotic regimen is not always indicated in viral pneumonia, it can help avoid or treat subsequent bacterial infections and sepsis. Azithromycin and other macrolides are very successful at preventing pulmonary infections in patients with viral pneumonias, as well as having a considerable anti-inflammatory effect on the airways.

Corticosteroids

In patients who demonstrate progressive deterioration of oxygen saturation, increased activation of the pro-inflammatory response, and rapid worsening of characteristics on chest imaging, steroids can be given for a short period of time, 3–5 days. Methylprednisolone was the first and only steroid recommended at first, with doses ranging from 0.5–1 mg/kg/day for moderate instances to 12 mg/kg/day for severe cases. Due to the delay in virus clearance caused by steroid-mediated immunosuppression, higher doses were not indicated.

Dexamethasone has recently been discovered to be useful in reducing mortality in severe and critically ill patients.

Convalescent plasma

Convalescent plasma could confer SARSCoV2 coronavirus humoral protection in the short to medium term. The vast majority of people who recover are able to return to work.COVID19 infection leads to the development of circulating neutralising antibodies. Antibodies to the proteins of the SARS CoV2 virus 2 to 3 weeks detectable by ELISA or other methods after infection tests that are quantitative Plasma transfer from these patients should kill the virus to prevent it from spreading further .replication as well as stopping the progression of tissue damage. This In patient, this method is expected to function best.

Covid 19 vaccines available in India

Name	Manufacturer	Type of vaccine	Efficacy rate
Covishield **	Serum Institute of India	Viral vector	81.3%
Sputnik V	Gamaleya	Viral vector	91.6%
Covaxin	Bharat Biotech	Inactivated	80.6%

Covaxin is an inactivated vaccine that is developed by Hyderabad based Bharat Biotech International limited in collaboration with ICMR (Indian Council of Medical Research) and National institute of Virology, Pune. It is based on a tried and tested platform of dead viruses. The vaccine is developed using a whole-virion Inactivated Vero cell divide platform technology. Inactivated vaccines do not replicate and are likely to revert and cause pathological side effects. They contain dead viruses that is incapable of infecting people but still able to instruct the immune system to mount a defensive reaction against an infection

Covishield is based on a viral vector platform, a chimpanzee adenovirus called ChAdOx1 (the vector), that has been modified to carry the corona virus pipe protein into human cells. While the injected cold virus is harmless it serves as an instruction manual for the body on how to fight against similar viruses. This virus is used for infections like Ebola.

The **Sputnik V** vaccine is based on a proven and well-studied platform of human adenoviral vectors, which cause the common cold and have been around for thousands of years. Sputnik V uses two different vectors for the two shots in a course of vaccination, providing immunity with a longer duration than vaccines using the same delivery mechanism for both shots. There are no strong allergies caused by Sputnik V.

EFFICACY

The efficacy data of Covaxin is about 81.6%. For Covishield the efficacy varies between 70-90% depending on the gap between the two doses given to patients. Both the vaccines are authorized for market use, and emergency permission is given by the government as well that prevent Covid 19 disease individuals above the age of 18. According to Gamaleya National Research Centre of Epidemiology and Microbiology of the Ministry of Health of the Russian Federation and the Russian

Direct Investment Fund, Sputnik V vaccine demonstrated efficacy of 97.6%, based on the analysis of data on the infection rate of coronavirus among those in Russia vaccinated with both components of Sputnik V. it is one of only three vaccines in the world with efficacy of over 90%; Sputnik V provides full protection against severe cases of COVID-19.

COMMON SIDE EFFECTS

Vaccines allow the body to build immunity by activating T and B lymphocytes, cells that, respectively, recognize the targeted virus and produce antibodies to combat it.A vaccine cannot cause COVID-19. No vaccine contains a complete form of the virus responsible for this illness.
the World Health Organization (WHO)Trusted Source, common side effects of a COVID-19 vaccine include:
a fever, fatigue, headaches, body aches, chills, A person might also experience side effects around the injection site, which is usually the upper arm. These might include swelling, pain, redness, an itchy rash, and other mild forms of irritation.

Allergic reactions and anaphylaxis

Rarely, a person experiences an allergic reaction to one or more of the ingredients in a vaccine. They might develop hives or another type of skin rash, swelling, and respiratory symptoms. A severe allergic reaction can lead to anaphylaxis, and it involves low blood pressure, nausea, and difficulty breathing, among other symptoms. Anaphylaxis is an extremely rare side effect of vaccination. According to the CDC, around 2–5 people per million Trusted Source, or fewer than 0.001% of people vaccinated in the U.S. have experienced anaphylaxis afterward. Allergic reactions to mRNA vaccines have been of particular concern, as they contain a chemical, called polyethylene glycol (PEG) that has never been used in an approved vaccine before. PEG is in many drugs have occasionally triggered anaphylaxis. In these vaccines, it coats the mRNA molecule and supports penetration into cell.

TYPES OF POST-COVID CONDITIONS

Long COVID

Long COVID is a range of symptoms that can last weeks or months after first being infected with the virus that causes COVID-19 or can appear weeks after infection. Long COVID can happen to anyone who has had COVID-19, even if the illness was mild, or they had no symptoms. People with long COVID report experiencing different combinations of the following symptoms:

Tiredness or fatigue, Difficulty thinking or concentrating (sometimes referred to as “brain fog”), Headache, Loss of smell or taste, Dizziness on standing, Fast-beating or pounding heart (also known as heart palpitations), Chest pain, Difficulty breathing or shortness of breath, Cough, Joint or muscle pain, Depression or anxiety, Fever Symptoms that get worse after physical or mental activities.

DIAGNOSIS AND IMAGING

Molecular tests (RT-PCR)

The upper respiratory tract is sampled using nasopharyngeal and oropharyngeal swabs, whereas the lower respiratory tract is sampled using expectorated sputum and bronchoalveolar lavage (only for mechanically ventilated patients). After being stored at 4°C, the samples are transported to the laboratory for reverse-transcription amplification of the viral genetic material. Finally, the conserved sections of the SARS-CoV-2 genetic code are detected on the amplified genetic material.

How the RT-PCR test works

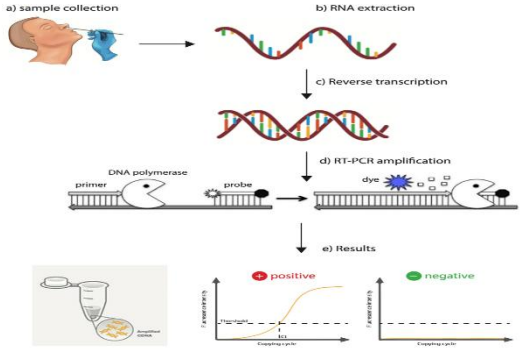

Figure 3 Process of RT PCR Test

Steps in the RT-PCR test:

a) Specimen is taken from the nose or throat of individual
b) RNA is extracted.
c) RNA transcribed into complementary DNA (cDNA).
d) Once the primers have bound to the DNA, they provide a starting point for the DNA polymerase to help copy it. DNA polymerase then degrades the bound probe which results in an increased fluorescence signal
e) The fluorescence increases as copies of the virus DNA are made. If the fluorescence level crosses certain threshold, the test is positive(Figure 2a).If the virus was not present in the sample, the PCR test would not have made copies, so the fluorescence threshold is not reached — the test is then negative (Figure 2b).
In situations of a positive test, the test should be repeated for verification, as well as to confirm viral

clearance in COVID-19 positive cases. The sensitivity of these tests is low; roughly 53.3 per cent of COVID-19-confirmed patients had positive oropharyngeal swabs, and around 71 per cent of COVID-19-confirmed patients had RT-PCR positive sputum samples. After 2–8 days, the RT-PCR results frequently reveal positive.

Rapid tests (antigenic and serological) these tests are less reliable than RT-PCR tests but can be performed at the point-of-care, or in community settings without the need of expensive equipment. The concept of the test is a bit similar to how pregnancy tests work. They make use of antibody-antigen recognition, using monoclonal antibodies to detect viral antigens. Test strips are coated with antibodies that bind to a viral protein (there are prototypes that use aptamers instead). If the patient's sample contains such proteins, they will bind to the antibodies, forming a coloured indicator on the strip. Colloidal gold nanoparticles are the most commonly used material to induce a change in colour in the presence of the analyte. This represents one of the wonderful uses of nanoplasmonics

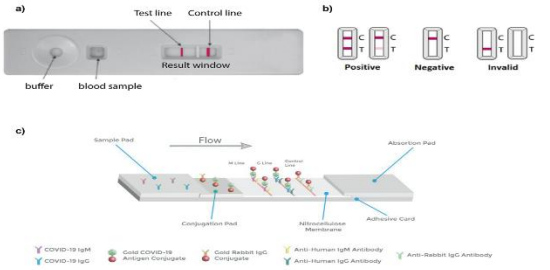

Figure 4 Rapid Antigen Test

Typical lateral flow assay for a serological test

a. Inside the cassette is a strip made of filter paper and nitrocellulose. Typically, a drop of blood is added to the cassette through one hole (sample well), and then a number of drops of buffer usually through another hole (buffer well). Buffer carries the sample along the length of the cassette to the results window.

b. Interpretation of results.

c. A schematic of the COVID-19 lateral flow test from the antibody first binds to an antigen conjugated to colloidal gold in the conjugation pad, and the resultant complex is captured on the strip by a band of bound antibody, forming a visible line (T - test line) in the results window. A control line (C-control line) gives information on the integrity of the antibody-gold conjugate.

These tests can be done in 10-30 min and far away from big laboratories, but in order for them to give reliable measurements, the concentration of the analyte needs to be higher than 10 copies/ul. This means that most of these tests may only work in symptomatic individuals.

Chest X-ray

In the early stages of the disease, a chest X-ray is frequently inconclusive and may not reveal any major alterations. Bilateral multifocal alveolar opacities appear as the infection proceeds, which may be coupled with pleural effusion. The high rate of false negatives in chest X-rays, as in PCR, is a drawback. The prematurity of the imaging test and the absence of pulmonary disease at the time of presentation; the limitations of the X-ray technique, especially in portable X-ray systems; and the fact that COVID-19's ground-glass opacities and reticular pattern can be difficult to detect on chest X-rays are all possible causes

CT

Even in the early stages of COVID-19 pneumonia, high-resolution CT (HRCT) is the method of choice for diagnosing the virus. Multifocal bilateral ‘ground-glass' areas associated with consolidation and a patchy peripheral dispersion are the most typical features, with lower lobe involvement being more common. A ‘reversed halo sign,' defined as a central area of patchy opacities surrounded by a peripheral ring with consolidation, can also be detected in some cases. Pleural effusion, cavitation, calcification, and lymphadenopathy are some of the other things that can be found.

OTHER METHODS

CRISPR/Cas tests

The CRISPR/Cas system is a bacterial immune mechanism that fights foreign DNA or RNA invasion. Bacteria use CRISPR RNA (crRNA) and Cas proteins to detect target DNA/RNA and cut invading foreign nucleic acids. CRISPR is a potent gene editing tool that can trim, cut, replace, or add to organisms' DNA sequences. CRISPR/Cas is therefore known as "molecular scissors." In recent years, it has been demonstrated that CRISPR and related proteins, primarily Cas12a and Cas13, may be utilised to recognise specific nucleic acids in samples. Cas12a and Cas13 bind to RNA or DNA targets, as determined by guide RNA (gRNA) s. Cas12a or Cas13 were used to detect the COVID-19 predicted sequence, and the virus was then validated by cleavage of the reporter molecule. Multiple detection methods have recently developed into diagnostic tools for the quick detection of SARS-CoV-2 RNA, integrating various isothermal amplification techniques (such as LAMP and RPA) and CRISPR

Cas12 is a protein that cuts double-stranded DNA. Cas12a also provides extracurricular activities. Cas12a not only cleaves the target sequence but also

any single-stranded DNA (ssDNA) in the system once crRNA binds to it specifically. CRISPR-FDS methods, includes 3 steps, the RNA extraction, target amplification, and fluorescent signal detection. Detection by this method requires that a sample contains at least 2 copies of the target RNA sequence; no detectable target signal is produced if the DNA target amplified by qPCR has less than 5 copies.

ELISA-based tests

Siddhartha Tripathi and Amit Agrawal proposed a microfluidic sandwich ELISA system to detect SARS-CoV-2 antibodies. On the microfluidic chip, a T-shaped microchannel is used to separate plasma from whole blood .The plasma is then used for a SARS-CoV-2 ELISA. Approximately 10 μL of plasma can be isolated from 1 mL of whole human blood in approximately 3 min. Xudong Fan's group invented a microfluidic ELISA method to quantitatively and sensitively detect SARS-CoV-2. IgG and viral antigen-S protein in serum was used as targets. The ELISA took 15–20 min to complete

Biosensor-based identification

Apart from the aforementioned methods, there is still an urgent need for rapid and sensitive SARS-CoV-2 identification techniques .Recently; miniature biosensors have exhibited potential as analytical platforms because of their unique characteristics, such as sensitivity, reliable specificity and rapid diagnosis, etc. biosensor, typically composed of a functional receptor, transducer, and signal detector/analyser, can sense the intruded target and directly provide sufficient feedback to the end-user with optical signals, electrical signals, etc.
Biosensor-based diagnosis is considered an alternative solution for relieving the heavy pressure on PCR-based testing, which has been proved as a promising platform during the pandemic.
Two types of biosensors are -

- Plasmonic biosensors
- Electrochemical biosensors

RT-LAMP Technology

Loop-mediated isothermal amplification, or LAMP, is an assay that can be used for viral RNA detection. Reverse-transcription LAMP (RT-LAMP) allows for quicker analysis of genetic material than traditional PCR and has been successfully used in the detection of the COVID-19 virus The methodology for RT-LAMP was based on the mechanism behind auto cycling strand displacement DNA synthesis. A polymerase carries out the reaction, and the polymerase has high strand displacement activity. There are also two pairs of primers used; one pair of inner and one of outer primers. These primers are specially designed for the reaction.
RT-LAMP can achieve high specificity due to the target sequences. Unlike other technologies, RT-LAMP recognizes the target sequence using six independent sequences at the start and by four independent sequences towards the latter stages.
RT-LAMP is the perfect technology for use in the COVID-19 pandemic due to its accuracy and relatively simple equipment. These means tests can be carried out in non-standard institutions, such as airports or rural hospitals or medical centres.

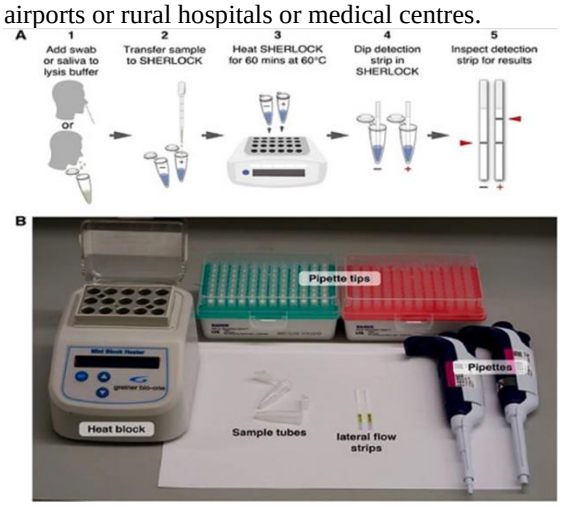

Figure 5 Process of RT LAMP Technology

CONCLUSION

The COVID-19 pandemic is still severe, and most of the drugs currently available for COVID-19 are not designed specifically against SARS-CoV-2. The search for effective antiviral agents specific to SARS-CoV-2 is still on-going. The current battle againstCOVID-19 pandemic also emphasizes the need for policies for being better equipped for any future pandemic, which includes increased funding to drugs and vaccines development, kits development, testing facilities, and fast-track FDA approval policies. Clinical evidence suggests that remdesivir can shorten the recovery time of advanced COVID-19 pneumonia. However, The clinical efficacy and safety of other agents for emergency use is controversial owing to the limitations of study designs. IL-6 inhibitors, which alleviate severe inflammation induced by cytokine release after viral infection, may improve clinical outcome of critical cases of COVID-19. Several clinical trials of IL-6 inhibitors for severe COVID-19 patients are conducted. It is still too early to draw conclusions until more evidences from well-designed clinical trials are available. COVID-19 vaccine is the most promising strategy to end the current pandemic in addition to anti-viral agents. Design of novel anti-viral agents which are specific for SARS-CoV-2 will provide more effective

therapy for COVID-19 patients. Development of effective vaccines and anti-viral drugs both needs multidisciplinary cooperation. Before effective vaccines and antiviral drugs are available, therapy with repurposing drugs are still the mainstreams. Drugs which suppress virus may benefit patients in the early phase of COVID-19.

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