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COVID -19 VIRUS PATHOGENESIS: A GLOBAL BIOTERRORISM FOR PUBLIC HEALTH

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ABSTRACT

The novel coronavirus (COVID-19) pandemic has had a devastating impact on the global population, with over 100 million cases and 2 million deaths reported worldwide. This novel virus outbreak has challenged the economic, medical and public health infrastructure of China as well as other countries remarkably the neighbors. Time alone will tell how the virus will impact our lives here in Bangladesh. The pandemic of COVID-19 has challenged our existing knowledge, laws, and regulations and forced us to take measures as far as complete lockdown in various parts of the world. The high death toll of COVID-19 has stressed the need for prompt research and dissemination of updated information. This review summarized the scopes and

developments of COVID-19 diagnosis tools and therapeutic options and also discussed the prevention and controlling steps considering an apparently upcoming second wave of infection. While the world is in search for a cure, it is recommended that countries should make use of existing scientific tools to develop models to predict community-based outcomes prior to make decisions. Healthcare workers must be supported with modern and effective facilities and remain updated with the up-to-date knowledge and practical skills. This paper provides an overview of the current state of the pandemic, including the epidemiology, clinical features, diagnosis, treatment, and prevention of COVID-19. It also discusses the economic, social, and psychological effects of the pandemic, as well as the challenges posed by the virus to global health systems.

KEYWORD: COVID-19 vaccine, Social distancing, Quarantine, mRNA vaccines, Delta variant, Isolation, Testing, Vaccination rate.

INTRODUCTION

The novel coronavirus spreads through respiratory droplets or contact with contaminated surfaces and can cause a wide range of symptoms, from mild to severe, including fever, cough, and difficulty breathing. The disease quickly spread globally and was declared a pandemic by the World Health Organization in March 2020. COVID-19 has had a significant impact on global health, economies, and societies, with millions of people infected and hundreds of thousands of deaths worldwide. To prevent the spread of COVID-19, public health measures such as wearing masks, social distancing, and frequent hand washing have been recommended. Vaccines have also been developed and authorized for emergency use in many countries, and their widespread distribution and administration are ongoing. WHO recommends nucleic acid amplification test (NAAT) based reverse transcription polymerase chain reaction (RT-PCR) as the primary testing method because of its accuracy and hence it remains the gold standard for COVID-19 detection.[1] However, the technique requires laboratory settings as well as skilled personnel to conduct the test with precision. To scale up the number of tests performed per day, the need for the development of an accurate point-of-care test is of paramount importance. Recently, some antibody-based serological studies provided insights that the number of people having COVID-19 infection could be much higher than what was previously thought. With overloaded healthcare and an increasing number of infections among the medical personnel, the ultimate way out remains to be in the discovery of an effective vaccine.

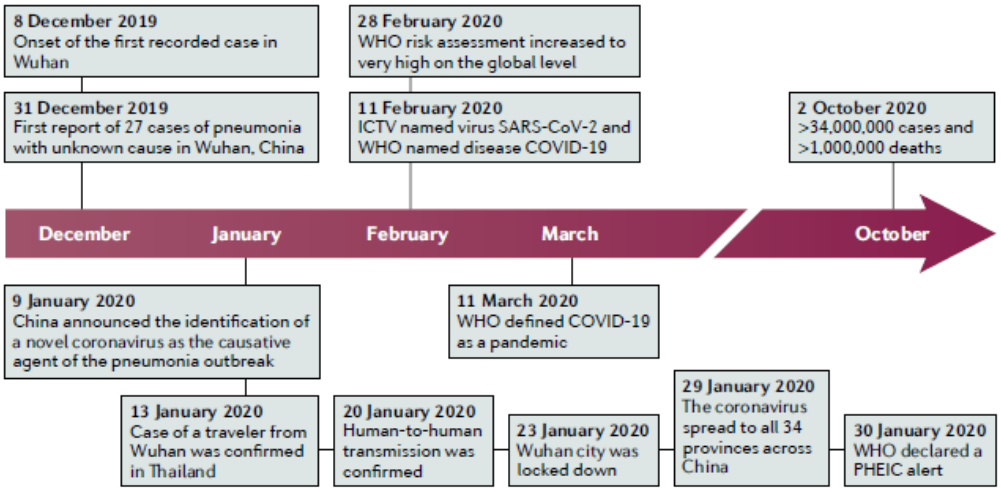


Fig. 1: Time-line of the key events of the COVID-19 outbreak.[9]

However, the discovery and development of vaccine or drugs is a lengthy process, and it generally takes around a decade to pass through the entire course. So, repurposing of existing drugs to treat COVID-19 appears as a logical scientific approach. So far, the choices are limited for the treatment of COVID-19 by a lack of specific drugs. From a variety of existing antiviral medications, repurposing the appropriate drug remains as a challenge to overcome. Small-scale studies reported a few drugs to be effective, but later proved to bring no significant difference in clinical outcomes.[2–8] High throughput virtual screening and in vitro studies are underway to look for scopes in both the development and repurposable options of antiviral drugs.[9] As the virus is moving in a pandemic speed, various control measures have been considered by different regions. Revising the decisions and their respective outcomes can further resolve the challenges in disease containment. In this review, we aimed at summarizing the current literatures to draw a compendium of understanding on the scopes of diagnostics tools, treatments, vaccines, and control measures for COVID-19.

History COVID-19 is a respiratory illness caused by the novel coronavirus SARS-CoV-2. The virus was first identified in Wuhan, China in December 2019 and quickly spread to become a global pandemic. The first cases of COVID-19 were reported in December 2019 in Wuhan, a city in the Hubei province of China. The initial outbreak was linked to a seafood and live animal market in the city. The virus quickly spread to other parts of China and then to other countries, with the World Health Organization (WHO) declaring a global pandemic in March 2020. By mid-2020, the virus had spread to almost every country in the world, and millions of people had been infected. Governments around the world implemented a range of measures to try to slow the spread of the virus, including lockdowns, social distancing, and

mask mandates. As the pandemic continued, scientists worked to develop vaccines to protect against the virus. Several vaccines were developed and approved for use in late 2020 and early 2021, and vaccination efforts began in many countries. As of early 2023, the pandemic is ongoing, and new variants of the virus continue to emerge. The impact of COVID-19 has been significant, with millions of deaths and long-term health effects for many survivors. Coronaviruses are enveloped positive sense RNA viruses ranging from 60 nm to 140 nm in diameter with spike like projections on its surface giving it a crown like appearance under the electron microscope; hence the name coronavirus.[10] Four corona viruses namely HKU1, NL63, 229E and OC43 have been in circulation in humans, and generally cause mild respiratory disease. There have been two events in the past two decades wherein crossover of animal betacorona viruses to humans has resulted in severe disease. The first such instance was in 2002– 2003 when a new coronavirus of the β genera and with origin in bats crossed over to humans via the intermediary host of palm civet cats in the Guangdong province of China. Almost a decade later in 2012, the Middle East respiratory syndrome coronavirus (MERS-CoV), also of bat origin, emerged in Saudi Arabia with dromedary camels as the intermediate host and affected 2494 people and caused 858 deaths (fatality rate 34%).[5]

Epidemiology and Pathogenesis

All ages are susceptible. Infection is transmitted through large droplets generated during coughing and sneezing by symptomatic patients but can also occur from asymptomatic people and before onset of symptoms.[9] Studies have shown higher viral loads in the nasal cavity as compared to the throatwith no difference in viral burden between symptomatic and asymptomatic people.[10] Patients can be infectious for as long as the symptoms last and even on clinical recovery. Some people may act as super spreaders; a UK citizen who attended a conference in Singapore infected 11 other people while staying in a resort in the French Alps and upon return to the UK.[11] These infected droplets can spread 1–2 m and deposit on surfaces. The virus can remain viable on surfaces for days in favourable atmospheric conditions but are destroyed in less than aminute by common disinfectants like sodium hypochlorite, hydrogen peroxide etc.[12-13] Infection is acquired either by inhalation of these droplets or touching surfaces contaminated by them and then touching the nose, mouth and eyes. The virus is also present in the stool and contamination of the water supply and subsequent transmission via aerosolization/ feco oral route is also hypothesized.[6] As per current information, transplacental transmission from pregnant women to their fetus has not been described.[14] However, neonatal disease due to post natal transmission is described.[14]

The incubation period varies from 2 to 14 d [median 5 d]. Studies have identified angiotensin receptor 2 (ACE2) as the receptor through which the virus enters the respiratory mucosa.[11] The basic case reproduction rate (BCR) is estimated to range from 2 to 6.47 in various modelling studies.[11] In comparison, the BCR of SARS was 2 and 1.3 for pandemic flu H1N1 2009.[2]

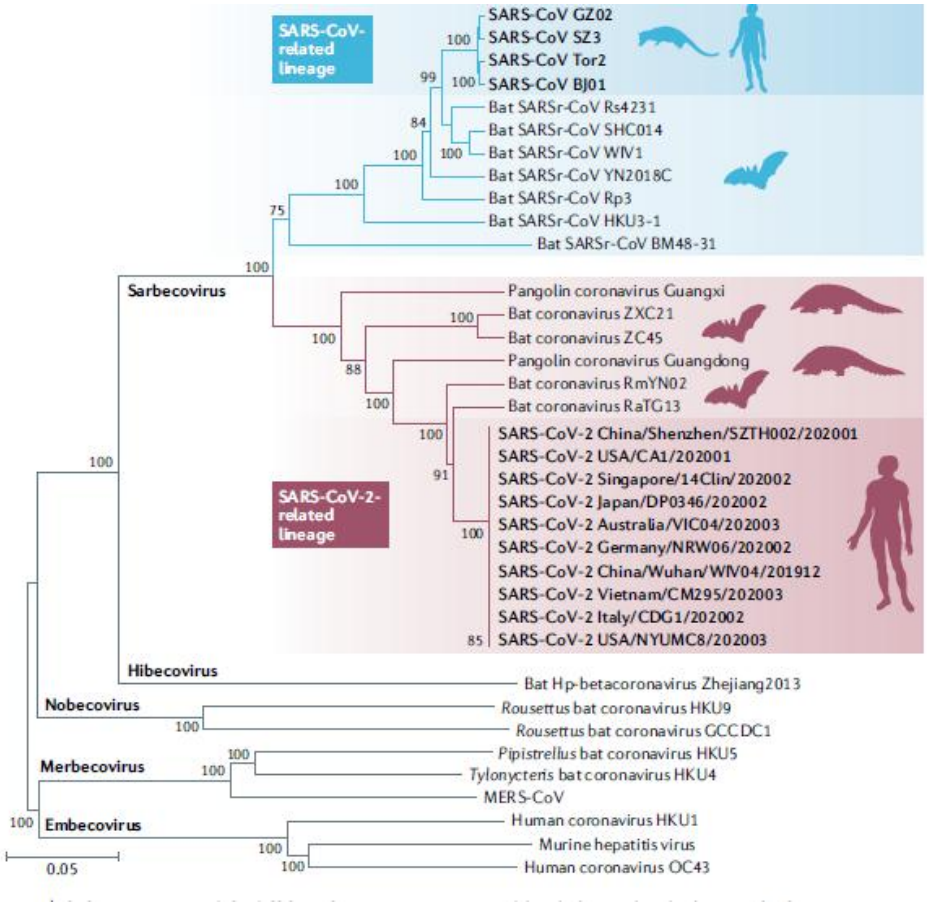


Fig. 2: Phylogenetic tree of the full-length genome sequences of SARS-CoV-2, SARSr-CoVs and other betacoronaviruses.[9]

Clinical and Epidemiological Features

The clinical and epidemiological features of COVID-19 vary widely depending on factors such as age, underlying health conditions, and viral strain. However, there are several common features that have been observed in many cases.

Clinical Features

Fever Cough Shortness of breath or difficulty breathing Fatigue Body aches Loss of taste or smell Sore throat Headache Nasal congestion or runny nose Nausea or vomiting Diarrhea.

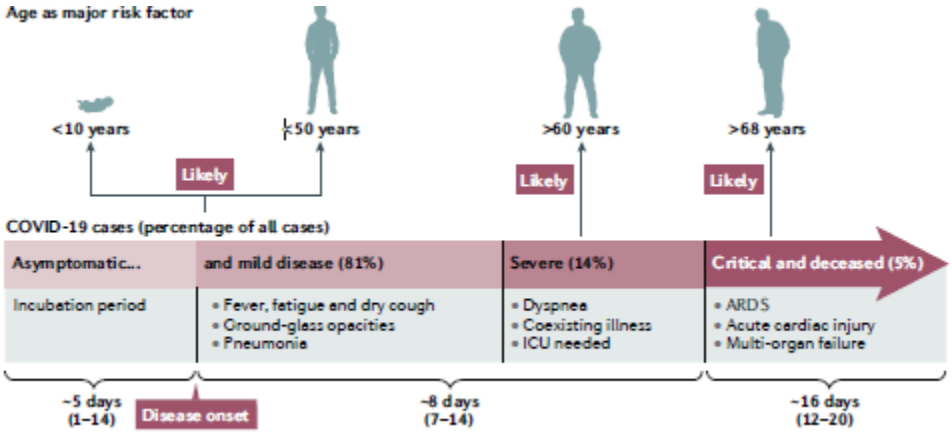
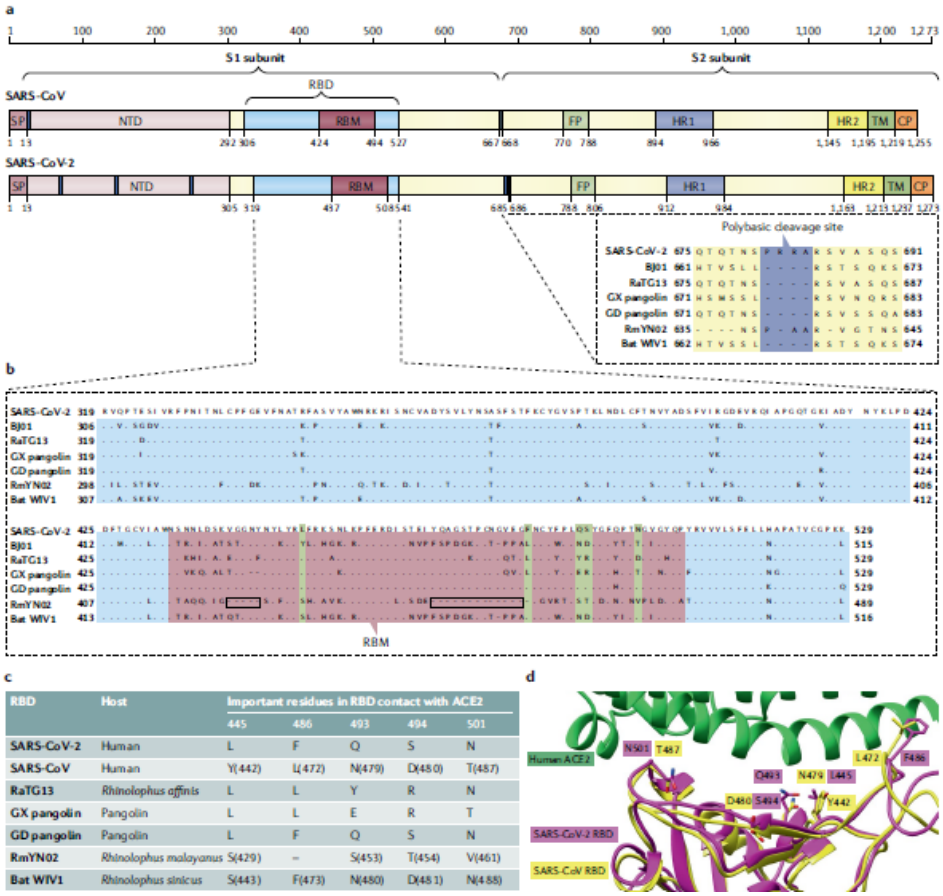


Fig. 3: Clinical features of COVID-19.[9]

Epidemiological Features

The virus primarily spreads through respiratory droplets when an infected person talks, coughs, or sneezes. The incubation period, or the time between exposure to the virus and onset of symptoms, ranges from 2 to 14 days, with most people experiencing symptoms within 5-6 days. The virus can be transmitted by people who are asymptomatic or pre-symptomatic, making it difficult to control its spread. Older adults and those with underlying health conditions, such as diabetes, heart disease, and obesity, are at higher risk of developing severe illness from COVID-19. The virus has caused widespread outbreaks and pandemics, with varying levels of severity and mortality rates in different regions. It is important to note that the clinical and epidemiological features of COVID-19 continue to evolve as researchers learn more about the virus and its variants. It is essential to stay up-to-date on the latest information from trusted sources such as the Centers for Disease Control and Prevention (CDC) and the World Health Organization (WHO). In a report of 72,314 cases in China, 81% of the cases were classified as mild, 14% were severe cases that required ventilation in an intensive care unit (ICU) and a 5% were critical (that is, the patients had respiratory failure, septic shock and/or multiple organ dysfunction or failure).[14] On admission, ground-glass opacity was the most common radiologic finding on chest computed tomography (CT).[15] Most patients also developed marked lymphopenia, similar to what was observed in patients with SARS and MERS, and non- survivors developed severer lymphopenia over time.[16] Compared with non- ICU patients, ICU patients had higher levels of plasma cytokines, which suggests an immunopathological process caused by a cytokine storm.[17] In this cohort of patient, around 2.3% people died within a median time of 16 days from disease onset.[18] Men older than 68 years had a higher risk of respiratory failure, acute cardiac injury and heart failure that led to death, regardless of a history of cardiovascular disease[19]

(Fig. 4). Most patients recovered enough to be released from hospital in 2 weeks[20-21] (Fig. 4). Early transmission of SARS- CoV-2 in Wuhan in December 2019 was initially linked to the Huanan Seafood Wholesale Market, and it was suggested as the source of the outbreak.[9,22] However, community transmission might have happened before that.[9] Later, ongoing human- to- human transmission propagated the outbreak.[9] It is generally accepted that SARS- CoV-2 is more transmissible than SARS- CoV and MERS- CoV; however, determination of an accurate reproduction number (R0) for COVID-19 is not possible yet, as many asymptomatic infections cannot be accurately accounted for at this stage.[8,9] An estimated R0 of 2.5 (ranging from 1.8 to 3.6) has been proposed for SARS- CoV-2 recently, compared with 2.0–3.0 for SARS- CoV.[23] Notably, most of the SARS- CoV-2 human- to-human transmission early in China occurred in family clusters, and in other countries large outbreaks also happened in other settings, such as migrant worker communities, slaughterhouses and meat packing plants, indicating the necessity of isolating infected people.[9,12] The high transmissibility of SARS- CoV-2 may be attributed to the unique virological features of SARS- CoV-2. Transmission of SARS- CoV occurred mainly after illness onset and peaked following disease severity.[24] However, the SARS- CoV-2 viral load in upper respiratory tract samples was already highest during the first week of symptoms, and thus the risk of pharyngeal virus shedding was very high at the beginning of infection.[12] It was postulated that undocumented infections might account for 79% of documented cases owing to the high transmissibility of the virus during mild disease or the asymptomatic period.[8,9] In addition, transmission of the virus through the ocular surface and prolonged presence of SARS- CoV-2 viral RNA in faecal samples were also documented.[10] Coronaviruses can persist on inanimate surfaces for days, which could also be the case for SARS- CoV-2 and could pose a prolonged risk of infection.[23] These findings explain the rapid geographic spread of COVID-19, and public health interventions to reduce transmission will provide benefit to mitigate the epidemic, as has proved successful in China and several other countries, such as Bangladesh.[24]



RBD	Host	Important residues in RBD contact with ACE2				
		445	486	493	494	501
SARS-CoV-2	Human	L	F	Q	S	N
SARS-CoV	Human	Y(442)	L(472)	N(479)	D(480)	T(487)
RaTG13	*Rhinolophus affinis*	L	L	Y	R	N
GX pangolin	Pangolin	L	L	E	R	T
GD pangolin	Pangolin	L	F	Q	S	N
RmYN02	*Rhinolophus malayanus*	S(429)	–	S(453)	T(454)	V(461)
Bat WIV1	*Rhinolophus sinicus*	S(443)	F(473)	N(480)	D(481)	N(488)

Fig. 4: Key differences in the spike protein of SARS-CoV-2 and related coronaviruses. A.[9]

Diagnosis

The diagnosis of COVID-19 involves several steps, including clinical evaluation, laboratory testing, and imaging.

Clinical Evaluation: The initial step in the diagnosis of COVID-19 involves a clinical evaluation by a healthcare provider. The provider will assess the patient's symptoms, medical history, and exposure to the virus. They may also perform a physical examination to check for signs of infection such as fever, cough, and shortness of breath.

Laboratory Testing: Laboratory testing is essential for confirming a diagnosis of COVID-19. The most common diagnostic test is the reverse transcription-polymerase chain reaction (RT-PCR) test. This test detects the presence of viral genetic material in a respiratory sample, such as a nasal or throat swab. In some cases, an antigen test may be used to detect viral proteins in respiratory samples. However, antigen tests are generally less sensitive than RT-PCR tests and may produce false-negative results.

Imaging: Imaging studies, such as chest X-rays or computed tomography (CT) scans, may be used to evaluate the severity of COVID-19 and to monitor disease progression. These tests can reveal signs of pneumonia or other complications of COVID-19. In addition to laboratory testing and imaging, healthcare providers may consider the patient's clinical presentation and epidemiological factors, such as exposure to the virus, when making a diagnosis of COVID-19. It is important to note that a negative test result does not rule out COVID-19, particularly if the patient has been exposed to the virus or has symptoms consistent with the disease. Healthcare providers may recommend additional testing or monitoring if there is a high suspicion of COVID-19, even with a negative test result.

Treatment

The treatment of COVID-19 depends on the severity of the disease and the patient's overall health. Mild cases of COVID-19 may not require specific treatment, while severe cases may require hospitalization and intensive care. Treatment is essentially supportive and symptomatic. The first step is to ensure adequate isolation (discussed later) to prevent transmission to other contacts, patients and healthcare workers. Mild illness should be managed at home with counseling about danger signs. Here are some of the common treatment options for COVID-19.

Supportive Care: For mild cases of COVID-19, supportive care may be all that is necessary. This may include rest, hydration, and over-the-counter medications such as acetaminophen to reduce fever and pain.

Oxygen Therapy: For patients with more severe respiratory symptoms, oxygen therapy may be necessary to maintain adequate oxygen levels in the blood. This may involve the use of nasal prongs, a mask, or a ventilator, depending on the severity of the disease.

Antiviral Medications: Several antiviral medications have been authorized or approved for the treatment of COVID-19, including remdesivir, molnupiravir, and Paxlovid. These medications work by inhibiting the replication of the virus and may help to reduce the severity and duration of the illness.

Corticosteroids: Corticosteroids such as dexamethasone have been shown to reduce mortality in patients with severe COVID-19. These medications work by reducing

inflammation in the lungs and other organs, which can be a major cause of morbidity and mortality in COVID-19 patients.

Monoclonal Antibodies: Monoclonal antibodies, such as bamlanivimab and casirivimab/imdevimab, may be used in certain high-risk patients with mild to moderate COVID-19 to prevent progression to severe disease.

Other Treatments: Other treatments that may be used in COVID-19 patients include convalescent plasma, which contains antibodies from recovered COVID-19 patients, and immune modulators such as tocilizumab, which can help to reduce inflammation. More evidence is needed before these drugs are recommended. Other drugs proposed for therapy are arbidol (an antiviral drug available in Russia and China), intravenous immunoglobulin, interferons, chloroquine and plasma of patients recovered from COVID-19.[21] Additionally, recommendations about using traditional Chinese herbs find place in the Chinese guidelines.[21] It is important to note that there is currently no single treatment or cure for COVID-19, and the optimal treatment approach may vary depending on the patient's individual circumstances. Healthcare providers will work closely with their patients to determine the best course of treatment based on their clinical presentation, underlying health conditions, and other factors.

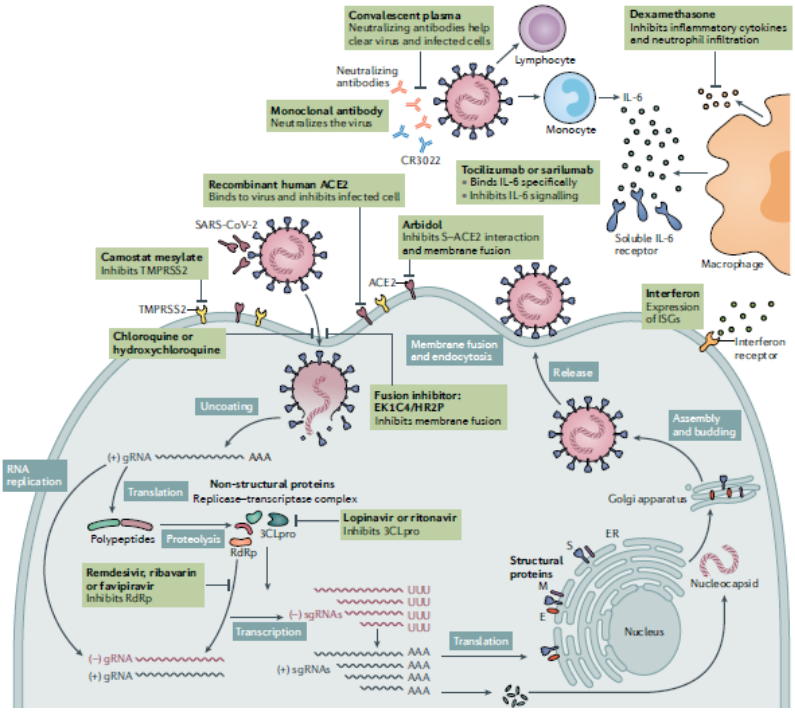


Fig. 5: SARS-CoV-2 replication and potential therapeutic targets.[9]

Vaccines

Vaccination is the most effective method for a long- term strategy for prevention and control of COVID-19 in the future. Many different vaccine platforms against SARS- CoV-2 are in development, the strategies of which include recombinant vectors, DNA, mRNA in lipid nanoparticles, inactivated viruses, live attenuated viruses and protein subunits.[25-27] There are currently several vaccines available for COVID-19, all of which have been authorized for emergency use by various regulatory agencies around the world. The vaccines use different technologies to stimulate an immune response against the virus that causes COVID-19. Some of the vaccines that have been authorized for emergency use include.

Pfizer-BioNTech vaccine: This vaccine uses messenger RNA (mRNA) technology to produce an immune response to the spike protein of the SARS-CoV-2 virus. It requires two doses, given three weeks apart.

Moderna vaccine: This vaccine also uses mRNA technology to produce an immune response to the spike protein of the SARS-CoV-2 virus. It requires two doses, given four weeks apart.

Johnson & Johnson vaccine: This vaccine uses a viral vector technology to produce an immune response to the spike protein of the SARS-CoV-2 virus. It requires a single dose.

AstraZeneca vaccine: This vaccine also uses a viral vector technology to produce an immune response to the spike protein of the SARS-CoV-2 virus. It requires two doses, given four to twelve weeks apart.

Sinovac vaccine: This vaccine uses an inactivated virus to stimulate an immune response against the SARS-CoV-2 virus. It requires two doses, given two to four weeks apart.

Sinopharm COVID-19 vaccine: Sinopharm COVID-19 vaccine is a vaccine developed by the China National Biotec Group (CNBG), which is a subsidiary of the state-owned China National Pharmaceutical Group (Sinopharm). This vaccine is an inactivated virus vaccine, which means that it contains a killed version of the SARS-CoV-2 virus that causes COVID-19. The Sinopharm COVID-19 vaccine has been authorized for emergency use in many countries, including China, the United Arab Emirates, and Egypt, among others. It has undergone clinical trials in several countries, including the UAE, Bahrain, Egypt, and Jordan, and has been shown to be safe and effective in preventing COVID-19. According to the

available data, the Sinopharm COVID-19 vaccine has an overall efficacy rate of around 79% in preventing symptomatic COVID-19 infections. This efficacy rate may vary depending on the population studied and the criteria used to define COVID-19 cases.

Prevention

Prevention of COVID-19 involves taking several measures to reduce the risk of getting infected with the virus that causes the disease. Since at this time there are no approved treatments for this infection, prevention is crucial. Patients should be asked to wear a simple surgical mask and practice cough hygiene. Caregivers should be asked to wear a surgical mask when in the same room as patient and use hand hygiene every 15–20 min. The greatest risk in COVID-19 is transmission to healthcare workers. Here are some ways to prevent COVID-19.

Get Vaccinated: COVID-19 vaccines are highly effective in preventing severe illness, hospitalization, and death from COVID-19. It's important to get vaccinated as soon as possible, especially if you're in a high-risk group.

Wear A Mask: Wear a mask that covers your nose and mouth in indoor public spaces or when you're around others who don't live in your household. Masks can help reduce the spread of the virus, particularly in areas with high transmission rates.

Practice Social Distancing: Stay at least six feet away from people who don't live in your household, especially in crowded places or poorly ventilated indoor spaces.

Wash Your Hands: Wash your hands often with soap and water for at least 20 seconds, especially after being in public places or after coughing, sneezing, or blowing your nose.

Avoid Crowds and Poorly Ventilated Spaces: Try to avoid large gatherings and poorly ventilated spaces, especially if they are indoors.

Stay Home If You're Sick: If you have COVID-19 symptoms or have been in close contact with someone who has tested positive for COVID-19, stay home and get tested.

Clean and Disinfect Frequently Touched Objects and Surfaces: Clean and disinfect frequently touched objects and surfaces, such as doorknobs, light switches, and countertops, at least once a day. These measures can help reduce the spread of the virus and protect

yourself and others from COVID-19. It's important to continue following these guidelines, even after getting vaccinated, to help slow the spread of the virus and protect those who may not be able to get vaccinated.

DISCUSSION

The COVID-19 pandemic has had a significant impact on many aspects of life, including public health, the economy, education, and social interactions. Governments around the world have implemented measures such as lockdowns, travel restrictions, and social distancing guidelines to try to slow the spread of the virus and reduce the burden on healthcare systems. The development of COVID-19 vaccines has been a significant breakthrough in the fight against the pandemic, with several vaccines now available for emergency use around the world. However, the distribution of vaccines has been unequal, with many low-income countries struggling to access enough doses. It's important to continue to follow public health guidelines and to stay informed about the latest developments in the pandemic. We can also discuss how we can support those who have been most affected by the pandemic, such as healthcare workers, low-income communities, and those who have lost loved ones to COVID-19.

CONCLUSIONS

COVID-19 is a global health crisis that has had a significant impact on individuals, communities, and economies around the world. The pandemic has highlighted the importance of public health measures such as social distancing, wearing masks, and washing hands to slow the spread of the virus. Vaccines have also played a crucial role in preventing severe illness, hospitalization, and death from COVID-19. The pandemic of COVID-19 has challenged our existing knowledge, laws, and regulations and forced us to take measures as far as complete lockdown in various parts of the world., e high death toll of COVID-19 has stressed the need for prompt research and dissemination of updated information., is review summarized the scopes and developments of COVID-19 diagnosis tools and therapeutic options and discussed the prevention and control measures considering an apparently upcoming second wave of infection. While the world is in search for a cure, it is recommended that countries make use of existing scientific tools to develop models to predict community-based outcomes prior to making. The pandemic has also exposed many inequalities in healthcare systems, with marginalized communities and low-income countries being disproportionately affected by the virus. It's important to continue to address these

inequalities and work towards a more equitable distribution of resources, including vaccines, to ensure that everyone has access to the tools they need to stay safe and healthy. At the governmental level, facilitating more testing and contact tracing, providing timely publication of epidemic information, enabling early diagnosis, and delivering supportive treatments for the patients are of utmost importance. As we continue to navigate the pandemic, it's important to stay informed, follow public health guidelines, and support one another through these challenging times. We can also use the lessons learned from the pandemic to strengthen our preparedness for future global health emergencies and work towards building more resilient and equitable communities.

Conflicts of Interest

The authors declare that there are no conflicts of interest.

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