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Review Article

A Review on Severe Acute Respiratory Syndrome 2 (SARS COV-2)

Arsalan Rasheed[1], Tahir Usman[2,*], Sadaf Niaz[1], Irfan Khattak[2], Saira Gul[2], Nawab Ali[1], Naimat Ullah Khan[2], Hazrat Ali[2], and Mian Saeed Sarwar[2]

[1]Department of Zoology, Abdul Wali Khan University, Mardan 23200
[2]College of Veterinary Sciences and Animal Husbandry, Abdul Wali Khan University, Mardan 23200

ABSTRACT

Coronavirus has attracted a lot of attention due to its ability to cause fatal zoonotic infections. These are the zoonotic viruses of both medical and veterinary importance. The virus spread through respiratory droplets and causes diseases, ranging from colds to more serious illnesses: Middle East Respiratory Syndrome, Severe Respiratory Syndrome, and Severe Respiratory Syndrome 2. The prevalence rate is high during winter and spring. Genomes of coronaviruses have large enveloped +RNA. First human corona viruses, causing respiratory diseases, were identified in 1960s, but they were not considered highly pathogenic to humans until severe respiratory syndrome broke out in China during 2003. Middle East Respiratory Syndrome, Severe Acute Respiratory Syndrome, and novel Corona Virus Disease (nCOVID-19) or Severe Acute Respiratory Syndrome-2 have increased the interest in this viral family. The Coronavirus-19 is a novel strain that was recently discovered in Wuhan (China) in December 2019. Studies revealed that reservoir of all the three fatal coronaviruses was bat with variation in the intermediate host i.e. civet cats for Severe Acute Respiratory Syndrome, dromedary camel for Middle East Respiratory Syndrome and bat or pangolin for Severe Acute Respiratory Syndrome 2. Numerous well-known corona viruses are circulating in animals that have not yet infected humans, while previously identified viruses could only be the tip of the iceberg, possibly with more novel and severe zoonotic events unfolding. Coronaviruses can be controlled with the global community's special attention and prophylaxis. However, in this review we will talk about the Severe Acute Respiratory Syndrome 2.

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Key words
Coronaviruses, Severe acute respiratory syndrome, SARS COV-2, COVID-19, nCOVID-19.

INTRODUCTION

The recognition of coronavirus (COV) as a separate virus family occurred during 1960s in the wake of the discovery of several new human respiratory pathogens, which appeared highly similar to the avian infectious bronchitis virus and mouse hepatitis virus. Coronavirus has entered the limelight owing to the 2003 outbreak of severe acute respiratory syndrome coronavirus (SARS COV) in Southeast Asia and the ongoing transmission since 2012 of the Middle East respiratory syndrome coronavirus (MERS COV), which caused about 37% mortality among patients seeking medical attention (Graham *et al*., 2012). Both viruses are closely related to COV, which is found in bats and other potential reservoirs (Ge *et al*., 2013; Menachery *et al*., 2015). The newly identified corona virus has caused Severe Acute Respiratory Syndrome 2 (SARS COV-2) pneumonia-like disease called Corona virus disease-19 (COVID-19). As of August 7, 2020, there have been 18,561,051 confirmed cases of COVID-19 and 701,263 deaths. MERS COV and SARS COV have reported a mortality rate of 10% and 37%, respectively in the last two decades. However, the confirmed cases of COVID-19 have surpassed both of them.

The SARS COV belongs to a group of β-Coronavirus that was identified as an effective agent in the SARS epidemic that occurred in Guangdong Province, China between 2002 and 2003. It was the most serious disease caused by a corona virus. Coronaviruses were only thought to cause mild and self-limiting respiratory infections in humans prior to the SARS COV outbreak. During the 2002 to 2003 epidemics, there were about 8,098 incidents in which 774 deaths occurred resulting in a death rate of 9%. In the elderly, the mortality rate was much higher. In addition, the outbreak caused an estimated loss of 40 billion in economic activity, as many activities around the world were at halt for months to put curb on the disease. While the SARS COV epidemic was controlled in 2003, the recent SARS COV-2 sparked a new COV strain similar to the SARS COV of 2003 (Ramphul and Mejias, 2020).

* Corresponding author: tahircau@gmail.com; tahirusman@awkum.edu.pk
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HISTORY OF SARS COV-2

SARS COV-2 is a 29,903 bpss-RNA Betacoronavirus (Fig. 1). On December 31, 2019, Chinese officials announced that 27 people in Wuhan had been infected with a new strain of coronavirus. Since then, the number of infectious disease cases has been labelled as 2019-nCOV, COVID-19, SARS COV-2 or Wuhan virus, with new cases appearing daily. On January 30, 2020, the World Health Organization (WHO) declared the epidemic as a global emergency and highlighted the urgent need for a rapidly coordinated international response to address this global health threat. As of 31st January, 7,711 cases of infection were reported in China, including 200 deaths. In addition, about 100 people in 19 countries, including the United States, Germany, France, South Korea, and Singapore, have tested positive for the virus. Since it was first seen in stallholders, the SARS COV-2 is thought to have originated from the Wuhan Seafood Market, which also trades an illegal wildlife, such as bats, marmots, birds, and snakes. Preliminary analysis of the microbes divulged that the new clout was similar to that of COV in snakes, but scientists have now discovered that SARS COV-2 is also mutated from bats similar to SARS COV.

Since January 22, 2020, Chinese authorities have imposed a travel ban on 11 million Wuhan residents and suspended all buses, trains and flights outside the city. Public transport has also been suspended in nearby cities, such as Huanggang, Ezhou, Zhejiang, Chibi, Xian Tao, and Qianjiang. Wuhan officials were closely monitoring the health of the families of all infected patients and residents, who had entered the now-closed market around the time the virus was first detected. They also closed all schools until March 2020. The Chinese government has installed thermometers at points across the country. Anyone having a slight fever is immediately taken to medical centre for diagnoses and treatment. Similar measures are being taken around the world to prevent the spread of the virus. On January 28, 2020, Hong Kong officials announced the closure of some of their border crossings with mainland China.

EPIDEMIOLOGY OF SARS COV-2

COVID-19 is a self-limiting disease in more than 80% of patients. In around 15% of patients, acute pneumonia has occurred as seen in trials with broad patient populations. At 25 February 2020, global fatality was recorded 3.4%. This average is 4.4% for Wuhan patients, 4.0% for Hubei patients, and 0.92% for Hubei patients. Wuhan's exceptionally high fatality can be interpreted by a shortage in hospitals, vast numbers of misdiagnosed patients, or a mixture of suboptimal care (Yuen *et al*., 2020). As of March 10, 2020, the World Health Organization (WHO) reported 113,702 globally confirmed cases and 4,012 deaths. 71% of all confirmed cases related to COVID-19 (80,924) and 78% of all deaths (3,140) were from China and its environs. Since the case was first reported in Wuhan, other countries had announced that they had at least one confirmed case of COVID-19. The WHO officially classified China as a "high risk" region for COVID-19 (WHO, 2020). The recent outbreak of a new type of corona virus, COVID-19 or SARS COV-2, in China, has sparked a massive global effort to contain

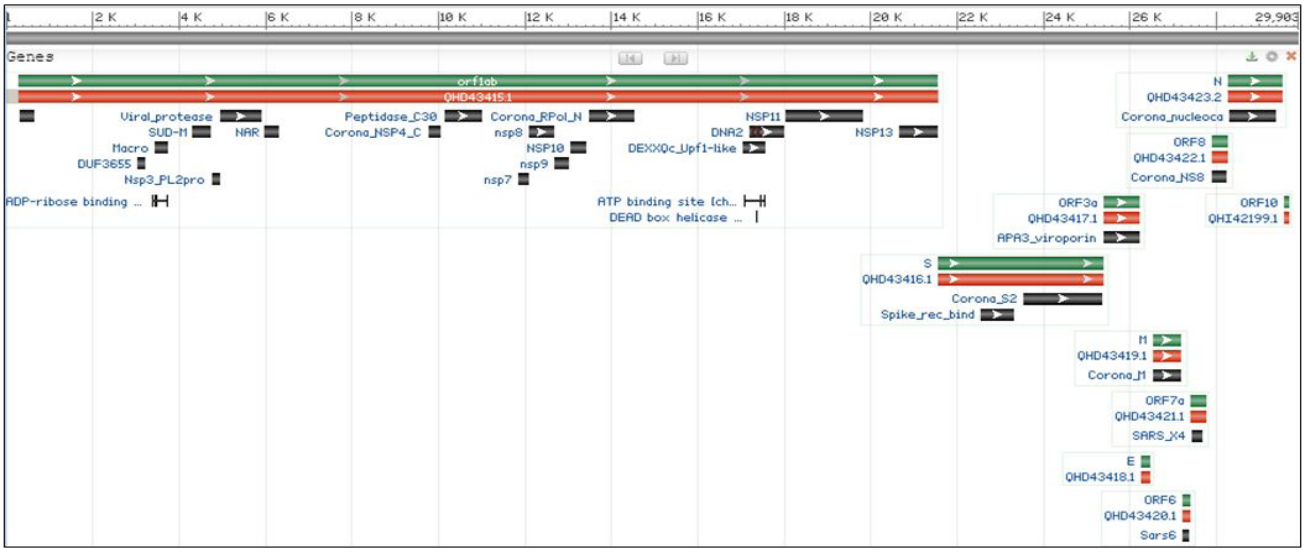

Fig. 1. Complete genome of SARS-CoV-2 (Source: NCBI/ https://www.ncbi.nlm.nih.gov/nuccore/MN908947.3?report=graph)

and slow its spread. Despite these efforts, the virus has been circulating in several countries and regions outside China in recent months. The locations of COVID-19 cases certified by the National Institutes of Health (NIH) and WHO are shown in Table I and Figure 2.

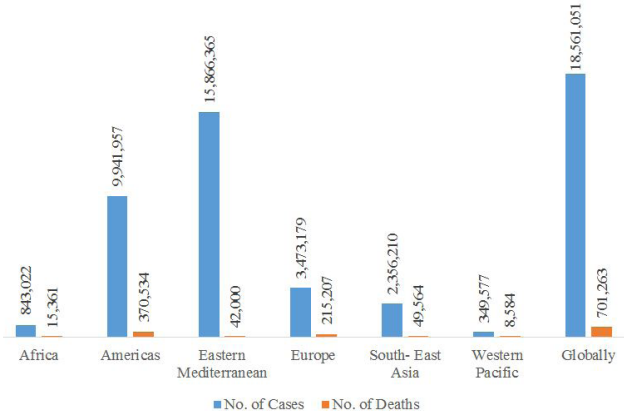

Fig. 2. Epidemic reports of COVID-19 up to 28 March 2020 (Source: WHO, 28 March 2020).

Table I.- COVID-19 worldwide situation report up to 7th August, 2020.

Area	No. of cases	No. of deaths
Africa	843,022	15,361
Americas	9,941,957	370,534
Eastern Mediterranean	15,866,365	42,000
Europe	3,473,179	215,207
South-East Asia	2,356,210	49,564
Western Pacific	349,577	8,584
Globally	18,561,051	701,263

*Most cases are locally transmitted with few imported cases except for Africa where majority of cases are imported and few are local.

TRANSMISSION OF SARS COV-2

COV transmission is primarily by the respiratory and oral organs. Oral and salivary transmission of MERS-COV and SARS-COV is also possible (Goh *et al*., 2013; Wang *et al*., 2004). Those people are at risk for self-infection who live with or care for someone with COVID-19. Continued transmission of SARS-COV-2 in Wuhan suggests that tertiary and quaternary spreading has occurred. Transmission of SARS-COV was relatively ineffective, as it only spreads through direct contact with infected people after the onset of the disease, or through salivary droplets containing particularly large particles. It can only be suspended in the air for three to six feet before dispersing. According to the Centres for Disease Control and Prevention (CDC), SARS COV-2 is transmitted from one person to a human in a range of 180 cm through respiratory droplets. The virus can be spread through the contact of infected person with material objects. SARS COV-2 can last for several hours on various types of surfaces *i.e.* 4 h on copper, up to 24 h on cardboard and 2-3 h on plastics and stainless steel. Experts say that as long as you are not in close contact with someone who has the corona virus, you can stay safe. In the same manner epidemic of SARS was brought under control in June 2003 as a result only a few cases occurred that confirmed that the outbreak of coronavirus is controllable through the use of quarantining. Retrospective analysis of all confirmed cases in Wuhan should be very informative regarding the transmission of SARS-COV-2.

In addition to transmission via droplets and close contact, fecal–oral transmission of SARS-CoV has proved to be significant in some cases. The role of the fecal-oral path in SARS-CoV-2 transmission is confirmed by the gastrointestinal presence of SARS-CoV-2 infection and SARS-CoV-2 isolation from fecal samples of patients. Although the probability of SARS-CoV-2 transmission by polluted water, air conditioning systems and aerosols was rarely observed in studies with large cohorts (CDC, 2020; Wang *et al*., 2020); it should not be underestimated, especially for instance for Diamond Princesses cruise ship with 3,700 people, of whom at least 742 were reported to be infected by SARS-CoV-2 (Yuen *et al*., 2020). In these cases, and the representative resident areas chosen for comprehensive epidemiological studies, further studies would be appropriate to establish the role of fecal–oral transmission in Wuhan as discussed above.

SYMPTOMS OF COVID-19

Symptoms of COVD-19 may appear 2-14 days after exposure to SARS COV-2. The symptoms are similar to those of influenza when infected with the flu. These include fever, cough, fatigue, muscle aches, persistent pain or pressure in the chest and shortness of breath. Some victims have also experienced headaches and diarrhoea while death can occur in severe cases. In fact, the incidence of illness was not higher for pregnant women (Hu *et al*., 2020). However, evidence of trans placental transmission of SARS-CoV-2 from infected mother to neonate has been identified, but this was an isolated event (Chen *et al*., 2020; Vivanti *et al*., 2020). However, the shedding of asymptomatic and pre symptomatic viruses provides a huge obstacle to infection control (Chan *et al*., 2020). Moreover, it is often difficult to classify and quarantine

patients with moderate and unspecified signs (Bai *et al*., 2020). Notably, the lack of fever is more common in SARS-CoV-2 infection (12.1%) than in SARS-CoV (1%) and Middle East coronavirus respiratory syndrome (MERS-CoV; 2%) (CDC, 2020). In light of this, it is important to review the efficacy of the use of fever diagnosis as a form of surveillance.

However, the viral loads in asymptomatic carriers are remarkably low, based on prior observations of influenza viruses and community-acquired human coronaviruses (Heimdal *et al*., 2019). The chance should stay low if this is also the case for SARS-CoV-2. Studies are desperately needed on the natural history of SARS-CoV-2 infection in humans. Over a span of time, detecting a cohort of asymptomatic carriers in Wuhan and following their viral loads, clinical presentations and antibody titers will provide hints as to how many of the subjects have symptoms in a later stage, whether virus shedding from the subjects is potentially less robust, and how much SARS-CoV-2 could be spread to others.

DIAGNOSIS OF COVID-19

Diagnosis is also important in areas where severe SARS COV-2 is spreading. RT-PCR has become the method of choice for diagnosis of human COV, because the multiplex real-time RT-PCR has been developed. They are able to detect all four human respiratory COV and could be further adapted to diagnose novel COV (Gaunt *et al*., 2010; Fehr and Pearlman, 2016). Serological assays are important in cases where it may be difficult to isolate RNA for the study of infectious diseases. PCR kits are commercially available for SARS, including internal controls and protocol to follow. PCR primers and procedures have been published and can be adapted to laboratories. The PCR procedure should have appropriate negative and positive control in each run, which should yield the expected results. At least two different clinical specimens (e.g. nasopharyngeal and stool), the same clinical specimen accumulated during illness for two or more days or repeat PCR using two different sizes or original clinical samples at each test site to confirm a positive PCR of the SARS virus. If a positive PCR result is found, it must be verified by repeating the PCR using the original sample or by testing the same sample in another laboratory. Amplifying a second genomic region can further enhance the test feature.

Diagnosis of SARS COV-2 can also be made with the help of isolation in cell culture of SARS-COV from any specimen along with PCR confirmation using a validated method. ELISA and IFA tests are being developed by research laboratories for diagnoses of SARS COV-2 but SARS COV-2 antibodies are not found in populations that have not been exposed to the virus because it is a new disease in humans. An antibody rise between acute and convalescent phase sera tested in parallel is very specific. Seroconversion by ELISA or IFA requires a negative antibody test on severe serum followed by a fourfold increase in antibody titer between the acute and convulsive phase sera tested in parallel. Identifying cases will help promote public health measures to control epidemics. To control these pathogens and protect foodstuffs, it is also important to diagnose cases of severe, severe veterinary COV-induced disease, such as porcine epidemic diarrhoea virus and avian infectious bronchitis virus.

Early diagnosis is essential for managing the dissemination of COVID-19. SARS-CoV-2 nucleic acid molecular identification is another method of diagnosis (Bordi *et al*., 2020). There are several commercially available kits for nucleic acid identification targeting *ORF1b, N, E* or *S* Genes (including RdRp) (Chan *et al*., 2020; Konrad *et al*., 2020). The detection time varies according to the technology, from few minutes to hours. Many variables will impact molecular detection (Pan *et al*., 2020). Although SARS-CoV-2 was identified from a number of respiratory sources, including swabs of the throat, oropharyngeal saliva, nasopharyngeal swab, sputum and bronchial fluid, lower respiratory tract tests have increased the viral load (To *et al*., 2020; Han *et al*., 2020). Viral nucleic acid was also present in gastrointestinal or blood tests, including though respiratory samples were negative (Wang *et al*., 2020). Finally, the viral load may already decrease at the onset of disease from its peak stage. False negatives can also be normal where oral swabs are used and multiple detection methods should be used to validate a diagnosis of COVID-19.

Some other detection techniques have been used to detect SARS-COV-2. Chest CT was used to easily classify a patient when molecular detection capability was overwhelmed in Wuhan. Patients with COVID-19 displayed typical features of the initial CT, including bilateral multilobar ground-glass opacities with a peripheral or posterior distribution. It was also proposed that CT scanning coupled with repetitive swab testing might be used for persons with elevated clinical suspicion of COVID-19 but who were screened negative during initial nucleic acid testing (Hu *et al*., 2020). Finally, SARS-CoV-2 serological tests to detect N or S protein antibodies can complement molecular diagnosis, especially in the late phases following onset of disease or in retrospective studies. However, the nature and length of immune responses are still uncertain, and the available serological tests vary in their sensitivity and precision, both of which need to be taken into consideration when deciding on

serological tests and evaluating their findings or potentially in the future test for T cell responses.

Another type of rapid diagnostic test (RDT) identifies the presence of viral proteins (antigens) in a sample from a person's respiratory tract which is expressed by the COVID-19 virus. If the target antigen is present in sufficient concentrations in the sample, it will bind to the specific antibodies attached to the paper strip contained in the plastic casing and, typically within 30 min, generate a visually detectable signal. The detected antigen(s) are only expressed when the virus is actively replicating, so it is best to use these tests to identify acute or early infection. The performance of the tests depends on a number of factors, including the time since the onset of the disease, the concentration of the virus in the sample, the quality of the sample collected from the individual and how it is processed, and the precise formulation of the reagents in the test kits. The sensitivity of these tests could be expected to vary from 34 to 80% based on experience with antigen-based RDTs for other respiratory diseases such as influenza, in which affected patients have comparable influenza virus concentrations in respiratory samples as seen in COVID-19 (WHO, 2020).

There is another, more common type of RDT marketed for COVID-19; a test that detects the presence of antibodies in the blood of people believed to have been infected with COVID-19 (Liu *et al*., 2020; Li *et al*., 2020; WHO, 2020). Antibody testing, also known as serology testing, is typically conducted after complete recovery from COVID-19. The immune system generates these antibodies (proteins) that are essential to battling and clearing the virus. If the test findings reveal antibodies, it means that patient been contaminated with COVID-19 at some stage in the past and also have some immunity. Yet there is a lack of data as to whether having antibodies means that affected person is safe from COVID-19 reinfection. It is not yet known the extent of immunity and how long immunity lasts. Benefit of accurate antibody testing is that people who've recovered from COVID-19 may be eligible to donate plasma, a part of their blood. This plasma (convalescent plasma) could be used to treat others with severe disease and boost the ability to fight the virus. More evidence on this will gradually be revealed by continuing research. Based on current data, WHO does not recommend the use of antibody-detecting RDTs for patient care but encourages the continuation of work to establish their usefulness in disease surveillance and epidemiologic research (WHO, 2020).

TREATMENT OF COVID-19

To date, there is no antiviral treatment that specifically targets the human coronavirus. Therefore, only limited options are available to prevent corona virus infection. According to National Institutes of Health, people infected with COVID-19 can use nonsteroidal anti-inflammatory drugs (NSAIDs) or acetaminophen. Several studies are focused on an antiviral medication known as remdesivir which was created to fight Ebola. Researchers in the U.S. say remdesivir helped patients in one study recover from COVID-19 31% faster (NIH). Several potential vaccines have been developed but none have yet been approved for use. These vaccines include individual viral proteins that appear to be reproduced by strain viruses, direct virus vectors or DNA plasmids. Therapeutic SARS-COV neutralizing antibodies have been developed can be used again in the case of SARS-COV outbreaks. Such antibodies will be most effective in protecting healthcare workers. In general, it is thought that the direct strain vaccine will be most effective in targeting the coronavirus.

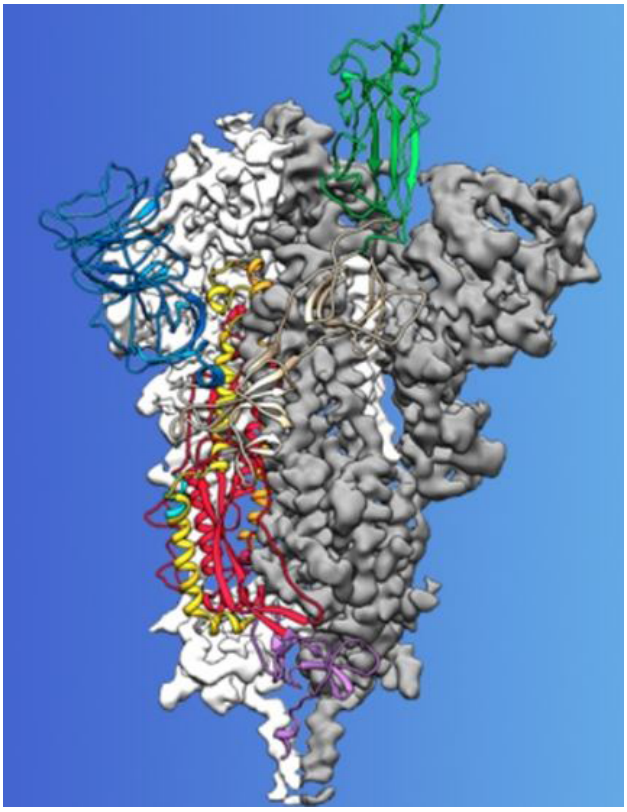

Fig. 3. Atomic-level structure of the spike protein of the virus that causes COVID-19 (Source: Wrapp *et al*., 2020).

Despite this success, the development of a vaccine for coronavirus faces many challenges. First, for mucosal infections, natural infection does not prevent subsequent infection. Therefore, vaccines should either provide better

immunity than the original virus or minimize the risk of secondary infections. Second, the increase in virus rehabilitation could lead to the vaccine being useless and potentially causing problems by increasing the evolution and diversity of the virus in the wild. Finally, it has been shown in feline infectious peritonitis virus that vaccination with S protein leads to enhanced disease. Nevertheless, a number of strategies are being used to develop vaccines that can reduce the likelihood of recurrence, for example by making large deletions in NSP1 (Zust *et al*., 2007) or E proteins (Netland *et al*., 2010), rearranging the 3′ end of the genome (De Haan *et al*., 2002), modifying the TRS sequences (Yount *et al*., 2006) or using mutant viruses with abnormally high mutation rates that significantly reduce the virus (Graham *et al*., 2012).

The SARS and MERS epidemics have encouraged research on these viruses and this research has identified a number of suitable antiviral targets, such as viral proteases, polymerase and entry proteins. In record time, an NIH-funded team of researchers mapped the first nuclear scale of a protein-related protein target for vaccine development (Wrapp *et al*., 2020). This is the so-called spike protein on the new coronavirus that causes COVID-19. One part of this sticky substance (green) on the surface allows the virus to bind to receptors on human cells, causing other parts of the spike to degrade viral and human cell membranes (Fig. 3). This process is needed for the virus to gain entry into cells and infect them. Importantly, his team had earlier developed a method to lock coronavirus spike proteins into a shape that makes them both easier to analyse structurally via the high-resolution imaging tool cryo-electron microscopy and to use it in vaccine development efforts. However, to develop drugs that target these processes and are able to inhibit viral replication, significant work remains.

IMPLEMENTING HOME CARE FOR COVID-19 PATIENT

COVID-19 patients that are medically healthy who may undergo home treatment (or discharged to home patients after hospitalization with a reported infection with COVID-19) should be isolated at home until it is felt that the risk of secondary transmission is limited. A healthcare provider should decide whether the residential environment is ideal for home treatment in consultation with state or local health department personnel. According to CDC interim guidelines (2020), home care concerns include whether the patient and home is well enough to obtain home care like there should be a bedroom and bathroom where the patient can recover without sharing immediate space with others. Similarly, resources for access to food and other necessities should also be available.

The patient and all members of the family should be able to adhere to prescribed procedures as part of home treatment or isolation, including the patient's need to wear a mask if indicated. The caregiver may also wear a mask and may take regular proactive actions to avoid getting sick. Masks can be bought or made at home. Family members having higher risk for serious illness should not take care of COVID-19 patients because members of the family could be at elevated risk of serious COVID-19 disease if exposed to the SARS-COV-2. These recommendations are based on what is still known about the role respiratory droplets play in the spread of SARS-COV-2.

PROPHYLAXIS

There is currently no specific treatment available for people infected with COVID-19. However, according to CDC, if diagnosed early, most people will recover on their own by taking the commonly available cold medicine to relieve symptoms. The most serious cases of the disease are still limited to people with weakened immune systems, the elderly or people with respiratory illness. Because COV is transmitted by mash drops, it is recommended to take simple precautions people to stay safe like frequent and thorough hand washing, avoiding touching their eyes, nose or mouth with their hands, and staying away from people who show flu-like symptoms. People with symptoms of the virus are advised to cover their mouth and nose while they cough and sneeze. They are also advised to stay away from school, work or any public area where they are at risk of infecting others.

The WHO's strategic goal of controlling the spread of SARS COV-2 is to impede the transition from human to human. It aims to reduce the COVID-19 by the following steps: (i) Secondary infections among close contacts and healthcare workers, (ii) Prevent an increase transmission and further international spread, (iii) Identify, isolate and care for patients quickly, (iv) Provide better care for affected patients, (v) Minimize animal transport, (vi) Accelerate the development of diagnostics, therapeutics and vaccines, (vii) Disseminate risk and incident information to all communities and counter misinformation, and (viii) Minimize social and economic impact through multilateral partnerships.

FUTURE OUTLOOK AND GUIDELINES

Over the past 50 years, a number of different coronaviruses have emerged, causing a wide variety of human and veterinary diseases. There are hundreds of COVs out there but only 7 have been prepared to infect

humans so far and three of them (MERS COV, SARS COV and SARS COV-2) caused an outbreak. These viruses are likely to continue their emergence and cause the spread of human and veterinary diseases that have the potential to rehabilitate, mutate, and infect many species and cell types. SARS COV-2 is spreading at an alarming rate worldwide. Elderly and VIPs are at higher risk for the deadly effects of the virus. Early estimates predict that the overall COVID-19 recovery rate will be between 97%-99.75%. Although some treatment protocols have shown some promise, but still there is currently no confirmed cure for the virus and no vaccine has been developed yet. Therefore, COVID-19 needs to be controlled through a combination of public health measures such as rapid identification, diagnosis and management of cases, identification and follow-up of contacts, prevention in health care settings to control infection, implementation of health measures by passenger, awareness in population *etc*.

Based on its rapid transmission and spread to more than 200 countries, COVID-19 is expected to revolutionize the global scientific, social, geographical, and economic landscape. With the global community's special attention and focus on zoonotic, infectious and contagious diseases, and using collective wisdom, it is hoped that after COVID-19, it will be a better world with the coexistence of all species on this beautiful planet. Future research on the corona viruses is needed to investigate various aspects of viral replication, pathogenesis, and explain how the coronaviruses causes disease and how to develop vaccines and diseases by understanding the host immunopathological response.

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Statement of conflict of interest

The authors have declared no conflict of interests.

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