



**A REVIEW OF SEVERE ACUTE RESPIRATORY SYNDROME CORONAVIRUS 2  
(SARS-COV-2)**

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**ABSTRACT**

Coronavirus disease 2019, (COVID-19) or SARS-CoV-2 is a zoonotic virus causing a combination of severe respiratory diseases. As of May 16, 2020 the continuing COVID-19 became pandemic and spread over 213 countries. Total of 4,675,063 infected patients were reported globally, with 310,291 deaths, and 1,785,231 is recovered. Unfortunately, the global numbers of both infected patients and fatalities will continue to grow in the future months because neither specific and effective antiviral therapies nor vaccine have been identified. India reported, total 85,940 COVID-19 cases (till May 16, 2020), 2,752 people were died and 30,153 people is treated successfully. The fatality rate is expected to 2 to 3%. Diagnosis is by demonstration of the virus in respiratory secretions special molecular tests. Treatment is basically supportive. Prevention is carrying out mainly by home isolation of suspected cases and those with mild illnesses and severe infection. Our study aimed to present an overview of the virus in terms of, transmission, symptoms, Pathophysiology, Diagnosis, treatment, prevention and vaccine.

**KEYWORDS:** Coronavirus, COVID-19, SARS-CoV-2, ACE2 receptors.

**INTRODUCTION**

Coronaviruses are enveloped RNA virus. Where size varies between 60 to 140 nm in diameter.<sup>[1]</sup> The diameter of the envelope is 80 nm and the spikes are 20 nm long.<sup>[2]</sup> The viral envelope consists of a lipid bilayer where the membrane, envelope and spike are structural proteins.<sup>[3]</sup> Under the electron microscope, its show spike like projections on its outer surface, giving a crown like appearance.<sup>[1]</sup> It is a group of related viruses that can cause diseases in mammals and birds. In humans, coronaviruses cause respiratory tract infections. According to the World Health Organization, viral diseases keep on to emerge and represent a severe issue to public health. In the last twenty years, several viral epidemics such as the severe acute respiratory syndrome coronavirus (SARS-CoV) in 2002 to 2003 beginning in China and involving two dozen countries with approximately 8000 cases along with 800 deaths. Most recently, the Middle East respiratory syndrome coronavirus (MERS-CoV) was first identified in Saudi Arabia in 2012 and has approximately 2,500 cases along with 800 deaths and still causes as sporadic cases.<sup>[4]</sup>

Although bats and snakes are the natural reservoir of most coronaviruses, but there is no evidence so far that COVID-19 originated and transmitted from a seafood market.<sup>[5]</sup> On 31st December 2019, 27 cases of

pneumonia of unknown etiology were identified in Wuhan City, Hubei province in China<sup>[6]</sup> with clinical symptoms of dry cough, dyspnea, fever, bilateral lung infiltrates on imaging and later developed various fatal complications including organ failure, septic shock, pulmonary oedema, severe pneumonia, and Acute Respiratory Distress Syndrome (ARDS). However majority of cases have spontaneously resolved.<sup>[7]</sup> The causative agent was identified from throat swab samples conducted by the Chinese Centre for Disease Control and Prevention (CCDC) on 7th January 2020, and subsequently named as Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2).<sup>[8]</sup> On January 30, 2020, the World Health Organization (WHO) declared COVID-19 a public health emergency of international concern<sup>[9]</sup>, On February 11, 2020, the WHO Director-General, Dr. Tedros Adhanom Ghebreyesus, announced that the disease caused by this new CoV was a "COVID-19," which is the short form of (coronavirus disease 2019)<sup>[4]</sup> and on March 12, the WHO declared COVID-19 to be a pandemic.<sup>[10]</sup>

**Transmission**

All ages are susceptible. The WHO and the U.S. Centers for Disease Control and Prevention (CDC) say that COVID-19 mostly spread through close contact of the infected patients approximately 3–7 feet by small

droplets, formed when people cough, sneeze and talk,<sup>[11-13]</sup> both saliva and sputum can transmit the large number of viruses<sup>[14]</sup> and loudly talking will spread out additional droplets than usual talking.<sup>[15]</sup> A study in Singapore establish that open cough will cause droplets movement up to (4.5) meters. It may also spread from the contaminated surface, known as fomite transmission, and then touches one's eyes, nose or mouth.<sup>[11]</sup> It may be spread via faeces, but risk is believed to be low. The infections can be spread from both symptomatic and asymptomatic patients.<sup>[11,16]</sup> On the surfaces, viruses survive for hours to days.<sup>[11,17]</sup> Specifically, the virus was found to be detectable for one day on cardboard, three days on plastic and stainless steel, up to four hours on 99% copper.<sup>[18,19]</sup> So far parenteral and maternal transmission has not been detected, however neonatal disease due to post natal transmission does occur. While it was known, that older age is a risk factor for disease severity and fatal outcome and there is evidence that males have a higher risk for disease severity and death than females.<sup>[20]</sup>

### Symptoms

The clinical features of COVID-19 are varied, from an asymptomatic condition to acute respiratory distress syndrome and multi-organ dysfunction.<sup>[21]</sup> According to WHO records, the period from symptom start to death ranges from 6 to 41 days with a median of 14 days. This period depends on the age and immune status of the individual and is shorter in those <70 years old.<sup>[22]</sup> The common clinical features include fever not in all patients, cough, sore throat, headache, fatigue, myalgia, breathlessness and conjunctivitis.<sup>[23]</sup> More serious symptoms include difficulty breathing, persistent chest pain, confusion, difficulty walking, and bluish face or lips.<sup>[24,25]</sup> Loss of smell and taste has also been reported with symptom of COVID-19 in March 2020.<sup>[26-28]</sup> Several neurological symptoms have been reported including seizures, stroke, encephalitis and Guillain-Barre syndrome.<sup>[29]</sup> Cardiovascular related complications may include heart failure, irregular electric activity, blood clots, and heart inflammation.<sup>[30]</sup>

### Pathophysiology

The COVID-19 belongs to genera Betacoronavirus based on its phylogenetic relationships and genomic and structure. Human Betacoronaviruses (SARS-CoV, MERS-CoV and SARS-CoV- 2) have several similarities, but also have differences in their genomic and phenotypic structure that can influence their pathogenesis. The human respiratory system is primarily targets organs of COVID-19 because the virus accesses host cells via the enzyme Angiotensin-converting enzyme 2 (ACE2), which is generally abundant number in type II alveolar cells of the lungs. It has been confirmed that the SARS-CoV-2 uses the same cellular entry receptor, ACE2, as SARS-CoV. The virion S-glycoprotein on the surface of coronavirus can attach to the receptor, ACE2 on the surface of human cells. The virus uses a special surface glycoprotein called a "spike"

to connect to ACE2 and enter the host cell.<sup>[31]</sup> The density of ACE2 in each tissue correlates with the severity of the disease in that tissue and some have suggested that decreasing ACE2 activity might be protective<sup>[32,33]</sup> through another view is that increasing ACE2 using Angiotensin II receptor blockers. Angiotensin II receptor blocker treatment could be defending and these hypotheses should be tested.<sup>[34]</sup> As the alveolar disease progresses, respiratory failure might develop and death may follow.<sup>[33]</sup> The virus also affects the gastrointestinal tract because ACE2 is present abundantly on the glandular cells of the gastric, duodenal and rectal epithelium<sup>[35]</sup> as well as enterocytes and small intestine of endothelial cells.<sup>[36]</sup> ACE2 is present in the brain, and there is growing evidence of neurological manifestations in people with COVID-19.<sup>[37]</sup> The virus can cause acute myocardial injury and damage to the cardiovascular system. Myocardial injuries may also be related to ACE2 receptors in the heart.<sup>[38]</sup> ACE2 receptors are highly expressed in the heart and are involved in heart function.<sup>[38,39]</sup> Another common cause of death is complications related to kidneys.<sup>[40]</sup> Post-mortem studies confirmed that SARS-CoV-2 directly infects kidney cells. Acute kidney injury is more significant in patients with already compromised kidney function, especially in people with pre-existing chronic conditions such as hypertension and diabetes, which can cause death.<sup>[41]</sup> Autopsies of people who died of COVID-19 have found diffuse alveolar damage (DAD), and lymphocyte-containing inflammatory infiltrates within the lung.<sup>[42]</sup>

### Diagnosis

The WHO has written many testing protocols for the diagnosis of COVID-19<sup>39</sup>; however, Quantitative RT-PCR is the most specific and sensitive assay accepted and basically in use by several reference laboratories worldwide.<sup>[43]</sup> Specimen handling for molecular testing would need BSL-2 or equivalent facilities. For the culture of the virus need BSL-3 facilities, but virus isolation isn't suggested as a routine diagnostic technique.<sup>[44]</sup> Initially, the pathogen of COVID-19 has been detected from upper and lower respiratory tracts samples such as a nasopharyngeal swab, nasal swab or sputum sample. Later on, viral RNA can also be detected from faecal and blood samples.<sup>[44]</sup> Chinese scientists isolated a strain of the coronavirus and distributed the genetic sequence across the world for independently establishing polymerase chain reaction (PCR) tests to detect viral infection.<sup>[45-47]</sup> Target gene for diagnosis of COVID-19 may be different for screening and confirmatory test by RT-PCR. According to Chinese laboratory protocol, open reading frame (ORF1ab) and nucleocapsid (N) is used, while RNA-dependent RNA polymerase (RdRP), envelope (E) and N are investigating in Germany. Besides, three targets in the N gene are considered in US protocol.<sup>[44]</sup> Along with laboratory testing, the chest X-ray (CXR) usually shows bilateral infiltrates but may be normal in early disease.<sup>[48]</sup> Chest CT scans may be helpful to diagnose COVID-19

in individuals with a high clinical doubt of infection but are not recommended for routine screening.<sup>[49,50]</sup> The CT scan imaging is more sensitive, specific and generally shows infiltrates, ground-glass opacities and subsegmental consolidation. It is also abnormal in asymptomatic patients with no clinical evidence of lower respiratory tract involvement. Abnormal CT scans have been used to diagnose COVID-19 in suspect cases with the negative molecular diagnosis; many of these patients had positive molecular tests on repeat testing.<sup>[48]</sup> Correlations of CT scan with RT-PCR as a gold standard, sensitivity of CT scan is appropriate.<sup>[51]</sup> Notably, a combined IgM–IgG rapid immunoassay has also been recently developed, for diagnosis. As of 4 April 2020, antibody test which may detect active infections and whether a person had been infected in the past, but not yet widely used.<sup>[53-54]</sup> The Chinese experience with testing has shown the accuracy is only 60 to 70%.<sup>[55]</sup>

### Treatment

Treatment is basically supportive and symptomatic. The primary step is to confirm adequate isolation to prevent transmission to another associate, patients and health care workers. Mild ill health must be managed at home with counselling regarding danger signs. The same old ideology maintaining nutrition and controlling fever and cough. Antibiotics and antifungals are needed if co-infections is suspected or established.<sup>[56,57]</sup> Broad spectrum antibiotic treatment should be start within one hour of initial assessment for infection.<sup>[58]</sup> It is necessary to notice that patients will develop additional bacterial and fungal infections throughout the middle and latter stages of the infections. Therefore, conventional and regular antibiotic regimens should still be followed.<sup>[59]</sup> The role of corticosteroids is unconfirmed; whereas current international agreement and WHO advocate against their use, Chinese instructions do suggest short term medical care with low-to-moderate dose corticosteroids in COVID-19, acute respiratory distress syndrome.<sup>[56,57]</sup> Glucocorticoids can also be given for patients with severe immune reactions. In youngsters, methylprednisolone must be restricted to 1–2 mg/kg/day for five days.<sup>[60,61]</sup> Patients with severe acute infection, respiratory distress, hypoxaemia or shock need the administration of immediate oxygen therapy. This could be at five L/min to achieve SpO<sub>2</sub> targets of  $\geq 90\%$  in non-pregnant adults and youngsters, and  $\geq 92-95\%$  in pregnant lady.<sup>[62-64]</sup> Alternative medication projected for therapy are arbidol (an antiviral agent are offered in Russia and China), intravenous immunoglobulin, interferons, antimalarial (chloroquine) and plasma of patients recovered from COVID-19.<sup>[65-67]</sup>

Remdesivir has been reported to treat the primary United state case of COVID-19 with success.<sup>[68]</sup> Antimalarial may be a reused drug with good result to treat COVID-19.<sup>[69]</sup> Many probable mechanisms are investigated: Chloroquine will inhibit pH-dependent steps of the replication of many viruses<sup>[70]</sup>, with a powerful result on

SARS-CoV infection and spread.<sup>[71]</sup> Additionally, Chloroquine has immunomodulatory property, suppressing the production and release of IL-6 and TNF- $\alpha$ . It conjointly works as a completely unique category of cell-death.<sup>[72]</sup>

### Prevention

The WHO and US Centers for Disease Control and Prevention (CDC) have issued instruction to prevent further spread of COVID-19.<sup>[73,74]</sup> They recommend avoiding travel to high-risk areas, contact with persons who are symptomatic, and the consumption of meat from regions with known COVID-19 epidemic. Basic hand hygiene procedures are also suggested, including frequent hand washing.<sup>[75]</sup> Frequent hand washing mainly after direct contact with poor health people or their surroundings, and avoiding unprotected contact with farm or wild animals. Moreover, people with symptoms of acute respiratory infection should practice cough with good manners, which is to maintain distance, cover coughs and sneezes with disposable tissues or clothing and wash hands, within healthcare facilities enhanced standard infection prevention and control practices are suggested in hospitals, mainly in emergency departments.<sup>[76]</sup> The rooms, surfaces and equipment should undergo regular decontamination preferably with sodium hypochlorite.<sup>[77]</sup> The virus is susceptible to many active ingredients (AI), such as sodium hypochlorite (0.1%–0.5%), 70% ethyl alcohol, povidone-iodine (1% iodine), chloroxylonol (0.24%), 50% isopropanol, 0.05% benzalkonium chloride, 1% cresol soap, or hydrogen peroxide (0.5%–7.0%). The confirmed case should be isolated preferably at negative pressure isolation room or, alternatively, a single room with good ventilation<sup>[78]</sup> Healthcare workers should be provided with fit tested N95 respirators and protective suits and goggles. Airborne transmission precautions should be taken during aerosol generating procedures such as intubation, suction and tracheostomies. All contacts including healthcare workers should be monitored for development of symptoms of COVID-19. Patients can be discharged from isolation once they are afebrile for at least 3 day and have two consecutive negative molecular tests at 1 day sampling interval. This recommendation is different from pandemic flu where patients were asked to resume work/school once afebrile for 24 h or by day 7 of illness. Negative molecular tests were not a condition for discharge. At the community level, people should be asked to avoid crowded areas and postpone non-essential travel to places with ongoing transmission. They should be asked to practice cough hygiene by coughing in sleeve/ tissue rather than hands and practice hand hygiene frequently every 15–20 min. Patients with respiratory symptoms should be asked to uses urgical masks. The use of mask by healthy people in public places has not shown to protect against respiratory viral infections and is currently not recommended by WHO.<sup>[77]</sup> Consecutive two negative results, can lead to discharge the patients. Cadaver should be burned or

buried deep. Treatments effective against coronavirus include steam and heat.<sup>[78]</sup>

### Vaccine

There is no any accessible vaccine, but different agencies are strongly trying to develop the vaccine. Previous work on SARS-CoV is being used because both SARS-CoV and SARS-CoV-2 use the same ACE2 receptor to enter human cells.<sup>[79]</sup> Three vaccination blueprint are being Consider. Primary, aim of the researchers to construct a whole virus vaccine. The inactive or dead virus is used for production of immune response, without delay against the new infection of COVID-19. A second approach involves subunit vaccines, which aims to create a vaccine that sensitizes the immune system to certain subunits of the virus. In the case of SARS-CoV-2, such research focuses on the S-spike protein that helps the virus interfere with the ACE2 enzyme receptor. A third approach is that of the nucleic acid vaccines DNA or RNA vaccines is a new technique for creating a vaccination. Investigational vaccines from any of these approaches would have to be tested for safety and effectiveness.<sup>[80]</sup> The first clinical trial of a vaccine started On 16 March 2020, with the four volunteers are Seattle, United States. The vaccine contains a harmless genetic code copied from the virus that causes the disease.<sup>[81]</sup> Antibody dependent enhancement has been suggested as a potential challenge for vaccine development for SARS-COV-2, but this is controversial.<sup>[82]</sup>

### CONCLUSION

COVID-19 is a great biological hazard and it is a worldwide threat. It is highly contagious during the latency period and close contact with an infected person compared to SARS-CoV and MERSCoV. It can cause more severe infections amongst children, old age individuals, pregnancy, people with chronic debilitating diseases such as diabetes mellitus, cardiovascular diseases, and malignancy. The effective selection of antiviral therapy and vaccination are currently under evaluation and development. Health-care workers must also follow CDC guidelines and should not attempt to perform any virus isolation or characterization. Any mutation occurring will be especially important. There is no evidence that part of COVID-19 is synthetic.

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