

# A Review of Coronavirus Disease-2019 (COVID-19)

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**Abstract:** *Coronavirus possess a descriptive morphology, the name derived from the outer fringe embedded envelop protein. This viral infectious disease (COVID-19) is produced by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). This transmission disease was first observed in December 2019 in Wuhan, China and has rapidly transmit all over the world in several days. This virus originates in from bats and was transmitted to humans through unknown animals in Wuhan. The disease is transmitted by inhalation of droplets or contact with infected persons and the it has incubation period ranges from 2 to 14 days. The symptoms are usually fever, cough, sore throat, breathlessness, fatigue, and feeling of tastelessness, headache and many more. Many people are also asymptomatic to this viral infection. The World Health Organization (WHO) declared this pandemic for the Public Health Emergency of International Concern on 30th January 2020 and realizes it as a pandemic on 11th march, 2020. The several numbers of peoples are diagnosed with coronavirus worldwide crossed the one million marks on 2nd April 2020; after that, two-million-mark cross on 15th April 2020; three-million-mark cross on 27th April and the lastly four million marks on 9th may 2020. We show a review of available information to highlight knowledge about the virus and the current pandemic condition. In this writing review, the influential agent, pathogenesis and immune responses to pathogen, epidemiology, diagnosis, treatment and handling of the disease, control and preventions strategies are all reviewed separately.*

**Keywords:** COVID-19, viral infectious disease, SARS-CoV-2, World Health Organization (WHO).

## I. INTRODUCTION

On December 31, 2019, the China Health committee informed to the World Health Organization (WHO) about different cases of pneumonia of different pathogenesis in Wuhan City in, capital of China. On 7th January, a main coronavirus, originally known as COVID-2019 by World health organization, was observed from the throat swab sample of the patient [2]. This virus was after renamed as severe acute respiratory syndrome - coronavirus 2 (SARS-CoV-2) by the group of scientists.[3] Later, this disease was again named as coronavirus disease 2019 (COVID-19) by the World health organization.

According to the National Health Commission of China, the death rate of confirmed cases in China was about 2.1% in February month and the mortality rate was 0.2% in active cases outside the China. All among patients admitted to hospitals, were death rate ranged in between 11% and 15%.

Coronavirus is an member of the Coronaviridae family and order Nidovirales. This Coronaviridae family includes of two subfamilies that are, Coronavirinae and Torovirinae and members of the subfamily Coronavirinae are subdivided into four genetic divisions:

- Alphacoronavirus genome which includes the human coronavirus (HCoV)-229E and HCoV-NL63.
- Betacoronavirus genome which contains the HCoV-OC43, Severe Acute Respiratory Syndrome human coronavirus (SARS-HCoV), HCoV-HKU1, and Middle Eastern respiratory syndrome coronavirus (MERS-CoV).
- Gammacoronavirus genome that contains a virus of whales and birds.
- Deltacoronavirus genome which contains a virus produced from pigs and birds [9]. SARS-CoV-2 originates from Betacoronavirus together with two highly pathogenic viruses.

The goal of this literature review is to revised the current knowledge of COVID-19 containing causative organism, pathogenesis of the infection, diagnosis and treatment of the transmission, also control and prevention strategies against the disease.

### History

Coronavirus has a descriptive history that is going back to the 1930's. Avian coronavirus, initially known as infectious bronchitis virus of chickens, mainly infecting domestic chickens was first identified in the 1930's. After that, two more animal coronaviruses, mouse hepatitis virus (MHV) and transferable gastro- enteritis virus (TGEV) in the 1940's was identified at that time. Human coronavirus was historically called because it causes a large area of minor upper respiratory tract infections. Tyrrell and Bynoe [11], first found in 1965, that a virus named B 814 caused common cold in adults.

In 2002 severe acute respiratory syndrome epidemic appears to have originated in Guangdong Province, China. In 2017, Chinese scientists' group which was led by Shi Zheng-Li and Cui Jie of the Wuhan Institute of Virology, China identified the source of the outbreak to horseshoe bats with civets acting

In the US, only 8 people HAS laboratory PROOF of SARS-CoV transmission during the 2003 pandemic. virus, choose as severe acute respiratory syndrome coronavirus infected about 8422 peoples that are mostly in China and Hong Kong and results of 916 deaths (death rate 11%) before being contained [4]. After a decade later in 2012, the Middle East respiratory syndrome coronavirus (MERS-CoV), that originate from bats, emerged in Saudi Arabia with arabinan camels as the middle host and infected 2494 peoples and results into 858 deaths (mortality rate 34%) [5].

### Origin and Spread of COVID-19 [1, 2, 6]

In December 2019, adult's peoples in Wuhan, China and a main transportation core of China started presenting to local hospitals with severe pneumonia of unknown cause. Many of the starting cases has a common manifestation to the Huanan wholesale seafood market that also transfer live animals. The observations system was activated and patient's respiratory samples were sent to reference laboratory for etiologic identification. In 31<sup>st</sup> December 2019, China observed the pandemic to the World Health Organization and on 1st January the Huanan Sea food market was closed due to infection. In 7th January the virus was observed as a coronavirus that had about >95% similarities with the bat coronavirus and about > 70% hology with the SARS- CoV. Different samples from the Huanan Sea food market also tested positive, that the virus originated from market [7].

The several numbers of cases started raising, some of which did not have showed to the live animal market, indicative of the fact that human-to-human transmission was occurring in that market [8]. The first case was identified in 11th January 2020. The Bigger transformation of Chinese during the Chinese New Year fuelled the epidemic. Cases in other states of China also in other countries such as Thailand, Japan and South Korea were reported in peoples who were returning from Wuhan. Spreading to healthcare workers caring for patients was described on 20th Jan, 2020. And finally on 23rd January, the 11 million population of Wuhan was kept under lock down with very strict restrictions of entry and exit from the Wuhan city. After some days, this lock down was expanded into other cities of Hubei province. Cases of coronavirus in countries outside China were reported in those with no travel history to China recommend that local human-to-human infection was produced in these countries [9].

Airports in several countries including India put in under screening to identify infectious patients that are returning from China and placed them in under isolation and testing them for coronavirus. Soon it was observed that the infection could be spread from asymptomatic people and also before onset of symptoms. Hence, countries including India who removes their peoples from Wuhan through special flights and placed all people symptomatic or otherwise in under observation for 14 days quarantine period. Cases continued to raise and modelling studies reported an epidemic doubling time of 1.8 days [10]. In fact, on the 12th of February, China changed its definition of confirmed cases to include patients with negative tests but with clinical, radiologic and epidemiologic properties of coronavirus leading to an extend in cases by 15,000 in a one day [6]. As of 05th march 2020, 96,000 newly cases worldwide (80,000 in China) and 87 other countries number of new cases has decrease in China lately, they have increased significantly in other countries containing South Korea, Italy and Iran.

In those infected peoples, about 20% are in very critical condition, 25% have recovered very well, and 3310 peoples were have died [2]. India, which had identified only 3 cases of virus till 2nd march 2020, has also seen a sudden pump in cases. From 5th march 2020, 29 cases have been observed; mostly in Delhi, Mumbai and pune in Italian travellers and their contacts. One case was reported in an Indian who traveled back from Austria and exposed a excess number of college students in a birthday party at a city hotel. Many of the people's contacts of these cases have been quarantined for 14days.

These numbers are possibly an misjudge of the transmitted and dead due to limitations of observations and testing. Though the SARS-CoV-2 produced from bats, the intermediary animal through which it crossed over to humans is uncertain. Pangolins and snakes are the current suspects of this transmission.

### **Epidemiology and Pathogenesis [10, 11]**

Coronaviruses structures are enveloped, non-segmented, positive-sense RNA type of viruses. They are identified by club-like spikes that are originate from their surface and the largest characterized RNA genomes which contains approximately 30 kilo base (kb) genome and also a unique replication strategy. The replication strategy of coronaviruses includes a closely packed set of messenger RNAs with common polyadenylated 30 ends. Only the unique part of the 50 end is translated. Mutations are common in nature. Coronaviruses are capable of genetic recombination if 2 viruses infect the same cell at the same time.

The coronavirus name is derived from Latin word, corona, meaning crown shape in structure. Due to special appearance of virions by electron microscopy on the surface of the virus [Fig. 3], produced an image of a crown shape or of a solar corona.

Coronavirus has acquired its name. Investigated the patterns of molecular divergence between SARS-CoV-2 and other related coronaviruses by studying the 103 genomes of SARS-CoV-2 and they showed the results that SARS-CoV-2 viruses involved into two major types (L and S types). The first S type are more ancient type of SARS-CoV-2. The second, L type was having to be more aggressive than the S type and more common in the early stages of the outbreak in Wuhan, the regularity of L type decreased after staring of January 2020 due to human intervention.

In the subgenus sarbecovirus, SARS-CoV-2 is genetically similar to othercoronaviruses, a subfamilyof beta coronaviruses formed by the coronavirus that results in SARS and other SARS-CoV like coronaviruses found in bats. Recombination between coronaviruses is common, and SARS-CoV is capable to be a recombinant between bat sarbecorviruses. Unsurprisingly, the whole genome of SARS-CoV-2 is relatively highly similar to that of a bat coronavirus, which was detected in 2013 (>96% sequence identity), which suggests that the immediate precursor of SARS-CoV-2 has been circulating in bats for at least next several years.

ACE2 has been observed as a functional receptor for coronaviruses, which containing SARS-CoV and SARS-CoV-2. SARS- CoV-2 infection is caused by binding between the spike protein and ACE2, which is highly performed in the heart and lungs. Also, Binding of the S1 unit of the viral S protein to the host ACE2 receptor provides viral engulfment to the target host cells surfaces. Viral S protein inform then requires breakdown of S1 protein from S2 by the host cell serine protease TMPRSS2. After that, the viral S2 subunit then produce fusion between viral and host cell membranes. Additionally, cytokine storm produced by an imbalanced response between type 1 and type 2 T helper cells and respiratory dysfunction and hypoxemia are produced by COVID-19 that can result in damage of myocardial cells [21]., Protected animals that is Pangolins that are traded illegally in Asia and elsewhere, have been proposed as a potential raising host by some studies.

However, receptor identification is not the only determines the species specificity. After Immediately binding to their special receptor, SARS-CoV-2 enters into host cells where they attack on the innate immune response. In order to effectively infect the new host, SARS-CoV-2 must be able to inhibit host innate immune waving. However, it is largely unknown how SARS- CoV-2 manages to inhibit the immune response and produces pathogenesis. Study shown that, COVID-19 and SARS have similar clinical features [7], SARS-CoV-2 have a identical pathogenesis mechanism as SARS- CoV. In response to SARS-CoV infections, the type I interferon (IFN) system increases the expression of IFN-stimulated genes (ISGs) to inhibit viral replication. To avoid this antiviral activity, SARS- CoV encrypt at least 8 viral antagonists that regulate induction of IFN and cytokines and avoid ISG effector function.

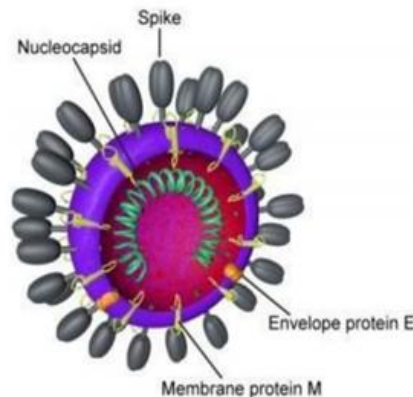


Fig. 3 Diagram by Belouzard et al.

The host immune system response to viral infection by regulating inflammation and cellular antiviral activity is critical to inhibit viral replication and spreading. However, additional immune responses together with breaking effects of the virus on host cells will result into pathogenesis. Studies have shown that, patients suffering from severe pneumonia, with common symptoms of fever and dry cough at onset of illness [7,8]. Some patients progressed rapidly with Acute Respiratory Stress Syndrome (ARDS) and septic shock, which was eventually followed by multiple organ failure and about 20% of patients have died.

#### Clinical Features [8, 15–18]

The clinical features of COVID-19 are different that are ranging from non-symptomatic state to acute respiratory distress syndrome and multi organ dysfunction. Some of the common clinical features are- fever (not in all), cough, sore throat, headache, fatigue, headache, myalgia and breathlessness. Conjunctivitis (pinkeye) has also been observed. Hence, they are alike from other respiratory infections. In some patients, after ending of a first week the disease can progress and lead to pneumonia, respiratory failure and death. This progress is related with higher rise in inflammatory cytokines including IL2, IL7, IL10, GCSF, IP10, MCP1, MIP1A, and TNF $\alpha$  [15]. The mid time from onset of symptoms to dyspnea was 5 days, hospitalization 7 days and acute respiratory distress syndrome (ARDS) 8days. The need for extra care was when 25–30% of affected patients in published series. Complications such as acute lung injury, ARDS, shock and acute kidney injury. Recovery started from the 2nd or 3rd wk. The mid duration of hospital stay in those patients who recovered was in 10 days. Adverse side effects and death are more common in the elderly patients and those with basic co-morbidities (50–75% of fatal cases). Death rate in hospitalized adult patients is ranging from 4 to 11%. The overall death rate is estimated to ranging between 2 and 3% [2].

Unsurprisingly, disease in patients outside Hubei city, China has been reported to be less harmful than those from Wuhan [17].

Similarly, the strength and fatality case rate in patients outside China has been reported to be lighter [6]. This may either be due to selective partiality whereas the cases collecting from Wuhan consisting only some cases or due to disposition of the Asian population to the virus due to higher expression of ACE2 receptors on the respiratory mucosa [11].

Disease in new born babies (neonates), infants and children has been also collected and reported. The effects significantly low than their adult result. A study of group of 34 children hospitalized to a Shenzhen, China in between 19th January to 7th February, in that experiment, there were 14 males and 20 females. The mid age was 8 years, 11 month and in 28 children, the infection was linked to their family members and 26 children has past history of travel/residence to Hubei province in China. All the patients were either non-symptomatic (9%) or has some mild disease. No severe or critical cases were seen. In this experiment, children were most common symptoms such as fever (50%) and cough (38%).

All patients recovered with symptomatic therapy and there were no deaths occurs. Only one case of severe pneumonia and multiorgan dysfunction in a child has also been recorded [19]. Similarly, the neonatal cases that have been reported have been mild effects [20].

### **Diagnosis [21]**

A suspect case is defined as one with fever, sore throat and cough who has history of travel to China or other areas of persistent local transmission or contact with patients with similar travel history or those with confirmed COVID-19 infection. However, cases may be asymptomatic or even without fever. A confirmed case is a suspect case with a positive molecular test.

Specific diagnosis is by specific molecular tests on respiratory samples (throat swab/ nasopharyngeal swab/ sputum/ endotracheal aspirates and bronchoalveolar lavage). Virus may also be detected in the stool and in severe cases, the blood. It must be remembered that the multiplex PCR panels currently available do not include the COVID-19. Commercial tests are also not available at present. In a suspect case in India, the appropriate sample has to be sent to designated reference labs in India or the National Institute of Virology in Pune. As the epidemic progresses, commercial tests will become available. Other laboratory investigations are usually nonspecific.

The white cell count is usually normal or low. There may be lymphopenia; a lymphocyte count <1000 has been associated with severe disease. The platelet count is usually normal or mildly low. The CRP and ESR are generally elevated but procalcitonin levels are usually normal. A high procalcitonin level may indicate a bacterial co-infection. The ALT/AST, prothrombin time, creatinine, D-dimer, CPK and LDH may be elevated and high levels are associated with severe disease.

The chest X-ray (CXR) usually shows bilateral infiltrates but may be normal in early disease. The CT is more sensitive and specific. CT imaging generally shows infiltrates, ground glass opacities and sub segmental consolidation. It is also abnormal in asymptomatic patients/ patients with no clinical evidence of lower respiratory tract involvement. In fact, abnormal CT scans have been used to diagnose COVID-19 in suspect cases with negative molecular diagnosis; many of these patients had positive molecular tests on repeat testing [22].

### **Differential Diagnosis [21]**

The various diagnosis includes all types of respiratory viral infections [influenza, parainfluenza, respiratory syncytial virus (RSV), adenovirus, human metapneumovirus, non COVID-19 coronavirus], atypical organisms (mycoplasma, chlamydia) and bacterial infections. It is impossible to separate COVID-19 from these infections clinically or through different laboratory tests. Hence travelling history becomes important. However, as the epidemic spreads, the travel history will become unrelated.

### **Treatment [21, 23]**

#### **Treatment is very essentially supportive and symptomatic.**

The first step in the treatment is to check sufficient isolation (discussed later) to avoid transmission to other person, patients and healthcare workers. Mild illness should be recovered at home with counselling about danger signs. The main principles are maintaining water level and supply proper nutrition and maintain fever and cough. Antibiotics and antivirals such as oseltamivir should be prevented in active confirmed cases. In hypoxic patients, providing of enough oxygen through nasal tip, face mask, high flow nasal cannula (HFNC) or non-spreading ventilation is indicated. Mechanical ventilation and even excess oxygen requirement may be needed. In some patients, renal replacement therapy may be needed.

Antibiotics and antifungal medication are required if co-infections get produced. The role of corticosteroids drugs is not clear; while current international agreement and WHO advocate are against their use, Chinese authority give permission to use short term therapy with low-to-moderate dose of corticosteroids in COVID-19 patients [24, 25]. Detailed instructions for critical care management for COVID-19 have been published by the WHO [26]. But now, there is no approved treatment for COVID-19. Antiviral drugs such as Remdesivir, ribavirin, lopinavir- ritonavir, covishield have been used based on the experience with SARS and MERS.



In a past time study in patients with SARS, patients treated with lopinavir-ritonavir medications with ribavirin has better results as compared to ribavirin alone [15].

In the experiment that 99 admitted patients with COVID-19 infection from Wuhan, oxygen was given to 76% type of patients, non-spreader patients ventilation in 13%, mechanical ventilation in 4% patients, extracorporeal membrane oxygenation (ECMO) having 3%, continuous renal replacement therapy (CRRT) in 9% patients, antibiotics in 71% patients, antifungals in 15% patients, glucocorticoids in 19% patients and intra-venous immunoglobulin therapy in 27% [15] patients were given to be. Antiviral therapy containing medication such as remdesivir, acyclovir and covishield was given to 75% of the patients. The duration of non-spreader ventilation was 4–22 days and in mechanical ventilation for 3–20 days. In the experiment of children discussed earlier, all children recovered with basic treatment and did not need intensive care or any other special treatments. [17].

There is unscientific experience with use of remdesivir, a member of broad-spectrum anti-RNA drug developed for

Ebola virus in management of COVID-19 [27]. More proofs are needed before these drugs are recommended. Other drugs used for treatments are arbidol (an antiviral medication available in Russia and China), intravenous immunoglobulin, interferon's, antimalarial drug such as chloroquine and plasma of patients recovered from COVID-19 [21, 28, 29]. Additionally, counselling about using traditional Chinese medications find place only in their Chinese guidelines [21].

### **Prevention [21, 30]**

Since at current time, there are no approved medication for this corona virus infection so prevention is very important. Various properties of this virus make prevention very complicating, non-specific features of the disease, the infection before onset of symptoms in the incubation time, spreading from non-symptomatic people, long incubation period, phototropism for mucosal surfaces such as the conjunctiva (pinkeye), longer duration of the illness and spreading even after clinical recovery of patients.

Isolation of active cases with low illness at home is advised. At home, the ventilation must be good with sunlight is allow for destruction of virus. Patients should wear a simple surgical mask and practice cough hygiene. Volunteers should be asked to wear a surgical mask when in the same room as patient and also use sanitizer every 15–20 minutes.

The largest risk in COVID-19 is spreading this virus to healthcare workers. In the SARS outbreak of 2002, 21% of persons those affected were healthcare workers [31]. Till current date, almost 15000 healthcare workers in China have been infected from this corona virus with 6 deaths. Also, doctor who first warned about this virus to the world has died too. So, it is very important to

protect healthcare workers to confirm continuity of care and to prevent spreading of this infection to other persons. In other side, COVID-19 spread as a droplet pathogen and is categorized in B group of infectious agents (highly pathogenic H5N1 and SARS), by the China National Health Commission, infection control measures advice are those agents that are falls into category A agents (cholera, plague). Patients should be placed in separate rooms or. Negative pressure rooms are not generally needed. The whole rooms and room surfaces and equipment should decontaminate regularly by using sodium hypochlorite. Healthcare workers should provide with fit tested N95 masks and protective suits and goggles. Airborne spreading precautions should be taken during aerosol opening 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 free from fever for atleast 3 days and also have two consecutive negative tests at 1 day sampling interval. This advice is different from pandemic flu where patients were asked to stops work/school once they are free from fever for 24 hours or by day 7 of illness. Negative tests were not essential for discharge the patients.

At the society level, people should be avoid crowded places and delayed non-essential travelling to places with ongoing spreading. They should be asked to practice cough hygiene by coughing in sleeve/ tissue other than hands and practice wash hands by using sanitizer frequently every 15–20 min. Those patients having respiratory symptoms should use surgical masks as much as possible. The use of mask by healthy people in public places has not protect against respiratory viral infections and is currently not adviceable by World health organization. Also in China, the public has been wearing masks in public places and especially in crowded places, large gatherings are avoided (entertainment

parks, theatres, jeam, play parks etc). China is also introducing law to inhibit the selling and transport of wild animals from one place to another places[32].

The international results have been dramatic. At starting, there were massive travel restrictions to China and also peoples who returning from China being observed for clinical symptoms, isolated and tested for COVID-19 for 2 weeks even if also they were asymptomatic. However, now with rapid transmission of this virus to whole world, these travel restrictions have extended to other countries also. Whether these efforts will lead to slowing of viral spread is not known completely. A candidate vaccine is under development.

### Practice Points from an Indian Perspective

At the writing this article, the risk of coronavirus in India is extremely high. But that may change in the next few weeks. Hence the following is guidelines are recommended:

- Healthcare providers should take travel history of each all passenger with respiratory symptoms, and any international traveller in the past 2 weeks as well as contact with illness people who have travelled internationally.
- They should set up a system of sorting of patients with respiratory sickness in the outpatient department and give them a simple surgical mask to wear to protect other peoples from viral infection.
- Suspected cases should be referred to government designated centres for isolation and testing (in Mumbai, at this time, it is Kasturba hospital).

Patients admitted with some symptoms of pneumonia and acute respiratory distress syndrome should be observed for travel history and placed under contact and droplet isolation to prevent the infection. Regular decontamination of surfaces should be done by using proper disinfectants. They should be tested for ethology using multiplex PCR tests if logistics permit and if no pathogen were observed and refer the suspected samples for testing for SARS-CoV-2.

- All physicians should keep themselves updated about recent developments including global spread of the disease newly developed treatments.
- Non-essential international travellers should be prevented at this time to avoid rapid transmission.
- People should stop spreading news and false information about the disease and try to solve problems, maintain public mental health, stress and anxiety of the public.

## II. CONCLUSION

This new virus transmission and pandemic has challenged the economic, medical field and public health infrastructure of the world and to some extent, of other countries. Time tells how the virus will impact our lives here in India. We need to developed more infrastructure in hospitals, oxygen production, vaccine developments and more so, future outbreaks of viruses and pathogens are likely to continue. Therefore, apart from suppress this outbreak, efforts should be made to design broad ideas to prevent future outbreaks of this dangerous viral transmission.

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