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# COVID – 19: A REVIEW OF CLINICAL FEATURES, DIAGNOSIS AND TREATMENT

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## ABSTRACT

A novel corona-virus is a new strain of corona-virus that has not been previously identified in humans. Corona-virus is a group of enveloped viruses with non-segmented, single stranded and the positive-sense RNA genomes. The virus originated in bats and transmitted to the human through yet unknown intermediately animals in Wuhan, Hubei province, China in December 2019. Corona-virus (COV) are a large family of a viruses transmitting between the animals and the people that cause of illness ranging from the symptoms are usually fever, common cold, cough, sore though, breathlessness, fatigue, malaise among other. They are infect the neurological, respiratory, enteric and hepatic system. The more severe diseases such as Middle East respiratory syndrome (MERS-CoV) and severe acute respiratory syndrome (SARS-CoV). SARS-CoV-2 is highly contagious and has resulted in rapid pandemic of COVID-19. The disease is transmitted by inhalation or the contact with infected droplets and their incubation period ranges from 2 to 14 days. There have been around more than 2 lack reported cases of corona-virus disease 2019-20. (COVID-19) and more than 1 lack reported deaths of people. Hydroxychloroquine tablet still used in the management of critically ill patients with COVID-19 the need for the evidence base. Health officials in the United States (US) and around the world are working to contain the spread of the virus through public health measures such as social distancing, contact tracing, quarantines and travel restrictions. Scientists are working to find out medications to treat the disease and to develop a vaccine. So, STAY HOME, STAY SAFE.

**KEYWORDS:** COVID-19, SARS-CoV-2, RNA, MERS-CoV, Corona virus, respiratory.

## 1. INTRODUCTION

Corona virus is a large family of positive-sense, single-stranded RNA viruses that belong to the Nidovirales order. It's includes to Roniviridae, Arteriviridae, and Coronaviridae families. The Coronaviridae family is subdivided into the Torovirinae and Coronavirinae subfamilies.[1] Coronavirinae is further sub classified into 4 types alpha-, beta-, gamma-, and delta-COVs. The 2019 novel corona virus (2019-nCoV) or the severe acute respiratory syndrome corona virus 2 (SARS-CoV-2) as it is now called, is rapidly spreading from its origin in Wuhan City of Hubei Province of China to the rest of the world.[2] Corona-viruses 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 corona virus.[3] Four corona viruses namely HKU1, NL63, 229E and OC43 have been in circulation in humans, and generally cause the mild respiratory disease. Corona-virus was 1$^{st}$ discovered in the year 1930s. When an acute respiratory infection of domesticated chickens was shown to be caused by infectious bronchitis virus (IBV).[4] Human corona viruses were discovered in the 1960s.[5,6] The coronavirus are due to the crown like projections. In this like due to the avoid and the precaution of this disease are drink the hot water and eat completely washed and cooked food.

### 1.2. Epidemiology

In December 2019, there are many pneumonia cases clustered in the Wuhan city were reported and searches for the source have shown Human Seafood Market as the origin.[7] The first case of the epidemic COVID – 19 was discovered with unexplained pneumonia on December 12, 2019 and there are 27 pneumonia cases were officially announced on December 31, 2019. The common symptoms like common cold, fatigue, loose motion, cough, sore though. These patients has the infection transmitted from animal to human.[8] These studies have shown higher viral loads in the nasal cavity as compared to the throat with the no difference in viral burden between symptomatic and asymptomatic people.[9] The incubation period varies from 2 to 14 days and the studies have been identified that angiotensin receptor 2 ($ACE_2$) as the receptor through which the virus enters the respiratory mucosa.[10]

### *1.3. Structure and genome of Coronavirus*

Corona virus (CoV) is a large family of positive-sense, single-stranded RNA viruses. The Coronaviridae family is subdivided into the Torovirinae and Coronavirinae subfamilies. Coronavirinae is further sub-classified into 4 types' alpha-, beta-, gamma-, and delta-COVs. Coronavirus visions are spherical to pleomorphic enveloped particles (Fig. 1). The envelope is flecked with projecting proteins (glycol-protein), and surrounds a core consisting of matrix protein enclosed within which is a single strand of positive-sense RNA (Mr 6 × 106) associated with nucleoprotein. The envelope glycoproteins are responsible for attachment to the host cell and also carry the main antigenic epitopes, particularly the epitopes recognized by neutralizing antibodies. OC43 also possesses a haemagglutin.[11] Under the electron microscope, the CoV vision appear to be spherical, with distinct "club-like" projection formed by the spike (S) protein.[12, 13, 14]

**Fig. 1: Electron micrograph showing human coronavirus 229E. Bar, 100 MN (Courtesy S.Sikotra, Leicester Royal Infirmary, Leicester, England.).**

Corona viruse visions contain three major structural proteins: the very large (200K) glycoprotein S (for spike) that forms the bulky (15 to 20 NM) peplomers found in the viral envelope, that unusual trans membrane glycoprotein (M) and the internal phosphorylated nucleocapsid protein (N). In addition, there is a minor trans membrane protein E, and some corona-viruses contain a further envelope protein with both hem agglutination and est-erase functions (HE). The 30 kb positive sense, that are the single-stranded RNA genome is the largest RNA viral genome known. It is capped at the 5′-end and polyadenylated at the 3′-terminus, and is infectious. Due to its size the expression of individual genes occurs through a complex process whereby sets of nested mRNA are produced, all sharing the same 5′-end sequence. The rearrangements may occur as a result of heterologous RNA recombination. At the 5′-end of the genome is an un-translated (UTR) sequence of 65 to 98 nucleotide, termed the leader RNA, which is also present at the 5′-ends of all sub-genomic mRNA s. At the 3′-end of the RNA genome is another un translated sequence of 200 to 500 nucleotide s, followed by a poly (A) tail. Both un-translated regions are important for the regulating RNA replication and transcription.

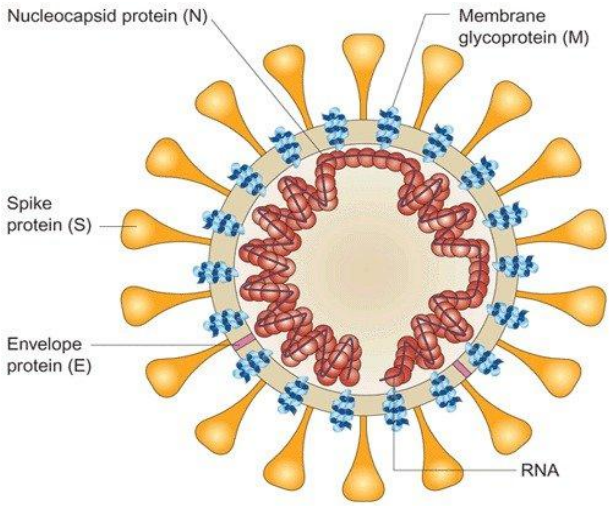


**Fig. 2. Structure of Coronavirus.**

The corona virus genome contains 7 to 14 open reading frames (ORFs). Starting from the 5′-end, Gene 1, which comprises two-thirds of the genome, is about 20 to 22 kb in length. It consists of two overlapping ORFs (1 a and 1 b), collectively functioning as the viral RNA polymer. These non-structural protein gene products are not essential for virus replication, but deletion of one or more often causes viral attenuation. At least one, the product of ORF3a, is now recognized to be a structural protein. The ORF3a product is an O-glycosylated, triple-membrane spanning protein capable of binding to N, M, and S proteins, suggesting a role in viral biogenesis.[15]

### *1.4. Pathogenesis and Immunity*

Most corona viruses first replicate in epithelial cells of the respiratory or enteric tracts. Because corona-viruses are enveloped, visions are less stable in the environment and in clinical specimens compared to most non-enveloped viruses. The pathogens and immune responses of corona viruses have been most studied in animal corona virus infections. For example, mouse hepatitis virus (MHV), the prototype of beta corona-viruses, includes a spectrum of strains with different tropism, causing enteric, hepatic, respiratory, or CNS infections.

Corona-viruses attach to specific cellular receptors via the spike protein. The first identified corona virus receptor was CEACAM 1, utilized by MHV[16] Viral attachment triggers a conformation change in the spike protein that promotes the fusion of viral and cellular membranes.[17,18]

The corona virus spike protein plays a vital roles in viral entry, cell-to-cell spread, and to determining tissue tropism. Corona-virus entry is, in general, but not pH dependent, and thus it has been believed to occur directly at the plasma membrane and not via an endosomal route. However, there are suggesting that endosomal route may be utilized by some viruses.[19,20] The entry of SARS-CoV is inhibited by lysosomotropic agents, suggesting an endosomal route of entry.[21,22] Furthermore, this inhibition may be overcome by pro-tease treatment of virus that has been attached to the cell. This, along with the observation that can be infection is blocked by inhibitors of the pH-sensitive endosomal protease cathepsin L, that can be suggests that there is a requirement for cleavage of the SARS-CoV spike during entry through the endosomes.[23, 24] The entry at the plasma membrane pro-tease treatment is more efficient than entry by the endosomal route.Those suggested that SARS-CoV spike may be cleaved by the pro-teases produced by inflammatory cells present in the lungs of SARS patients and thus enter cells by the more efficient plasma membrane route.[23]

The highly hepatotropic MHV-2 strain may enter to the cell by an endosomal route similar to that used by SARS-CoV. MHV-2, like SARS-CoV, encodes an un-cleaved spike protein and is sensitive to lysosomotropic agents; however, trypsin treatment of cell-associated MHV-2 spike overcomes inhibition by lysosomotropic agents. This suggests that entry at the cell surface may require a cleavage of spike in the viral membrane, while endosomal entry may provide for cleavage during entry. Finally, the corona viruses with cleaved spikes may also enter to the cell by the endosomes route. For example, while wild-type MHV-JHM enters to cells in culture by a pH-independent pathway, the OBLV60 mutant of JHM is inhibited by lysosomotropic agents and is believed to enter though a lysosomes pathway.[24,25]

### *1.5. Symptoms of Coronavirus*

People with corona virus (COVID-19) have had a wide range of symptoms reported – that ranging from mild symptoms to severe illness. Symptoms may visible 2-14 days after exposure to the virus.

Corona-virus infects the lungs. There are two main symptoms are a fever or a dry cough, which can sometimes lead to breathing problems. Coughing a lot for more than an hour, or having 3 or more coughing episodes in 24 hours. If you have a cough, it may be worse than usual.

You have a fever if your body temperature is above 37.8 C. This may make you feel warm, cold or shivery. A headache, sore throat and diarrhoea have also been reported and a loss of smell and taste may also be a symptom. It takes five days on average that can to start showing the symptoms, but some people will get them much later so, the disease can increase very fast. The World Health Organization in short WHO says the incubation period lasts up to 14 days.

People with these combinations of symptoms may have COVID-19:

- Cough
- Shortness of breath or difficulty breathing

**Or at least two of these symptoms**

- Fever
- Chills
- Repeated shaking with chills
- Muscle pain
- Headache
- Sore throat
- New loss of taste or smell

The Children that have similar symptoms to adults and generally have mild illness. The median time from symptom as to invasive ventilation and extra corporeal membrane oxygenation in these patients is 4.5 to 7 days. Risk of severe disease is higher in men over age 45, people with pre-existing medical condition including that of diabetes, obesity chronic kidney disease, chronic cardiac disease and COPD.[26]

### *1.6. Clinical manifestation and diagnosis*

The complete clinical manifestation is not clear yet, as the reported symptoms range from mild to severe, with some cases even resulting in death.[27] The most commonly reported symptoms are fever, cough, fatigue, pneumonia, and complicated dyspnoea, whereas less common reported symptoms include headache, diarrhoea, haemoptysis, runny nose, and phlegm-producing cough.[28]

### *1.6.1. Chest X-Ray*

A chest X-ray (radio-graph) is the most commonly ordered study for patients with respiratory complaints. In the early stages of corona virus (COVID-19), a chest X-ray may be read as normal. But in some cases the patients with severe disease, their X-ray readings may resemble pneumonia or acute respiratory distress syndrome.

#### *1.6.1.1.Chest X-ray Findings of COVID-19 Disease*

- **Bilateral multi-focal consolidations that may progress to involve entire lungs:** The term "consolidation" refers to the filling of pulmonary airspace's with fluid or other products of inflammation. The phrase "bilateral multi-focal" means that the abnormalities occur in different locations in both lungs.
- **Small pleural effusions:** Abnormal fluid which develops in the spaces around the lungs.[29]

### *1.6.2. CT Scan*

A CT scan of the chest is a specialized type of imaging study. Which is use X-rays to create 3 D images of the chest. Chest CT scan is more effective than chest X-ray in the detection of early COVID-19 disease. However, up to the 50% of patients may have a normal chest CT within the first two days after the onset of symptoms. Also, the other types of pneumonia may mimic COVID-19 on chest CT. Nevertheless, suspicious findings on chest CT are a valuable clue (along with the clinical presentation and exposure history) that a patient may have COVID-19.

The severity of COVID-19 varies significantly from person to person. Chest CT scan may also be used as an initial tool to assess disease severity, as well as to monitor for progression or resolution of disease.

#### *1.6.2.1. Chest CT Findings of COVID-19 Disease*

- **Multi-focal ground-glass opacities and consolidations:** The term "ground-glass opacity" refers to the hazy appearance of the lungs on imaging studies, almost as if sections are obscured by ground glass. It may be due to the filling of pulmonary airspace's with fluid, the collapse of the airspace's, or both.
- Abnormalities tend to occur in the peripheral and basal areas of the lungs, more commonly in the posterior lung bases.[29,30]

### *1.6.3. Blood and Sputum Cultures*

Collect the blood and sputum specimens for culture in all patients. They have to rule out other causes of lower respiratory tract infection and sepsis, but the patients with an atypical epidemiological history. Specimens should be collected prior to starting empirical antimicrobial if possible.

### *1.7. Corona-virus Treatment*

Corona-virus is a group of enveloped viruses with non-segmented, single stranded and the positive-sense RNA genomes. Corona virus are a large family of a viruses transmitting between the animals and the people that cause of illness ranging from the symptoms are usually fever, common cold, cough, sore though, breathlessness, fatigue, malaise among other. They are infect the neurological, respiratory, enteric and hepatic system.

***A. Remdesivir*** - Several studies are focused on an antiviral medication called remdesivir, which was created to fight Ebola. Remdesivir is being tested as a specific treatment for COVID-19, and has been issued an Emergency Use Authorization in the U.S. for those hospitalized with severe disease.

***B. Favipiravir*** – An antiviral drug called favipiravir which was reported February 17, 2020. The brand name favipiravir is Avigan, is an antiviral medication used to treat influenza in Japan.

***C. Lopinavir/ritonavir*** - Under the brand name is Kaletra. The fixed dose combination medication for the treatment and prevention of HIV/AIDS. The lopinavir is combine with a low dose of ritonavir. It is mainly recommended for use with other anti-retroviral.

***D. Hydroxychloroquine*** - it is used to prevent malaria in areas where malaria remains sensitive to chloroquine. It was reported in the journal clinical infection disease on March 9 that the malaria drug hydroxychloroquine was effective in killing the corona virus in laboratory experiment. Other uses include treatment of rheumatoid arthritis, lupus.

***E. Ivermectin*** - Ivermectin is a drug used to treat many types of parasite infestations. This includes head lice, scabies, river blindness, strongyloidiasis, trichuriasis, ascariasis, and lymphatic filariasis. The drug ivermectin break off the SARS-CoV-2 virus growing in cell culture within 48 hours. The use of Ivermectin to combat corona virus (COVID-19) would depend on the results of further pre-clinical testing and ultimately clinical trials.

***F. Hydroxychloroquine and Chloroquine*** - Chloroquine and hydroxychloroquine have been found to be efficient on SARS-CoV-2, and reported to be efficient in Chinese COV-19

patients. The drug is type of antimalarial. The result shows that all patients taking the combination were cured within 6 days of treatment.

***G. Convalescent Plasma Therapy*** – Specific countries, including India, are seriously looking at plasma therapy as a potential treatment for Covid-19, the disease caused by the novel corona virus. Plasma therapy is use in which blood donated by recovered patients to introduce antibodies in those under treatment.

This therapy's concept is simple and is based on the premise that the blood of a patient who has recovered from Covid-19 contains antibodies with the specific ability of fighting novel corona virus. The theory is that the recovered patient's antibodies, once ingested into somebody under treatment, will begin targeting and fighting the novel corona virus in the second patient.

The convalescent plasma therapy is akin to passive immunization as, according to researchers, it is a preventive measure and not a treatment for the Covid-19 disease.[32,33,34]

### *1.8. Prevention*

To prevention infection and to slow transmission of COVID-19, do the following:

***1. Wash your hands frequently and carefully***

Use warm water, soap and rub your hands for at least 20 seconds. Work the lather to your fingernails, wrists, and between your fingers,

***2. Avoid touching your face***

SARS-CoV-2 can live on hard surfaces up to 72 hours. Avoid touching to any part of your face, head including your mouth, nose, and eyes. Also avoid biting your fingernails. This can give SARS-CoV-2 a chance to go into your body from your hands.

***3. Stop shaking hands and hugging people***

Similarly, avoid touching other people because skin contact can pass SARS-CoV-2 from person to another person.

***4. Don't share personal items***

Do not share personal items like makeup, phones, or combs. Do not to share eating utensils and straws. Teach children to recognize their reusable straw, cup, and other dishes for their own use only.

***5. Cover your nose and mouth when you cough and sneeze***

SARS-CoV-2 is mostly found in high amounts in the mouth and nose. because it can be carried by air droplets to other people when you cough or sneeze. It can also land on hard surfaces and leave there for up to 3 days.

Use a tissue when you are sneeze and keep your hands as clean as possible. Wash your hands after you sneeze or cough, regardless.

***6. Clean and disinfect surfaces***

Use alcohol-based disinfectants to clean hard surfaces in your home like counter-tops, door handles, furniture, and toys. Also clean your phones, laptop, and anything else you use regularly several times a day.

***7. Take social distancing seriously***

If you are surviving the SARS-CoV-2 virus, it will be found in high amounts in your spit (sputum). Social distancing means staying at home and working remotely when possible. Stay a distance of 6 feet from other people.

***8. Do not gather in groups***

Avoid the group of people. In some cases the infection person contact on our self.

***9. Avoid eating or drinking in public places***

Now is not the time to go out to eat. This means avoiding restaurants, bars, coffee shops and other eateries. The virus may be transmitted through food, cups, dishes, and utensils. It can also be airborne from other people in the venue. Choose foods that are completely cooked and can be reheated, also to avoid the ice-cream, cold drink.

***10. Wash fresh groceries***

Soak all vegetables, raw, and whole fruits in a solution of food-grade hydrogen peroxide or white vinegar. Let dry before putting them away in your cupboards, fridge. You may use vegetable antibacterial wash to clean produce. Wash your hands properly before and after handling fresh produce.

***11. Wear a (homemade) mask***

Careful hand washing and social (physical) distancing must also be followed.

- Wash your hands with hand wash before you put on your mask.

- Wash your mask after use.
- Virus can transfer from your hands to the mask. If you're wearing a mask, then avoid touching the front of it.
- The virus can also transfer from the mask to your hands. Wash your hands properly if you touch the front of the mask.
- Your mask shouldn't be worn by a child under 2 years old, a person who has trouble breathing, or a person who can't remove the mask on their own.
- To maintain at least 1 metre distance between you and people coughing or sneezing.

***12. Self-quarantine if sick***

If you have any symptoms then call your doctor. Stay home until you recover. Stay home Safe home.[35,36]

## 2. CONCLUSION

There are hundreds of corona viruses, most of which circulate in animals. Only seven of these viruses infect humans and four of them cause symptoms of the common cold. But, 3 times in the last 20 years, a coronavirus has jumped from animals to humans to cause severe disease.

The new corona-virus was first detected in Wuhan, China in December 2019. Tens of thousands of people were covid 19 infected in China, with the virus spreading easily from person-to-person in many parts of that country. Health officials in the United States (US) and around the world are working to contain the spread of the virus through public health measures such as social distancing, contact tracing, testing, quarantines and travel restrictions. Scientists are working to find medications to treat the disease of COVID 19 and to develop a vaccine. So, STAY HOME, STAY SAFE.

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