

COVID-19: Transmission Mechanism and Pathogenic Potential

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Abstract: Coronavirus has taken hold all over the world. About 213 countries are marching with a death procession at this time. After analyzing the genome, we can see that the coronavirus begins with the bat's and later transmitted to human, but there is an intermediate source in the Wuhan sea food market, China, in December of 2019. This virus not a new type of virus, because it's a same group of virus of 2003, Severe Acute Respiratory Syndrome (SARS-CoV), both belongs to the *Betacoronavirus* group, and having that's similarity it was named SARS-CoV2. As there is not much clinical reports and vaccines, scientists are thinking to use some type of drug for COVID-19 as to previous case. We will try our best to review something that is about origin of CoVs, genomic structure, symptoms, pathogenicity, spreading cause, and how to prevent yourself focusing on SARS-CoV2, and will try to summaries the recent investigation of drugs with our opinion about COVID-19 treatment.

Keywords: SARS-CoV2, COVID-19, Symptoms, Prevention, Antiviral therapies.

1. Introduction

COVID-19 infection symptoms were first seen in Wuhan's people, then it gradually began to take on a larger size. Last December, a large number of Covid-19 cases were found in the south china sea-food city. Twenty-seven cases of the south China sea-food city were found in worse condition; the rest of the cases were in control. On 9th January 2020 after detailing in Wuhan city the China government has found socking reports, on that day China government publish a report about Covid-19. Report on the CDC revealed Coronavirus (COVID-19) has been found at main reasonable specialist for 15 to 59 pneumonia cases. On 10th January 2020 the genome of coronavirus became accessible. [1] Then it was kept in the GenBank database (accession number- MN908947). Then Global Initiative takes of the data and called it to be all influenza (GISAID). In primary examination about this virus, it was told that novel coronavirus (SARS-CoV2) affected by the SARS related CoV clade and differ from the inside genome of known bat CoVs. [2] After COVID-19 discovery more than 6365000 patients have been greatly affected and about 377000 were died due to Covid-19. The COVID-19 has its ability to spread rapidly and it tends to cause great disease in older adults and patients with worse health condition [3,4]. The corona virus has the ability to mutate and recombine and the genome sequence has already muted. Some of the scientists have found in the

virus there are two circulating strains, deadly strains "L" and less virulent one is "S" [5], [6]. Till now there are no several antiviral treatment or vaccines of coronavirus. Scientists are mainly focusing on the symptoms of respiratory system as the protocol issued by health authority in each country, as many countries are following WHO protocol [3], [4]. About all severe cases accepts oxygen. For rescue treatment, immunoglobulin G and convalescent plasma are used for passive immunization [7]. As per todays condition the invention of medicine is the main priority. Several number of research institute, organization, are working on searching a medication or an applicable vaccine for COVID-19. The Coronavirus caused the such epidemic in our world for the third times. The first such type of virus detected twenty one century ago, which was named SARS-CoV (2003) [8]-[10], and second time it was found in Arab country, which name was MERS-CoV (2012-2013)[11]-[13]. As we have already fought with the two epidemics, previously we can use the experience to create treatment plans against this. At this time scientist are using different types of drugs and medication to the positive patients and get promising result. Combination of Choloroquine and Azithromycine can be taken as an example [14]. Recently the combination of Remdesivir and well known Choloroquine drag get attention globally in medical science and many organizations are thinking to work on finding another method, antiviral RNA can be taken as an example [15]. As there are no specific treatment in this case many research groups are working hard to find the control, the replication and the spreading of the virus. We are also working on finding for most promising option in the treatment of Covid-19 and to provide an outer layer about our research. We are working on reviewing transmission mechanism and pathogenic potential of coronavirus and try to explain in which path the treatment strategy should go on to prevent and to slow down the viral infection.

2. SARS-CoV2

Coronavirus are huge in number's which is common among many animals even in human bodies. Respiratory illnesses and gastrointestinal illnesses are the two most popular symptom of Covid-19 in human and animals. Various of Covid-19 have large peplomers and it is almost look like a crown under the electron microscope. The name corona meaning "crown" or

“halo” [16,18]. Covid-19 were not considered as a deadly virus before 2003, This are almost round in shape they were causing little symptoms in immunocompetent people. Runny nose, sore throat, cough, headache and fever are the main symptoms of Covid-19. The symptoms can last for several days. Immunocompromised patients have a chance that the virus could cause a lower respiratory illness like bronchitis and pneumonia [16], [17]. In 2003 the world faced the first pandemic of the 21th century. Severe Acute Respiratory Syndrome Coronavirus (2003) emerged in Guangdong, China and it was the causes of 774 deaths and the illness of more than 8000 patients [16], [19], [20]. After nine years the strains of Coronavirus emerged in Saudi Arabia, 2500 cases and 861 deaths with a deadly case-fatality rate of 34.4%, were the fearful result of Middle East Respiratory Syndrome Coronavirus (MERS-CoV) [20].

A. The Era of Coronavirus

Coronavirus are not a new type of virus as it belongs to the subfamily *Coronavirinae* and with the family *Coronaviridae* and the order *Nidovirales*. The members of *Coronavirinae* subfamily are classified into four types, based on their protein sequences and phylogenetic relationship as,

- Alphacoronaviruses*,
- Betacoronaviruses*,
- Gammacoronaviruses*, and
- Deltacoronaviruses*.

Gammacoronavirus and *Deltacoronavirus* are unable to effect human though it can affect birds and might affect mammals [20], [21], [46] but *Alphacoronaviruses* and *Betacoronaviruses* can cause respiratory illness to human bodies and gastrointestinal illness in animals.

Six common coronaviruses (members of *Alphacoronaviruses* and *Betacoroaviruses*) can effect human greatly as reported at December 2019. HCoV-229E, and HCoV-NL63 belongs to the group of *Alphacoronaviruses* and the lineage A of *Betacoronaviruses* consists of HCoV-OC43 and HCoV- HKU1 and the most deadly SARS-CoV and MERS-CoV lineages to B and C of *Betacoronavirus* respectively [20]. CoVs are zoonotic pathogen and it originates in animal bodies and later transmitted to human bodies directly. [47]

All Coronaviruses that effect massively in human life are originated in bats and they are the hosts of many Coronaviruses [17,22] but there is an intermediate animal hosts between bats and human. Market civets’ cats and dromedary camels are the intermediate animal host of SARS-CoV and MERS-CoV respectively [23], [11], [13]. Primarily in the seafood Wuhan market in China, the Covid-19 is suspected, so the Chinese authority decided to close the market [1], [20]. According to the analysis the Covid-19 is similar to the SARS and for this it was named SARS-CoV2. But in this case the intermediate source is still yet to find so the scientists are researching on it.

B. Genomic Structure and Replication

As the world is aware of the trending novel zoonotic

Coronavirus (SARS-COV-2), popularly called as Covid-19 whose infection started in Wuhan in December 2019. [26] The Corona virus family consists of many contagious viruses- IBV-Beaudette, BCoV-ENT, HCoV-229E, MHV- A59, TGEV-Purdue 115, PEDV-CV777, etc. The range of their lengths is 27,317 to 31,357 nucleotides making the Coronavirus genome the largest one among all the RNA viruses. The members of this family have known to infect humans, other vertebrates and causing respiratory and GIT related issues. The organisation of this genome is somewhat similar to order Nidovirus [24]. Before the pandemic spread, there were only 2 viruses that were common to cause human infections- hCoV-229E and hCoV-OC43 but after the infection started discovery of more strains was observed- SARS-CoV, hCoV-NL63, hCoV-HKU1 and MERS-CoV. Out of these, SARS-Cov and MERS-Cov are highly virulent and have the highest mortality rate. Interestingly, both of them have been derived from bats. At the 5’ terminal end, two-third portion of the genome codes for replication and transcription while the left over one-third codes for structural and accessory proteins of the virus.

The research on these one-third proteins is necessary to find out the drug treatments and develop vaccines against the virus. [25], [46] SARS- COV-2 and MERS_COV, both are highly pathogenic and derived from bat. But some phylogenetic researches have revealed that though coronavirus can enter the cell through human receptors but it doesn’t transfer directly, preferably it needs an animal host that stays close to humans to spread it. So, for SARS-COV, it is being racoon dogs and for MERS-COV it is domestic riding camels. SARS COV-2, the reason for pandemic is 96% identical to bat SARS-like coronavirus genomically. The virus is spherical in shape, single stranded positive- sense RNA 26 to 32 kb in size. The structural features show that it is crown-like possessing clover leaf shaped projections (made up of glycosylated proteins) from the viral envelope known as spike proteins. Except spike proteins, they have 3 other types of proteins present called the membrane, envelope and nucleocapsid ones (Figure 1). [46], [47]

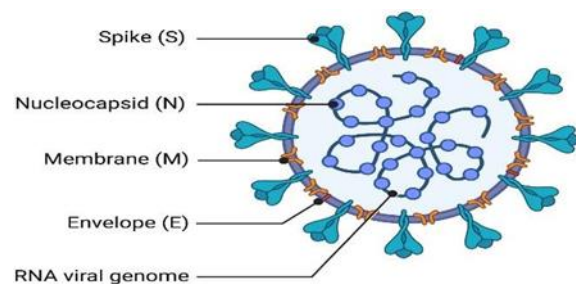


Fig. 1. Structure of coronaviruses

Almost 66% of the genome consists of two open reading frames that are overlapping code for 16 non-structural proteins, which includes- RNA dependent RNA polymerase, proteases, primase, helicase, etc. together forming a viral replication system. These unstructured proteins are the main therapeutic targets to find the cure of the disease. The remaining one-third

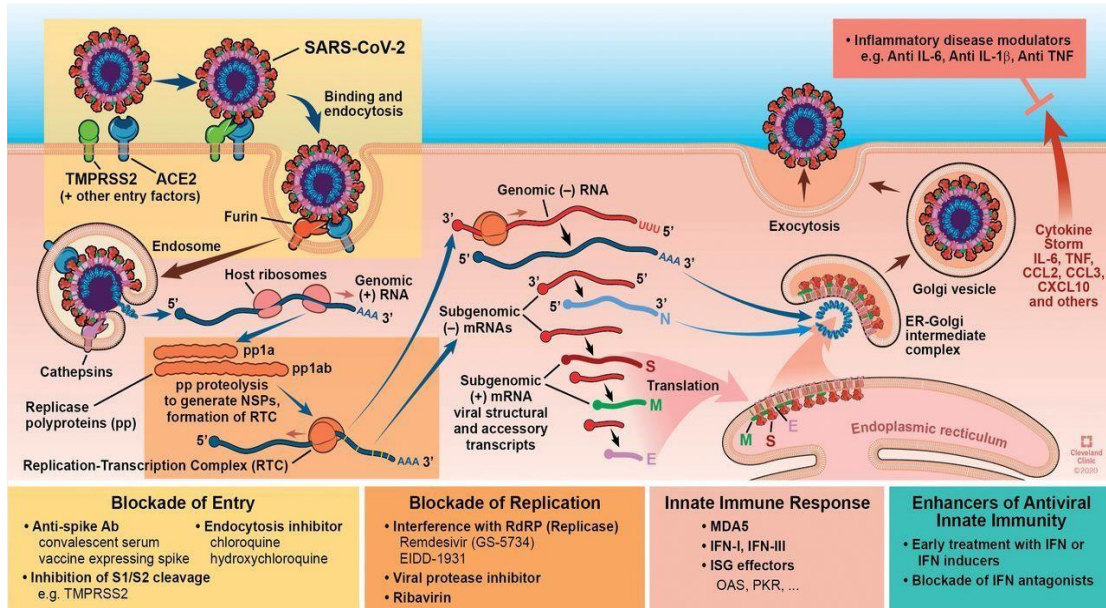


Fig. 2. Overview of COVID-19, SARS-CoV-2 replication, and therapeutic targets

on the genome contains the proteins not involved in replication but cause suppression of the immune system and enhance pathogenesis (Figure 2). [27]. A unique feature possessed by this virus is that it can also outspread by the people showing no symptoms at all. Reports have disclosed that this virus can spread among cats but chances among dogs is very low but whether this can spread from domestic animals to humans is still untold.

3. Symptoms

The common symptoms of SARS-COV-2 are fever, cough, loss of appetite, pneumonia, diarrhoea, vomiting, abdominal pain and other respiratory symptoms. In most of the patients, loss of smell and taste has been seen. [31] It was shocking to note that some positive cases showed only digestive symptoms and no respiratory symptoms. As the number of patients increased, it was observed that digestive issues became more common than the respiratory ones. The case with digestion issues had low monocyte count, high liver enzyme levels, long prothrombin count and their duration of treatment was longer than other cases.

Clinical studies revealed that one of the most common symptoms among the patients is diarrhoea and anorexia. So, this virus is not only affecting the respiratory system but damages the other systems and in the worst-case scenarios it has caused multiple organ dysfunction as well.

This is quite significant that the people and health care workers should know about other symptoms so that they are not solely depend on the respiratory symptoms to detect the disease. Also, it has been observed that in some cases the patients are showing digestive issues followed by respiratory issues when the condition becomes critical which has been a drawback to detect the cases earlier.

More and more people should be made aware about these

symptoms so that they don't spread it to other people or members of their family unknowingly. [28] Some other researchers say that the Coronavirus has impact on nervous system as it has been detected in the brain and cerebrospinal fluid but more research is going on to give more definite results. [29] Another study revealed that the asymptomatic patients are four times more than the symptomatic ones and have been playing a major role in its transmission. [30]

4. Cause of spreading of COVID-19

We have only few ideas about spreading of corona virus. Cough and sneezing of people during social events and small program are the main cause of its spreading according to WHO (33). In human body some fluctuations occur through droplets, (Figure-3) circulation of air and transmission mechanisms etc. but its importance in this case is still not clear.

Viral RNA samples are detected in human stool and transmitted through seasonal tobacco transmission [34], [35]. Is this kind of transmission the drops may stop in upper part of human body such as mouth and nose and sometimes may transmitted in lungs.

Some medical treatments such as infiltration and cardiopulmonary resuscitation (CPR) may cause circulation and endothelial dysfunction. When a man comes into contaminated area, the virus can also spread to the human body.

In this type of viruses there is no mother-to-child transmission and it the most important as a pregnant woman is more likely to be exposed to genital infections [36], [37]. Recent research said about 88% patients have chronic respiratory distress syndrome and all human patients can be related.

This human to human as way of integrating is supported by domestic and non-family run small business in Wuhan (38). In upcoming studies said that the metric component can be

affected by temperature, humidity, radiation components. This kind of virus is directly linked with drinking water, waste water and when it is thrown into manure. Commonly dirty water is used for irrigation purpose and human infections are often found in waste water. Shown in Fig. 3. [39].

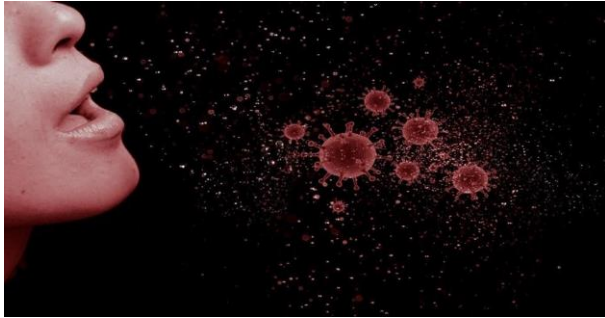


Fig. 3. Most common way of spreading Coronavirus COVID-19

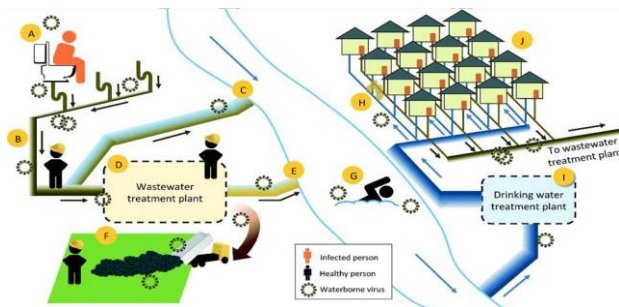


Fig. 4. Getting infections from wastewater

- i) Contaminations also observed in treat plants drinking water. the treatment of water is done by various natural and chemical treatment techniques repeatedly, in order to vanish contaminants including infections.
- j) A virus is coming into urban drinking water through the leaks in underground pipes and it conserve its aggravation through drinking water treatment.

If the load with Viruses are put into milk or infected vitamins, it can affect the water system and the Sewage Treatment industry (WWTP). In 2014, United States are highly affected by Ebola for the lack of Quantity and Quality in the waste of human body and in the Sea Water also (40). SARS, H5N1 influenza, RNA viruses were mainly immunodeficiency viruses and it is due to the high mutation rate. Some human parasites contain human Products are known as Zoo Noses and that can increase the Spreading the World Wide Movement, forestry, markets of Animal as well as meat hunting tor (41). Rubella infection is comparatively less effective. The incident of human infection is much more than typical catastrophic viruses that grow from unwanted wastes and class bio solids (42). In many cases the patient themselves swallow the virus-enriched nose and cause its presence in respiratory system. The PCR method is to detect these viruses in human body it's almost correct every time. In Urban Area the infectious germs must be in the wastewater and the NON effective SARS-CoV and Avian influenza virus are identified in infected individuals in fecal or intestinal tract [43]-[45].

Non-infectious that are in Urban Water,

- a) The viruses are in human waste as well as in Vomit that penetrate the drainage drain. TOILETs with or without the inside plumbing system can create problems.
- b) As the viruses can transport through local urban side to the wastewater treatment plant (WWTP), the employees can be affected.
- c) The flood water that mix will go to the untreated basin to the surface water.
- d) After the entry of viruses into the downtown, by the means of physical, biological and chemical treatment system expression of WWTP occurs. Exposure of WWTP agents to the virus that present in either treated or untreated water or may be present on residues of bio solids.
- e) Those viruses get survived after treatment of surface water, can cause the polluted water contaminants.
- f) By the process of land-application disposal of residual bio-solid from WWTP is done. Employees and others those are exposed bio solids after the survival of therapeutic procedures they may be exposed to virus free solids.
- g) Non contaminated microbes into the water system may get released by the recreational activities.
- h) Underground water supply channels may get contaminated by rapid sewage pipes.

5. Prevention

To prevent the spread of disease, use of face masks, maintaining good hand hygiene, social distancing and quarantines are really important. As till now there is no treatment found so, the medicines are used to just give a symptomatic relief. To reduce the transmission, various rules were imposed on the public that included isolation, environmental disinfectant (in the form of sprays, aerosols or liquids) and use of PPE (personal protective equipment). As there is no cure so, only option we have is prevention and that is only possible when we follow the guidelines given by WHO, health care workers or the government. Neither any treatment nor vaccine is available to protect us from the virus, the only way is to avoid exposure. As we know the disease is airborne so, use of face masks, covering your nose while coughing or sneezing with tissues and properly disposing off the used tissues is significant, handwashing regularly with hand wash or sanitizer (containing at least 60% alcohol), maintaining social distancing is necessary. Never touch your hands, eyes, nose and mouth without washing your hands. [32]

6. COVID-19 Treatment

Not one, but there have been many drugs that were tested to treat Covid-19, the most common ones include Remdesivir, Baricitinib, Ritonavir, Favipiravir, chloroquine, etc. Ivermectin and Remdesivir are the drugs that interfere with the viral

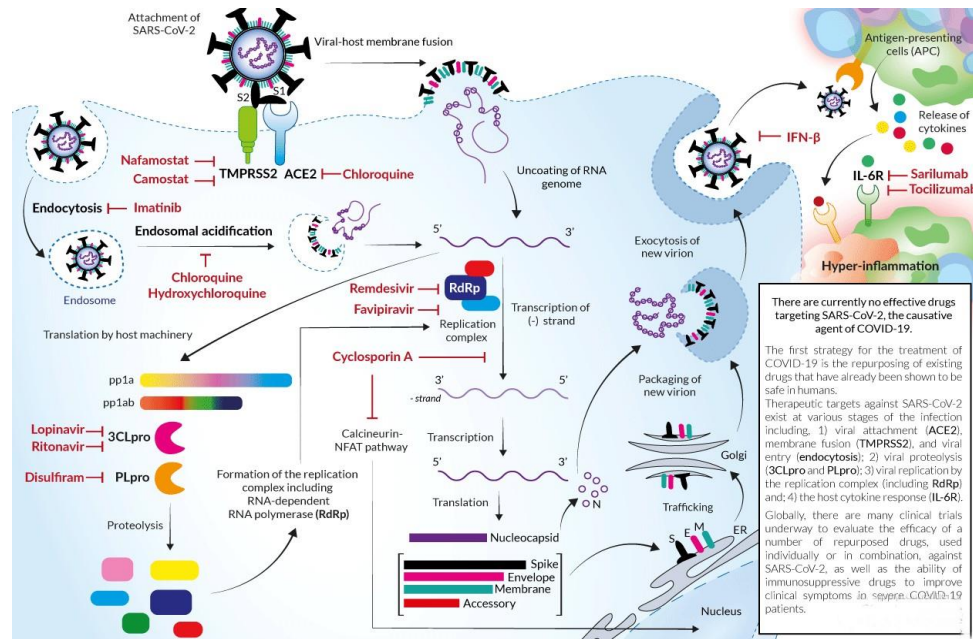


Fig. 5. Repurposing approved drugs for targeting SARS-CoV-2

replication. Favipiravir binds to the RNA dependent RNA polymerase and inhibits its reproduction. Darunavir and Ritonavir inhibit the protease activity and interfere in the viral replication. Baricitinib inhibits the endocytosis regulators thus prohibiting the viral entry. But the most accepted of all is Hydroxychloroquine as it is anti- malaria, anti-viral and anti-inflammatory. It works by increasing endosomal PH, interfering with the glycosylate receptors of the virus and modulating the immune system. This drug has been approved by FDA to use in emergency conditions and can be used in treatments under some regulations. First of all, there was a report suggesting hydroxychloroquine to be the possible treatment for this disease and various researches were done on it. One of the studies told us about the synergistic effect of two combinations that works better together. Azithromycin has been observed to kill Ebola and Zika virus and has shown results when given to the patients suffering from general viral infection. Although, more and more research should be done to check if this combination has some side effects or not. Studies have suggested these two to act as anti-viral as well as anti-bacterial therapy. If this drug doesn't help much still knowing its mode of action, we can develop a vaccine against the disease. When a drug research article comes into the market then, more and more interested people read it, some carry various experiments to know more about it which might be quite beneficial to find out the potential treatment or vaccination in the near future (Figure-4). These results came out of a small survey which showed that the use of hydroxychloroquine reduces the viral load and its action is triggered by azithromycin [14].

7. Conclusion

The COVID-19 pandemic poses a significant threat to the

global public health systems. The increasing number of cases and deaths have put the international community on alert that the worst scenarios are possible. Despite our knowledge of the SARS-CoV-2 infectious cycle, there is no clear strategy for COVID-19 patients' treatment. Based on recent experimental findings and recommendations, physicians are investigating different potential drugs that showed antiviral activity against SARS-CoV-2. Only time to tell which one of these drugs is going to work. In the meantime, scientists around the globe are working aggressively to find clinical therapies or vaccines against the virus.

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