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Dr. N Karnakar

Assistant Professor and HOD,
Venkateshwara Institute of
Pharmaceutical Sciences,
Nalgonda, Telangana, India

Dr. Ramana Hechhu

Assistant Professor,
Department of Pharmacy,
College of Health Sciences and
Medicine, Wolaita Sodo
University, Ethiopia

A review article on Corona Virus

Dr. N Karnakar and Dr. Ramana Hechhu

Abstract

Corona virus is a Novel RNA Virus member of the family Coronaviridae it causes Diseases in mammals and birds, In humans it causes respiratory tract infections It is First discovered in 1930 at North Dakota in domesticated chickens with New Respiratory Infection infectious bronchitis virus (IBV). In present review work Research conducting on latest case study on Corona virus (COVID-19) outbreak at Wuhan city of China in December 2019.

Keywords: SARS-CoV-2, MERS, CDC, WHO, Favipiravir

Introduction

Corona viruses are a group of related RNA viruses that cause diseases in mammals and birds. In humans, these viruses cause respiratory tract infections that can range from mild to lethal. Mild illnesses include some cases of the common cold (which is also caused by other viruses, predominantly rhinoviruses), while more lethal varieties can cause SARS, MERS, and COVID-19. There are as yet no vaccines or antiviral drugs to prevent or treat human coronavirus infections. Coronavirus disease 2019 (COVID-19) is an infectious disease caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). Coronaviruses constitute the subfamily *Orthocoronavirinae*, in the family *Coronaviridae*, order *Nidovirales*, and realm *Riboviria* ^[1, 2]. They are enveloped viruses with a positive-sense single-stranded RNA genome and a nucleocapsid of helical symmetry ^[3]. The genome size of coronaviruses ranges from approximately 26 to 32 kilobases, one of the largest among RNA viruses ^[4]. They have characteristic club-shaped spikes that project from their surface, which in electron micrographs create an image reminiscent of the solar corona, from which their name derives ^[5].

Structure of Coronaviruses are large, roughly spherical, particles with bulbous surface projections ^[6]. The average diameter of the virus particles is around 125 nm (.125 μ m). The diameter of the envelope is 85 nm and the spikes are 20 nm long. The envelope of the virus in electron micrographs appears as a distinct pair of electron-dense shells (shells that are relatively opaque to the electron beam used to scan the virus particle) ^[7, 8]. The viral envelope consists of a lipid bilayer, in which the membrane (M), envelope (E) and spike (S) structural proteins are anchored ^[9]. The ratio of E:S:M in the lipid bilayer is approximately 1:20:300 ^[10]. On average a coronavirus particle has 74 surface spikes ^[11]. A subset of coronaviruses (specifically the members of betacoronavirus subgroup A) also have a shorter spike-like surface protein called hemagglutinin esterase (HE).

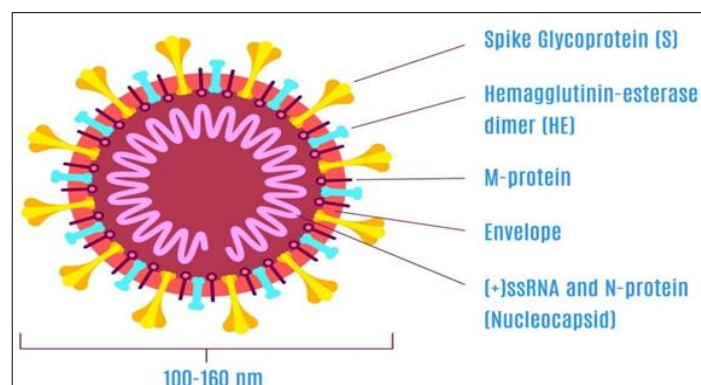


Fig 1: Coronavirus structure

Corresponding Author:

Dr. N Karnakar

Assistant Professor and HOD,
Venkateshwara Institute of
Pharmaceutical Sciences,
Nalgonda, Telangana, India

Coronaviruses were first discovered in the 1930s when an acute respiratory infection of domesticated chickens was shown to be caused by infectious bronchitis virus (IBV) [12]. Arthur Schalk and M.C. Hawn described in 1931 a new respiratory infection of chickens in North Dakota. In the 1940s, two more animal coronaviruses, mouse hepatitis virus (MHV) and transmissible gastroenteritis virus (TGEV), were isolated [13]. Human coronaviruses were discovered in the 1960s [14]. They were isolated using two different methods in the United Kingdom and the United States. E.C. Kendall, Malcom Byone, and David Tyrrell working at the Common Cold Unit of the British Medical Research Council in 1960 isolated from a boy a novel common cold virus B814 [15]. The two novel strains B814 and 229E were subsequently imaged by electron microscopy in 1967 by Scottish virologist June Almeida at St. Thomas Hospital in London [16]. Other human coronaviruses have since been identified, including SARS-CoV in 2003, HCoV NL63 in 2004, HCoV HKU1 in 2005, MERS-CoV in 2012, and SARS-CoV-2 in 2019 [17, 18]. It was first identified in December 2019 in Wuhan, China, and has resulted in an ongoing pandemic.

Coronaviruses are single-stranded RNA viruses, about 120 nanometers in diameter. They are susceptible to mutation and recombination and are therefore highly diverse. There are about 40 different varieties (see Appendix 1) and they

mainly infect human and non-human mammals and birds. They reside in bats and wild birds, and can spread to other animals and hence to humans. The virus that causes COVID-19 is thought to have originated in bats and then spread to snakes and pangolins and hence to humans, perhaps by contamination of meat from wild animals, as sold in China’s meat markets

The corona-like appearance of coronaviruses is caused by so-called spike glycoproteins, or peplomers, which are necessary for the viruses to enter host cells. The spike has two subunits; one subunit, S1, binds to a receptor on the surface of the host’s cell; the other subunit, S2, fuses with the cell membrane. The cell membrane receptor for both SARS-CoV-1 and SARS-CoV-2 is a form of angiotensin converting enzyme, ACE-2, different from the enzyme that is inhibited by conventional ACE-1 inhibitors, such as enalapril and ramipril.

Briefly, the S1 subunit of the spike binds to the ACE-2 enzyme on the cell membrane surface. A host transmembrane serine protease, TMPRSS2, then activates the spike and cleaves ACE-2. TMPRSS2 also acts on the S2 subunit, facilitating fusion of the virus to the cell membrane. The virus then enters the cell. Inside the cell the virus is released from endosomes by acidification or the action of an intracellular cysteine protease, cathepsin.

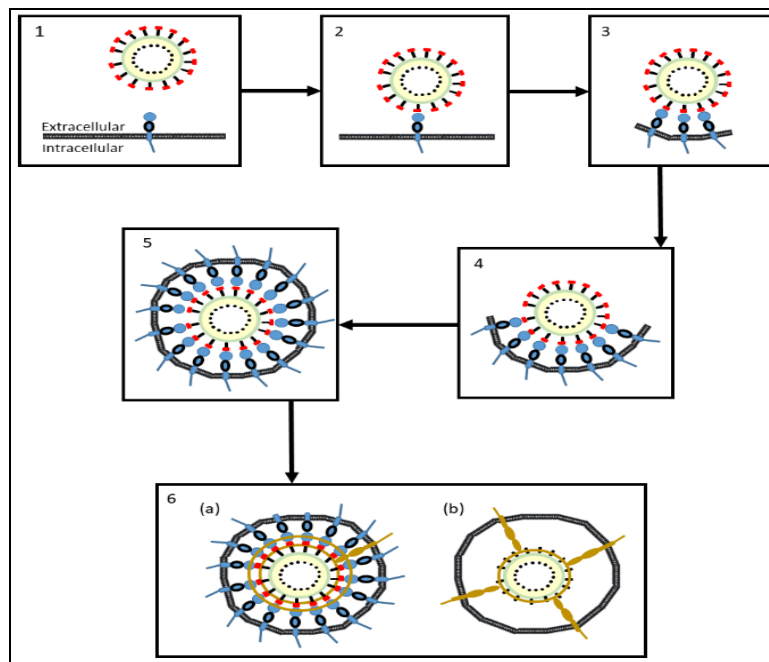


Fig 2: Shows detailed description of mechanisms whereby coronavirus SRA-CoV-2 enters cells

Figure shows detailed description of mechanisms whereby coronavirus SRA-CoV-2 enters cells

1. The coronavirus approaches the cell membrane
2. An S1 subunit (red) at the distal end of a glycoprotein spike of the virus binds to a membrane-bound molecule of ACE-2 (blue)
3. As more S1 subunits of the glycoprotein spikes bind to membrane-bound molecules of ACE-2, the membrane starts to form an envelope around the virus (an endosome)
4. The process continues ...
5. ... until the endosome is complete
6. The virus can enter the cell in two ways:

- a. A cell membrane-bound serine protease (brown), TMPRSS2, cleaves the virus’s S1 subunits (red) from its S2 subunits (black) and also cleaves the ACE-2 enzymes; the endosome enters the cell (endocytosis), where the virus is released by acidification or the action of another protease, cathepsin
- b. The same serine protease, TMPRSS2, causes irreversible conformational changes in the virus’s S2 subunits, activating them, after which the virus fuses to the cell membrane and can be internalized by the cell

A serine protease inhibitor, camostat mesylate, used in Japan to treat chronic pancreatitis, inhibits the TMPRSS2

and partially blocks the entry of SARS-CoV-2 into bronchial epithelial cells in vitro.

Symptoms

As is common with infections, there is a delay between the moment a person is first infected and the time he or she develops symptoms. This is called the incubation period. The typical incubation period for COVID-19 is five or six days, but it can range from one to fourteen days ^[19] with approximately ten percent of cases taking longer ^[20].

Fever is the most common symptom of COVID-19, but is highly variable in severity and presentation, with some older, immunocompromised, or critically ill people not having fever *et al.* ^[21] Other common symptoms include cough, loss of appetite, fatigue, shortness of breath, sputum production, and muscle and joint pains ^[22]. Symptoms such as nausea, vomiting, and diarrhoea have been observed in varying percentages. Less common symptoms include sneezing, runny nose, sore throat, and skin lesions ^[23]. Some cases in China initially presented with only chest tightness and palpitations ^[24]. A decreased sense of smell or disturbances in taste may occur. Loss of smell was a presenting symptom in 30% of confirmed cases in South Korea ^[25].

Table 1: Covid-19 Symptoms Range

Symptom	Range
Fever	83-99%
Cough	59-82%
Loss appetite	40-84%
Fatigue	44-70%
Shortness of breath	31-40%
Coughing up sputum	28-33%
Muscle aches and Pains	11-35%

Latest case study

Detailed timeline of China's coronavirus outbreak-First in World China (Wuhan city)

- On December 1, the symptom onset date of the first patient identified. Five days after illness onset, his 53-year-old wife who had no known history of exposure to the market also presented with pneumonia and was hospitalized in the isolation ward.
- It wasn't until the second week of December, the Wuhan doctors were finding cases that indicated the virus was spreading from one human to another.
- On December 25, Chinese medical staff in two hospitals in Wuhan were found to be suspected of contracting viral pneumonia and were quarantined. Later, hospitals in the Wuhan witnessed an "exponential" increase in the number of cases in late December that cannot be linked back to the Huanan Seafood Wholesale Market.
- Whistleblower doctor Li Wenliang warned a group of other doctors about a possible outbreak of an illness that resembled "severe acute respiratory syndrome (SARS)". He urged them to take protective measures against infection.
- On December 31, the Wuhan Municipal Health Commission declared that their investigation has not found "any obvious human-to-human transmission and no medical staff infection. "China contacted the World Health Organization (WHO) three weeks after doctors first started noticing the cases.

- At the beginning of January, summons issued to Li Wenliang by the Wuhan Public Security Bureau accusing the doctor of "spreading rumours."
- On January 3, Dr Li signed a statement at a police station acknowledging his "misdemeanor" and promising not to commit further "unlawful acts." China's National Health Commission ordered institutions not to publish any information related to the unknown disease. On the same day, the Hubei Provincial Health Commission ordered to stop testing samples from Wuhan related to the new disease and destroyed all existing samples. The Wuhan Municipal Health Commission released another statement, reiterating that preliminary investigations have shown "no clear evidence of human-to-human transmission and no medical staff infections." 59 people in the central city of Wuhan have been sickened by a "pneumonia-like illness", as per a report by The New York Times published on January 6. On the same day, the Chinese Center for Disease Control and Prevention issued a level 1 travel watch. It advised travellers to Wuhan to avoid contact with 'living or dead animals, animal markets, and sick people.'
- On January 8, Chinese medical authorities claim to have identified the virus, reiterating that it still found "no clear evidence of human-to-human transfer".
- On January 11, the Wuhan City Health Commission released Q&A sheet emphasizing that most of the unexplained viral pneumonia cases in Wuhan have a history of exposure to the South China seafood market and "no clear evidence of human-to-human transmission has been found."
- Dr Li Wenliang was hospitalized on January 12. He started coughing and developed a fever after unknowingly treating a patient with the coronavirus. Later, Wenliang's condition deteriorated so badly that he was admitted to the intensive care unit and was given oxygen support.
- On January 13, the first case of novel coronavirus was reported outside China involving a 61-year-old Chinese woman in Thailand, who had visited Wuhan. However, Thailand's Ministry of Public Health said the woman had not visited the Wuhan seafood market and had come down with a fever on January 5. The woman had visited a different, smaller market in Wuhan, in which live and freshly slaughtered animals were sold.
- On January 14, the World Health Organization in its report stated: "Preliminary investigations conducted by the Chinese authorities have found no clear evidence of human-to-human transmission of the novel coronavirus (2019-nCoV) identified in Wuhan, China."
- On January 15, Japan reported its first case of coronavirus and its Health Ministry said the patient had not visited any seafood markets in China. The Wuhan Municipal Health Commission in a statement said that the possibility of "limited human-to-human transmission" cannot be ruled out. Despite the fact that Wuhan doctors knew that the virus is "contagious", city authorities allow 40,000 families to gather and share home-cooked food in a Lunar New Year banquet, as per the article in National Review.
- On January 19, the Chinese National Health Commission declared the virus "still preventable and controllable". A day later, the head of China's national

health commission team investigating the outbreak, confirmed that two cases of infection in China's Guangdong province had been caused by "human-to-human transmission and medical staff had been infected".

- On January 21, the CDC announced the first case of the coronavirus in the US. The patient had returned from China six days ago.
- On January 22, a WHO delegation conducted a field visit to Wuhan and concluded, "deployment of the new test kit nationally suggests that human-to-human transmission is taking place in Wuhan. "Nearly two months after the first case of the virus was reported, Chinese authorities announced their 'first steps for a quarantine of Wuhan.' By this time, a significant number of Chinese citizens have traveled abroad as "asymptomatic, oblivious carriers".
- Dr Wenliang tested positive for coronavirus on February 1 and died six days later.

The mode of transmission

COVID-19 is a new disease and we are still learning about how it spreads according to the US Centers for Disease Control and Prevention (CDC) [26], In general, respiratory virus infection can occur through In general, respiratory virus infection can occur through

- Contact (direct or indirect)
- Droplet spray in short range transmission
- Aerosol in long-range transmission (airborne transmission)

Close Contact (6 feet, 1.8 meters) and Respiratory Droplets: The virus is thought to spread mainly from person-to-person, Between people who are in close contact with one another Through respiratory droplets produced when an infected person coughs, sneezes or talks This idea, that large droplets of virus-laden mucus are the primary mode of transmission, guides the US CDC's advice to maintain at least a 6-foot distance, Maintaining good social distance (about 6 feet) is very important in preventing the spread of COVID-19. Larger respiratory droplets (>5 μm) remain in the air for only a short time and travel only short distances, generally <1 m". "Virus-laden small (<5 μm) aerosolized droplets can remain in the air and travel long distances, >1 m" (more than 3.3 feet). A study of transmission occurring in a restaurant between people at a distance above 1 meter, observed that "strong airflow from the air conditioner could have propagated droplets".

Airborne Transmission: The WHO²⁶ states that "Respiratory infections can be transmitted through droplets of different sizes: when the droplet particles are >5-10 μm in diameter they are referred to as respiratory droplets, and when they are <5μm in diameter, they are referred to as droplet nuclei. According to current evidence, COVID-19 virus is primarily transmitted between people through respiratory droplets and contact routes". The WHO defines airborne transmission as "the spread of an infectious agent caused by the dissemination of droplet nuclei that remain infectious when suspended in air over long distances and time.

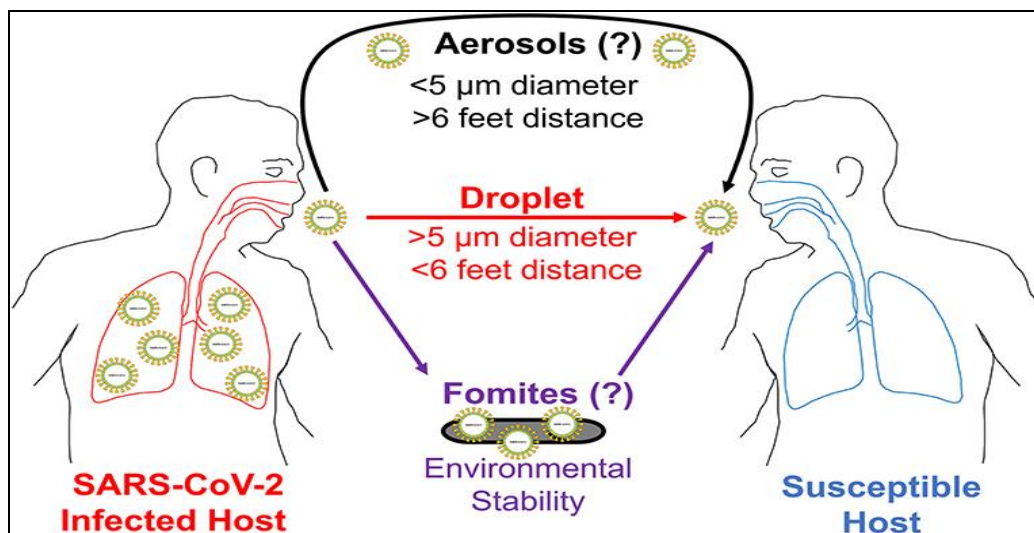


Fig 3: Diagram Shows Primary Mode of Transmission for COVID-19

Objects and Surfaces: The virus could spread by touching an object or surface with virus present from an infected person, and then touching the mouth, nose or eyes. Surface contamination as observed in the study cited above

- Computer mouse (ICU 6/8, 75%; GW 1/5, 20%)
- Trash cans (ICU 3/5, 60%; GW 0/8)
- Sickbed handrails (ICU 6/14, 42.9%; GW 0/12)
- Doorknobs (GW 1/12, 8.3%)

76.5% of all personal items sampled at the University of Nebraska Medical Center (UNMC) were determined to be positive for SARS-CoV-2, Of these samples, 81.3% of the miscellaneous personal items were positive by PCR, which

included: Exercise equipment, Medical equipment (spirometer, pulse oximeter, nasal cannula), PC and iPads, Reading glasses other findings include Cellular phones (83.3% positive for viral RNA), Remote controls for in-room TVs (64.7% percent positive), Toilets (81.0% positive), Room surfaces (80.4% of all sampled), Bedside tables and bed rails (75.0%) and Window ledges (81.8%)

Duration of contamination on objects and surfaces: Although the virus titer was greatly reduced, viable SARS-CoV-2 was measured for this length of time [26].

- Plastic: up to 2-3 days
- Stainless Steel: up to 2-3 days

- Cardboard: up to 1 day
- Copper: up to 4 hours

Laboratory Diagnosis

Samples: A Chinese study reported that positive rates varied by sample type tested. In 205 patients with confirmed COVID-19 among 3 hospitals, pharyngeal swabs were collected 1-3 days after admission. Other types of samples were also collected throughout illness-sputum, blood, urine, feces, nasal swabs, and bronchial brush or bronchoalveolar lavage (BAL) fluid. Samples were tested with RT-PCR. Of 1070 total samples tested, types with the highest rates of positive results included BAL fluid (14/15; 93%), sputum (75/104; 72%), nasal swabs (5/8; 63%), brush biopsy (6/13; 46%), pharyngeal swabs (126/398; 32%), feces (44/153; 29%), blood (3/307; 1%), and urine (0/72; 0%). Nasal swabs were found to contain the most virus.

Upper respiratory tract specimens have been reported to contain a smaller viral load than lower respiratory tract specimens do. If PCR tests are negative for SARS-CoV-2 using upper respiratory tract specimens despite persistent clinical suspicion, the WHO recommends retesting using lower respiratory tract specimens.

The CDC has developed a diagnostic test for detection of the virus and received special Emergency Use Authorization (EUA) from the FDA on February 4, 2020, for its use. The test is a real-time reverse transcription-polymerase chain reaction (rRT-PCR) assay that can be used to diagnose the virus in respiratory and serum samples from clinical specimens. The CDC has developed a diagnostic test for detection of the virus and received special Emergency Use Authorization (EUA) from the FDA on February 4, 2020, for its use [27]. The test is a real-time reverse transcription-polymerase chain reaction (rRT-PCR) assay that can be used to diagnose the virus in respiratory and serum samples from clinical specimens.

Two kinds of tests are available for COVID-19: viral tests and antibody tests. Coronavirus 2019 Test, SARS CoV-2 Test, COVID-19 RT-PCR, COVID-19 IgG, IgM antibody test, SARS CoV-2 antigen test, COVID-19 Ag test [28].

- Molecular (RT-PCR) test: To diagnose a SARS-CoV-2 infection (COVID-19)
- Antibody (serology) test: To detect antibodies to SARS-CoV-2 that indicate you have been exposed to the virus; to help track the pandemic, A COVID-19 antigen test that detects SARS CoV-2 proteins in respiratory samples has received an emergency-use authorization but the test is not in widespread use yet.

Prevention and control

The best way to prevent illness is to avoid being exposed to this virus [29]: The virus is thought to spread mainly from person-to-person, Between people who are in close contact with one another (within about 6 feet), Through respiratory droplets produced when an infected person coughs, sneezes or talks, These droplets can land in the mouths or noses of people who are nearby or possibly be inhaled into the lungs. Some recent studies have suggested that COVID-19 may be spread by people who are not showing symptoms.

Wash your hands often: Wash your hands often with soap

and water for at least 20 seconds especially after you have been in a public place, or after blowing your nose, coughing, or sneezing. If soap and water are not readily available, use a hand sanitizer that contains at least 60% alcohol. Cover all surfaces of your hands and rub them together until they feel dry. Avoid touching your eyes, nose, and mouth with unwashed hands.

Avoid close contact: Avoid close contact with people who are sick, even inside your home. If possible, maintain 6 feet between the person who is sick and other household members. Put distance between yourself and other people outside of your home, Remember that some people without symptoms may be able to spread virus. Stay at least 6 feet (about 2 arms' length) from other people. Keeping distance from others is especially important for people who are at higher risk of getting very sick.

Cover your mouth and nose with a cloth face cover when around others: Everyone should wear a cloth face cover when they have to go out in public, for example to the grocery store or to pick up other necessities. Cloth face coverings should not be placed on young children under age 2, anyone who has trouble breathing, or is unconscious, incapacitated or otherwise unable to remove the mask without assistance, The cloth face cover is meant to protect other people in case you are infected.

Cover coughs and sneezes: If you are around others and do not have on your cloth face covering, remember to always cover your mouth and nose with a tissue when you cough or sneeze or use the inside of your elbow and do not spit, Throw used tissues in the trash, Immediately wash your hands with soap and water for at least 20 seconds. If soap and water are not readily available, clean your hands with a hand sanitizer that contains at least 60% alcohol.

Clean and disinfect: Clean AND disinfect frequently touched surfaces daily. This includes tables, doorknobs, light switches, countertops, handles, desks, phones, keyboards, toilets, faucets, and sinks. If surfaces are dirty, clean them. Use detergent or soap and water prior to disinfection. Then, use a household disinfectant. Most common EPA-registered household disinfectants.

Monitor Your Health: Be alert for symptoms. Watch for fever, cough, shortness of breath, or other symptoms of COVID-19. Especially important if you are running essential errands, going into the office or workplace, and in settings where it may be difficult to keep a physical distance of 6 feet. Take your temperature if symptoms develop. Don't take your temperature within 30 minutes of exercising or after taking medications that could lower your temperature, like acetaminophen. Follow CDC guidance if symptoms develop.

Treatment

There is currently no vaccine to prevent coronavirus disease 2019 (COVID-19) approved by US FDA. Even though some of the drugs recommended for supporting to treat corona virus disease are given in below table

Table 2: What it does When should it be used

Drug name	What it does	When should it be used	Route of administration
Remdesivir	Shutting down viral replication in the body	Given it to hospitalized patients on oxygen with moderate covid19	Intravenous in ICU Inhaler
Glucocorticoids	Calms acute inflammatory response to slow disease progression by preventing the body pumping out inflammatory chemicals.	For severely ill patients with progressive deterioration of oxygenation indicators, rapid worsening of imaging and cytokine storm.	Intravenous
Hydroxychloroquine	Found to inhabit the activity of SARS – COV – 2 in lab studies by decreasing the acidity in endosomes, which are compartments inside cells that some viruses co-opt to enter cells and cause infection.	Prophylaxis for high risk close contact, health workers and frontline workers who had unprotected exposure to infection, people with mild disease at start of infection	Oral tablets
Dexamethasone	Modulates immune mediated lung injury and slows progression to respiratory failure and death.	Given it to severely ill patients on invasive ventilation or oxygenation.	Intravenous in ICU Oral Tablets
Favipiravir	broad spectrum anti viral works by selectively inhabiting RNA polymerase to shut down replication.	Given it to mild to moderate disease patients.	Oral tablets.
Tocilizumab	Calms the aberrant hyper immune response called cytokine storm by acting against inflammatory chemicals to fight infection	Given it to moderate to severe to disease patients.	Intra venus drip.
Plasma therapy	Infection fighting anti bodies from the blood of recovered people given to ill patients to boost their immunity.	Given it to for patients with moderate disease whose oxygen requirement is progressively increasing despite the use of steroids.	Transfusion

Conclusion

Corona virus infection is Global Emerging viral infectious Disease in Humans primarily it is transmitted between people through respiratory droplets. It can spread to humans through close contact with infected humans.

COVID 19 disease outbreak was reported from Wuhan City, Hubei Province, People's Republic of China on December 31, 2019. Corona virus related infectious diseases seems to be biggest challenge of 21 century that have been constantly emerging and threatening public health around the globe. Coronavirus disease-19 (COVID-19) that was detected as cause of respiratory tract infection in China by end the December 2019 impelled World Health Organization to declare in January 2020 public health emergency of international concern and consequently pandemic in March 2020. Over a past six months COVID-19 pandemic spread all over the world as of now 10th, Aug 2020, there have been 19,717,999 confirmed cases of COVID-19, including 728,012 deaths, reported to WHO. hence, all over the world united together and continued to fight against COVID 19 is needed until the successful vaccine release in to the Market.

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the largest genomes [26.4 kb (ThCoV HKU12) to 31.7 kb (SW1)] among all known RNA viruses (Figure 1) [2,13,16].

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