

## Classroom Article

# Coronaviral Infections and the Novel Coronavirus outbreak 2019-20

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## Abstract

The novel coronavirus disease (COVID-19) which originated from china in December 2019 has infected millions and has caused countless deaths. The main mode of spread is through droplets. The infection mostly causes mild symptoms like fever, cough, sore throat, myalgia etc, but can also cause potentially fatal pneumonia renal failure etc. RT-PCR is currently the best diagnostic test. Since there is no specific drug against the virus, the best way to control the disease is through preventing it by taking care of droplet spread, isolation of infected people and contact tracing. The population should avoid unnecessary travel, maintain social distancing, follow protective measures and proper hygiene.

**Key words :** Covid-19, pandemic, morbidity, isolation, prevention

## Introduction

There are several emerging viral infections affecting humans. One among them is the coronavirus infection. They are large viruses which produces disease mostly in animals and sometimes in humans. Bats are common reservoirs.<sup>1</sup> They do not exhibit any symptoms. Coronavirus also circulates between animals like civetcats, camels, pangolins. Humans can get infected from these animals. Most of the infections are asymptomatic or manifests as common cold. However severe diseases have been documented as SARSCoV, MERS CoV. A new mysterious disease with fever and pneumonia was first reported from Wuhan city, Hubei province China in Dec-2019. This virus has been designated as SARS CoV 2 by the international Committee on Taxonomy of Viruses.<sup>2</sup> WHO on 11th February 2020 declared official name for the new coronavirus as COVID -19.<sup>3</sup> Coronavirus has been named because it looks like a Crowned Virus (Corona = Crown) due to Spike Protein.

## Classification

Coronavirus is the largest virus belonging to the Nidovirales order. 229E (alpha coronavirus) and OC43 (beta corona virus) causes common cold, NL63 (alpha) in 2004 caused bronchiolitis, HKU1 (beta) in 2005 caused lower respiratory tract infection. SARS CoV in 2003, MERS CoV in 2012 and COVID-19 in 2019-20 has caused significant morbidity and mortality.

## Biology and functions

Corona virus virions are spherical with a size of 125 nm. They are enveloped viruses, Contains positive sense RNA. It has various structural proteins such as Spike protein (S), Membrane glycoprotein (M), Envelope protein (E) Hemagglutininesterase glycoprotein (HE), Nuclear protein (N) with RNA together called Nucleocapsid. The S protein is useful for attachment to the host cell. HE protein helps in this process. M protein is the abundant one which is maintaining the curvature of viral membrane. It also binds to the nucleocapsid. Assembly and release of virus is the function of E protein. This protein also has ion channel activity.

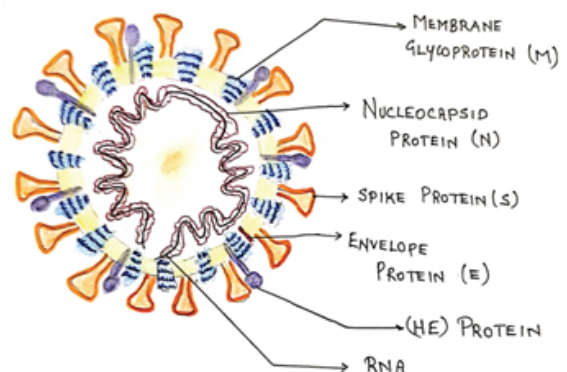


Figure 1 : Structure of Corona virus

## Pathogenesis

Virus particle gets attached to the host cell by surface protein ACE-2, endocytosis occurs. Since the virus has a single positive strand RNA, it can directly produce viral genome and proteins, resulting in less doubling time and so more viral particles gets produced quickly.<sup>4,5</sup> Viral replication and assembly occurs and finally new virus particles are released. Incubation period is around 2-28 days, but in most cases 7-14 days.

## Modes of Transmission

### 1. Origin

Coronavirus is a Zoonotic infection. Bats are the main reservoirs. From bats infection spreads to many animals (bat to camel, bat to pangolin, bat to snakes, bats to civet cats) and accidental spread to man happens due to contact with these animals. Genomic sequence of novel coronavirus disease shows 99.9% similarity to Bat corona virus<sup>5</sup>.

### 2. Man to Man Spread

1. Droplet spread:<sup>6</sup> Coughing, sneezing coryza and close personal contact such as touching and shaking hands.
2. Fomites:<sup>6</sup> Coronavirus can be present for one day in cardboard box, three days in plastics and

silver ware, three hours in brass, in dry surfaces for 6 hours and in wet surfaces for 6 days.

3. The infection can also be transmitted by people without symptoms during their incubation period.

Contagiousness of virus is determined by Reproductive number ( $R_0$ ),<sup>7</sup> that represents the average number of people who will be Infected with the disease from a single infected person.  $R_0$  number for COVID-19 is 4.08 as compared to 1.3 for common influenza and 2 for SARS. For measles  $R_0$  is 14 and for Chicken Pox – 9. Transmission rate for COVID-19 is 2-3.1. Fatality rate for COVID-19 is 3%, whereas for seasonal flu it is 0.01%, and for SARS– 10% and for MERS– 34%.

## Risk Factors

Children less than one year, elderly, persons with immunosuppressive therapy and with co-morbid conditions like diabetes, hypertension, smoking and chronic systemic diseases are at risk.

## Clinical Features

Most of the coronavirus infections are either asymptomatic or mild manifesting as common cold, headache, body pain, cough, running nose, sore throat with fever of mild to moderate degree.<sup>6,7</sup> Human

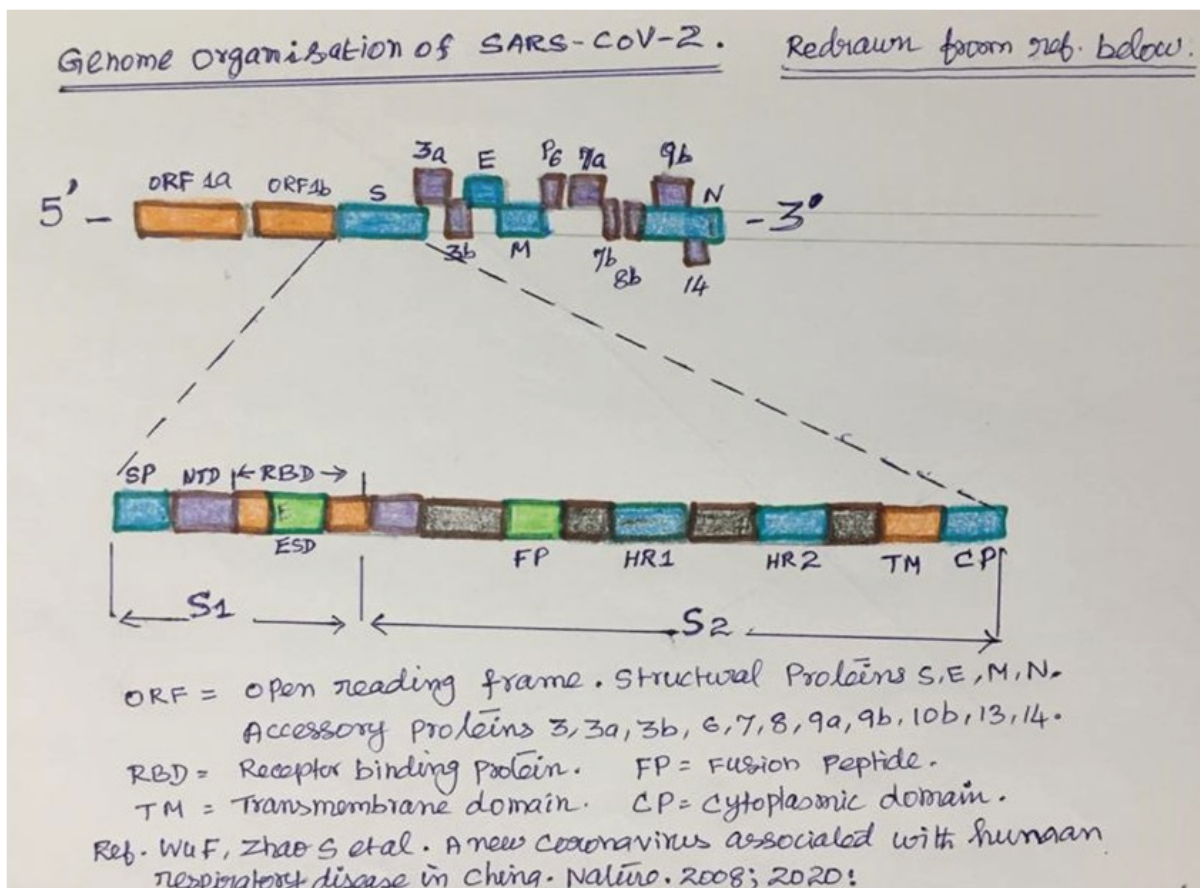


Figure 2: Genomic organization of SARS-CoV-2

S.no	Author	Title	Study details
1	COVID-19 response team	Corona virus disease 2019 in children in USA	Children constituted 1.7% of positive corona virus cases of which 5% of these required admissions.77% of admitted kids had comorbidities Fever- 56% Cough- 54% Headache- 28% Sore throat- 24% Myalgia-23% Diarrhea- 13% Breathing difficulties -13% Nausea/vomiting-11% Rhinorrhea- 7%
2	Lux X Zhang L et al	SARS Cov2 infection in children at Wuhan Children's Hospital, China	Among RT-PCR positive cases in children Less than 1 year- 18.1% 1-5 years- 23.4% 6-10 years- 33.9% 11-15 years-24.6% Symptomatically 41.2% had fever, 46.2% had pharyngitis, 48.5% had cough, 64.9% had pneumonia.
3	Wu Z Mc Googan J Met al	Characteristics of and important lessons from corona outbreak in china	Among the RT-PCR positive cases studied Less than 10 years- 1% 10-19 years- 1% 20-29 years- 8% 30-79 years- 87% >80 years-3% Case fatality rate was 2.3%, no deaths were recorded below 9 years
4	Dong Y, Mox X et al	Epidemiological characteristics of 2143 pediatric patients with 2019 corona virus disease	Among the RT-PCR positive children studied at shanghai children medical centre, china Less than 1 year- 17.7% 1-5 years- 7.3% 6-10 years- 4.2% 11-15 years- 4.1% >15 years- 15.6% 10.6% of infants had severe or critical illness It was observed that cases peaked on the third week after rising and then started declining

Table 1: VARIOUS SYMTOMS NOTED IN THE CORONA VIRUS OUTBREAK(source:-1.MMWR 2020;14:22-426,2.New Eng J med 2020,3.JAMA 2020;264,4.Pediatrics 2020;0702.)

coronaviruses can also cause other severe manifestations like respiratory distress, pneumonia (specifically ground glass opacities in peripheries of lungs), pneumothorax, ARDS, hypertension, myocardial injury and cardiac dysfunction, renal shutdown and multi-organ dysfunction syndrome

Nansen chen's study in lancet reveals that coronavirus infections initially resemble common cold and other respiratory tract illness. Presentation is mild in most of the cases.

ARDS were seen in 17% of cases and 11% of them worsened quickly and expired. Some patients showed ground-glass opacity, multiple mottling in chest imaging and 1% of patient had Pneumothorax. Deaths were due to Pneumonia, Severe Acute respiratory distress and acute respiratory failure. Some had severe myocardial injury, renal shut down ultimately leading to multi-organ dysfunction and death.<sup>8</sup>

Huijun et al studied 9 pregnant women with the complaints of cough, cold, myalgia, malaise and sore throat. They tested positive. None had severe pneu-

monia. 5/9 had lymphocyte count less than. 1000/cu.mm, 3/5 had elevated transaminases. All women delivered by cesarean section. All neonates were normal. Samples of amniotic fluid were tested for rtPCR and all were negative. Cord blood and throat swabs of neonates were also negative for rtPCR. There was no vertical transmission. Larger studies are needed.<sup>9</sup>

## The Global Spread

Apart from China Coronavirus had spread to many countries via air travelers. USA, South Korea, Japan, Iran and Italy are worst affected. In USA a 35 year old man in, Washington confirmed to have 2019 nCoV- with a 4 day history of fever, cough progressed to pneumonia, had history of travel to China. He was given supportive and antiviral (remdesivir-first trial) treatment and recovered.<sup>10</sup>

## Laboratory Investigations

Specimens taken are nasopharyngeal swab, throat swab, sputum, endo-bronchial or endo-tracheal aspirates, stool or serum. All contacts and pneumonia cases are also to be tested. (RT-PCR next

PARAMETERS	SARS	MERS	COVID – 19
ORIGIN	China 2002-2003	Saudi Arabia 2012	Wuhan City, Hubei province China. 2019-2020
MORBIDITY AND MORTALITY	8096 cases 774 deaths 10% mortality	2494 cases 858 deaths 30% mortality More deadly	As of May 4 2020, 3,442,234 cases, 239,740 deaths, 2% are serious or critical. Overall appears less virulent
SOURCE	Bats Civet cats Raccoon dogs	Bats to camels and finally to humans	Bats to humans or snake to humans. Pangolins to humans. Huanan sea food market December 2019.
INFECTIVITY	Not able to sustain human to human transmission for a long time	Not able to sustain human to human transmission for a long time.	Human to human transmission appears to be significant in china and in many countries. Has become pandemic.

Table 1: COMPARISON BETWEEN SARS, MERS AND NOVEL CORONAVIRUS

State/regoin	Total RT-PCR positive cases	Deaths
Tamil nadu	2162	27
India	23,546	1079
World	30,18,952	2,07,973
Europe	14,06,899	1,29,311
Americas	12,13,088	62,404
Mediterranean	1,76,928	7,304
Western pacific	1,46,720	6,037
South-east Asia	51,351	2,001
Africa	23,254	903

Table 3: Covid -19 cases/deaths as of 29.4.2020

generation sequencing of target enrichment and identification of nucleoproteins) is the gold standard test. A tiered way, where second sample is sent to the national reference lab and confirmed positive. Maximum yield in stool sample is at 14<sup>th</sup> day and it can be positive upto 44 days. Serology is used for confirmation of convalescent and past cases.

As per lancet study the results are shown.<sup>8</sup> Total leucocyte count were above the normal range in 24% of the patients and below normal range in 9% of the patients. Neutrophils were above the normal range in 38% of the patients. Platelets were increased in 4% of the patients and decreased in 12% of the patients. Lymphocytes were decreased in 35% of the cases.

Transaminases, Serum bilirubin showed mild increase. BUN and serum creatinine also showed mild increase.<sup>7</sup>

### Previously emerged viral epidemics:

1. SARS: Rui-Heng Xu et al have studied in detail the SARS outbreak which originated from China in 2002. The first case was a man who cooked food with chicken, cat and snake. Later it was shown that the viral infection spread from bats to civet cats and then to man. The disease started as myalgia, headache and cough with fever. Some progressed to pneumonia. The overall death rate was 3.8% and over 65 years it climbed to 12.7%.<sup>11</sup> Clinical features in adults were running nose, dry cough, respiratory distress and rapidly progressive pneumonia.
2. MERS: The first case of MERS was from Saudi Arabia, who presented with headache, myalgia, vomiting, diarrhea and tiredness. It was traced to consumption of camel milk and meat. Camels got the infection from bats. Humans acquired the infection from these animals. Thereafter human to human transmission was the main cause of spread.<sup>12,13</sup> Some of them had severe pneumonia, renal failure, pericarditis, myocardial damage, disseminated intra-vascular coagulation and bleeding and kidney failure. ( mortality 30%)
3. Swine Flu: In a study done by Rathinasamy M et al in 2015 at Chennai in office practice, among the 27 suspected cases, 13 were positive by RT-PCR. In that year thousands of cases and hundreds of deaths were reported world wide.<sup>14</sup>
4. Zika virus disease was named after it was first discovered from the Zika forest, Uganda. Infection in pregnant women resulted in neurological problem in babies.<sup>15</sup>
5. Ebola was discovered in Congo, near Ebola river. So it was named after that location. In 2013-16, Ebola epidemic had 28,616 cases and 11,310 deaths.

Drug clan	Name	Mechanism	Dosage	Comments	Sources
Anti-viral nucleoside analogue	Ribavirin	Inhibits RNA synthesis	8 mg/kg – 8 <sup>th</sup> hourly IV for 14 days	Hemolytic anemia and hypocalcemia may occur	SARS Data- Not recommended
Neuraminidase inhibitor	Oseltamivir	Reduces replication of the virus	12-15kgs-60mg/day 15-23kgs-90mg/day 23-40kgs-120mg/day >40kgs-150mg/day Given BD for 5days	Given if coinfection with influenza is suspected	MERS Cov Data
Protease inhibitor	Lopinavir/ Ritonavir	CoV protease inhibitor	Low dose-200/100mg High dose-400/100mg Given BD for 6-15days	---	SARS Data- weak recommendation
Adenosine analog	Remdesivir	Synthesis of premature RNA chains which are unviable	200mg IV on day 1 100mg/day IV on days 2-10 (Adult)	To be avoided in children and during pregnancy	Used in USA. currently undergoing trials
Amino-quinoline	Chloroquine, Hydroxy-chloroquine	Endosomal pH increase which inhibits receptor binding	CQ-10mg/kg STAT then 5mg/kg BD HCQ-8mg/kg STAT then 4mg/kg BD For 5 days Prophylaxis- 400mg weekly	Inhibits severity of pneumonia and shortens duration of disease Immuno modulator also.	Ongoing trials, ICMR recommends for prophylaxis
Immuno-globulin	IVIg / convalent plasma	Immune modulator	1-2G/kg/day IV infusion for 2-5 days	After all therapies fail	Critically ill SARS: under trial
Immune modulator for anti-viral	Interferon α	Reduces viral load	200000-400000 IU/kg in 2 ml water nebulisation	In early phase of respiratory infection	Weak recommendation

Table 1: COMPARISON BETWEEN SARS, MERS AND NOVEL CORONAVIRUS

6. Sanish flu in 1902 claimed two million lives.

### Treatment of Coronavirus Disease

No specific anti-viral treatment nor vaccination is available. Only supportive treatment has to be given.

### Supportive Treatment

1. Hydration (frequent home available fluids and normal diet) to be given.
2. Complete bed rest and isolation is advised
3. Anti-pyretic and anti-histamines for needy cases.
4. If they become sick has to be admitted in major hospital which has intensive care facilities.

### Pharmacological Treatment

There is no specific treatment. So various modalities and methods are being tried in this COVID-19 infections.

### Prevention

Since there is no specific drug and no specific treatment, prevention is the only mode to contain and to limit the infection

If there is no risk of source of exposure,

1. Avoid travel and stay at home
2. Wash hands often with soap and running water for 20 seconds for atleast 10-15 times/-day or use 60% alcohol based sanitisers.

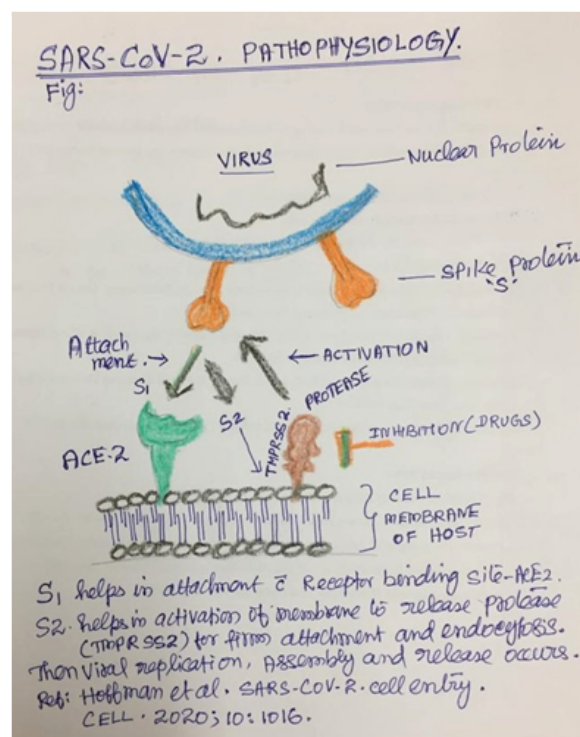


Figure 3: SARS-CoV-2 pathophysiology

3. Advise use of personal protection gear for people who may come in contact with infected people
4. Keep at least one meter distance from other person and wear mask.

If there is risk of source of exposure/contact:

1. People with infection should follow cough etiquette such as using handkerchief to cover their mouth, nose while coughing or sneezing.
2. Avoid close contact with people suffering from acute respiratory infections.
3. Avoid touching eyes, nose and mouth. (T-zone)
4. Keep yourself hydrated, drink tender coconut, Oral rehydration solution or 'kanji'.
5. For health care professional, use of personal protective equipment such as surgical mask or N-95 mask, gloves, face mask, goggles, special robes is recommended.

## Conclusion

The Coronavirus infection is spreading fast. Even though the mortality rate for the disease is low, the large volume of cases causes a significant number of mortalities. The virus, being highly infective, has caused governments to take drastic measures of isolation causing decrease in tourism and trade, leading to an economic collapse. Lock down and prevention is still the best way to avoid the disease.

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