

# What we know about COVID-19

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## Abstract:

**Covid-19**, a Coronavirus, is currently causing a pandemic. It was named “Corona virus” due to the club shaped projections on their surface which looks like a “halo” or “crown” on the virus when seen under electron microscope. It is a zoonotic virus. The usual carriers are bats, pangolins, mammals and other birds. They accidentally switch to human beings, infect them and cause disease. Symptoms of the disease are wide ranging from mild to severe. The common presenting symptoms are fever, cough, tiredness, breathlessness and loss of smell and taste (early signs). Treatment is still symptomatic. There is no cure for this disease or a suitable vaccine is available.

**Keywords:** Covid-19, Coronavirus, Pandemic, Management, Prevention, Vaccine, Co-morbidities, RNA virus, Pneumonia, Handwassings, Acute Respiratory distress Syndrome (ARDS), Ventilation.

**Abbreviations Used:** WHO (World Health Organization), COPD (Chronic Obstructive Pulmonary Disease), CAD (Coronary artery disease), CKD (Chronic Kidney disease), ARDS (Acute Respiratory distress syndrome), AKI (Acute Kidney Injury), DIC (Disseminated Intravascular Coagulation), RT- PCR (Reverse Transcriptase Polymerase Chain Reaction), ICU (Intensive Care Unit), CDC (Centre for disease control), ICMR (Indian council of Medical Research), HCQ (Hydroxychloroquine)

## 1. About the Coronavirus:

Covid-19, a Coronavirus, is currently causing a pandemic. There are a host of Corona viruses. Covid-19 is caused by Severe Acute Respiratory Distress Syndrome Corona Virus 2 (SARS-CoV-2)<sup>[1]</sup>. They are named Corona virus due to the club shaped projections on their surface which looks like a “halo” or “crown” on the virus when seen under electron microscope. These club shaped projections are protein molecules (Figure 1). The Covid2 virus is large (125 nm) in size and spherical in shape with bulbous projections or spikes.

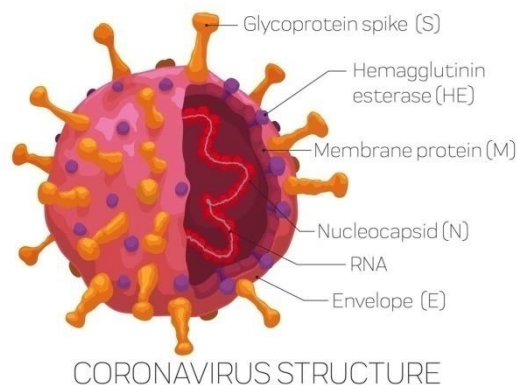
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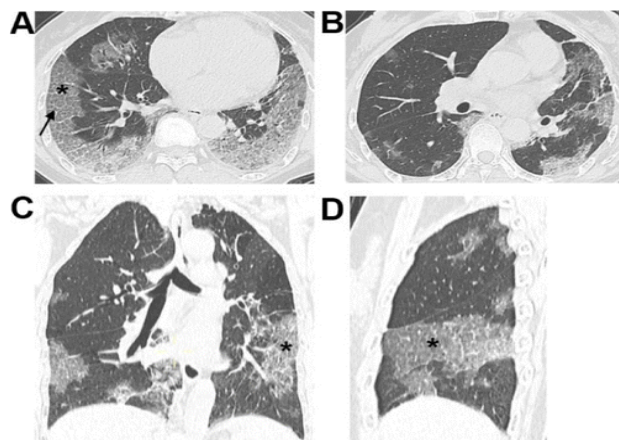
<sup>1</sup> Coronaviridae Study Group of the International Committee on Taxonomy of Viruses. The species severe acute respiratory syndrome-related Coronavirus: classifying 2019-nCoV and naming it SARS-CoV-2. Nat Microbiol. 2020 Apr; 5(4):536-44



**Figure- 1 : Showing Structure of Coronavirus**

There are 74 spikes on COVID-2. COVID-2 is a RNA virus having 3 layers: outer lipid bilayer(envelope), the middle protein layer and inner layer consisting of nucleoside and RNA. The nucleocapsid protein is arranged in a continuous “beads on a string” conformation. There are 3 types of membrane protein M, E and S. The S protein on the membrane is a class I fusion protein and its subunit S1 has a receptor binding domain (RBD) which binds to target cells (Figure- 2).

They grow only in respiratory cells. As the virus enters host cells they uncoat, transcribed and translocated and start replicating. The lining cells and alveoli become vacuolated and cilia are damaged. This in turn triggers inflammatory mediators. Their effect on the respiratory epithelium leads to thickening of mucosa and accumulation of fluid. Ultimately pneumonia sets in which turns out to be most serious in elderly people with **comorbidities**.



**Fig- 2. CT chest of Covid-19 patient showing consolidation, septal thickening and crazy paving pattern.**

## 2. Epidemiology:

Corona virus is a zoonotic virus [2]. The usual carriers are bats, pangolins, mammals and other birds. They accidentally switch to human beings, infect them and cause disease. The pandemic

<sup>2</sup> Livingston E, Bucher K. Coronavirus disease 2019 (COVID-19) in Italy. JAMA. 2020 Mar 17 [Epub ahead of print].

first started in the Wuhan city of China and ultimately spread across the world leading to the Covid-19 pandemic.

The Chinese government tried to control the disease as it broke out in the local population but did not share information with the international authority and the scientific community. Ultimately the virus spread to different countries and continents and finally World Health Organization (WHO) declared Covid-19 as Pandemic on 11<sup>th</sup> March, 2020.

The incubation period is 4 to 14 days. The spread is by droplets and aerosol<sup>[3]</sup>. Coughing, sneezing, talking and singing spread the virus. Kissing, intimate contact and fecal-oral transmissions occur but not sexually. Covid-19 spread is thought to be easier than influenza (flu) but not as easily as measles. About 40-45% of Covid-19 cases are asymptomatic. About 80% of patients suffer a mild attack, 14% develops pneumonia and 5% have septic shock with organ failure (respiratory). In 2-3 %, the disease is fatal.

### 3. Clinical Features:

Symptoms of the disease are wide ranging from mild to severe <sup>[4 & 5]</sup>. Most common presenting symptoms are fever, cough, tiredness and loss of smell and taste (early signs). Other important symptoms are shortness of breath, muscle aches, chills, sore throat, diarrhoea and headache. Some of the serious symptoms are difficulty in breathing, chest pain and loss of speech or movement. Skin rashes, nausea, vomiting and diarrhoea are uncommon.

Children suffer from similar symptoms but in milder form. The elderly population is at higher risk of developing severe disease. COPD (*Chronic Obstructive Pulmonary Disease*), CAD (*Coronary artery disease*), cardiomyopathy, asthma, hypertension, heart failure, type 2 diabetes, severe obesity, CKD (*Chronic Kidney disease*), sickle cell anaemia, HIV/AIDS and patients of solid organ transplants are at higher risk. Risk factors for contracting Covid 2 are history of recent travel, close contact (>5 minutes) with Covid-19 patient, coughing and sneezing help community spread.

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<sup>3</sup> Van Doremalen N, Morris D, Bushmaker T et al. Aerosol and Surface Stability of SARS-CoV-2 as compared with SARSCoV-1. *New Engl J Med* 2020 doi: 10.1056/NEJMc2004973

<sup>4</sup> Asadi-Pooya AA, Simani L. Central nervous system manifestations of COVID-19: A systematic review. *J Neurol Sci*. 2020 Apr 11;413:116832

<sup>5</sup> Huang C, Wang Y, Li X, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. *Lancet* 2020; 395: 497–506.

#### 4. Complications:

Complications which can follow are pneumonia, ARDS (*Acute Respiratory distress syndrome*), AKI (*Acute Kidney Injury*), organ failure, DIC (*Disseminated Intravascular Coagulation*), arrhythmias, viral and bacterial infections.

#### 5. Collection of Specimen:

The specimen should be collected from upper respiratory tract from nose and oral cavity in ambulatory persons and from lower respiratory tract from ill patients through endotracheal suction or bronchoalveolar suction. Sputum, stool, urine and blood samples should also be collected. All collections must follow standard protocol.

#### 6. Investigations:

Investigations are indicated in suspected cases for diagnosis and for treatment and prognosis in ill patients. Some investigations may predict severe degree of illness. For confirmation of diagnosis, RT-PCR (*Reverse Transcriptase Polymerase Chain Reaction*) and Antigen tests are indicated. While RT-PCR is 89% sensitive, the Antigen test is faster (in hours) but less sensitive. It is to be confirmed later by RT-PCR. There are other tests but not recommended.

Investigations can be classed as 1<sup>st</sup> line investigations, investigations for confirmation and emerging tests. 1<sup>st</sup> line investigations are pulse oximetry, ABG, CBC, complete metabolic panel, blood glucose level, coagulation profile, CRP, ESR, serum LDH, serum IL 6, cardiac biomarkers, serum procalcitonin, serum ferritin, serum amyloid A, serum creatine kinase, sputum and blood culture, RT-PCR and chest X-ray. Investigations to consider are CT chest and serology. Emerging tests are antigen test, RT-LAMP and Lung ultrasound.

Pulse oximetry is very important as an initial test as many patients of Covid-19 develop “silent hypoxia”. SpO<sub>2</sub> < 90% indicates severe disease. ABG may show hypercapnia and acidosis signifying severe illness. Lymphopenia, leucocytosis, Leukopenia, thrombocytopenia, low Hb% and low eosinophils count act as biomarkers of poor outcome. A low ratio of neutrophil to lymphocyte also indicates poor prognosis. Low CD 4+ and CD 8+ count indicate severe disease. Of the metabolic panel increased liver transaminases and low albumin level, raised urea and creatinine and hypokalemia indicate severe disease in 54% of Covid-19 cases.

Uncontrolled hyperglycaemia showed worse prognosis. Increased D-dimer, CRP, ESR, fibrinogen, PT levels indicate poor prognosis. Serum LDH level is raised in Covid-19 pneumonia and raised procalcitonin indicate secondary bacterial infection. This can help in restricting antibiotic overdose. A rise in IL 6 and serum troponin is indicative of cardiac injury. Raised serum creatine kinase also indicates muscle or cardiac injury (13-33%).

Point of care test is not recommended. Serologic tests (IgG and IgM) also not recommended. Ultrasonography of lung has a low diagnostic accuracy, but it has got its advantages. It can be done at bed side, repeated, less radiation and less costly. CT scan is a better investigation than X-ray or ultrasonography with very high rate of diagnosis (97%). It shows consolidation, more in the lower lobe, septal thickening and crazy paving pattern (Fig.-2). Involvement may be unilateral (25%) or bilateral (75%). A typical finding in CT should be taken as confirmatory even if RT-PCR is negative on preliminary examination.

## 7. Treatment:

As there is still no drug acting on Corona virus, standard definitive treatment has not yet been established. But certain medications are recommended in the treatment of Covid-19 patients. The following guidelines have been issued by NIH.

- (1) Antiviral agent: Remdesivir if SpO<sub>2</sub> < 94% and patients on mechanical ventilation or ECMO. Duration is 5 days, can be extended up to 10 days if positive result
- (2) Continuous renal replacement therapy (RRT) in AKI is recommended rather than intermittent hemodialysis.
- (3) Dexamethasone (6mg/day for 10 days) is recommended for patients on ventilation or O<sub>2</sub> supplementation
- (4) Awake prone position may be beneficial
- (5) IL 1 inhibitors not recommended
- (6) IL 6 inhibitors (Tocilizumab) did not show any change and not recommended
- (7) Lopinavir/ Retinavir not recommended
- (8) Immune based therapy ( Convalescent plasma/ Immunoglobulin) not recommended
- (9) Immunomodulators (Interferon) not recommended.

Drugs like ACE inhibitors, corticosteroids, Statins and NSAIDs should be continued in patients who receive it for other reasons but not recommended for Covid-19 treatment except for corticosteroids. Patients with mild illness are observed in home isolation with monitoring of vitals. Antipyretics and analgesics are advised. Patients with moderate degree illness are likewise kept in home isolation or hospital monitoring, supportive care, antipyretics and analgesics and antibiotics. Severely ill patients need mandatory hospitalisation and put on Oxygen therapy. They also need DVT prophylaxis, dexamethasone and antibiotics for co infections. Experimental therapies may be tried.

Critical patients should be managed in ICU (*Intensive Care Unit*) setting with high flow oxygen therapy/ NIV, intermittent mechanical ventilation, ECMO, management of sepsis and shock, dexamethasone and experimental therapies.

Patients can be assessed by NEWS 2 (National Early Warning Score) scoring system. This is a simple bedside method taking into consideration the physical parameters (respiration, oxygen saturation, SBP, PR, temperature and level of consciousness or confusion).

## 8. Prevention:

Prevention is the best way of fighting against the disease as no drug has been found to be effective against the corona virus till date. WHO and CDC have recommended a few precautions to be observed to prevent spread of the disease:

- i) Avoid large gatherings
- ii) Avoid close contacts (2 M or 6') with sick and symptomatic persons
- iii) Stay home; keep safe distance (2M or 6')
- iv) Washing hands frequently: soap and water for 20 seconds or with alcohol based sanitizer (70%), cover all surfaces and rub till dry
- v) Cover face and elbow when coughing or sneezing
- vi) Avoid touching, nose, mouth and eyes
- vii) Avoid sharing dishes, glasses, towels, sharing bed with the sick
- viii) Clean and disinfect high touch surfaces daily
- ix) Stay away from work, school and public spaces if sick
- x) Avoid public transport. If travelling by rental car do not choose front seat by the driver
- xi) Air travel is safer due to constant air flow
- xii) Travel by car: fewer stops, home cooked meal, plenty of water stock, disposable gloves and masks
- xiii) Please follow guidelines given in WHO<sup>[6]</sup> /CDC (Centre for disease control)/local websites. Travel only when absolutely required. Use online facility.

## 9. Quarantine and Isolation:

Quarantine is a state, period, or place of isolation in which people WHO have arrived from elsewhere or been exposed to infectious or contagious disease are placed and isolation separates sick people with a contagious disease from people who are not sick. These are part of preventive measures to stop spread of infection in the community. Quarantine and isolation can be home or institutional. The period is being changed from time to time on the basis of disease spread. It is now different in different states and countries. A minimum of 7 to 14 days

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<sup>6</sup>WHO Infection Prevention and Control Guidance for COVID-19 available at <https://www.who.int/emergencies/diseases/novel-coronavirus-2019/technical-guidance/infection-prevention-andcontrol>



is recommended. Post infection fever free 3 days is considered safe and further test not mandatory.

#### 10. Vaccine:

The only active prevention would be a pre-emptive vaccination. Research is afoot worldwide and some hope has been generated. Several vaccine candidates are in different phases of development, notable among them are the Russian Vaccine, the Oxford vaccine, the Italian, the Indian and American vaccines. Russia has successfully completed the first human trial of their vaccine. It is hoped that by end of 2021, one or more vaccine(s) will be available.

#### 11. Indian council of Medical Research (ICMR) Guidelines:

A number of corona virus guidelines are available. ICMR guidelines <sup>[7]</sup> (revised 22<sup>nd</sup> May, 2020) recommend prophylactic use of HCQ (*Hydroxychloroquine*) for particular groups of health care workers, police personnel and for intimate contacts of Covid-19 patients. Contraindications are children below 16 and pregnant women. Recommended dosage is 400 mg twice on day 1 and thereafter 400 mg weekly for 7 weeks for health care workers. For contacts it is advised for 3 weeks. Clinical and ECG monitoring is important since the drug may cause QT prolongation. The drug should be stopped if there is any adverse effect and it is cautioned that taking the drug should not give rise to false sense of security. Other precautions must be continued. ICMR recently started second phase study on convalescent plasma therapy after initial encouraging result. Many drugs and experimental procedures are being tried but either the results are not encouraging, the trials are small or are not effective.

The only armamentarium as proposed by experts would be a vaccine. Research is afoot worldwide and some hope has been generated. But there are a few more steps to be crossed before it becomes a reality. Intensive studies have been undertaken on fast track mode using Live attenuated virus, Killed virus and Genetically engineered virus. It is encouraging that many international and Indian companies have forged collaboration in vaccine research and it is hoped that an effective vaccine could be marketed earlier.

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