

2019 Novel Corona Virus (2019-nCov) Pandemic: A Preliminary Review

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ABSTRACT

Today, human beings have become soft targets of invisible microbial pathogen, the Novel Coronavirus (2019-nCov). Since December 2019, the COVID-19 disease has spread like wildfire in 216 countries. The zoonotic RNA virus has been identified, characterized at molecular level. Although, work is in progress globally, no specific medicine or vaccine has been prepared yet. So, individual or community level preventive measures are only rays of hope for sustenance of mankind. The 'global pandemic' is still on, world is shaken but *Homo sapiens* has to adapt, evolve and survive. In the brief communication a panoramic review of COVID-19 has been presented.

Keywords: Covid-19, SARS, Coronavirus, RNA virus, Pandemic, Wuhan, WHO.**INTRODUCTION**

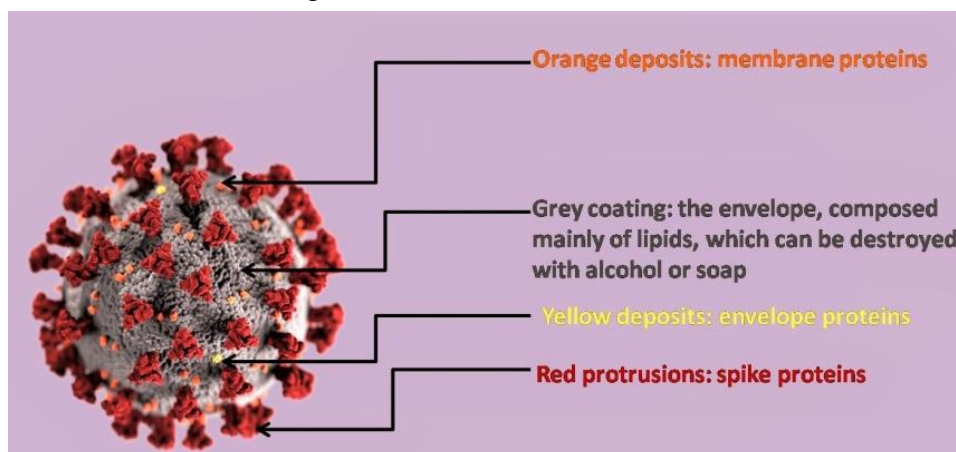
The unseen enemy which shook the whole world in early 2020; left everyone surprised and by the time the scientific community realized its severity; Novel Corona Pandemic overcast the globe. It all started in the fall of 2019 from the city of Wuhan in Hubei Province of China. Since December 2019, several cases of pneumonia of unknown etiology with a history of exposure to the Human Sea food Wholesale Market were reported in the city of Wuhan City of Hubei province, China (WHO, 2020 and Li *et al.*, 2020). It spread as a wildfire wiping approximately thousands of people in the city of Wuhan. By the time China confirmed the spread of this unknown deadly infection to the world; this disease had already set its foot in other countries of world slowly and silently. It spread its deadly fangs across the globe, courtesy, globalization and global networking by frequent exchange of people who travel by air for business, work as well as tourists. Till this time not much was known about this deadly disease, its origin and its mode of infection. The first or say the earliest report of this unknown disease was on 12th December 2019 from China. The unknown devil exhibiting flu like symptoms and creating chaos across the globe was identified as a virus and was initially called Wuhan Virus (WHO, 2020 AND Li *et al.*, 2020). It is well established fact that Wuhan has one of the World's largest Virus Research Centre.

Later, after characterization infectious agent was named as Novel coronavirus "SARS-CoV-2" (Fig. 1) because it exhibited SARS like symptoms and majorly affected the lungs. So the virus which caused this pandemic was named SARS-CoV-2 or 2019 novel Coronavirus (2019-nCov) and the disease caused by it was named COVID-19. COVID-19 has been declared a pandemic by the World Health Organisation (WHO). The confirmed cases approached 8242999 patients with 445535 deaths across over 216 countries on 18th June 2020 (WHO, 2020). After the initial description in Wuhan and China, Italy was hit first

in Europe and the impact has been immense (Pellino and Spinelli, 2020). Currently, COVID-19 has become a public health emergency of international concern, and the WHO has upgraded its threat status to the “highest” level and declared it as a ‘Global Pandemic’. All the efforts to contain the outbreak of COVID-19 have caused major disruption in socio-economic conditions globally and still it has not been tamed. An over view of the COVID 19 Pandemic has been presented in the present review.

SARS-CoV-2: The Pathogen:

The Novel Coronavirus Disease 2019 (COVID-19) is highly infectious disease causing acute respiratory syndrome along with other symptoms which are gradually being known day by day to the world. Mutation and adaptation have driven the co-evolution of Coronaviruses and their hosts, including human beings, for thousands of years. Human Coronaviruses were discovered in the 1960s. The name "coronavirus" is derived from *Latin* word “*corona*”, meaning “crown” or “wreath”. The name was coined by June Almeida and David Tyrrell who first observed and studied human Coronaviruses (Tyrrell and Fielder, 2002). Coronaviruses 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. Before 2003, two human coronaviruses were known to cause mild illness, such as common cold. Mild illnesses included some cases of the common cold (which is also caused by other viruses, predominantly rhinoviruses), while more lethal varieties can cause Severe Acute Respiratory Syndrome (SARS), Middle East Respiratory Syndrome (MERS), and COVID-19 (Fig. 2) (Williams *et al.*, 2020). The outbreaks of severe acute respiratory syndrome (SARS) and the Middle East respiratory syndrome (MERS) and COVID-19 have revealed the devastating and life threatening side of human coronavirus infection. Human coronavirus infection has a zoonotic origin. Most human coronaviruses originated from bats where they are non-pathogenic. The intermediate reservoir hosts of some human coronaviruses are also known and are suspected to be the intermediaries for spill over infection in humans. Thus, identifying the intermediate animal hosts has direct implications in the prevention of human transmission and human diseases. Since the outbreak of Severe Acute Respiratory Syndrome (SARS) 18 years ago, a large number of SARS-related coronaviruses (SARSr-CoVs) have been discovered in their natural reservoir host, the bats (Li *et al.*, 2005; Ge *et al.*, 2013; Yang *et al.*, 2013; Hu *et al.*, 2017 and Zhou *et al.*, 2020).



(Photo Credits: Adapted from the photo ID# 23311, CDC/Alissa Eckert, MS; Dan Higgins, MAMS)

Fig. 1. A SARS-CoV2 virion

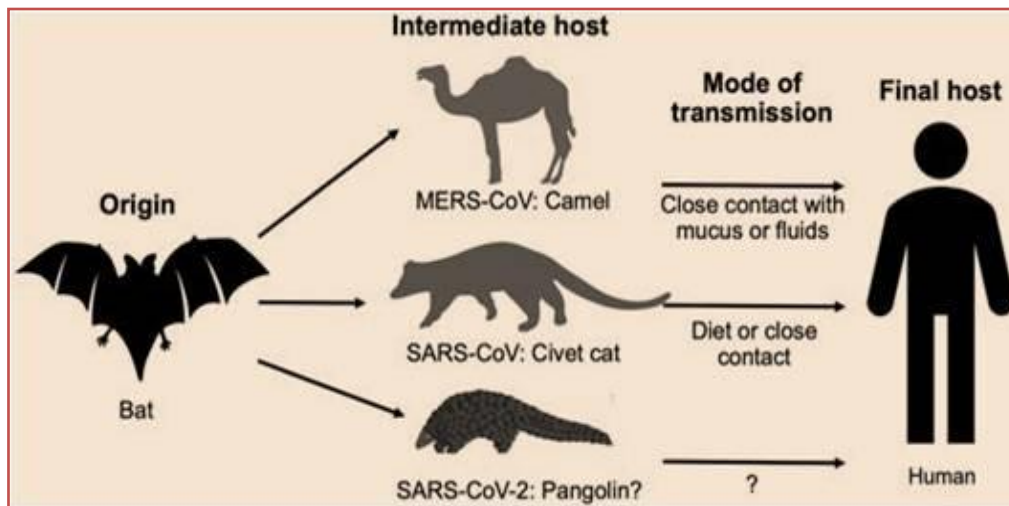
The original source of viral transmission of SARS-CoV-2 to humans is not clearly understood. It could be ascertained only when the strain becomes pathogenic before or after the spill-over event. So, understanding the origin and transmission of SARS-CoV-2 virus that caused the COVID-19 pandemic is of utmost importance for its control and treatment. SARS-CoV2 is a zoonotic virus belonging to the genus β -coronavirus (Herna'ndez and Austin, 2020 and Xie *et al.*, 2020). The COVID-19 virus genome is comprised of ~30,000 nucleotides. Results of whole genome sequencing of the virus showed the homology between SARS-CoV-2 and bat coronaviruses to be 96% (Zhou *et al.*, 2020) indicating bats as the best suitable hosts for this virus. Most experts agree that bats are a natural reservoir of SARS-CoV-2, but an intermediate host was needed for it to jump from bats to humans and the Pangolin also known as Scaly Anteater is suspected to be the intermediate host for SARS-CoV-2 but the mode of transmission is yet unknown (Fig. 3).

Time Line of Human Coronavirus Discoveries



Fig. 2. Human Coronavirus Discoveries (Williams, 2020)

(Source: <https://www.the-scientist.com/news-opinion/a-brief-history-of-human-coronaviruses-67600>)



(Photo credits: Adapted from American Chemical Society)

Fig. 3. Zoonotic origin of SARS-CoV, MERS-CoV & SARS-CoV-2 with intermediate hosts

Taxonomic Classification of SARS-CoV-2:

The International Committee on Taxonomy of Viruses (ICTV) named this Virus Severe Acute Respiratory Syndrome Corona Virus 2 (SARS-CoV-2) (Fig. 4). Coronaviruses are a group of related RNA viruses. These viruses (CoVs) are enveloped, positive-sense, single stranded RNA viruses ranging from 60 to 140 nm in diameter with spike-like projections on its surface, giving it a crown like appearance under electron microscope (Zhou *et al.*, 2020).

<u>Taxonomic Classification of 2019 Novel Corona Virus (2019- nCoV/ SARS-CoV2)</u>	
Category:	<i>Coronavirus</i>
Realm:	<i>Riboviria</i>
Kingdom:	<i>Orthornavirae</i>
Phylum:	<i>Pisuviricota</i>
Class:	<i>Pisoniviricetes</i>
Order:	<i>Nidovirales</i>
Suborder:	<i>Cornidovirineae</i>
Family:	<i>Coronaviridae</i>
Subfamily:	<i>Orthocoronavirinae</i>
Genus:	<i>Betacoronavirus</i>
Sub-Genus:	<i>Sarbecovirus</i>
Species:	<i>Severe Acute Respiratory Syndrome related corona virus (SARSr-CoVs)</i>
Strain:	<i>SARS Corona Virus 2 (SARS-CoV2) also known as 2019 Novel Corona Virus (2019- nCoV)</i>

Fig. 4. Classification of “2019 Novel Coronavirus”

(Source: *Coronaviridae* Study Group (CSG), a working group ICTV)

Physico-chemical Properties of SARS-CoV-2:

The physicochemical properties of SARS-CoV-2 are largely not known. SARS-CoV-2 is relatively stable against heat and UV or Gamma radiation as compared to SARS-CoV and MERS-CoV (Scheller *et al.*, 2020). But some reports suggest that SARS-CoV-2 is sensitive to ultraviolet rays and heat at 56 °C for 30 minutes (Philip *et al.*, 2020). In addition, ether (75%), ethanol (70%), chlorine-containing disinfectant, peroxyacetic acid chloroform etc. have been observed to effectively inactivate SARS-CoV2 (Scheller *et al.*, 2020). Both SARS-CoV and SARS-CoV-2 are unusually stable, for example on surfaces, but being enveloped viruses, they are rather lipophilic and therefore sensitive to solvents and surfactants. SARS-CoV and MERS-CoV can survive *in vitro* for 48 hours in a dry environment and up to 5 days under 20°C and 40% - 50% humidity. SARS-CoV-2 may possess similar properties (Scheller *et al.*, 2020 and Philip *et al.*, 2020).

Mode of Infection and Transmission Routes of SARS-CoV-2:

Human to human transmission is the major source of infection. The official incubation period for SARS-CoV-2 is 2-14 days and therefore 14 days is the chosen cut-off for self-quarantine. The patients with COVID-19 both symptomatic as well as asymptomatic are the sources of infection. Respiratory droplets and close contact are the main transmission routes. SARS-CoV-2 has been detected in the air in the ICU, and long term exposure in the relatively closed environment may lead to aerosol transmission (Xie *et al.*, 2020). SARS-CoV-2 has also been detected in the gastrointestinal tract, urine, saliva, and tears of patients with COVID-19 (Xie *et al.*, 2020). Coronavirus ‘SARS-CoV-2’ has emerged as an enigmatic pathogen and manifests itself by affecting humans in unexpected and lethal ways. SARS-CoV-2 clinical manifestations range from common cold-like symptoms and bronchitis to more severe disease such as pneumonia, severe acute respiratory distress syndrome, silent hypoxia, multi-organ failure and even death (Jason *et al.*, 2020). People from all ages are susceptible to COVID-19 infection. It is mainly transmitted through large droplets as well as aerosols generated during coughing and sneezing by symptomatic patients, but also transmitted from asymptomatic people before the onset of symptoms (WHO, 2020 and Jain *et al.*, 2020). Studies have shown higher viral loads in the nasal cavity as compared to the throat with no difference in viral burden between symptomatic and asymptomatic people (Jain *et al.*, 2020). SARS-CoV-2 clinical manifestations affecting different organs/parts of human body is given in Table 1 (Jason *et al.*, 2020).

Table 1

SARS-CoV-2 Clinical Manifestations Affecting Different Organs/Parts of Human Body

Organs/Parts affected by SARS-CoV-2	Manifestations
Blood	Fever and inflammation may disrupt blood vessels, rendering blood cells more prone to clumping while interfering with the body’s ability to dissolve clots. That may trigger a clotting cascade that can lead to blood-vessel blockages in tissues and organs throughout the body. Life-threatening clots in the arteries of the lung, known as pulmonary emboli, may occur even after symptoms of the infections have resolved. Damaged blood vessels may become leaky and prone to bleeding. In children, inflammation of veins and arteries triggered by excessive immune activation may cause an illness similar to Kawasaki disease, an inflammatory disorder.

Brain	Dysfunction in the lining of blood vessels and associated bleeding and clotting disorders may cause strokes and bleeding in the brain. Patients may also experience headache, dizziness, confusion, impaired consciousness, poor motor control, delirium and hallucinations.
Eyes	Red, puffy eyes, sometimes referred to as pink eye, may result from infection in the conjunctiva, the tissue that lines the inside of the eyelids and covers the white part of the eye.
Gastrointestinal Tract	Infection of cells lining the digestive tract may cause diarrhoea, nausea, vomiting and abdominal pain. Blood-vessel blockages caused by abnormal clotting have been found to damage the bowel, requiring emergency surgery and resection.
Hands	Prickling or burning sensation in the hands and limbs may indicate Guillain-Barré syndrome, a rare nervous-system disorder that may be triggered by aberrant immune responses to viral infection. Other symptoms of the syndrome include poor coordination, muscle weakness and temporary paralysis.
Heart	Cardiac injury, sometimes leading to irregular heartbeat, heart failure, and cardiac arrest, may occur as a result of excess strain, inflammation of the heart muscle and coronary artery, blood clots, and overwhelming multi-organ illness. Infection, fever, and inflammation in people with existing heart-vessel blockages may cause their fatty plaques to break off, blocking or stopping blood flow in organs and tissues.
Liver	Liver dysfunction may occur as a direct result of the viral infection, or more likely because of immune-mediated, systemic inflammation and circulatory blockages cutting blood flow to the organ.
Lungs	The virus targets the epithelial cells that line and protect the respiratory tract as well as the walls of the tiny grape-like air sacs, or alveoli, through which gas exchange occurs to oxygenate the blood. Damage to alveoli and inflammation in the lungs can cause pneumonia, characterized by chest pain and shortness of breath. In severe cases, the lack of oxygen can trigger acute respiratory distress syndrome, leading to multi-organ-system failure.
Kidneys	Acute kidney injury may result from clots and impaired blood supply, or as a direct result of infection.
Nose & Tongue	While the virus can cause the sneezing and runny nose typical of a common cold, it can also disrupt the olfactory system, causing an abrupt full or partial loss of the sense of smell known as anosmia. Taste may also become distorted in a condition known as dysgeusia.
Skin	Hive-like rashes, small red dots and purplish discolorations on the legs and abdomen are part of a complex category of so-called paraviral dermatoses that may result from the body's immune response to the virus or from benign, superficial blood-vessel damage beneath the skin.
Toes	Purple rashes that resemble chickenpox, measles or chilblains may appear on the feet, especially of children and younger adults.

Diagnosis of COVID-19:

Patient compliance with any one of the following symptoms can be diagnosed as severe COVID-19 (Xie *et al.*, 2020):

- 1) Respiratory distress, respiratory rate ≥ 30 breaths/min;
- 2) Pulse oximetry oxygen saturation at rest $\leq 93\%$;

- 3) Oxygenation index ($\text{PaO}_2/\text{FiO}_2$) ≤ 300 mmHg (1 mmHg = 0.133 kPa);
- 4) Lung imaging tests showing significant progression ($>50\%$) in lesions in 24–48 h;
- 5) Age ≥ 50 years and Neutrophil-to-lymphocyte ratio (NLR ≥ 3.13);
- 6) Respiratory failure and need for mechanical ventilation (non-invasive or invasive);
- 7) Septic Shock and Co-morbid failure in other organs and need for ICU monitoring and treatment.

Diagnostic Tools:

After genetic sequence of the SARS-CoV-2 was made available by CDC, China; primers were designed against the SARS-CoV-2 genome and utilized for reverse transcriptase polymerase chain reaction (RT-PCR) assays to make a diagnosis of COVID-19. Therefore, RT-PCR has become the gold standard for the diagnosis of COVID-19, but it is only 66-80% sensitive (Ai *et al.*, 2020). This means that 20-34% of patients with COVID-19 out of 100 would test negative despite being infected. This difference in the sensitivity of the test can be attributed to the patients being tested early in the disease course, wherein the viral load is below detection level or due to lack of automation in sample preparation and handling error for RT-PCR. Also, a single negative RT-PCR does not rule out COVID-19 infection, hence a repeat RT-PCR must be performed. The concern is raised regarding the timeframe of the repeat RT-PCR, the ideal window lies between 24 to 72 hours of the negative test (Ai *et al.*, 2020).

Treatment:

Due to the lack of experience and prior studies with the SARS-CoV-2, mainly supportive care may be provided to COVID-19 patients, while attempting a variety of therapies that have been used or proposed before for the treatment of other corona viruses such as SARS-CoV and MERS-CoV and other viral diseases. Treatment of severe COVID-19 includes aggressive treatment of complications, prophylaxis for secondary infection, and organ function support based on treatment of underlying disease (Philip *et al.*, 2020).

1. Supportive Care
2. Antiviral therapy
3. Use of traditional medicines
4. Tackling Cytokine Storm by Immunosuppressant
5. Convulsant Plasma Therapy

Drug trials and Vaccine development are being carried for the treatment and control of SARS-CoV-2 globally. At present individual or community level prevention is the best approach against COVID 19 infection till a cure is confirmed by a drug.

Perspective:

There are many unanswered questions related to this deadly pathogen, which has to be answered. Currently the whole world is going through uncertainties and the scientific world is waging a war to find out the cure against this invisible demon and we are racing against time as well as against SARS-CoV-2. We don't know how long will this pandemic last? How is the virus genetically evolving during transmission among humans? Will it die out like SARS

or relapse periodically like the common flu? We need to get answers of all these as well as many other questions. We have no other choice but to stop the Pandemic as soon as possible and bring our life back to normal.

But as it is said “Every dark cloud has a silver lining”; amidst all this disease, dearth, death and sufferings because of COVID 19, there are some positive aspects also. For example the pollution level across the globe reduced drastically, the holes in the ozone layer started to heal, “Mother Nature” started to repair, regenerate and rejuvenate our natural environment. It compels us to think about our mad race to evolve materialistically. Man has always been playing God by trying to control everything but has been defeated by a micro-organism.

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