

COMPREHENSIVE REVIEW ON NOVEL CORONA VIRUS - COVID 19 OUTBREAK

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ABSTRACT

Corona viruses are the group of viruses which infect human respiratory system. There are 6 different types of corona viruses which are identified earlier. Recently a 7th group of corona virus made a sensation in Wuhan city of china. This corona virus is named first as Nova corona virus (2019-nCoV) and later as COVID-19. The virus seems to be a mix of two corona viruses known to infect bats and another corona virus is from unknown origin. They are called as zoonotic and they can be transmitted from animals to human. It is a contagious viral infection, caused by inhalation or ingestion of viral diseases as a result of coughing and sneezing, handshake, touching infectious surfaces is the primary source for infection. The symptoms of COVID-19 include fever, cough, shortness of breath, pneumonia. There is no vaccine for the corona virus. The treatment of corona virus mainly consists of care in alleviating symptoms and preventing the transmission of viruses.

KEYWORDS: COVID-19, Corona virus, Contagious infection.

INTRODUCTION

Virus is discovered in the year of 1892. Viruses are the infectious agent which are metabolically inert in nature, they can infect all types of living forms, by replicating only within the cells of living hosts (e.g.: Plants, Animals, Microorganisms including Bacteria and Archaea).^[1] and they are surrounded by an envelope and are composed of an RNA or DNA core, a protein coat and are more complex types.^[2] Corona virus are ether sensitive viruses which are morphologically similar in group and cause infectious diseases such as bronchitis in birds, gastroenteritis in swine, hepatitis in mice, and respiratory infections in humans^[3]. Recently in the city of Wuhan of china a new corona virus was first identified in 2019 and named as Nova corona virus (2019-nCoV).^[4,5] Later on 13th February it was named as COVID 19^[6] and known informally as Wuhan corona virus^[7] by which there is a rise in number of infected with a number of deaths still having been reported. On 11 February Nova corona virus (2019-nCoV) seems to be a mix, or recombination, of two corona viruses - one is known to infect bats and another corona virus is from unknown origin^[8]. The large family viruses that are common among the animals are corona viruses. In rare cases, they are called as zoonotic by scientist,^[9,10] which mean they can be transmitted from animals to human. It is a type of contagious viral infection that caused by inhalation or ingestion of viral diseases as a result of coughing and sneezing, handshake, touching infectious surfaces are the primary source for infection.^[11] It causes respiratory diseases and pneumonia. There is no vaccine for corona viruses.^[12] The treatment of corona virus mainly consists of care in alleviating symptoms and preventing the

transmission of viruses through handshaking and other measures. Corona virus mostly have natural reservoir in the animals that they can able to infect bats, camels or cats. The new corona virus coming out of china came through food molecule where the Chinese had live animals, so the hypothesis came out that the virus is transmitted from animal through humans. Nova corona viruses is different from other corona viruses because they suppress the immune system and cause severe disease.

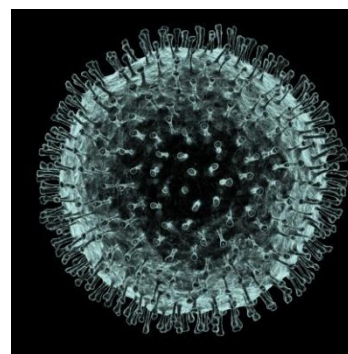


Figure 1: New corona virus.

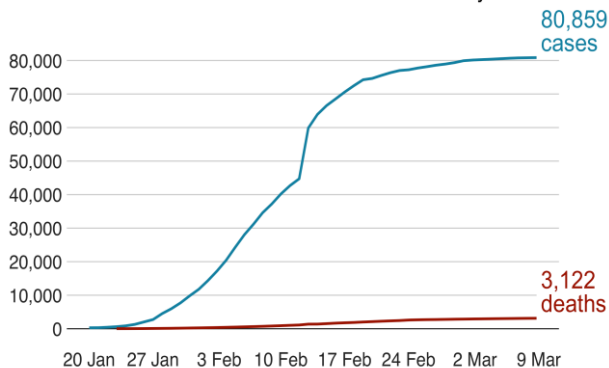
Epidemiology

The word “corona virus” is derived from the Latin language *corona*, which means *crown* or *halo*, characterized from the appearance of virus particles.^[13] They are characterized by having a fringe reminiscent of a royal crown or of the solar corona. Unknown aetiology in several cases of pneumonia has been reported. Since Dec 8, 2019^[14, 15, 16]. On 31 December 2019, a cluster of pneumonia cases of unknown origin was reported by the

local authorities of Wuhan, Hubei province, China. From the sample of throat swab, a novel corona virus was identified by the Chinese Centre for Disease Control and Prevention (CDC) on Jan 7 and was named subsequently as 2019-nCoV by WHO.^[17] On 9 January 2020, the China Centre for Disease Control reported that the novel Corona virus (2019-nCoV) is a causative agent. More than 2000 cases of 2019-nCoV infection have been confirmed. As of Jan 26, 2020, most of the people infected are living in or visiting Wuhan, and the transmission confirmed between the people.^[18] Overall, on January 29, 2020 the cases were found to be doubling in size on every 7.4 days in Wuhan city of China. For the first 425 cases the median age was 59 years, with a range of 15 to 89 years. In men the majority of cases, 240 (approximately 56%), were documented.^[19] 7824 laboratory-confirmed cases have been reported of 2019-nCoV including 170 deaths as of 30 January 2020.^[20] The new corona virus (2019-nCoV) has been speeded in 23 countries, and international health authorities have been declared that it is a public health emergency of international concern. National health commission of China meanwhile, said that 189,583 people have been identified as having close contact with infected patients.^[21] At the time of March 8th 2020, 3,653 deaths have been attributed to COVID-19 but however, 60,659 people have been recovered from the illness.^[22]

New cases in China have slowed

Total confirmed cases of coronavirus in the country



Source: China National Health Commission, WHO, Updated: 9 Mar 06:00 GMT

Figure 2: Total confirmed cases of corona virus in China.

History of Corona Virus

The history of corona virus is started in 8000 BCE.^[23] All corona viruses such as Alpha corona virus, Beta corona virus, Gamma corona virus, and Delta corona virus was placed at about 2400 BCE, 3300 BCE, 2800 BCE, and 3000 BCE, respectively. The source of corona virus gene seems like to be bats and birds, flying vertebrates which are warm-blooded to fuel corona virus evolution and dissemination. The source for Alpha corona virus and Beta corona virus is bats where as the source for Gamma corona virus and Delta corona virus is birds.^[24]

Scientific Classification

Family : Corona viridae

Group : Group IV (+) RNA

Genus : Alpha , Beta , Delta and Gamma corona virus

Order : Nidovirales.^[25,26]

The history of human corona viruses began in 1965. The seven corona viruses that can infect people are:

1. 229E (alpha corona virus),
2. NL63 (alpha corona virus),
3. OC43 (beta corona virus),
4. HKU1 (beta corona virus),
5. MERS-CoV (the beta corona virus),
6. SARS-CoV (the beta corona virus),
7. 2019 Novel Corona virus (2019-nCoV is beta corona virus).^[27]

Corona viruses initially were known to cause common cold hence remained primarily because there were no severe human diseases that were attributed to it.

- There are two corona viruses which cause severe disease in humans. They are Severe Acute Respiratory Syndrome (SARS) which is identified in 2002 and Middle East Respiratory Syndrome (MERS) which is identified in 2012. The currently causing COVID 19 is the third example.^[28]
- An outbreak of SARS occurred in southern china results in 8,098 cases with 774 deaths over 17 countries. In 2017, Chinese scientists identified that the virus is an intermediary of civets to cave-dwelling horseshoe bats in Yunnan province. The symptoms include fever, muscle pain, lethargy, cough, sour throat. It may also lead to shortness of breath and pneumonia.^[29]
- MERS is a beta derivative also known as camel flu. The symptoms include fever, cough, diarrhoea and shortness of breath. The mortality rate is about one-third of the diagnosed case.^[30] 35% of the patients approximately with MERS have died.^[31]
- Recently COVID 19 80%cases are comparatively mild they don't require major medical interventions, but 20% cases can be quite serious.^[32] COVID 19 is an infectious disease which is caused by Severe Acute Respiratory syndrome Corona virus 2 which has close relation with SARS.^[33]

Structure Of Corona Virus

Corona virus are enveloped with extraordinarily large single stranded RNA genomes of approximately 26 to 32 kilo bases^[34] indicating the fact that they are sensitive to lipid solvents. Corona virus particles usually appear spherical, as seen under an electron microscope with a crown^[35] or club shaped^[36] or petri shaped spikes on their surface which give corona like appearance. The size of the virus ranges from 100-160nm. They have helical symmetry and they can infect several animals. Among the six genera corona contain alpha, beta, gamma, delta, bafini virus, and toro virus. Human corona virus belongs to alpha and beta corona viruses. Nova corona virus is a beta corona virus.

Alpha corona virus -229E, NL63

Beta corona virus – (SARS, MERS, OC43, HKU1).

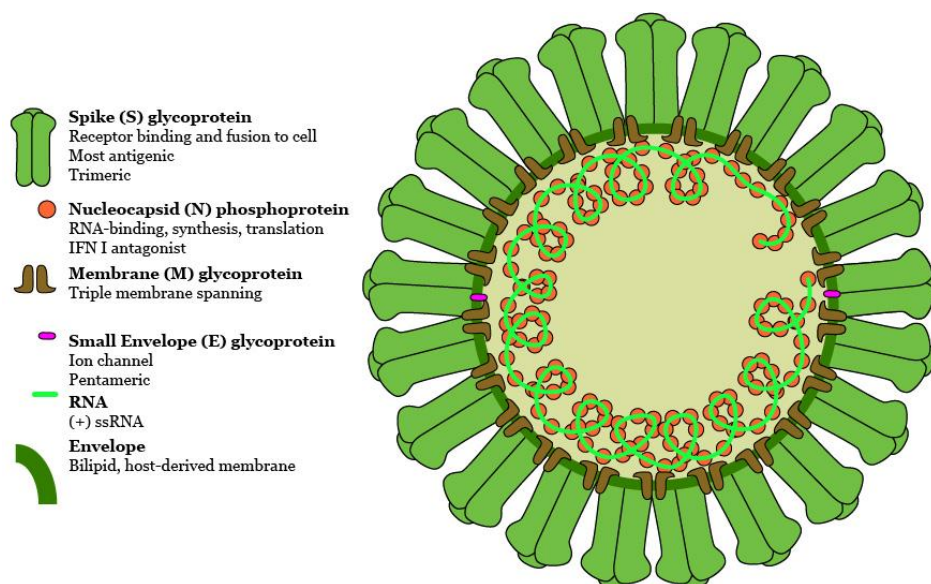


Figure 3: Structure of corona virus.

Corona virus genome encodes four structural proteins.

- Nucleo capsid (N) Phospho- protein which encloses the nucleic acid.
- Membrane glycoprotein which is embedded in lipid bilayer.
- The spike glycoprotein (S1) which will make the petal shaped peplomers and
- Small envelop (E) protein.^[37]

Incubation Period

After infection it requires 1-14 days to experience symptoms^[38] In 10 cases which are observed closely, the mean of incubation period was estimated to be 5.2 days.^[39]

Diagnosis

Lab diagnosis rarely required:

- RT-PCR – by detecting the viral genome.^[40]
- ELISA or IFAT for serology.^[41]
- DNA test^[42]
- CT scans^[43]
- Chest x ray^[44]
- Medical history revising.
- Checking for symptoms.
- Physical examination.
- Blood tests.
- Sputum test by collecting a sample from a throat swab or by respiratory specimens may be done.

Also there may be a chance of doing laboratory tests on respiratory specimens and serum (part of your blood) to detect human corona viruses. Laboratory testing is used for severe disease or suspected for having MERS.^[45]



Figure 4: Corona virus infection on lungs.

Replication of Corona Virus

The Replication of Corona virus which takes place in the cytoplasm in a membrane – protected microenvironment begins with entry to the cell. The virus particle in the cell is uncoated and in the cytoplasm the RNA genome is deposited. The genome of corona virus has a 5' methylated cap and a 3' polyadenylated-A tail. This allows for translation of the RNA to attach to ribosomes. Replicase is a protein of Corona viruses which is encoded in its genome allows the RNA viral genome to be translated by using the host cells machinery into RNA. The replicase which is the first protein to be made as once the gene encoding the replicase is translated; the translation is stopped by a stop codon. This is called as a nested transcript, in this transcript only one gene is encoded- it is monocistronic. A long polyprotein is formed, when the RNA genome is replicated where all of the proteins are attached. A protease which is a non-structural protein of corona virus is able to separate the proteins in the chain. This is a form of genetic economy for the virus allowing it to encode the most amounts of genes in a small amount of nucleotides.

The transcription of corona virus involves in a discontinuous RNA synthesis (template switch) during the extension of a negative copy of the sub genomic mRNAs. Base pairing is required during transcription. The N protein of corona virus is required for RNA synthesis, and it has RNA chaperone activity which may be involved in template switch. For replication and transcription both viral and cellular proteins are required. Corona viruses translation is initiated by the mechanisms of cap-dependent and cap-independent. After the corona virus infection the Cell macromolecular synthesis may be controlled by locating some virus proteins in the host cell nucleus. Infection by different corona viruses cause alteration in the host transcription and translation patterns, in the cell cycle, apoptosis, the cytoskeleton, and coagulation pathways, inflammation, and immune and stress responses.^[46]

Transmission

Corona viruses are a large family of viruses that are common in many different species of animals, including camels, cattle, cats, and bats. Rarely, animal corona viruses can infect people and then spread between people such as with MERS, SARS, and now with 2019-nCoV.

Person-to-person spread is thought to occur mainly via respiratory droplets produced when an infected person coughs or sneezes, similar to how influenza and other respiratory pathogens spread. These droplets can land in the mouths or noses of people who are nearby or possibly be inhaled into the lungs. It's currently unclear if a person can get 2019-nCoV by touching a surface or object that has the virus on it and then touching their own mouth, nose, or possibly their eyes. Typically, with most respiratory viruses, people are thought to be most contagious when they are most symptomatic (the sickest).^[47]

Pathophysiology

In the pathogenesis the viral spike proteins are known to play a role of corona viruses by inducing the neutralizing antibodies and also mediating the viral fusion of the viral cell envelope with the host cell membrane. They are also responsible for haem agglutination. This contributes to the infectivity and also progressiveness of the virus spirals to the Severe Respiratory illnesses and pneumonia. The incubation period is contagious by enhancing the rate of spread and infection to the other individuals through exposure to infected aerosols and by contact. The virus remains asymptomatic during the incubation period. By the activation of antibody production the host immune system which induces cytokine production by causing severe inflammation of the lungs which results in causing inflammatory-lung injury with severe pneumonia and also other upper and lower respiratory infections is seen which are associated with fever, coughing, headache, myalgia, haemoptysis, and renal failure. The mechanisms of immune pathogenesis are rapidly increased and cause functional

impairment, pulmonary tissue damage, and reduction in lung capacity. In the early investigations of the 2019-nCoV, indicated that a cascade of cytokines is present in the plasma of most of the patients, which were measured by using the Human Cytokine Standard 27-Plex Assays panel and also by the Bio-Plex 200 system (Bio-Rad, Hercules, CA, USA). The pathophysiology of this COVID19 (2019-nCoV) along with that of SARS-CoV and MERS-CoV are all still yet to be understood.^[48]

Symptoms

- The symptoms of corona virus of upper respiratory infection include fever, cough, and shortness of breath.
- The severe form of corona virus infection includes additional symptoms such as cough with mucus and tightness in the chest when you breathe or cough.
- Corona virus leads to upper respiratory tract infections. The infection can also spread to the lower respiratory tract which can cause pneumonia or bronchitis.
- Severe infection leads to acute respiratory syndrome, kidney failure and even death in people by causing a weak immune system.^[49]

Prevention

- Wash your hands.
- Avoid touching eyes, nose, and mouth.
- Don't visit the areas where virus is common.
- Get flu shot for protecting your lungs.
- Avoid crowds.
- Avoid healthcare facilities unless you are sick.
- Usage of Face masks.^[50]

Management and Treatment

No official treatment is available for nova corona virus, but the first reported cases with severe illnesses to reduce inflammatory induced lung injury, to lower moderate quantities of patients with acute respiratory syndrome were administered with corticosteroids (methyl prednisolone 40–120 mg per day).

Symptoms are relieved by

- Using medicines for pain, fever, and cough.
- Precautions like using a humidifier room, taking hot water bath will help ease a sore throat and cough.
- Take large quantity of fluids.
- Taking more and more rest.^[51]
- Supporting care involved is to keep functioning of systems vital organs i.e. by monitoring vitals such as blood pressure, temperature, oxygen levels those as normal as we can. Providing oxygen particularly for a lung ailment may be critical and hence methods like simple tube in the nostrils more aggressive approaches such as medical ventilation, which involves in a breathing tube threaded into airways of a person.
- There is no vaccine for corona virus. But researchers are racing to change that. A vaccine could be ready to test as soon as April.

- Rheumatoid arthritis drug actemra which is approved by U.S FDA in 2010 was now used for treating serious corona virus patients with lung damage. Actemra inhibits the receptor of interleukin 6 (IL-6), a pro inflammatory cytokine which is a main culprit for immune over action among COVID-19.^[52, 53] Aspirin is avoided in children and do not give cough medicine under age.
- The team of medical doctors in Bangkok give a latest development against the fight of corona virus. They used cocktail of drugs which are usually given to HIV patients to 71 years old infected women with the virus and saw the positive signs and better recovery within in 48 hours. These drug cocktail targets an enzyme of corona virus called protease which is used for attacking the protein cells in the body and multiply their numbers in the body.
- The drugs for treating COVID19 include lopinavir and ritonavir. These drugs used for impairing the virus's ability to attack or reproduce the body's immune system.
- Experiments by the doctors with the added usage of anti-flu drug Oseltamivir are also going on.^[54]
- A trail on chloroquine is done in china in February 2020 which showed quite positive results.^[55]
- The usage of steroids and methyl prednisolone has advised by WHO unless the disease is complicated by acute respiratory distress syndrome.^[56]

DISCUSSION AND CONCLUSION

Corona viruses are a large family of viruses that are common in many different species of animals, including camels, cattle, cats, and bats. Corona viruses can infect people and then spread between person to person. The spreading of infection occurs mainly through respiratory droplets produced when an infected person coughs or sneezes. The viral spike proteins play an important role of corona viruses by mediating the viral fusion of the vial cell envelope with the host cell membrane. Infection by corona viruses cause changes in the host transcription and translation patterns, in the cell cycle, apoptosis, the cytoskeleton, and coagulation pathways, inflammation, and immune and stress responses. These results in cause of fever, cough, shortness of breath, pneumonia, severe infection leads to acute respiratory syndrome, kidney failure and even death in people by causing a weak immune system. There is no vaccine for corona virus. The treatment includes mainly relieving the Symptoms by using medicines for pain, fever, and cough. Some drugs like methyl prednisolone, Oseltamivir, lopinavir, ritonavir and actemra are used.

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