

Emerging COVID-19 infection

An updated appraisal

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Coronavirus is a global concern these days. The massive outbreaks due to the novel coronavirus disease named COVID-19 has led to its affirmation by the World Health Organization (WHO) as a pandemic situation. It became the first pandemic by any of the coronaviruses affecting humans or animals. The Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2) is responsible for COVID-19 leading to acute respiratory distress and substantial mortality in the absence of any effective therapeutic. The disease has spread over 150 countries affecting nearly 2,00,000 people with around 8,000 human deaths. The adoption of suitable public health preventive measures and strengthening medical facilities are the best options for managing the disease. In this article, information on coronavirus is provided with a few facts on virus and infection, risks and do's and don'ts for an awareness campaign.

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The coronaviruses (CoV) are large RNA viruses of around 120 nm and form a family termed *Coronaviridae*. The coronavirus family is further divided into four subdivisions based on the host species affected as *Alphacoronavirus*, *Betacoronavirus*, *Gammacoronavirus*, and *Deltacoronavirus*. The distinctive look of coronavirus gave it the name “corona” meaning “crown” and is a Latin word. The viral spike proteins provide this shape to the virus. The virus particles are pleomorphic spherical having bulbous surface projections visualized clearly in an electron microscope.

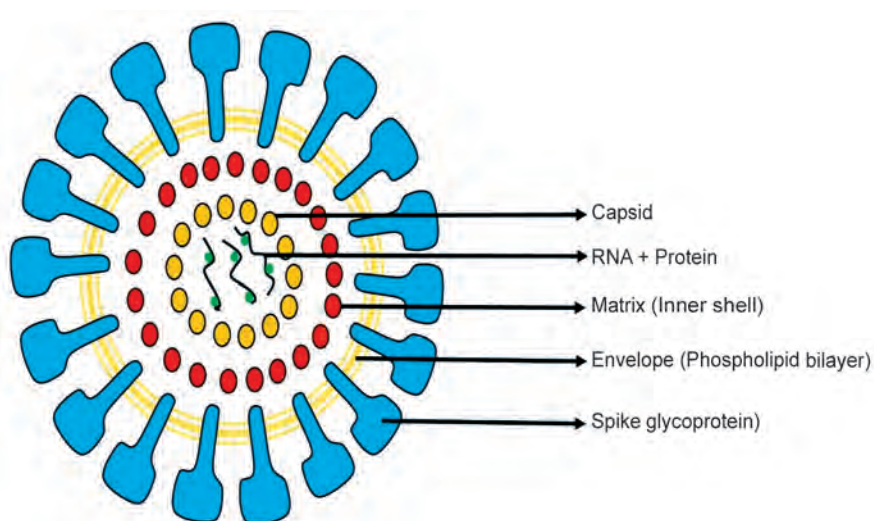
There are many coronaviruses which affect humans and animals. In humans, two of the coronaviruses are well known to cause common cold (HCoV 229E and HCoV-OC43). In contrast, another two coronaviruses in humans are more dreadful and called Severe Acute Respiratory Syndrome coronavirus (SARS-CoV) and Middle East Respiratory Syndrome (MERS-CoV). Outbreaks due to SARS-CoV

and MERS-CoV occurred during 2002 and 2012, respectively, with moderate to high mortality.

Origin of the novel coronavirus (SARS-CoV-2)

On 7th December 2019, a severe pneumonia like illness occurred from

the central Chinese city of Wuhan. Initially, the aetiology of this disease was unknown, and patients with acute respiratory distress emerged in clusters rapidly from this region of China. In due course of events, the Huanan seafood market in Wuhan, China was closed on 1st January 2020



Schematic representation of coronavirus structure showing bulbous spike protein responsible for its crown shape appearance.

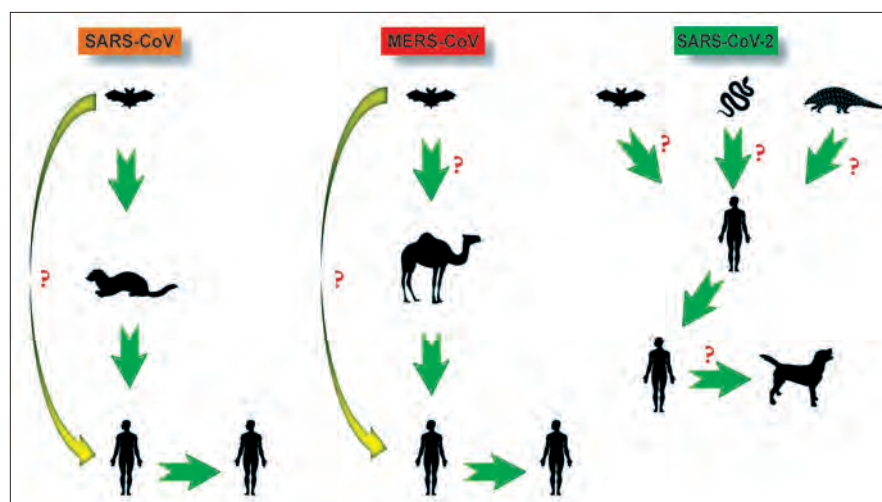
following which several patients were confirmed to carry this unknown problem which was linked to wild animals sold from this market. On 3rd January 2020, it was confirmed that a novel coronavirus, provisionally named “2019-nCoV”, is the causative agent for this severe respiratory illness. Gradually, 2019-nCoV spread noted in more than 100 countries.

Based on the virus genetic nature, Wuhan Health Committee rejected SARS-CoV and MERS-CoV as the possible cause of the current outbreak. Later, on 9th January 2020, the World Health Organization (WHO) confirmed the cause of this disease as a new and novel virus, naming it as 2019-nCoV. The first death due to “2019-nCoV” came from China. Following China, adjacent countries like Thailand, Japan, and South Korea also reported death cases due to novel coronavirus. Soon it was declared as a global health emergency by the WHO on 30th January 2020. India also confirmed its first case on January 30, 2020. Due to its closeness to earlier reported SARS-CoVs, ICTV renamed the virus as SARS-CoV-2 and the disease produced by it as COVID-19 by the WHO. The newly identified SARS-CoV-2 belongs to the genus *Betacoronavirus*.

Animal linkage of SARS-CoV-2

When the source of SARS-CoV-2 virus was investigated, it was observed that the epicentre was a South China Wet Seafood wholesale market in Wuhan, Hubei Province, where different wild and live animals are known to be sold in an open market which includes poultry, bats, snakes, and marmots for human consumption. Findings indicated the probability of zoonotic spillover as coronavirus is known to circulate between various animal species, vertebrate and humans due to wide host range. Hence, scientists assumed that SARS-CoV-2 was initially transmitted from animals to humans, followed by human-to-human transmission.

In the previous coronavirus outbreaks (SARS-CoV and MERS-CoV), virus jumping the species



Intra- and Inter-species transmission of different coronaviruses of humans. Arrows with question mark represent suspected transmission whereas other arrows without the question mark represent confirmed transmission between those two species.

barrier was noted. As seen earlier, bats were found involved in the transmission of SARS-CoV and MERS-CoV, the researchers forecasted the role of bats in the origin and transmission for the current transfer of SARS-CoV-2. There are several reasons behind the emergence of SARS-CoV-2 like CoVs can infect several host species, can survive in the natural conditions and have a high frequency of mutation and highly prone to genetic recombination. Potential zoonotic pathogens like SARS-CoV and MERS-CoV originated from bats. However, their amplifier hosts were palm civet cat and dromedary camels, respectively.

Previous literature documents that a few of the bat origin SARS-CoVs were capable of infecting human beings. In the current COVID-19 epidemic, laboratory findings confirmed that SARS-CoV-2 is also 96% identical to the bat coronavirus at the genetic level. Hence, bats may be the primary source of the zoonotic spillover of this virus to humans. Bats are ideal reservoir host for coronaviruses, as viruses are persistently present in bats and being asymptomatic, they travel across the forests in search of food and transmit the virus to a variety of hosts they come in contact. Due to their reliable and robust immune system, they harbour many viruses which don't cause any clinical infections to them instead upon their spillover to humans; they cause fatal diseases. In

China, bats are not only sold for food purpose in live-animal markets, but they are an integral part of Traditional Chinese Medicine, wild bats are used to obtain bat-derived compounds. Although bats have commercial value, pose a severe risk of acquiring many new zoonotic infections.

Does SARS-CoV-2 infect animals?

There is no report or evidence on SARS-CoV-2 infection in animals. They are only considered as the host or carrier of the disease. However, in a recent report from Hong Kong, mild SARS-CoV-2 infection was diagnosed in a pet dog, and the owner was severely affected by COVID-19 virus. The dog didn't show any clinical signs of the disease. This representative case was proposed as a link from human to animal transfer of COVID-19 disease, although upon examination, the viral load and symptoms were very less in the pet dog.

Coronaviruses infection in animals

Moreover, other species of coronaviruses (other than SARS-CoV-2) have a broad host range. They can infect several animals including cattle, horses, swine, ferrets, mink, bats, snake, dogs, cats, camels, rabbits, rodents, birds, frogs, marmots, hedgehogs (*Erinaceus europaeus*), Malayan or Javan or Sunda pangolin (*Manis javanica*) and a few of the wild animals. Among, large animals, bovine coronaviruses

Do's and Don'ts in COVID-19 infection

Do's

1. Avoid close contact with a sick person.
2. Practice frequent hand washing. Wash hands with soap and water. Wash hands even if they are visibly clean. If soap is not available, then use an alcohol-based hand sanitizer with at least 70% alcohol.
3. Cover your nose and mouth with handkerchief/ tissue while sneezing and coughing. Throw used tissue/ handkerchief into closed bins immediately after use.
4. Consult a doctor if you feel unwell (fever, difficult breathing and cough). While visiting a doctor must wear a mask/ cloth to cover your mouth and nose.
5. If you have any suspecting signs/symptoms of COVID-19, call State helpline number or Ministry of Health & Family Welfare's 24X7 helpline at 011-23978046.
6. Avoid participating in large gatherings.
7. Avoid unnecessary visits/travel.
8. Stay at home when you are uncomfortable or sick.
9. Clean and sanitize frequently used objects and surfaces with a household cleaning spray or wipe.
10. Wearing a mask is not essential unless you are dealing with an infected person. The Centers for Disease Control recommends that only infected individual wear masks to prevent the spread of the virus.
11. Follow at the top priority the travel advisory set out by the Ministry of Health and Welfare.

Don'ts

1. Have close contact with anyone, if you're experiencing cough and fever.
2. Touch your eyes, nose and mouth.
3. Spit in public.

have zoonotic potential as having been isolated from children and mainly transfer the disease to several domestic and wild ruminants, in which calf diarrhoea in neonates, bloody diarrhoea in adult cattle and respiratory form of shipping fever in all age groups of animals are apparent implications. Clinical disease may vary from enteritis in cattle and swine, upper respiratory tract disease in poultry and the common cold to fatal respiratory infections in humans.

Current status of COVID-19

Although internationally authorities have implemented appropriate preventive and control strategies to overcome the threat from COVID-19, there is a sharp increase in the number of cases of COVID world over. In the absence of vaccines or direct-acting antiviral drugs available for the treatment of COVID infections, the case fatality rate (CFR) is increasing due to substantial mortality recorded over

the past few weeks. As per the 59th situation report by WHO on 19th March 2020, there are 2,09,839 confirmed cases globally with 8,778 deaths. The western pacific region (China, South Korea, Japan, Malaysia etc) is the most affected region with 92,333 confirmed cases and 3,377 deaths, followed by European region (cases 87,108/deaths 4,084), Eastern Mediterranean region (cases 19,518/deaths 1,161), Region of Americas (cases 9,144/ deaths 119), South East Asia (cases 657/ deaths 23), and African region (cases 367/ deaths 7).

In India, till 20th March 2020, there have been 171 confirmed cases with 4 deaths and 19 recovered cases from 20 states/union territories.

Disease and symptoms of SARS-CoV-2/ COVID-19

Coronaviruses (CoV) cause illness ranging from a common cold to severe infections. In humans, the respiratory symptoms include fever, cough, runny nose, sore throat and

shortness of breath, with acute respiratory distress syndrome in severe cases. It is a potentially fatal respiratory infection in humans.

Earlier the disease caused by SARS-CoV-2 was also named as the Severe Specific Contagious Pneumonia (SSCP), Wuhan pneumonia, and recently re-named as Coronavirus Disease 2019 or COVID-19 by WHO. Compared to the SARS-CoV, SARS-CoV-2 has less severe pathogenesis but has superior transmission capability that is evident from the continuously increasing confirmed cases. The incubation period of SARS-CoV-2 is 3 to 10 days. The mean incubation period of COVID-19 was estimated to be 6.4 days and ranging from 2.1-11.1 days. Among the early affected people of 425 patients, 59 years was the median age group affected, where males showed higher susceptibility. Similar to SARS and MERS, the severity of this novel coronavirus is high in aged people above 50 years.

The symptoms of COVID-19 include fever, cough, myalgia or fatigue, less commonly headache or body pain, hemoptysis, diarrhea and shortness of breath.

Can we diagnose SARS-CoV-2 (COVID-19)?

At present, many nucleic acid-based detection techniques recommended by WHO, like RT-PCR and qRT-PCR, are considered as the most effective methods for confirming the COVID-19 infection. Presence of SARS-CoV-2 RNA can be confirmed by next-generation sequencing (NGS) platforms also. Several companies across the world are currently focusing on developing and marketing SARS-CoV-2 specific nucleic acid detection kits. Also, multiple laboratories are developing their in-house RT-PCR assays. Nucleic acids of SARS-CoV-2 can be detected from the samples such as throat swabs, sputum, lower respiratory tract secretions, and blood. A suspected case of COVID-19 infection is to be confirmed if the respiratory tract aspirate or blood samples are tested positive for SARS-CoV-2 nucleic acid using RT-PCR or by the identification of genetic

sequence in respiratory tract aspirate or blood samples tested. The patient will be confirmed as cured when two subsequent oral swabs results become negative. For the accurate diagnosis of COVID-19, a combination of repeated swab tests using RT-PCR and CT scanning is required to prevent the possibility of false-negative results during the disease screening. In addition to all the above, sequencing and phylogenetic analysis are critical for identification and confirmation of the causative viral agent, and useful to establish relationships with previous isolates and strains.

Is there treatment available for SARS-CoV-2?

Currently, there is no drug or vaccine available for the treatment or controlling the current coronavirus outbreak. Several efforts have been made to develop vaccines against human coronavirus infection in the past decades. However, the level of protection by such vaccines is extraordinarily constrained because of the broad antigenic variations even within the strains of a phylogenetic sub-branch. For MERS and SARS coronaviruses, there is no authorized explicit antiviral treatment or immunization accessible until now. However, few of the advances made in developing vaccines and drugs for SARS-CoV and MERS-CoV could be exploited for controlling the SARS-CoV-2. Since the efforts to develop and design an antiviral drug or vaccine to handle the currently rising coronavirus pathogen would take some time, so up to that point, we have to depend broadly on effective prevention and control

measures to limit the danger of SARS-CoV-2 transmission and spread. Different vaccines and antiviral drugs based on spike protein have been previously evaluated. Among the probable vaccine candidates, the S protein-based vaccines comprise full-length spike protein vaccines, and other include DNA-based vaccine, viral vector-based vaccine, recombinant spike protein-based and recombinant RBD protein-based vaccines. Even though such curative agents have demonstrated efficacy in the *in vitro* investigations, however, most of these have not undergone randomized animal or human trials and hence are of limited use for SARS-CoV-2. Remdesivir is a novel nucleotide simple prodrug that was proposed to be utilized for the treatment of Ebola infection. Likewise, it has anti-coronavirus action because of its inhibitory activity on the SARS-CoV and MERS-CoV replication. Combination therapy with SARS-CoV-2 specific monoclonal antibodies and remdesivir can be considered as the ideal therapeutic option for SARS-CoV-2. Most recently, SARS-CoV-2 vaccine has entered in clinical trial stages in humans, and hopefully we may get an effective vaccine to counter the infection in coming time.

Management measures of COVID-19

For managing the spread of SARS-CoV-2 infection effectively, the WHO in its guidelines for public prescribed to stay away from the unprotected contacts with both farm and wild animals. The live-animal markets, for example, in China could

give opportunities to animal CoVs to get transmitted to humans and these areas may act as hot spots for the origin of novel zoonotic pathogens and pose high health risk during an outbreak. These deadly viral pathogens could be countered by selecting prompt and timely worldwide collaborative and cooperative efforts between human and animal health sectors. In the present scenario of not having any direct-acting antiviral agent and vaccines, strict implementation of high vigilance for SARS-CoV-2 and appropriate prevention and control measures are more relevant to check the further spread and control of the virus. Researchers and authorities (WHO, CDC and others) across the globe are working to combat the current ongoing SARS-CoV-2 outbreaks, design and develop effective vaccines and therapeutics.

There is a need for strengthening of infrastructure and capacity building with trained workforce/hospital/health workers to identify the SARS-CoV-2 affected patients with the isolation and quarantine of patients after being suspected of carrying COVID-19 infection. To implement a preventive measure, rapid diagnosis with accuracy is the foremost step. As a suspected case is a good source of nosocomial spread, the health workers must follow all the precautionary practices while handling the COVID-19 case. Notably, a facility with negative air pressure is recommended for keeping confirmed patients of SARS-CoV-2.

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Are hand-sanitizers the only solution to protect yourself from COVID-19?

Practising frequent hand washing with soap and water is the most effective way to stay protected from COVID-19



However, if you don't have the facilities of washing your hands with soap and water, use an alcohol-based sand sanitizer