

Review Article

The Deadly Corona Virus (Covid-19)

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DOI: <https://doi.org/10.24321/0019.5138.202010>

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How to cite this article:

Rajagopalan PK. The Deadly Corona Virus (Covid-19). *J Commun Dis* 2020; 52(1): 78-81.

Date of Submission: 2020-03-11

Date of Acceptance: 2020-04-16

A B S T R A C T

*[On 7th March 2020, the ministry of health, Govt. of India, said that the number of highly contagious Coronavirus disease cases in India had risen to 34. In December 2019, the World Health Organization (WHO) had described **the outbreak of febrile respiratory illness of unknown etiology from Wuhan in China**. Now named **Covid-19**, it has now spread to more than 90 countries. As on 7th March 2020, there were 101,923 confirmed cases and 3486 deaths from 94 countries, areas and territories. WHO has declared the outbreak as **Public Health Emergency of International Concern?** Italy has reported over 9000 infected cases, with 463 deaths as on 10th March 2019, next in enormity only to that of China] From: <https://www.biorxiv.org/content/10.1101/2020.01.22.914952v1.full.pdf>.*

As the SARS epidemic created panic 18 years ago, a great number of Severe Acute Respiratory Syndrome-related corona viruses (SARSr-CoV) have been discovered in their natural reservoir host, bats. Earlier researches have shown that ceratin bat SARSr-CoVs can infect humans. Novel corona virus (Covid-19)) has caused an epidemic of acute respiratory syndrome in humans in Wuhan, China. The epidemic began from 12 December 2019 became a pandemic giving rise to 2,050 laboratory-confirmed infections with 56 deadly cases by 26 January 2020. Full-length genome sequences of 5 patients at the early stage of the outbreak, were found to share 79.5% sequence resembling SARS-CoV. A bat coronavirus has been found 96% identical at the whole-genome level to this virus. The entry receptor of novel CoV is same as that of ACE2. The pair wise protein sequence analysis of seven conserved non-structural proteins show that this virus belongs to the species of SARSr-CoV.

How the Disease has Originated and how it has Spread?

The origin of the pandemic has been associated with Huanan seafood market in Wuhan, China where animals such as birds and rabbits were also being sold. What is the host of the virus and how did it enter humans is the puzzle which is being resolved by Chinese research teams by means of genomic analysis on viruses isolated from patients, the puzzle pieces are coming together. The novel coronavirus, nCoV-2019, has been linked to bats. Bats carry and transmit some of the world's deadliest zoonotic viruses: Ebola, Marburg, Nipah, and the pathogen behind severe acute respiratory syndrome, SARS corona virus, to name

a few. And, of course, KFD. What has puzzled researchers for a long time is why bats don't appear to get sick from their unusually high microbial loads. The question has been nagging Peng Zhou, a virologist at China's Wuhan Institute of Virology, for more than a decade, ever since he took part in a **survey of bat populations in southern China**. Zhou and his colleagues were looking for the strain of the SARS corona virus responsible for the 2003 outbreak that sickened more than 8,000 people worldwide and killed nearly 800. And now we have the deadly corona virus. Are bats involved "We started to think, why bats?" he says (Based on: <https://www.the-scientist.com/notebook/why-bats-make-such-good-viral-hosts-64251>).

An earlier report, published on January 23 (available from: <https://www.genengnews.com/news/coronavirus-outbreak-emerged-from-bats-genomic-findings-suggest/>), came from a team at the Wuhan Institute of Virology, Chinese Academy of Sciences in Wuhan, China. Their study, published on the *bioRxiv* preprint server, is titled "Discovery of a novel coronavirus associated with the recent pneumonia outbreak in humans and its potential bat origin." Another report (Available from: <https://www.genengnews.com/news/coronavirus-outbreak-emerged-from-bats-genomic-findings-suggest/>), published in *The Lancet* on January 30, "Genomic characterization and epidemiology of 2019 novel coronavirus: implications for virus origins and receptor binding," came from a group in the Chinese Center for Disease Control and Prevention, Beijing, China. The Wuhan researchers obtained samples from 5 patients at the onset stage of the pandemic and did genomic sequencing. nCoV-2019 was found to be 96% identical to a bat coronavirus. Moreover, it was found to be 79.5% similar to severe acute respiratory syndrome coronavirus (SARS-CoV). The research proved that SARS-CoV and nCoV-2019 have the same cell entry receptor, ACE2. The *Lancet* paper analyzed 10 genome sequences from nine patients, eight of whom had visited the Huanan seafood market in Wuhan. The sequences had more than 99.98% sequence identity. In addition, they found that the nCoV-2019 genome had 88% identity to two bat-derived SARS-like corona viruses, 79% identity to SARS-CoV, and only about 50% identity to another coronavirus that is a human pathogen-Middle Eastern respiratory syndrome (MERS-CoV). The team also found that nCoV-2019 had a similar receptor-binding domain structure to that of SARS-CoV. They write that "although our phylogenetic analysis suggests that bats might be the original host of this virus, an animal sold at the seafood market in Wuhan might represent an intermediate host facilitating the emergence of the virus in humans."

During the SARS-CoV outbreak in 2003, scientists and epidemiologists tested various animals to find out the natural reservoir of the virus and related civet cats to the

virus; however the theory was overturned and horseshoe bats were proved to be the natural hosts of corona virus. This discovery made further research easier. **Since bats were shown to be the carrier of SARS in 2003, not only have many severe acute respiratory syndrome related corona viruses (SARSr-CoV) been isolated from bats, the mammals have been recognized as the natural reservoir for over 100 other viruses including MERS, Ebola virus, Marburg virus, Hendra virus, and Nipah virus, to name a few.** (<https://www.genengnews.com/news/coronavirus-outbreak-emerged-from-bats-genomic-findings-suggest/>).

Why and how are the bats able to carry and spread so many viruses? The reasons may be many. As reviewed in the article, "Going batty: Studying natural reservoirs to inform drug development", Wudan Yan noted:

- Bats' high-density lifestyle sets up a perfect storm of viral transmission.
- The tremendous diversity in and among the bat species, which accounts for roughly 20% of all mammals.
- Bats fly far and wide carrying the viruses to more areas than most mammals.
- Immunity and body temperature created by high flight.

The immune system of the bat is yet an unexplored area. Indeed, the first bat genomes were published in 2013, by an international group that included BGI-Shenzhen, Novo Nordisk Foundation Center for Basic Metabolic Research, and the University of Copenhagen, Denmark. In 2016, the research group of Michelle Baker, PhD, a bat immunologist at Commonwealth Scientific and Industrial Research Organization (CSIRO) published findings in PNAS that bats' immune systems are always turned on and have only three interferons-a fraction of the number of interferons found in people. At that time, Baker noted, "If we can redirect other species' immune responses to behave in a similar manner to that of bats, then the high death rate associated with diseases, such as Ebola, could be a thing of the past." Baker tells *GEN*, "We have been working to try to understand how bats co-exist with viruses without disease and will be very interested to learn more about the role of bats in the emergence of 2019-nCoV." (<https://www.genengnews.com/news/coronavirus-outbreak-emerged-from-bats-genomic-findings-suggest/>).

Another news report dated January 30, 2020, says the emerging virus that spread to humans from an animal host are commonplace and represent some of the deadliest diseases known. Given the details of the Wuhan coronavirus (2019-nCoV) outbreak, including the genetic profile of the disease agent, the hypothesis of a snake origin was the first raised in the peer-reviewed literature. It is a highly controversial origin story, however, given that mammals have been the sources of all other such zoonotic corona viruses, as well as a host of other zoonotic

diseases. According to the **Centers for Disease Control and Prevention**, most patients right now start with a fever, cough, and shortness of breath. An early report, published in *The Lancet*, provided even more detailed information. It looked at a subset of the first 41 patients with confirmed 2019-nCoV in Wuhan. The general symptoms were fever, cough, muscle pain, and fatigue; headache, diarrhea, and coughing up mucus or blood are less common to occur. CT scan shows pneumonia and lung abnormalities. The disease was severe: 6 patients among 13 admitted to an ICU. By January 22, most (68 percent) of the patients had been discharged from the hospital. More recently, there have also been reports of people with **very mild symptoms**, like the **cases in southern Germany**. There's even **evidence of asymptomatic** cases. It's possible that as we learn more, 2019-nCoV will seem more like the flu than like SARS. That's because infectious diseases typically look more severe when they're first discovered, since the people showing up in hospitals tend to be the sickest. And already, the new virus appears to be less deadly than both SARS and MERS. We don't yet know yet how the Corona Viruses **spread**. How exactly 2019-nCoV spreads, but we do have a lot of data on how MERS, SARS, and other respiratory viruses move from person to person. And that's mainly through *exposure to droplets* from coughing or sneezing. So when an infected person coughs or sneezes, they let out a spray, and if these droplets reach the nose, eyes, or mouth of another person, they can pass on the virus, said Jennifer Nuzzo, an infectious disease expert and senior scholar at the Johns Hopkins Center for Health Security. *In rare cases, a person might catch a respiratory disease indirectly, "via touching droplets on surfaces - and then touching mucosal membranes" in the mouth, eyes, and nose, she added. That's why hand-washing is an important public health measure - all the time, and especially in an outbreak.* If previous outbreaks of coronavirus are any indication, the Wuhan strain that is now spreading may eventually be traced back to bats. Dr. Peter Daszak, president of EcoHealth Alliance, who has been working in China for 15 years studying diseases that jump from animals to people, said, "We don't know the source yet, but there's pretty strong evidence that this is a bat origin coronavirus." He said, "It's probably going to be the **Chinese horseshoe bat, *Rhinolophus sinicus***" a common species that weighs up to an ounce. (<https://www.vox.com/2020/1/31/21113178/what-is-coronavirus-symptoms-travel-china-map>) If he's right, this strain will join many other viruses that bats carry. SARS and MERS epidemics were caused by bat corona viruses, as was a highly destructive viral epidemic in pigs. Bats carry the virus but survive the disease. They form the natural reservoirs for the Marburg virus, and Nipah and Hendra and Ebola viruses, which have caused human disease and outbreaks in Africa, Malaysia, Bangladesh and Australia. They are

reservoirs of rabies virus but cannot survive rabies. They are more tolerant to most of the viruses than any other mammal. They are the only flying mammals, they devour disease-carrying insects by the ton, and they are essential in the pollination of many fruits, like bananas, avocados and mangoes. Eating, trading and entering their habitat can have devastating results. (<https://www.nytimes.com/2020/01/28/science/bats-coronavirus-Wuhan.html>).

In a 2018 paper in Cell Host and Microbe, scientists in China and Singapore reported their investigation of how bats handle something called DNA sensing. The energy demands of flight are so great that cells in the body break down and release bits of DNA that are then floating around where they shouldn't be. Mammals, including bats, have ways to identify and respond to such bits of DNA, which might indicate an invasion of a disease-causing organism. But in bats, they found, evolution has weakened that system, which would normally cause inflammation as it fought the viruses. Bats have lost some genes involved in that response, which makes sense because the inflammation itself can be very damaging to the body. They have a weakened response but it is still there. Thus, the researchers write, this weakened response may allow them to maintain a "balanced state of 'effective response' but not 'over response' against viruses." Shown below is the image of greater Horseshoe bat, *Rhinolophus sinicus*. (Another species of the same genus, *Rhinolophus rouxi*, and its tick ectoparasite, *Ornithodoros sp. was found positive foe KFD Virus*. [Rajagopalan et al, 1969]. (<https://www.nytimes.com/2020/01/28/science/bats-coronavirus-Wuhan.html>).



Rhinolophus sinicus

With the spread of new coronavirus in China and the world over, scientists are attempting to find out its origins. However, a recent study shows that bats may be as the most probable hosts. In the study, published (Jan. 29) in the journal *The Lancet*, the researchers analyzed 10 genome sequences of the novel coronavirus, dubbed 2019-nCoV, obtained from nine patients in China who were sick with the virus. They found that all 10 of the genome sequences

were identical to a large extent—they shared “more than 99.98% of the same genetic sequence,” the authors said. The study evinces that the virus entered humans very recently, because there is not much difference in the the virus sequences. “It is striking that the sequences of 2019-nCoV described here from different patients were almost identical,” study co-lead author Weifeng Shi, a professor at the Key Laboratory of Etiology and Epidemiology of Emerging Infectious Diseases in Universities of Shandong Province, affiliated with Shandong First Medical University, said in a statement. “This finding suggests that 2019-nCoV originated from one source within a very short period and was detected relatively rapidly.” In a short time, the virus has jumped to 15 more nations, according to the World Health Organization. To learn more about the virus’ origins, the researchers compared the 2019-nCoV genetic sequence with those in a library of viral sequences, **and found that the most closely related viruses were two corona viruses that originated in bats**; both of those corona viruses shared 88% of their genetic sequence with that of 2019-nCoV. (When compared with two other corona viruses known to infect people - SARS and MERS - 2019-nCoV shared about 79% of its genetic sequence with SARS and 50% with MERS.) There may be a yet unidentified animal in the chain from bats to human transmission of the virus.

“It seems likely that another animal host is acting as an intermediate host between bats and humans,” said study co-lead author Guizhen Wu, of the Chinese Center for Disease Control and Prevention. Overall, the outbreak of 2019-nCoV **“again highlights the hidden virus reservoir in wild animals and their potential to occasionally spill over into human populations,”** the authors wrote.

There is no evidence so far, that Corona virus was the result of Genetic engineering as alleged in certain circles. Coronavirus not genetically engineered in Wuhan lab, says expert Clive Cookson in Seattle. The theory that the virus was genetically engineered in a Wuhan laboratory has been refuted. Trevor Bedford, of the Fred Hutchinson Cancer Research Center in Seattle, said “There is no evidence whatsoever of genetic engineering that we can find,” he said at the American Association for the Advancement of Science meeting in Seattle. “The evidence we have is that the mutations [in the virus] are completely consistent with natural evolution. The genes it shares with HIV are extremely short sequences naturally shared by other organisms and “repeated again and again throughout the tree of life.” He also disputed claims that Covid-19 might have infected humans from snakes or even fish. The most likely scenario, based on genetic analysis, was that the virus was transmitted by a bat to another mammal between 20-70 years ago. This intermediary animal-not yet identified-passed it on to its first human host in the city of Wuhan in late November or early December 2019.

Dr. Bedford is a leader of the worldwide Next strain collaboration that took initiative to analyze Covid-19 genomes when they were released in January by Fudan University and the Chinese Centre for Disease Control. Genetic sequence of corona virus from 100 infected individuals has been published by various scientists. Occurrence of slow mutations has been observed as the infection transmits from one person to another. Typically, the virus in one patient today is different in around five of the 30,000 biochemical letters of its genetic code, but these are random changes rather than any sign that it is becoming more virulent or infectious, Dr. Bedford said. By comparing virus taken from different patients and knowing its mutation rate, he and his colleagues can also estimate the total number of cases so far. He said the result was similar to that produced by more conventional epidemiology. “We get upwards of 200,000 total infections, which fits with the estimates already published by Neil Ferguson and colleagues at Imperial College London,” Dr. Bedford said. But he was reluctant to forecast the future course of the epidemic, which is now becoming a world pandemic!! (<https://www.ft.com/content/a6392ee6-4ec6-11ea-95a0-43d18ec715f5>).

As of 10th March 2020, the situation regarding Covid-19 is still fluid and fast changing day by day. It is very difficult to predict anything. While the Government of India and the State governments, appear to do a tremendous job in tackling the epidemic, there appears to be a lack of enthusiasm and initiative on the part of our researchers to go deep into the reservoir status, and the how and why of its epidemiology.