



## Review Article

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## The 2019 novel coronavirus disease (COVID–19) pandemic: A zoonotic prospective

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## ABSTRACT

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), a novel coronavirus (CoV), has recently emerged as a significant pathogen for humans and the cause for the recent outbreak of the 2019 novel coronavirus disease (COVID-19) throughout the globe. For developing any preventive measure, an understanding of the zoonotic pattern for this virus is a necessity. We should have a clear knowledge of its reservoir host, its distribution pattern and spreading routes. Information about zoonotic reservoirs and its transmission among them can help to understand the COVID-19 outbreaks. In this article, we discuss about the bats as the zoonotic reservoir of several CoV strains, co-existence of bats and CoV/viruses, the sequence similarity of SARS-CoV-2 with bat SARS-like CoV, the probable source of the origin of SARS-CoV-2 strain and COVID-19 outbreak, intermediate host of CoVs and SARS-CoV-2, human to human transmission and the possibility to maintain the zoonotic barriers. Our knowledge about the zoonotic reservoir of SARS-CoV-2 and its transmission ability may help develop the preventive measures and control for the future outbreak of CoV.

**KEYWORDS:** SARS-CoV-2; COVID-19; Coronavirus; Zoonotic reservoir

## 1. Introduction

A recent outbreak of severe respiratory illness has occurred in Wuhan, China, making Wuhan as the central point of global attention. Patients with pneumonia of unknown etiology in Wuhan were first notified to WHO in China office on 31 December 2019. At that time, the

causative agent was unknown. On 9th January, the Chinese Centers for Disease Control and Prevention reported that a strain of coronavirus (CoV) that is distantly associated with the severe acute respiratory syndrome (SARS)-CoV monophyletic group might be the causative agent of the 2019 novel coronavirus disease (COVID-19). Later on, it was established that a novel type of CoV caused the outbreak and was named as SARS-CoV-2[1,2]. According to a recent report of WHO, till 16<sup>th</sup> March 2020 more than 167 511 cases of COVID-19 were reported and more than 6 606 deaths are confirmed, suggesting a medical emergency to control this virus.

SARS-CoV-2 outbreak is closely associated with the SARS-CoV and Middle East respiratory syndrome CoV (MERS-CoV) disease as it causes similar symptoms[3]. Previously, in 2002 and 2003, SARS-CoV caused SARS outbreaks in Guangdong Province, China[4] and in 2012, MERS-CoV caused MERS- outbreak in the Middle East[5]. So, there are three significant CoV outbreaks which are (i) current SARS-CoV-2 outbreak spread throughout the world; (ii) SARS-CoV caused the SARS outbreak in China in 2002 and 2003; (iii) MERS-CoV caused MERS- outbreak in the Middle East in 2012. The recent SARS-CoV-2 outbreak is the biggest outbreak among these and has already spread

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throughout the world.

It is very important to understand the reservoir host for CoV, its distribution, and spreading routes (Figure 1). Knowledge about the zoonotic reservoirs is necessary to prevent and control future CoV outbreaks. Here, we talk about the bats as the zoonotic reservoir, co-existence of bats and CoV, the sequence similarity of SARS-CoV-2 with other CoV, the probable source of the origin of SARS-CoV-2 strain, intermediate host of CoVs and SARS-CoV-2, human to human transmission etc.

## 2. Bat: The zoonotic reservoir of several CoV strains

Bats, a unique mammal with flying ability, are the zoonotic reservoirs or natural hosts of several CoVs such as SARS-CoV, MERS-CoV, etc. Other than CoVs, bats are the natural reservoir of various other deadly viruses, for instance, Hendra virus, Ebola virus, Nipah virus, and Marburg viruses (Table 1)[6–8]. More than 200 viruses have been found associated with bats, and probably most of them are RNA viruses[9]. Bat is also called the primary host of these viruses including SARS-CoV-2 as they act as a natural reservoir. It has been observed that the reservoir of the SARS-like CoV is bats, belonging to the genus *Rhinolophus*[7,10].

Among bat genera, six genera are important, which are *Cynopterus*, *Rousettus*, *Nyctalus*, *Myotis*, *Miniopterus*, and *Rhinolophus*. More than 1 100 different species have been reported for bats[11]. Among these

different species of bats, horseshoe bats [genus *Rhinolophus* (*R.*)] is the reservoir of the SARS-like-CoVs. Some important species of this bat genus are *R. pearsoni*, *R. macrotis*, *R. pussilus*, and *R. ferrumequinum*. These genera are the host of the CoV and have been confirmed by the serologic or PCR analysis[12]. In 2002 and 2003, SARS-CoV was initially identified in China. Then, it was found that bats were acting as primary hosts of that outbreak in China. The outbreak was associated with the wildlife meat industry[9]. MERS-CoV, which is the lineage of beta-CoVs ( $\beta$ -CoVs), is also associated with the bat CoV (BatCoVs)[13]. Several scientists have demonstrated that MERS-CoV might also be of bat origin either from Saudi Arabia[14] or Africa[15]. However, it is still a mystery that how MERS-CoV got transferred from bats to the camels. For several years, camels have been acted as a zoonotic reservoir for MERS-CoV[16]. However, after the CoV outbreak, a broad sampling was performed using bats and was rigorously studied to understand the route of the CoV outbreak. Similarly, the bats were also studied as a zoonotic reservoir for Nipah and Hendra viruses[17]. Many studies describe that infected bat transmitted the virus to the recipient host, which then acted as an intermediate host. From the intermediate host, the virus may have got transmitted to humans. Some possibilities are also there that the virus got transmitted directly from the bats to humans[9]. Bats can fly and migrate to more than 1 000 km and it may permit the bat to spread different diseases in vast areas. At the same time, they may acquire new microorganisms as a reservoir[18].

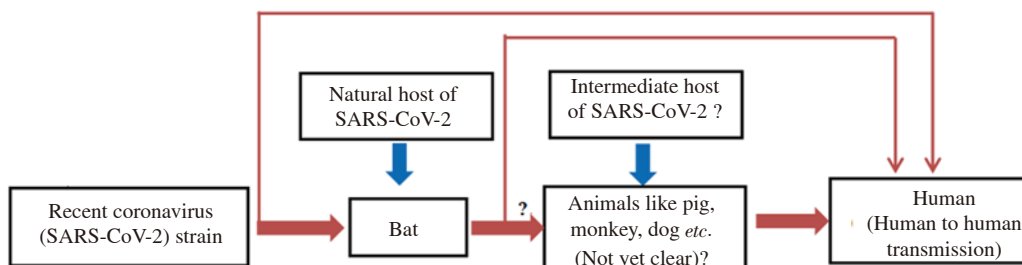


Figure 1. Transmission line of SARS-COV-2.

Table 1. Various significant features of the primary host of SARS-COV-2, bat (general and immunological features).

Primary host of SARS-COV-2	Features
General feature of bat	<ul style="list-style-type: none"> <li>•Only flying mammal</li> <li>•Can fly and migrate more than 1 000 km</li> <li>•Reservoir for more than 200 viruses</li> <li>•Bat can survive 20-30 years (20 years for 22 species and 30 years for 6 species)</li> <li>•Bat can spread different diseases in vast areas</li> <li>•Six genera are significant such as <i>Cynopterus</i>, <i>Rousettus</i>, <i>Nyctalus</i>, <i>Myotis</i>, <i>Miniopterus</i>, and <i>Rhinolophus</i></li> <li>•More than 1 300 species of bat are distributed across every continent</li> </ul>
Immunological feature of bat	<ul style="list-style-type: none"> <li>•Bats immune system evolve more than millions of years along with the viruses</li> <li>•Strong evolved immune mechanism of the bat helps to harbor viruses</li> <li>•Antiviral cytokines, such as interferons activate the expression of IFN-stimulated genes that inhibit virus replication</li> <li>•Faster evolution of innate immunity related genes causes superior antiviral phenotype of bat</li> <li>•Antibodies, such as IgA, IgE, IgG, and IgM have been detected in bats</li> <li>•P. alecto bats displayed a predominance of CD8<sup>+</sup> T cells in the spleen</li> <li>•B lymphocytes detected</li> <li>•Immune cell like NK cell, macrophage are detected</li> </ul>

**Table 2.** Important CoV strains and their primary host, intermediate host, symptoms of infection.

Sl. No.	Coronavirus strains	Primary host	Intermediated host	Symptom of infection
1.	HCoV-229E	Bat	Camelids	Placid infections in respiratory tract
2.	HCoV-HKU1	Rat	Not specified	Acute pneumonia
3.	HCoV-OC43	Rat	Cow	Mild upper respiratory disease
4.	HCoV-NL63	Bat	Not specified	Infections in respiratory tract
5.	MERS-CoV	Bat	Camels	Harsh acute respiratory syndrome, (37% mortality rate)
6.	SARS-CoV	Bat	Civets	Harsh acute respiratory syndrome, (10% mortality rate)
7.	SADS-CoV	Bat	Pig	Acute diarrhoea syndrome
8.	SARS-CoV-2	Bat (probable)	Not specified	Shortness of breath, fever, vomiting, kidney failure, coughing, pneumonia

### 3. Bat and CoV/viruses co–existence

Bats are the zoonotic reservoir of CoV and several viruses. It has been noted that bats usually harbor viruses and demonstrates no clinical symptoms. More than millions of years, bats and viruses have been co-existing and co-evolving. The strong evolved immune mechanism of the bats has helped them to harbor viruses without any clinical symptoms[19]. It has been observed that one of the effects or molecules of the primary innate immunity is the interferon and it has been found to play a significant role in the controlling mechanism of viral replication. In bats, different types of interferon have been recognized such as Type I interferon and Type III interferon[20]. The evolved immune mechanisms of bats permit the viruses for virus-host relationships. They may have a faster evolution of genes related to innate immunity and this may cause the superior antiviral phenotype of bats[21]. Taken together, viruses have reached a stable co-existing equilibrium with each other.

### 4. SARS–CoV–2, a member of $\beta$ CoV subfamily, has sequence similarity with bat SARS–like CoV

As per the classification of the International Committee on Taxonomy of Viruses, CoVs are associated with the family Coronaviridae, subfamily Coronavirinae and order Nidovirales. Based on the genomic structures and phylogenetic relationships, the subfamily is divided into four genera which are alpha coronavirus ( $\alpha$ -CoVs),  $\beta$ -CoVs, gamma coronavirus ( $\gamma$ -CoVs), and delta coronavirus ( $\delta$ -CoVs)[22]. The SARS-CoV-2 is a member of the  $\beta$ -CoV subfamily. According to Zhu *et al.*, SARS-CoV-2 has 86.9% genome sequence likeness to bat SARS-like CoV (bat-SL-CoVZC45, GenBank: MG772933.1) genome[23]. It has been also noted that several  $\alpha$ -CoV or  $\beta$ -CoV species were found only in bats. Thus, bats are probably the main natural reservoirs of  $\alpha$ -CoV or  $\beta$ -CoV[24].

### 5. The probable source of the origin of COVID–19 outbreak

The source of the origin of COVID-19 is still unidentified. However, there may be an epidemiological connection with the Huanan wholesale seafood market, where the live animals are also traded, including

snakes, birds, marmots, and bats[23], suggesting the possibility of animal associated transmission. Some Chinese researchers explored the epidemiological data with the 41 SARS-CoV-2 patients who have taken admission to a Wuhan hospital. The researcher found that among them, 27 patients (66%) had a contact history with the Wuhan Huanan seafood market where live wild animals or slaughtered wild animals were sold for food consumption[25]. Although, it was previously reported that MERSr-CoVs and SARSr-CoVs were originated from the bats[22]. The scientists are currently searching for the source of origin of SARS-CoV-2, including probable transitional animal vectors. Some researchers suspect that SARS-CoV-2 has a phylogenetic relation with SARS-CoV, bat SARS-like CoV, *etc.* which were discovered in humans, bat (mammals) or other wild animals[23]. Conversely, mammals are infected only either by  $\alpha$ -CoV or  $\beta$ -CoV. Although  $\gamma$ -CoV and  $\delta$ -CoV are known to affect birds, a few of them can affect mammals (Table 2)[26]. However, it is of utmost importance to understand and determine the origin of this ongoing pandemic. This information might help us to cut off the source of the origin of this outbreak from the transmission line.

### 6. Intermediate host of CoV and SARS–CoV–2

The intermediate host is an animal that plays a significant role in the transmission of the virus from natural hosts to others. The intermediate hosts may be domestic animals and these animals themselves might suffer diseases caused by bat-borne or closely related CoV. Swine acute diarrhea syndrome coronavirus was transmitted from bats to pigs[27]. The intermediate hosts of the different CoVs are camelids, cows, camels, civets, pigs, *etc.* However, the intermediate hosts for SARS-CoV-2 strain are not properly clear and have not been specified yet[28].

### 7. Human to human transmission of SARS–CoV–2

Human to human transmission of SARS-CoV-2 has been already reported by several scientists[29–33]. Viruses can spread very fast, irrespective of the borders of the countries. This novel virus can move from a country to another country through the host. Air travel is being one of the main routes of the global spread of this virus. Several

infected patients have been confirmed in other provinces in China, which confirms that the virus has no boundaries and is moving from Wuhan to other provinces of China. Several exported instances of this virus are also noted from China to other countries such as Thailand, Japan, South Korea, Macau, Malaysia, Australia, France, Canada, Vietnam, Nepal, India, the USA, Iran, and Italy.

Human to human transmission of SARS-CoV-2 got amplified due to the new-year celebration time in China. It was a significant cause for the movement of the human population resulting in the primary outbreak and spreading of the SARS-CoV-2. Human to human transmission may occur in several ways such as through the sneeze, droplets from the cough, surfaces of public transport and other public places[28].

Human CoV disease can cause mild respiratory and intestinal infections in animals as well as humans. This virus was believed to cause mild infection to humans, until the epidemic of SARS in 2002 and 2003 in Guangdong Province, China[4,6].

## 8. Maintaining the zoonotic barriers

After two outbreaks of SARS-CoV in 2002 and 2003 and one outbreak of MERS-CoV in 2012, this CoV outbreak is a recurrence of the previous incident with a novel strain, and all these of the CoV strains are probably of bat origin. However, our question is, can scientists prevent any CoV outbreak to maintain the barriers between zoonotic reservoirs? Some studies demonstrated that several factors are responsible for the barriers between the zoonotic reservoirs such as spike protein features[34] and proteolytic cleavage of the primary barrier[35]. However, more efforts are required to understand the specific features of zoonotic barriers.

## 9. Conclusions

At the whole-genome level, it was found that SARS-CoV-2 is closer to bat SARS-like CoV (bat-SL-CoVZXC21 and bat-SL-CoVZC45). The typical evolutionary rate for CoV is approximately calculated as  $10^{-4}$  nucleotide substitutions for every site each year[36]. Therefore, it was decided that the SARS-CoV-2 is a fresh lineage of  $\beta$ -CoV, which is intimately connected to bat SARS-related CoV[37]. With the increase of human population and societal changes, human-wildlife contact may increase. It may cause zoonotic viruses, including SARS-CoV-2, prone to the infection to humans as well as animals. However, more studies are obligatory to enhance our knowledge about zoonotic aspects of SARS-CoV-2 and its spread out from the zoonotic reservoir. Our knowledge about the zoonotic reservoir may provide the answer about the preventive measure for any future outbreak.

## Conflict of interest statement

No potential conflict of interest was reported by the author(s).

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## Authors' contributions

CC designed the manuscript. CC and ARS wrote the manuscript. Both MB and GS contributed to the final version of the manuscript. SSL edited the manuscript.

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