



Review Article

Wildlife as a Source of SARS-CoV-2 Evolution- A Review

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ABSTRACT

Coronavirus consists of single-stranded, enveloped and RNA virus, largest genome among all RNA viruses and has 4 proteins i.e. envelope, spike, nucleocapsid and membrane. Coronaviruses are classified into 4 genera: Alphacoronavirus, Betacoronavirus, Gammacoronavirus and Deltacoronavirus. *Betacoronavirus* most probably originated from bats and the virus may have jumped to avian species and evolved as *Deltacoronavirus* group. The avian coronaviruses jumped among other avian species, giving rise to *Gammacoronavirus* from *Deltacoronavirus*, while *Betacoronavirus* may have given rise to *Alphacoronavirus*. It is known that SARS-CoV-2 belongs to *Betacoronavirus*. This most similar virus is verified in bat and Malayan Pangolin. Analysis showed that SARS-CoV-2 most probably originated by recombination of both bat and pangolin viruses. Viral protein seroconversion and viral specific nucleotide positive documented in all COVID-19 patients tested provides confirmation of a link between the presence of this virus and the disease.

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INTRODUCTION

Coronaviruses consist of 4 proteins i.e. envelope, spike, nucleocapsid and membrane (Tidona and Darai, 2011; Scientific American, 2020), single-stranded and RNA virus. Coronaviruses have the largest genome sequence among all RNA viruses. Coronaviruses infect different animal species including human (WHO, 2020).

Coronaviruses belong to order Nidovirales, family Coronaviridae, subfamily Coronavirinae. Coronaviruses have the largest RNA genome, ranging from 25-33 kilobases (Woo *et al.*, 2009). On the basis of cluster analysis coronaviruses are classified into following genera: *Alphacoronavirus*, *Betacoronavirus*, *Gammacoronavirus* and *Deltacoronavirus* (Woo *et al.*, 2009; King *et al.*, 2012).

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Alphacoronavirus belongs to subfamily Coronavirinae, and has unique characteristics as a distinctive kind of nsp1, different in sequence and size from betacoronavirus nsp1 (nonstructural RNA-binding protein 1) and not counterpart in gammacoronaviruses, and has ORF3, ORF3b and ORF3c in TGEV (transmissible gastroenteritis virus) and amp (alphacoronavirus membrane protein). Alphacoronaviruses are monophyletic of viruses as compared with all coronaviruses group (King *et al.*, 2012). Following species of alphacoronaviruses are recorded till now i.e. *Human coronavirus 229E (HCoV-229E)*, *Alphacoronavirus-1*, *Miniopterus bat coronavirus 1 (Mi-BatCoV-1)*, *Porcine epidemic diarrhea virus (PEDV)*, *Miniopterus bat coronavirus HKU8 (Mi-BatCoV-HKU8)*, *Scotophilus bat coronavirus 512 (Sc-BatCoV-512)*, *Rhinolophus bat coronavirus HKU2 (Rh-BatCoV-HKU2)*, *Harbor seal coronavirus 1*, *Ferret coronavirus (FrCoV)* and *Mink coronavirus (MiCoV)* (Tidona and Darai, 2011; Saey, 2013; de Barros *et al.*, 2019).

Betacoronaviruses are monophyletic, the only well-known feature that would set them separate from other species of coronaviruses is their different nsp1 (i.e. nonstructural RNA-binding protein 1), different in sequence and size from alphacoronavirus nsp1 and

not equal in the other groups of coronaviruses (King *et al.*, 2012). Following species of Betacoronaviruses are recorded till now i.e. *Betacoronavirus 1*, *Murine coronavirus*, *Human coronavirus HKU-1 (HCoV-HKU1)*, *Rousettus bat coronavirus HKU9 (Ro-BatCoV-HKU9)*, *Pipistrellus bat coronavirus HKU5 (Pi-BatCoV-HKU5)*, *SARS coronavirus (SARS-CoV)*, *MERS coronavirus MERS-CoV*, *Tylosycteris bat coronavirus HKU4 (Ty-BatCoV-HKU4)* and *SARS-CoV-2*, (Tidona and Darai, 2011).

Gammacoronavirus genome organization, morphology and gene composition, replication or biology is different from other coronaviruses. Viruses of the species Avian coronavirus not have an nsp1 (i.e. nonstructural RNA-binding protein 1) (King *et al.*, 2012). Following species of Gammacoronaviruses are recorded till now i.e. *Avian coronavirus*, *Asian leopard cat coronavirus (ALCCoV)*, *Beluga Whale coronavirus SW1 (BWCoVSW1)*, *Black-headed gull coronavirus*, *Chinese ferret badger coronavirus Guanxi/2006 (CFBCoV Guanxi/2006)*, *Glaucous gull coronavirus*, *Glaucouswinged gull coronavirus*, *Pintail coronavirus PBA-124*, *Rock sandpiper coronavirus*, *Brent goose coronavirus*, *Snow goose coronavirus* and *Western sandpiper coronavirus*.

Analysis of complete genome explained that the Deltacoronavirus groups have relatively smallest genomes (e.g. 25.421 to 26.674 kilobases) among all groups of coronaviruses. Delta coronaviruses have one papain-like protease domain in nsp3 (i.e. non-structural protein 3), NS6 located between M and N genes (King *et al.*, 2011; Woo *et al.*, 2012). Following species of Deltacoronavirus are recorded till now i.e. *Bulbul coronavirus HKU11*, *Wigeon*

coronavirus HKU20, *Munia coronavirus HKU13*, *Porcine coronavirus HKU15*, *Night heron coronavirus HKU19*, *White-eye coronavirus HKU16*, *Thrush coronavirus HKU12*, *Common moorhen coronavirus HKU21*, *Magpie robin coronavirus HKU18* and *Sparrow coronavirus HKU17* (King *et al.*, 2011; Woo *et al.*, 2012).

Betacoronavirus most probably originated from bats species at nearly 3300 BC and virus may be jumped to avian species and evolved as *Deltacoronavirus* group at about 3000 BC. The avian coronaviruses jumped among other avian species, giving rise to *Gammacoronavirus* from *Deltacoronavirus* about 2800 BC. While *Betacoronavirus* may jumped among other mammals and evolved as *Alphacoronavirus* approximately 2400 BC. This evolution lineage shown in (Fig. 1 and Table I) and Woo *et al.* (2012) analysis evolutionary lineage with molecular clock analysis (MCA).

SARS CORONAVIRUSES-2

At the end of 2019, unique pneumonia was documented in Wuhan, China and might be transferred from wild animals to human and human to human. SARS-Cov-2 was observed as different and new coronavirus and has close phylogenetic relation with SARS-like coronaviruses (Fig. 2). This disease was diagnosed with novel coronavirus (SARS-Cov-2). Jiang *et al.* (2020) and Xu *et al.* (2020) also noted that the pathogen was at that time identified as a SARS-Cov-2 belonging to lineage SARS-CoV. Wu *et al.* (2020) analysis showed that phylogenetic comparison recognized 380 amino acid changeovers between SARS-Cov-2 and SARS, which may have caused functional and

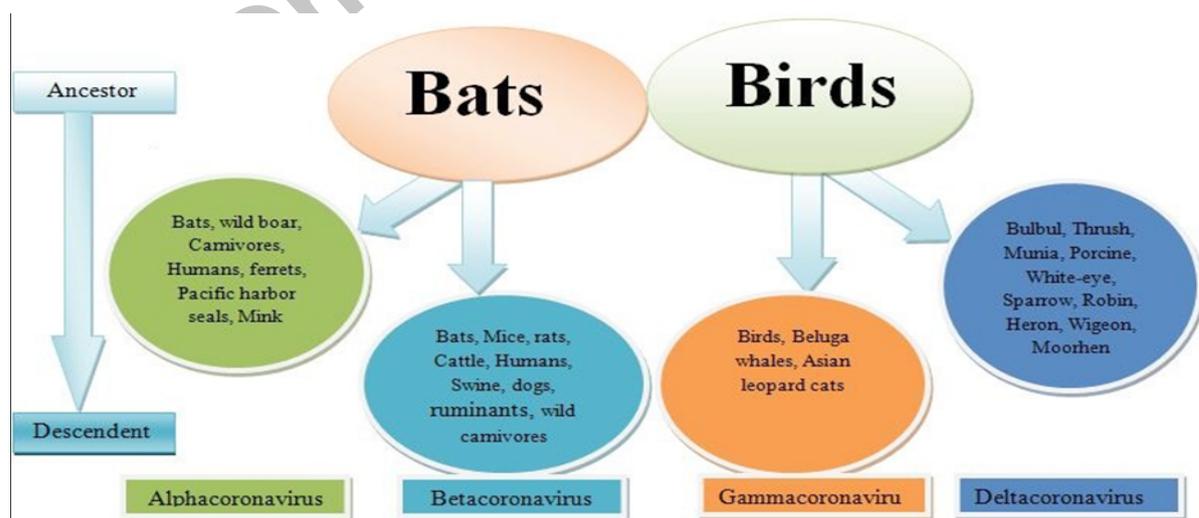


Fig. 1. Coronaviruses are the gene source of genera i.e. *Alphacoronavirus*, *Betacoronavirus*, *Gammacoronavirus* and *Deltacoronavirus* through wild animals.

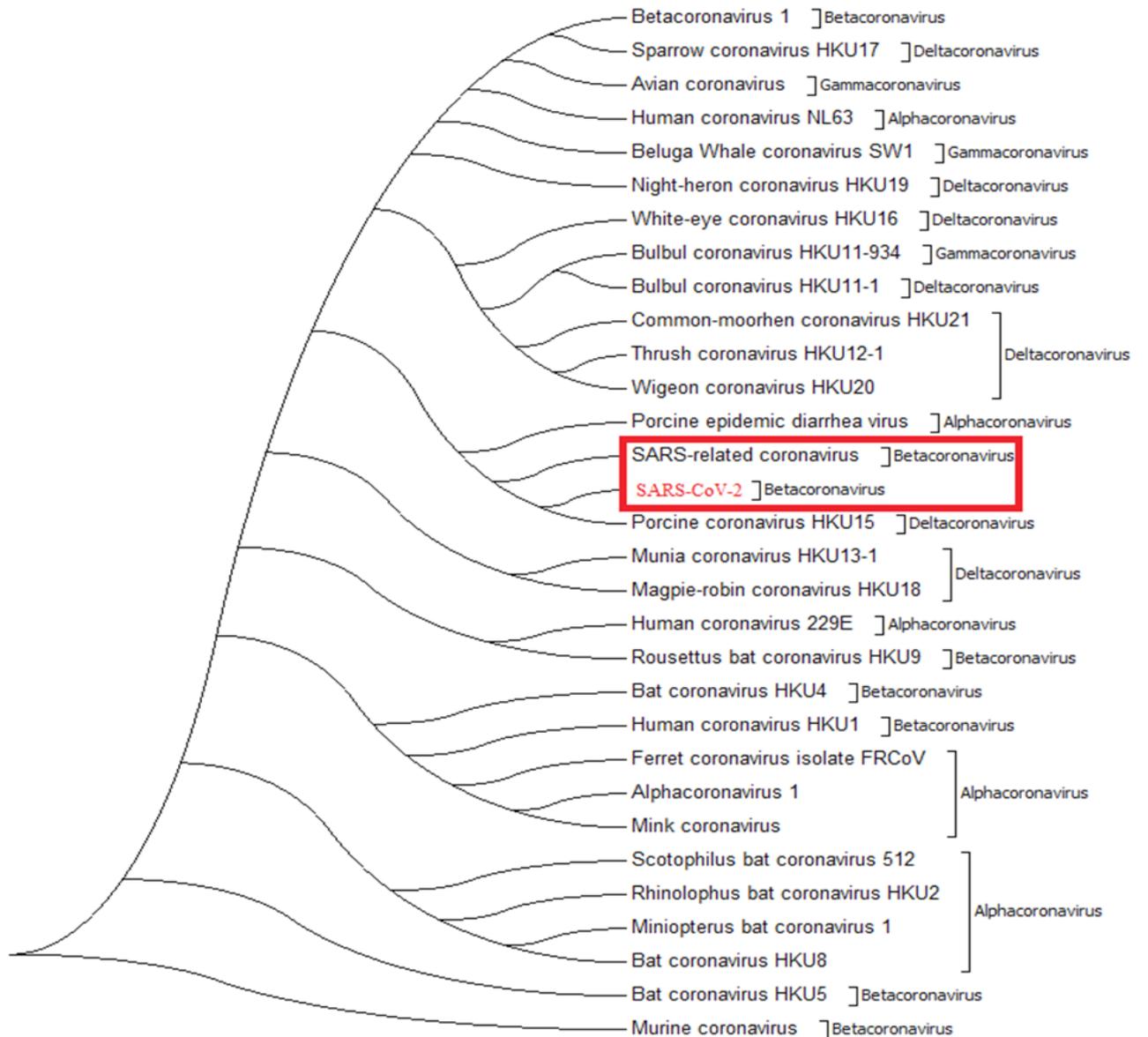


Fig. 2. Phylogenetic analyses of whole genome through (MEGA 6.06) software. Whole genomes of all coronaviruses were collected from NCBI (National Center for Biotechnology Information).

pathogenic divergence of SARS-Cov-2. [Paraskevis et al. \(2020\)](#) demonstrate proof that the SARS-Cov-2 is not-mosaic consisting in approximately half of its genome of a lineage within the *Betacoronavirus*. These genomic characteristics showed their potential virulence in humans.

Adaptation and mutation have driven the co-evolution of coronaviruses and animals, for thousands of years ([Woo et al., 2012](#)). Two coronaviruses i.e. severe acute respiratory syndrome (SARS) and Middle East respiratory syndrome (MERS) were recognized to reason mild disease, like common cold, before 2003. At the

end of 2019, the appearance of SARS-CoV-2 in China has originated, new virus has 95% similarity to SARS-CoV and spike in SARS-CoV-2 gene, the most different region among whole genome. SARS-CoV-2 has high transmissibility and low pathogenicity as compared to SARS-CoV. Research showed that SARS-CoV-2 may be evolved from the bat ([Paraskevis et al., 2020](#)) and Malayan Pangolin ([Lam et al., 2020](#)), but later analysis of SARS-CoV-2 showed that recombination actions were probable to happen in pangolin-bat-origin-coronaviruses either in human, bat or pangolin ([Fig. 3](#)) ([Zhang et al., 2020](#)).

Table I. Classification of Coronaviruses, mode of transmission, hosts and diseases.

Viruses	Hosts	Diseases	Transmission route/vector	References
<i>Alphacoronavirus-1</i>	<i>Sus scrofa</i> , carnivores	gastroenteritis, Feline enteritis, infectious, Swine respiratory disease, Canine enteritis	Faecal-oral, Aerosol	(Tidona and Darai, 2011; Saey, 2013; de Barros <i>et al.</i> , 2019)
<i>HCoV-NL63</i>	Human	Respiratory disease	Aerosol	
<i>HCoV-229E</i>	Human	Common cold	Aerosol	
<i>Mi-BatCoV-1</i>	Bats	Porcine epidemic diarrhea	Faecal-oral	
<i>PEDV</i>	<i>Sus scrofa</i>			
<i>Mi-BatCoV-HKU8</i>	Bats			
<i>Sc-BatCoV-512</i>	Bat			
<i>Rh-BatCoV-HKU2</i>	Bat			
<i>FrCoV</i>	Ferret	Ferret systemic coronavirus, Ferret epizootic enteritis	Faecal-oral	
<i>MiCoV</i>	Mink	Mink epizootic catarrhal gastroenteritis	Faecal-oral	
<i>Harbor seal coronavirus 1</i>	Pacific harbor seals			(Tidona and Darai, 2011)
<i>Murine coronavirus</i>	Mice, rat	Puffinosis	Likely aerosol	
<i>Betacoronavirus 1</i>	Human, horse, dog, cattle, swine, ruminant	Human common cold	Faecal-oral, aerosol	
<i>HCoV-HKU1</i>	Human	Human respiratory disease	Aerosol	
<i>Rousettus bat coronavirus HKU9</i>	Bat			
<i>Pi-BatCoV-HKU5</i>	Bat			
<i>SARS-CoV</i>	Wild carnivores, Bat	Severe acute respiratory disease	Aerosol	
<i>SARS-CoV-2</i>	Bats, pangolin	COVID-19	Aerosol	
<i>Ty-BatCoV-HKU4</i>	Bats (<i>Tylonycteris</i> spp.)			
<i>MERS-CoV</i>	Arabian Camel	Respiratory syndrome	Aerosol	
<i>Avian coronavirus</i>	Domestic and wild bird	Bronchitis infection, respiratory and kidney disease	Aerosol, Faecal-oral	(Tidona and Darai, 2011)
<i>BWCoV/SW1</i>	Beluga whale			(Woo <i>et al.</i> , 2012)
<i>Black-headed gull coronavirus</i>	Black-headed gull			
<i>ALCCoV</i>	Asian leopard cat			
<i>Brent goose coronavirus</i>	Russian Brent goose			
<i>Glaucous gull coronavirus</i>	Glaucous gull (<i>Larus hyperboreus</i>)			
<i>CFBCoV/Guanxi/2006</i>	Chinese ferret badger			
<i>Glaucouswinged gull coronavirus</i>	Glaucous winged gull			
<i>Rock sandpiper Coronavirus</i>	Rock sandpiper			
<i>Pintail coronavirus PBA-124</i>	Pintail			
<i>Western sandpiper coronavirus</i>	Western sandpiper			
<i>Snow goose coronavirus</i>	Snow goose coronavirus			
<i>Common moorhen coronavirus HKU21</i>	Common moorhen			
<i>Wigeon coronavirus HKU20</i>	Wigeon			
<i>Night heron coronavirus HKU19</i>	Night heron			
<i>Magpie robin coronavirus HKU18</i>	Magpie robin			
<i>Sparrow coronavirus HKU17</i>	Sparrow			
<i>White-eye coronavirus HKU16</i>	White-eye			
<i>Porcine coronavirus HKU15</i>	Porcine			
<i>Munia coronavirus HKU13</i>	Munia			
<i>Thrush coronavirus HKU12</i>	Thrush			
<i>Bulbul coronavirus HKU11</i>	Bulbul			



Fig. 3. Recombination of genes actions were probable to happen in livings (human, Pangolin or bat).

Zhou *et al.* (2020) noted Viral protein seroconversion and viral specific nucleotide positive documented in all patients tested provides confirmation of a link between the presence of this virus and the disease. Owing to shortage of specific treatment and considering the relatedness between SARS-CoV as well as SARS-CoV-2, some drugs and pre-clinical vaccine against SARS-CoV probably can be applied to this virus.

The mode of transmission is aerosol from bats to human, and human to human (Table 1). Chen *et al.* (2020) observed that SARS-CoV-2 is more likely to impact aged males with multiple coexisting diseases, and can result in severe and fatal respiratory diseases e.g. acute respiratory distress syndrome.

CONCLUSIONS

It is concluded that *Betacoronavirus* is most probably originated first from bats species and virus may be jumped to other species and evolved as *Deltacoronavirus*, *Gammacoronavirus* and *Alphacoronavirus*. SARS-CoV-2 is belongs to genus *Betacoronavirus*, and has close phylogenetic relation with SARS-like coronaviruses. Adaptation and Mutation have driven the co-evolution of coronaviruses and animals. Two coronaviruses belong to genus *Betacoronavirus* i.e. severe acute respiratory syndrome (SARS) and Middle East respiratory syndrome (MERS) were recognized to reason mild disease, like common cold, before 2003. At the end of 2019, SARS-CoV-2 in China has originated, new virus has 95% similarity to SARS-CoV and spike in SARS-CoV-2 gene, the most different region among whole genome. SARS-CoV-2 has

high transmissibility and low pathogenicity as compared to SARS-CoV. Genomic analysis showed recombination actions were probable to happen in pangolin-bat-origin-coronaviruses either in human, bat or pangolin.

Statement of conflict of interest

The authors have declared no conflict of interest.

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