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RESEARCH ARTICLE

Unraveling the Enigma of Coronavirus: Structure, History and Zoonotic Transmission

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Abstract: The family 'Coronaviridae' is a monophyletic cluster in the Nidovirales. The subfamily Orthocoronovirinae includes 4 genera in which SARS-CoV and SARS-CoV2 belong to genus betacoronavirus. The life cycle of coronavirus starts from the spike (S) protein forms the eponymous crown that interacts with a receptor through its SI domain. However, the recent identification of three novel human coronaviruses, one causing severe acute respiratory syndrome (SARS), has prompted further examination of these viruses. The first evidence of SARS-CoV infection in animals came from a study conducted in a live animal market in early 2003. Rats were implicated as potentially susceptible animals that may have played a role in the transmission and spread of SARS-CoV in the well-publicized SARS outbreaks. Bats have also been the main target because of their species diversity, large population size, broad geographic distribution, ability for long distance migration and habit of roosting in large groups. Corona viruses thrive well in avian species. Gammacoronavirus is highly contagious in chickens and also other similar virus, infect other domestic birds. Coronavirus have crossed the species barriers twice in past during SARS and MERS outbreaks, and thus SARS-CoV2 looks to be the outcome of species barrier jumping for the third time.

Keywords: Corona virus, SARS CoV, SARS CoV2, Geographic distribution, Bats, MERS.

INTRODUCTION

Coronaviruses are a family of enveloped RNA viruses distributed widely among mammals and birds, causing principally respiratory or enteric diseases but, in some cases, neurologic illness or hepatitis (Lai and Holmes, 2001). They primarily cause respiratory or gastrointestinal infections, but they can also occasionally cause neurologic disease or hepatitis. Individual coronavirus infections can be either acute or persistent, and they often affect their hosts in a species-specific manner. Most infections are spread orally and through the respiratory system. In negative-stained electron microscopy, the early viruses had a distinctive morphology that was characterised by a "fringe" of surface structures that were described as "spikes" or "club-like" projections. Nearly four decades later, the coronavirus that caused the fatal severe acute respiratory syndrome (SARS) epidemic in 2002–2003 was discovered. It shared the same distinctive virion shape as its predecessors. The rapid emergence of SARS has sparked a wave of new studies on the fundamental replication mechanisms of viruses in this family to prevent and manage the disease. SARS-CoV and MERS-CoV, which can infect the lower respiratory tract and cause severe respiratory illness in people, are more deadly. It is well known that various CoVs harm wild creatures, including birds, bats, mice, giraffes, whales, and many others. However, they can also infect livestock and result in significant financial loss. Additionally, domestic animals may serve as intermediary hosts for transmitting viruses from their original wild animal hosts to people. Additionally, domestic animals themselves are susceptible to coronavirus illnesses that are spread by bats or closely related species(Hasöksüz, 2020).

Structure of coronaviruses

In a positive sense, a single-stranded RNA genome covering members of the family Coronaviridae is a monophyletic cluster in the order Nidovirales, and measures, on average, 30 kilobases. Alphacoronavirus, Betacoronavirus, Gammacoronavirus, and Deltacoronavirus are the four genera that make up the Orthocoronavirinae subfamily. SARS-CoV and SARS-CoV-2 are members of the genus Betacoronavirus. The nucleocapsid (N) protein, the transmembrane (M) protein, the envelope (E) protein, and the spike (S) protein are the four main structural proteins found in the virion of the coronavirus (CoV), which has a single-stranded, non-segmented RNA genome with positive polarity (Vlasova et al., 2007).The structure of corona virus is given in

Fig 1.

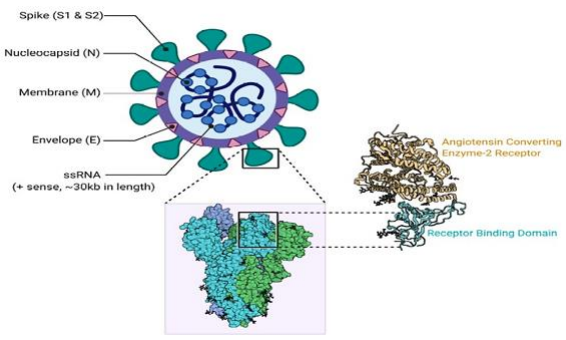


Figure 1: Structure of Coronavirus

In some coronaviruses, forming a complete, infectious virion does not require the whole ensemble of structural proteins. Instead, additional proteins with overlapping compensatory roles may be encoded. The coronavirus RNA genome is bounded mainly by the N protein, the only protein contributing to nucleocapsid formation. The N protein participates in viral genome-related activities but also affects viral RNA replication and the host's cellular response to viral infection (Perlman and Netland, 2009).

The host diversity of coronaviruses and the variety in tissue tropism are caused mainly by the S glycoprotein. A type 1 membrane glycoprotein known as the S glycoprotein has various functional domains close to its amino (S1) and carboxy (S2) termini. The S1 subunit is peripheral and linked to receptor-binding activities. In contrast, the S2 subunit is a transmembrane protein mediating the fusion of viral and cellular membranes.S glycoprotein promotes viral binding to cell surface receptors, results in cell fusion and stimulates the production of neutralising antibodies. Of the 2 functional subunits containing several antigenic sites - S1 and S2, the S1 monoclonal antibody appears to occur most efficiently because it has a higher level of neutralising activity (Hasoksuz *et al.*, 2002)

The coronavirus M protein is essential for virus assembly because it converts cellular membranes into factories where virus and host components combine to create new virus particles. The Golgi apparatus targets the M proteins from SARS-CoV, SARS-CoV-2, MERS-CoV, MHV, FCoV, IBV, TGEV, and BCoV. The M protein promotes assembly by interacting with the viral ribonucleoprotein (RNP) and S glycoproteins at the budding site and by setting up a network of M-M interactions capable of excluding some host membrane proteins from the viral envelope, according to reverse genetic studies and studies on the assembly of virus-like proteins (VLPs). The E protein is the tiniest and most enigmatic of the main structural proteins. Only a limited fraction of the E protein gets incorporated into the virion envelope, even though it is abundantly produced inside the infected cell throughout the replication cycle. The majority of the protein is found at the intracellular trafficking location of the ER, Golgi, and ER-Golgi intermediate compartment, where it participates in CoV assembly and budding (Neumanet *et.al*., 2011)

MHV has the receptor binding domain (RBD) at the N-terminus of S1, whereas SARS-CoV and SARS-CoV-2 have the RBD at the C-terminus of S1. The RBD positions within the S1 region of a coronavirus S protein vary depending on the virus. Numerous coronaviruses, including HCoV-229E, TGEV, PEDV, FIPV, and CCoV, use aminopeptidase N (APN) as their receptor. In contrast, HCoV-NL63, SARS-CoV, and SARS-CoV-2 use angiotensin-converting enzyme 2 (ACE2) as their receptor (Satija and Lal,2011). After attaching to the receptor, the virus must enter the host cell's cytoplasm. The attachment is typically done by fusing the viral and cellular membranes after cathepsin, TMPRRS2, or another protease cleaves the S protein in an acid-dependent manner (Bosch *et al.*, 2003).

History of coronaviruses

SARS first appeared in Guangdong Province, China, in November 2002, spreading quickly to several nations. Within a few weeks, the illness had infected over 8,000 people in 29 countries on 5 continents, and the World Health Organisation reported 774 fatalities(Peiris et al., 2003). Unknown coronavirus (CoV), which spread from an animal reservoir through wet markets in Southern China to the human population, was found to be the disease's etiological agent. Through airborne droplets and intimate contact, the virus was spread from one person to another (Guan *et al.*, 2003).

Clinically, SARS patients with atypical pneumonia and symptoms of fever, dyspnea, lymphopenia, and quickly advancing alterations on radiography were considered to have the sickness. Although there were no obvious upper respiratory tract symptoms, there were reports of watery diarrhoea. During their infection, 40% to 70% of individuals experienced diarrhoea, and the virus was found in their faeces, presumably indicating a channel of virus transmission. There was no response when traditional antibiotics were administered to treat pneumonia (Poutanen *et al.*, 2003).

The primary factor in all fatal SARS patients was respiratory insufficiency, which resulted in acute respiratory distress syndrome (ARDS) and respiratory failure. The virus was isolated or identified using a reverse transcription polymerase chain reaction (RT-PCR). During the acute phase of the illness, it was also possible to find lymphopenia, low platelet counts, extended coagulation profiles, and modestly raised serum hepatic enzymes in the affected people. In SARS, death and disease severity were both influenced by age. Mortality rates during the outbreak were 0%, 6%, 15%, and 52% among affected people in Hong Kong aged 0 to 24, 25 to 44, 45 to 64, and older than 65. No SARS-CoV-infected children in Hong Kong under 12 required intensive care or mechanical ventilation due to their sickness(Gao *et al.*, 2005).

At first, neither the aetiology of SARS nor a specific treatment option is known. Numerous early sporadic cases in Guangdong showed epidemiological ties to the live animal market trade, while healthcare workers were disproportionately afflicted in outbreaks linked to person-to-person transmission. The WHO coordinated a comprehensive global effort that included patient isolation, rigorous infection control in hospitals, quarantine procedures, and travel advisories to finally bring the outbreak under control (Poon *et al.*, 2004).

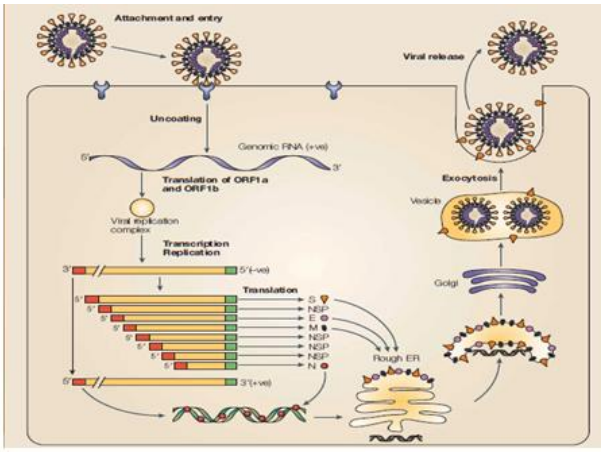
The life cycle of coronaviruses

The spike (S) protein, which gives coronaviruses their recognisable, eponymous crown, binds with a receptor through its S1 domain to begin the coronavirus life cycle. Membrane fusion leads to the entrance, most likely mediated by the S2 domain. The RNA genome is released into the cytoplasm, where replication occurs. Using a ribosomal frame-shifting mechanism, the host translation machinery translates the overlapping open reading frames ORF1a and ORF1b to create a single polyprotein (Thiel *et al.,* 2003).

The pieces required to assemble the viral replication complex, which produces full-length negative-strand RNA, are produced by the cleavage of proteinases encoded by the virus. A discontinuous transcription method also has a nested collection of sub-genomic negative-sense RNAs during negative-strand synthesis. The transcription regulatory sequence (TRS), located upstream of each translated gene and, with a few exceptions, at the 3′ end of the leader sequence, is crucial in this process. The nascent sub-genomic minus strands' 3′ ends are thought to be fused to the antisense leader sequence. Then, these irregularly created minus strands serve as templates for creating positive-sense mRNAs. (Rota *et al.* 2003).

The **Figure-2** depicts the positive-sense mRNA products. An alternative theory states that these mRNA molecules are produced by discontinuous transcription during positive-strand synthesis. Rarely is more than 5′ ORF translated. The helical nucleocapsid is formed in the cytoplasm by assembling the nucleocapsid (N) protein with genomic RNA. The endoplasmic reticulum (ER) and the Golgi apparatus are internal membranes through which this core structure budding receives its envelope. The ER transports the membrane (M), envelope (E), and spliceosomal (S) proteins to the budding compartment, where the nucleocapsid likely interacts with the M protein to initiate assembly. All three proteins will fit within the lipid bilayer. Sugar moieties are altered when the virus is transported through the Golgi apparatus, and in some coronaviruses, the S protein is split into the S1 and S2 domains. Any extra S protein is delivered to the cell surface and not integrated into the virions. Virion-containing vesicles fuse with the plasma membrane to release the virus from the host cell (Grotthuss *et al.*,2003).

Figure 2: Life cycle of Coronavirus



Coronaviruses affecting animals

The pathogens are present in various animal species, but only a few develop severe infections. Important Coronaviruses (CoVs) that cause hepatitis, enteritis, and respiratory illnesses in laboratory animals include the mouse hepatitis virus, the rat sialodacryoadenitis coronavirus, the guinea pig coronavirus, and the rabbit coronavirus(Shi *et al.,* 2019).

Bovine coronaviruses (BoCoVs) have zoonotic potential among large animals because they have been isolated from asymptomatic children and have also been found to affect several domestic and wild ruminants, with universal implications for calf diarrhoea in neonates, bloody diarrhoea in adult cattle, and respiratory form of shipping fever in all age groups of cattle (Suzuki *et al*., 2020).

Enteritis and infectious peritonitis caused by the feline CoVs impact the respiratory system, central nervous system, abdominal cavity, and gastrointestinal tract. The respiratory and gastrointestinal tracts are affected by canine enteric coronaviruses of the Alpha coronavirus and Betacoronavirus families (Tekes and Thiel, 2016).

Infectious bronchitis virus (IBV), a member of the Gamma coronavirus, causes significant economic loss in the chicken industry by causing respiratory illnesses, uti infections, and reproductive issues. A coronavirus from the genus Alpha called the swine acute diarrhoea syndrome coronavirus (SADS-CoV) causes severe enteritis in nursing piglets and high mortality (Dhama *et al*., 2014).

The coronavirus known as HKU2 coronavirus was discovered to be 95–96% identical to the coronavirus of the horseshoe bat (Rhinolophus sp.). It claimed that a coronavirus could jump from infecting bats to infecting pigs by recombining genetic material or altering the receptor-binding domain (RBD). Utilisingpanviral microarray technology, another unique CoV with the name SW1 has been found in the liver tissue of a captive beluga whale (Delphinapterus leucas) (Wang and Jin, 2020).

METHODS

We searched SARS-CoV-related data for review in the previously reported literature. We retrieved from databases (Science direct.com, Google Scholar) using the keywords Coronavirus structure, origin and transmission, SARS CoV 2 source, and coronavirus in various animals and birds. A total of articles were retrieved from these databases. The additional sources from the year 2000 to 2022 were included. Overall, articles were included in the reference section. Unrelated information about the corona and its transmission was excluded.

SARS-CoV

The source of SARS-CoV

Chinese ferret badgers (Melogalemoschata), raccoon dogs (Nyctereutesprocyonoides), and masked palm civets (Pagumalarvata) were all found to have the SARSCoV, according to a study on animals taken from live animal markets in Guangdong, China. The animal CoV found in civet cats shared a significant degree of sequence identity with the SARS-CoV but was otherwise unique. In contrast to early human SARS-CoV strains and animal SARS-like viruses, later-isolated viruses throughout the outbreak showed a 29-nucleotide deletion in the open reading frame(ORF)(Zhonget *al*., 2003).

It has been suggested that the live animal markets were a possible location for the interspecies transfer of an animal precursor virus to humans because urologic evidence of infection was also discovered in animal workers with no history of a SARS-like illness. However, later investigations failed to uncover any proof of widespread disease in either domesticated or wild civets. Although experimental SARS-CoV infection of palm civets with two distinct human isolates led to clinical illness (Li et al., 2003). Two study teams discovered a virus from Chinese horseshoe bats in September 2005 that was genetically similar to human SARS-CoV, raising the possibility that bats may be a reservoir for the SARSCoV that infected humans and palm civets. (Lau *et al.*, 2005) .

The bats are reservoir hosts of several zoonotic viruses, including the Hendra and Nipah, paramyxoviruses that have recently emerged in Australia and East Asia, which cause encephalitis and respiratory disease in humans. Bats are genetically diverse, live longer than other small mammals, roost in groups, and can fly great distances, making them ideal for spreading zoonotic diseases (Chua *et al.*,2000).

Despite rarely exhibiting clinical signs, bats can have persistent infections with various viruses. These traits and the increased availability of bats and bat items in traditional medicine and food markets across Asia, including southern China, prompted researchers to examine bats to find the SARSCoV's natural reservoir (Sulkin and Allen,1974).

SARS-CoV-like virus nucleic acids were discovered in the faeces of bats from the wild and Chinese markets. Blood samples from the animals also contained antibodies against the human SARS-CoV. Sequence study of the bat SARS-CoV revealed that these CoV family members had a wide range of genetic diversity and that some of them shared a common ancestor with the SARS-CoV found in humans and palm civets (Simmons *et al.*,2004).

Only the genetic sequence data and serology are now available due to the virus' failure to be successfully isolated from bats. The production of variant viruses that can adapt to new hosts and transcend the species barrier may be made possible by the ability of CoVs to recombine and RNA viruses' rapid mutation rate. It is possible that palm civets, marketed as food in Southern Chinese marketplaces for live animals, contracted the disease from bats or another animal host while living in the wild. With more animal surveillance, we will better comprehend the animal reservoir of SARS-CoVlike viruses in nature (Yang *et al.*,2004).

Animals suspected of SARS-CoV.

A study in a live animal market in early 2003 provided the first proof that animals were infected with the SARS-CoV virus. Three masked palm civets (Pagumalarvata) and one raccoon dog (Nyctereutesprocyonides) were found among the 25 animals analysed to have viruses closely related to SARS-CoV. Two Chinese ferret badgers (Melogalemoschata) were found to have neutralising antibodies against the SARS-CoV. According to this initial study's findings (Guan et al., 2003), coronaviruses closely related to the SARS-CoV were found to infect at least three different animal species in the Shenzhen market. It has been established that mammalian species are vulnerable to SARS-CoV infection or similar viruses. In the well-publicised SARS outbreaks in the Amoy Gardens apartment block in Hong Kong Special Administrative Region, People's Republic of China, rats were also named as possibly susceptible animals that may have contributed to the transmission and spread of SARS-CoV. The first confirmed incidence of SARS in a person occurred in Guangdong in 2004, and it was claimed that the person had no contact with animals besides rats(Swayne *et al.*, 2004). The list of animals suspected for SARS CoV is given in **Table 1**.

Table-1

List of SARS corona virus infected animals

Common name	Taxonomic name	Mode of infection

Masked palm civet	*Paguma larvata*	Natural
Racoon dog	*Nyctereutes procyonoides*	Natural
Chinese ferret badger	*Melogale moschata*	Natural
Cynomolgus macaque	*Macaca facicularis*	Experimental
Rhesus macaque	*Macaca mulatta*	Experimental
African green monkey	*Cercopithecus aethiops*	Experimental
Ferret	*Mustela furo*	Experimental
Golden hamster	*Mesocricetus auratus*	Experimental
Guinea pig	*Cavia porcellus*	Experimental
Mouse	*Mus musculus*	Experimental
Rat	Rattus rattus	Experimental
Pig	*Sus scrofa*	Natural

Transmission of coronavirus in animals

In 2005, new coronaviruses, known as SARS-CoV-related viruses or SARSlike coronaviruses, were discovered in horseshoe bats (genus Rhinolophus), linked to human SARS-CoV. (Geet al., 2013). Civets served as an intermediary, but bats may have served as a natural host for SARS-CoV. Another investigation revealed the coexistence of many SARSr-CoVs in bat populations that resided in a cave in Yunnan province, China. This study also provided the first evidence that the human angiotensin-converting enzyme 2 (ACE2) is a receptor for bat SARS-like coronavirus(Lau *et al.*, 2005).

The frequent recombination of the coronavirus genome suggests a high likelihood of the formation of new SARS-CoVs by recombination of bat SARS-CoVs already present in the same or different bat caves. He postulated that SARS-CoV direct progenitor was produced by recombination in bats and that it then spread to farmed civets and other mammals, infecting them through faecal-oral transmission. These virus-carrying civets are brought to the Guangdong market, where they are infected and further transformed market civets before spreading to humans(Lai and Cavanagh, 1997).

The evolutionary analysis of novel CoVs reveals that there have been several cross-species transmission events. However, the majority of these transmission events were brief overflows. The high frequency of CoV recombination in bats shows that bats are an essential reservoir for CoV development and recombination (Banerjee *et al.*, 2019).

Coronaviruses in Bats

Several species of horseshoe bats of the genus Rhinolophus have SARS-like-CoVs. Each of the four species examined in a study of horseshoe bat species conducted in 2004 in various parts of mainland People's Republic of China showed evidence of infection by a SARS-like-CoV: 2 species (R. Pearson and R. macrotis) had positive results from both serologic and PCR tests, whereas two species (R. pussilus and R. ferrumequinum) had positive results from either serologic or PCR tests (Woo *et al.*, 2006).

The provinces of Hubei and Guangxi, which are more than 1,000 miles apart, are where the bats with positive results were found. PCR testing revealed that 23 (or 39%) of 59 anal swabs from wild Chinese horseshoe bats (R. sinicus) contained genetic material closely linked to the SARS-CoV virus. A team in Hong Kong made this finding. Additionally, they discovered that up to 84% of the horseshoe bats studied had antibodies to the SARS-CoV recombinant N protein (Lau *et al.*, 2005).

SARS-CoV and some group 1 coronaviruses exhibit a certain level of antigenic cross-reactivity, and other group 1 coronaviruses have recently been discovered in bats. The actual seropositive rate for R. sinicus is about 84%. However, seropositive bats' relatively high sero frequency and widespread distribution align with the serologic pattern anticipated from the animal that serves as a pathogen's natural reservoir (Hudson *et al.*, 2005).

A genome sequencing revealed that the genome organisation of all SARS-like CoVs obtained from bats and humans is nearly identical. 88% to 92% of their total sequence identities were shared. The S gene's 5' terminus, which codes for the S1 domain necessary for receptor interaction, and open reading frame 10 (ORF10 or ORF8) were shown to have the most variable areas. Immediately upstream of the N gene, susceptible to deletions of different magnitudes, depending on the terminology used. Most human SARS-CoVs discovered in the late stages of the outbreaks in 2002–2003 have a 29–nt deletion in this area; In human or civet isolates from the early stages of the epidemic, this deletion is not present. The absence of the 29-nt deletion in bat viruses further suggests that SARS-CoVs and SARS-like-CoVs have a similar ancestor (Guan *et al.*, 2003).

The search for new coronaviruses with human and animal origins has increased in response to the discovery of SARS-CoV. Due to the diversity of their species, high population size, broad geographic distribution, capacity for long-distance migration, and propensity for roosting in big groups, bats have been selected as the primary target (Tang *et al.*, 2006).

Throughout the summer, surveillance research was carried out in Hong Kong. By sequencing PCR products from the RNA-dependent RNA polymerase (RdRp) gene, they discovered a novel group 1 coronavirus from 162 swab samples taken from 12 different species of bats. Three species of Miniopterus (M. pusillus, M. magnater, and M. schreibersii) were determined to share the same virus or viruses from the same genetic ancestry (Poon *et al.*, 2003) 985 bat samples from 35 species in 14 genera and 3 families were gathered from 82 sites across 15 provinces in the People's Republic of China. A PCR targeting a highly conserved 440-bp RdRp region yielded positive results in 64 (6.5%) bats. Only three (from the genus Rhinolophus) of the 64 PCR-positive products were sequenced; the other 40 belonged to Group 1, and the remaining 22 formed a separate cluster in Group 2, probably grouping with the Group 2c viruses (Zhang and Woo,2006). The strains of SARS CoV affecting bats detected in different locations is given in **Table 2**.

Table -2 Different strains of SARS Corona virus in Bat

Name/strain	**Bat species**	**Location of detection**
Bat-CoV HKU2	*Rhinolophus sinicus*	Hong Kong
Bat-CoV HKU6	*Myotis ricketti*	Hong Kong
Bat-CoV HKU7	*Miniopterus magnate*	Hong Kong
Bat-CoV HKU8	*Miniopterus pusillus*	Hong Kong
BtCoV/701/05	*Myotis ricketti*	Anhui, Guangdong
BtCoV/821/05	*Scolophlus kuhlii*	Hainan
BtCoV/970/06	*Rhinolophus pearsoni*	Shandong
BtCoV/A773/05	*M. schreibersii*	Fujian, Guangxi
Rm1 (BtCoV/279/04)	*Rhinolophus macrotis*	Hubei
Rf1 (BtCoV/273/04) Bat-SARS-CoV HKU3	*R. ferrumequinum*	Hubei
BtCoV/A1018/06	*R. sinicus*	Hong Kong
BtCoV/279/04	*R. sinicus*	Shandong
Bat-CoV HKU4	*R, macrotis*	Hubei
Bat-CoV HKU5	*Tylonycteris pachypu*	Hong Kong
BtCoV/133/05	*Pipistrellus abramus*	Hong Kong

BtCoV/434/05 BtCoV/355/05	*T. pachypus* *Pipistrellus pipistrellus* *P. abramus*	Guangdong Hainan Anhui, Sichuan

Corona Virus in Birds

Gamma and delta coronaviruses are two genera of coronaviruses that are well-adapted to avian species. Avian coronavirus is a typical example of a gamma coronavirus. Taxonomically, they are known as infectious bronchitis viruses (IBVs) because they are incredibly contagious in chickens and also infect other domestic birds, such as pheasants, peafowl, and quails, as well as turkeys (where the turkey coronavirus (TcoV) causes enteritis infection) and guinea fowls (where the guinea fowl coronavirus (GfCoV)). Columbiformes, Pelecaniformes, Ciconiiformes, Psittaciformes, Anseriformes, and Passeriformes (munia, bulbul, and thrush) are among the non-Galliformes and non-Galliformes reported to have the avian coronavirus (Woo *et al*., 2012).

The virus is disseminated by aerosol, which costs the chicken business significantly in terms of money. Viruses have been found in turkeys and pheasants, where they replicate or increase in the upper respiratory system before infecting the bronchi and causing severe sickness in young animals. Certain strains of infectious bronchitis viruses (IBV) reproduce in tissues such as the gut, kidney, and oviduct and cause nephritis, decreased egg production, and other systemic illnesses. The contagious bronchitis viruses are widespread and can be found in many parts of the world. The primary causes of infection in domestic poultry's urogenital, digestive, and respiratory tracts are strains of the infectious bronchitis virus. (Saif, 2004).

The tissue's defences against IBV-induced illness are only partially understood. Inactivated and live attenuated infectious bronchitis viruses (IBV) are covered by vaccines. Live vaccines may only provide temporary immunity; inactivated vaccines alone cannot prevent chicken sickness. However, to increase avian immunity, inactivated vaccinations may be combined with live attenuated vaccines (Vijay Krishna *et al.*, 2007).

Because of its wide antigenic diversity, IBV was the first coronavirus to be isolated in the 1930s. It has been extensively researched for over 50 years (Cavanagh &Naqi, 2003). Although it severely harms the mucosae of the respiratory tract, its effects are amplified because it makes sickness brought on by co-infections with bacteria and mycoplasmas more severe (Meulemans *et al.,* 2001).

The widespread use of live attenuated vaccines, linked to the escalation of secondary bacterial infections, partly contributes to the control. (Matthijs et al., 2003).Although proventriculitis has been related to IBV strains, pathology is not often associated with IBV infections of the gastrointestinal tract. Some viral strains have a long history of being particularly neuropathogenic. Some IBV strains are likely linked to pathological symptoms that have not been identified yet. The virus's ability to reproduce in so many tissues may factor in the diversity of its protein sequences, particularly the S protein. (Liu and Kong, 2004).

IBV strains vary in virulence, and the host's genetic makeup can affect how an infection turns out. IBV is, therefore, not a straightforward pathogen, and it is essential to keep in mind its heterogeneity in protein sequences, extensive tissue tropism, and toxicity in the context of the host range of the virus. (Bacon *et al.*, 2004). List of SARS CoV affecting birds and their associated diseases are shown in the **Table 3.**

Table -3 List of avian SARS Corona virus

Avian species	**CoV genus**	**CoV subgenus**	**CoV species**	**Common name**	**Associated disease**
Chicken (*Gallus gallus domesticus*) and other birds of different orders	*Gamma Coronavirus*	*Igacovirus*	*Avian coronavirus*	Infectious bronchitis virus (IBV)	Respiratory disease.

Turkey (genus *Meleagris*)	*Gamma coronavirus*	*Igacovirus*	*Avian coronavirus*	Turkey coronavirus (TCoV)	Enteric disease
Quail (*Coturnix coturnix*)	*Gamma Coronavirus*	*Igacovirus*	*Avian coronavirus*	Quail coronavirus (QCoV)	Enteric disease
Guineafowl (fam. *Numididae*)	*Gamma coronavirus*	*Igacovirus*	*Avian coronavirus*	Guineafowl coronavirus (GfCoV)	Enteric disease
Pheasant (Pheasant colchicus)	*Gamma coronavirus*	*Igacovirus*	*Avian coronavirus*	Pheasant Coronovirus	Respiratory disease

Turkey Coronavirus

In the United States, where it has been most completely examined, a coronavirus was connected to the enteritis of turkeys. It can cause mortality in young poults, but it can also be crippling in older birds, which causes them to produce less meat and eggs (Guy et al., 2000). The virus was identified in the UK in 2001 and has been seen in Brazil and Italy. Field research has used reverse transcriptase-polymerase chain reactions (RT-PCRs) to detect viruses in field research. Turkey sera have also been used to detect antibodies using immunological fluorescence with IBV-infected cells and an enzyme-linked immunosorbent assay (Cavanagh *et al.,* 2001).

Pheasant Coronavirus

A coronavirus (PhCoV), occasionally linked to renal and respiratory diseases, infected pheasants. Gene sequencing later proved that the virus was a coronavirus. Many pheasants from various ranges suffering from respiratory disease hadPhCoV, which was found in them(Pennycott, 2000). Except for the S protein, where PhCoV and IBV are more genetically similar to one another than TCoV, the degree of genetic relatedness to IBV is the same between IBV and TCoV (Welchman *et al*., 2002).

The gene sequences of the dozen or so pheasant isolates that were sequenced differed from IBVs used in the lab by around 10% and from all IBV sequences in the databanks by about the same amount. Similar to the variances between IBV serotypes, the pheasant coronaviruses had different gene sequences(Cavanagh *et al*., 2002).

Coronaviruses in Galliform Birds

The whole genomes of coronaviruses isolated from domestic peafowl (Pavocristatus), partridge (Alectoris sp.), guinea fowl (Numidameleagris), and teal (Anas sp.) were just recently sequenced by Chinese researchers. The genomic organisation of all of these viruses, which differs in several ways from that of the coronaviruses in Groups 1 and 2, was IBV-like, as were the gene sequences encoded by each virus. The peafowl virus's proteins shared 99% of their composition with the proteins in the widely used IBV H120 vaccination (databank accession number for the complete genome sequence: AY702085). It is almost probable that it was the vaccination strain from the peafowl, which had chickens in the area, because of the extraordinarily high degree of identification (Liu *et al*., 2005).

The H120 infectious bronchitis vaccine, a coronavirus antigenically linked to IBV and isolated from 5- and 10-day-old guinea fowl had most likely infected the peafowl. The guinea hens had a high death rate, a limited feed intake, and enteritis. Experimental inoculations of the isolate resulted in respiratory discomfort and watery faeces in chickens and guinea pigs. (Ito *et al*., 1991).

Coronaviruses in Non-galliform Birds

A neutralisation test using serum from the teal and the IBV-like virus extracted from the teal might be beneficial. Using chicken embryos and tracheal/cloacal swabs from racing pigeons with ruffled feathers, dyspnea, and profuse mucus near the beak, a coronavirus was discovered in Australia in 1988. The serum against an Australian serotype of IBV neutralised the virus, which induced alterations in the embryos typical of IBV (Barr et al., 1988).

When pigeons and chickens were injected with the virus, only the chickens developed respiratory illness. It is possible that the coronavirus was unable to cause the clinical symptoms seen in the racing pigeons from which the virus was isolated or that the coronavirus was able to cause chickens to produce antibodies after being inoculated with several PhCoVs, indicating replication but not disease (Gough *et al.,* 1996).

When FCoV and CCoV's ability to infect pigs was tested, the level of pathology generated varied according to the strain. It is evident that only a small number of TCoV and PhCoV strains have been studied in hens, and those studies were conducted in controlled laboratory settings rather than in the field where additional circumstances could worsen the effects of virus infection (Woods *et al*., 1981).

It is still being determined whether IBV, TCoV, and PhCoV should be regarded as three separate species or as one species with various strains producing disease in one host species but not the other, given their genetic similarity and ability to infect hens (Cavanagh, 2001

Cross-species Transmission

Four things must happen for zoonotic viruses to develop from a wildlife reservoir: The following were looked at: 1) interspecies contact, 2) spillover (cross-species virus transmission), 3) sustained transmission, and 4) virus adaptability within the spillover species. These four transitional occurrences occurred throughout the SARS outbreaks and aided in the disease's quick spread over the globe (Childs, 2004).

It was demonstrated how civets contribute to SARS-CoV infection of people directly. The most compelling instance was the infection of a waitress and a patron at a restaurant where SARS-CoV-positive civets were kept in cages. Two crucial questions remain: What animal is the SARS-CoV strains' natural reservoir host, and how were the viruses spread to civets or other intermediary hosts? The data collected so far strongly suggests that horseshoe bats are most likely the reservoir host of SARS-CoV, even though it is not yet conclusive. As previously mentioned, bat coronaviruses appear species-specific, and the only SARS-like-CoVs identified so far are linked to horseshoe bats (Wang *et al.*, 2005).

The possibility that the natural reservoir species may not be indigenous to the People's Republic of China is raised by the facts that SARS-CoV cross-species transmission appears to be a relatively uncommon event and that legal and illicit wildlife animal trade occurs between the People's Republic of China and other nations. previously conducted infection studies on various bat species that serve as the natural reservoir of SARS-CoV. The likelihood that the human/civet SARS-CoVs can still infect the primary reservoir species is high if the progenitor viruses originate from bats (Yan *et al.*,2005).

It is easier to determine the precise transmission mode from the reservoir host to the intermediate host with knowledge about the natural reservoir of SARS-CoV. However, the faecal-oral pathway stands out as the primary transmission means in mammals. The primary source of interspecies transmission in the animal trading chain, which includes warehouses, vehicles, and markets, may come from contaminated faeces, urine, blood, or aerosols, even though mixing live reservoir hosts (such as bats) and intermediate hosts (such as civets) would be an efficient method of transmission. This also applies to transfers from civets to people. The restaurant patron who contracted the disease in 2004 had no direct contact with civets, as was demonstrated in that case (Liang *et al.*,2004).

Studies of the receptor-S protein interaction, molecular epidemiologic research, and the possibility of direct transmission from the natural reservoir host to humans all suggest that the progenitor viruses are unlikely to be able to infect humans and that a quick viral evolution in an intermediate host (like civets) seems to be necessary to adapt the virus for human infection. For both animal-to-human and human-to-human transmission, the ability to effectively use the receptor molecules (ACE2 for humans and civets) is a crucial limiting factor. This also explains why the closely similar bat SARS-like-CoVs could not spread the human pandemic, but the SARS-CoV was (Li *et al.*, 2006).

Identifying SARS-like coronaviruses in bats and the wide genetic variety in bats have provided new insights into the evolution and spread of the SARS-CoV. Although the precise native host for the SARS-CoV progenitor virus is still unknown, we think that ongoing research in various bat populations in the People's Republic of China and surrounding nations, along with experimental SARS-CoV infection of different bat species, will eventually identify the native reservoir species. (Breed *et al.*, 2006).

The finding of SARS-like CoVs in bats emphasises the growing significance of bats as new viral reservoirs. The recent emergence of SARS-CoVs, as well as other bat-associated viruses like henipaviruses, Menangle, Tioman viruses, and variants of rabies viruses and bat lyssaviruses, supports the idea that viruses, particularly RNA viruses, pose a more significant threat than other pathogens for disease emergence in humans and domestic mammals due to their higher mutation rates (Harris *et al.*, 2006).

SARS-CoV-2

The recently discovered SARS-CoV-2 (2019-nCoV) belongs to the families Coronaviridae and Orthocoronavirinae of the order Nidovirales, which also includes the four coronavirus genera Alpha, Beta, Gamma, and Delta. The subgenus Sarbecovirus of the genus Beta coronavirus contains the SARS-CoV-2. Both SARS-CoV and MERS-CoV belonged to the Beta coronavirus genera, although SARS-CoV-2 is genetically distinct from these two. (Drexler et al., 2014).

SARS-CoV-2 has been determined to be 82% identical to human SARS-CoV Tor2 and human SARS-CoV BJ01 2003 at the nucleotide level while being 88-89% identical to two SARS coronaviruses of bat origin (bat-SL-CoVZC45 and bat-SL-CoVZXC21, also known as ZC45 and ZXC21). According to Hu et al. (2017), there was only a 50–51.8% identity between SARS-CoV-2 and MERS-CoV and a 79% identity between SARS-CoV-2 and SARSCoV. According to molecular-level phylogenetic analysis, SARS-CoV-2 is more closely related to the SARS-CoV of bat origin.380 amino acid substitutions between the sequences of SARS-CoV-2 were found through genome analysis (HB01)(Ramadan and Shaib, 2019).

Theories of SARS-CoV-2 origins

Through laboratory manipulation of a related SARS-CoV-like coronavirus, SARS-CoV-2 was created. In contrast to what was previously hypothesised, the RBD of SARS-CoV-2 is efficiently optimised for binding to human ACE2. Additionally, if genetic modification had been done, it is likely that one of the many reverse-genetic methods for beta coronaviruses would have been applied (Sheahan *et al.*,2008).

Genetic evidence conclusively demonstrated SARSCoV-2 is not generated from any previously used viral backbone. There are two plausible explanations for how SARS-CoV-2 originated (Almazanet *al.*,2014)

Natural selection in an animal host before zoonotic transfer

Early COVID-19 instances were frequently connected to Wuhan's Huanan market. There's a chance that an animal source was present here. Its ancestor likely used bats as reservoir hosts. RaTG13, a sample from a Rhinolophusaffinis bat, is approximately 96% identical to SARS-CoV-2 overall, but its spike diverges in the RBD, suggesting that it may not bind to human ACE27 effectively (Zhou et al., 2020). He said that Manisjavanicamalayan pangolins (brought into Guangdong province illegally) have coronaviruses identical to SARSCoV-2. The RaTG13 bat virus continues to have the genome most similar to SARS-CoV-2. However, some pangolin coronaviruses show considerable similarities to SARS-CoV-2 in the RBD, including all six critical RBD residues. This demonstrates unequivocally that natural selection produced the SARS-CoV-2 spike protein favoured for binding to ACE2, which is similar to the human. Both the pangolin and bat beta coronaviruses that have been sampled so far lack polybasic cleavage sites. The diversity of coronaviruses in bats and other animals is drastically under-sampled, even though no animal coronavirus has been found that is sufficiently comparable to have served as the direct progenitor of SARS-CoV-2. Coronaviruses' S1-S2 junction can experience mutations, insertions, and deletions, demonstrating that the polybasic cleavage site can develop naturally through evolutionary processes. An animal host likely has a large population density and an ACE2-encoding gene identical to the human ortholog for a precursor virus to acquire both the polybasic cleavage site and alterations in the spike protein suited for binding to human ACE2.

Natural selection in humans following zoonotic transfer

The genetic characteristics mentioned above were acquired by a SARS-CoV-2 progenitor during undetected human-to-human transmission. With these modifications, the pandemic would spread quickly, resulting in a sizable cluster of cases that would alert the surveillance system that would eventually catch it. This was also likely in the virus that jumped to humans because an RBD in pangolins was highly similar to SARS-CoV-2. This leaves human-to-human transmission as the only time when a polybasic cleavage site can be inserted. With the help of the most recent sequence data, estimates of the time of the most recent common ancestor of SARS-CoV-2 place the virus's emergence in late November or early December 2019, which is consistent with the earliest retrospectively confirmed cases(Wu *et al.*, 2020).

SELECTION DURING PASSAGE.

Studies of SARS-CoV11 have shown that SARS-CoV-2 acquired RBD mutations during adaptation to passage in cell culture. The discovery of coronaviruses that resemble SARS-CoV from pangolins and with virtually identical RBDs offers a far more convincing and economical explanation for how SARS-CoV-2 acquired them through recombination or mutation19. A further argument against culture-based hypotheses is provided by discovering the polybasic cleavage site and the expected O-linked glycans. New polybasic cleavage sites were found after a lengthy passage of low-pathogenicity avian influenza virus in vitro or in vivo (Corman, 2018).

Host range

Most of the time, infections caused by coronaviruses (CoVs) in humans and domestic and wild animal species remain subclinical. The clinical form ranges from ordinary cold to extremely lethal respiratory infections in humans, including enteritis in cattle, horses, and pigs, upper respiratory tract disease in cattle, dogs, cats, and poultry, and the common cold. (Salata *et al.*, 2020).

Alpha coronavirus and Beta coronavirus, two of the four genera in the Coronaviridae family, typically infect mammals and are thought to have swine origins. In contrast, the Gamma and Delta coronavirus typically infect birds, fish, and mammals. (Cui *et al.*, 2019).

Potential zoonotic viruses like SARS-CoV and MERS-CoV, which have bats as their primary host and palm civet cats and dromedary camels as their intermediate hosts, respectively, are members of the genus Beta coronavirus. Wigeon coronavirus HKU20, Bulbul coronavirus HKU11, Munia coronavirus HKU13, White eye coronavirus HKU16, Night-heron coronavirus HKU19, and Common moorhen coronavirus HKU21 are only a few of the many CoVs that have been found in birds (Wang and Eaton, 2019). Porcine Coronavirus HKU15, Transmissible Gastroenteritis Virus (TGEV), Porcine Epidemic Diarrhoea Virus (PEDV), and Porcine Hemagglutinating Encephalomyelitis virus (PHEV) are the prevalent pig-infecting coronaviruses that are being reported from numerous locations across the world (Ma *et al.*, 2008).

Cattle, horses, swine, dogs, cats, camels, rabbits, rodents, birds, ferrets, mink, bats, snakes (such as Chinese cobra

and krait), frogs, marmots, hedgehogs (Erinaceuseuropaeus), Malayan or Javan or Sunda pangolin(Manisjavanica)was reported as species harbouring the CoVs. (Monchatre-Leroy *et al.*, 2017).

Animals and zoonotic links of SARS-CoV-2

SARS-CoV-2 appears to result from a third species barrier crossing by coronaviruses, which have already done so twice during the SARS and MERS outbreaks. Recent zoonotic CoVs, including SARS-CoV, MERS-CoV, and SARS-CoV-2, have received more prominence due to the severity of the disease in humans and their widespread distribution worldwide (Rothan and Byrareddy, 2020).

Instability of the replicase enzyme, RNA-dependent RNA polymerase, polybasic furin cleavage site, and O-linked glycans, lack of a proofreading mechanism, a greater rate of mutations in the RBD of spike gene, and genetic recombination may all be contributing factors to the creation of novel CoVs and their broad host range. (Patel and Jernigan, 2020).ACE2 was a comparable cell entrance receptor for SARS-CoV and SARSCoV-2 (2019-nCoV). The host range of CoVs becomes enlarged to include different host species of animals or humans and the virulence and transmissibility of the virus may further change and rise, becoming a cause for concern on a worldwide scale (Zhou *et al.*,2020a)

When attempting to locate the SARS-CoV-2 source, it was discovered that the earliest affected people shared an exposure site. Wet Seafood Wholesale Market in Wuhan, Hubei Province, China, where restaurants are renowned for providing a variety of tiny and large domestic animals, wild animals, and live animals for human consumption (Patel and Jernigan, 2020).

The original conclusions from Wuhan Seafood Market hypothesised that wild animals and animal sources were responsible for spreading SARS-CoV-2. Findings pointed to the likelihood of a zoonotic basis, as CoVs continue to spread through different vertebrate species, humans, and other animals due to a broad host range. It was thought that SARS-CoV-2 was first spread by animals to people before being maintained by human-to-human transmission. (Nishiura *et al.*, 2020).

The respiratory pathway is where SARS-CoV-2 may spread if it is a food-borne CoV infection. According to literature documents, several SARS-CoVs with bat origins were likely capable of infecting humans. Researchers predicted that bats would play a part in the inception and spread of the current SARS-CoV-2 pandemic after it was shown that bats were involved in transmitting SARS-CoV and MERS-CoV. (Malik *et al.*, 2020)

The horseshoe bat, a species thought to serve as a maintenance host for earlier SARS-related CoVs, was the source of the bat coronavirus that was discovered. These two viruses are closely related. As a result, SARS-CoV-2 might have developed due to sequential recombination between the coronaviruses relevant to SARS (Ji et al., 2020a). SARS-CoV-2 was proposed as the reservoir of SARS-CoV 2 based on the codon use bias snake. Several researchers disputed this assertion. This is the rationale behind the suspicion that the zoonotic spillover to humans was caused by the existence of an intermediate animal host. (Murdoch and French, 2020).

Pigs have also contracted the SARS-related coronavirus from people in addition to bats. It is important to note that pigs had historically been the main species for the emergence of numerous novel strains of the influenza A virus. The likelihood of evolution of any unknown virus, including influenza and corona, cannot be eliminated when present in close connection with avian and human species, and because bat CoVs are infecting pigs, including the current situation of increasing SARS-CoV-2 cases. Such a notion requires exploratory studies. (Chen *et al.*,2005).

Pigs can serve as a mixing vessel for influenza viruses if certain conditions are met. The situation may worsen because of their proximity to people and their contact with numerous wild animals during domestic-sylvatic cycles. (Ma *et al.*, 2009).

The most recent animal carriers of human CoV infections have included bats, civets, and camels. The SARS-CoV-2 is believed to have originated from bats and pangolins. We still need to learn more about the actual intermediate host and how emergence occurs. There are two potential emerging scenarios for SARS-CoV-2. The first is that there may have been a natural selection of viruses in an animal host before transmission to humans, and the second is that there may have been a natural selection of viruses in humans following zoonotic transmission (Andersen *et al.*,2020).

SARS-CoV-2 in animals

SARS-CoV-2's receptor is an enzyme called angiotensin-converting enzyme 2 (ACE2). To determine the possible host range of SARS-CoV-2, critical ACE2 residues that recognise the spike/S protein were examined.Rhinopithecusroxellana(golden snub-nosed monkey), Macacamulatta(rhesus macaque), Mustelaermine(stoat), Pagumalarvata(masked palm civet), Rhinolophusmacrotis(big-eared horseshoe bat), Rhinolophussinicus(Chinese rufous horseshoe bat), Rousettus leschenaultia (Leschenault'srousette), Susscrofa(wild boar), Susscrofadomesticus(domestic pig), Mustelaputoriusfuro(ferret),Canis lupus familiaris(dog), Feliscatus(cat), Manisjavanica(pangolin), Rhinolophuspearsonii(Pearson's horseshoe bat), Pteropusvampyrus(large flying fox), Pongoabelii(Sumatran orangutan), Equuscaballus(horse), Bostaurus(cattle),

Pantroglodytes(chimpanzee), Ovisaries(sheep), Papio Anubis (olive baboon), Oryctolaguscuniculus(rabbit), Vulpes(redfox), Phodopuscampbelli(Campbell's hamster), Mesocricetusauratus(golden hamster), Callithrixjacchus(common marmoset), Heterocephalusglaber(naked mole-rat), Ictidomystridecemlineatus(thirteen-lined ground squirrel), andCricetulusgriseus(Chinese hamster) were predicted to possess ACE2 residues that may have the potential to bind to the S protein of SARSCoV (Luan *et al*., 2020a).The list of animal species for which information on natural or experimental infection is available is given in **Table 4**.

Table -4 List of SARS COVID-19 infected animal species

Species	**Type of infection**	**Susceptibility**	**Transmission**
Pigs	Experimental	None	No
Poultry (chicken, ducks, and turkeys)	Experimental	None	No
Dogs	Natural and experimental	Low	No
Cats (domestic)	Natural and experimental	High	Yes, between cats
Tigers and lions	Natural	High	Yes, between animals
Ferrets	Experimental	High	Yes, between ferrets
Minks (American minks, *Neovison vison*)	Natural	High	Yes, between minks and suggested from mink to humans
Egyptian fruit bats (*Rousettus aegyptiacus*)	Experimental	High	Yes, between Fruit bats
Golden Syrian hamsters	Experimental	High	Yes, between hamsters
Macaques (*Macaca fascicularis* and *Macaca mulatta*)	Experimental	High	Yes

Except for chickens, there was a high degree of sequence similarity when the amino acid sequence alignment of ACE2 was compared among species including humans, non-human primates (gibbon, green monkey, macaque, orangutan, and chimpanzee), cats, dogs, bovines, sheep, goats, swine, horses, chickens, ferrets, civets, mice, rats, and Chinese horseshoe bats. At first, it was thought that SARS-CoV-2's intermediate hosts were snakes or turtles. According to a recent study, neither turtles nor snakes can be viewed as intermediate hosts. The animal species have tested positive for SARS-CoV-2 primarily due to close contact with SARS-CoV-2 sick humans. Pigs and poultry are not susceptible to SARS-CoV-2 infection, according to preliminary findings from studies on experimental conditions. (Li *et al*., 2020a). The list of animal species for which information on natural or experimental infection is available is given.

Virus in bats

SARS-CoV from humans, SARS-rCoVs from wild predators, and SARS-rCoVs from horseshoe bats, SARS-CoV-2 is a member of SARS-rCoV (Genus Rhinolophus) species. Epidemiological studies at the Huanan seafood wholesale market (South China Seafood Market), the biggest seafood market in central China, found that many first patients had been exposed to animals. SARS-CoV-2 is one of hundreds of known viruses mostly isolated from bats (Zhou *et al*., 2020).

Although several viruses have names derived from SARS-CoV, only the viral isolates from the outbreak in 2002–2003 have been proven to cause SARS in people. Through the S protein's receptor binding domain (RBD), SARS-CoV-2 interacts with the ACE2 receptor. Likely originating from bats is SARS-CoV-2 as well. Following genomic sequences now available, strain Bat CoVRaTG13, which was found in a bat named Rhinolophusaffinis in the Yunnan province of China, is

the virus that is most closely related to SARS-CoV-2 (96.2% nucleotide sequence identity) (Tang et al., 2020). With less than 75% nucleotide sequence identity to all previously characterised SARS-rCoVs, the receptor-binding spike protein of SARS-CoV-2 is exceptionally different from other CoVs, except a 93.1% nucleotide identity to BatCoVRaTG13 (Gorbalenya *et al.*, 2020).

The ACE2 receptor is used by SARS-CoV-2, which also differs from SARS-CoV in five of the six critical amino acid residues in the RBD. These same residues, however, are identical to those of pangolin SARS-rCoVs, and one of them is similar to those of BatCoVRaTG13, despite the latter showing the highest nucleotide sequence identity with SARS-CoV-2 across the entire genome. Therefore, it was tempting to hypothesise that the RBD region of SARS-CoV-2 would have resulted from a recent recombination event in pangolins or that SARSCoV-2 and SARS-rCoVs of pangolins are the product of coincidental evolution. (Tang *et al.*, 2020).

Malayan pangolins

Manisjavanica, a species of Malayan pangolin, was taken from southern China, and SARS-CoV-2-related CoVs were found in them. The detected pangolin-associated CoVs belonged to sub-lineages of SARS-CoV-2-related CoVs, and their genomic sequences showed a striking similarity to the RBD of SARS-CoV-2. These results indicate that pangolins could play a significant host role in creating novel CoVs like SARS-CoV-2. A SARS-CoV-2-like CoV, known as Pangolin-CoV, was discovered through genomic and evolutionary research in dead Malayan pangolins (Lam *et al.*, 2020).

SARS-CoV-2 (91.02%) and BatCoV RaTG13 (90.55%) are more closely related to each other than Pangolin-CoV (91.02%). These findings imply that pangolins may serve as a natural reservoir for CoVs similar to SARS-CoV-2. While an investigation of the RBD area did not rule out the idea that pangolins could serve as intermediate hosts for SARS-CoV-2, genetic analysis of genomic regions other than the RBD shows that pangolin CoVs cannot be considered the direct origins of SARSCoV-2. The theory that SARS-CoV-2 originated from pangolins was rejected based on two key findings. The human-isolated SARS-CoV-2 possesses a unique peptide (PRRA) insertion that contributes to the spike protein's proteolytic cleavage. The coronavirus obtained from pangolins lacked this RRAR pattern. Additionally, it was discovered that pangolin CoVs were less related to SARSCoV-2 than the bat-isolated BetaCoV/Yunnan/RaTG13/2013 virus. (Tiwari *et al.*, 2020).

Malayan tiger

SARS-CoV-2 was identified in a tiger kept at the Bronx Zoo in New York City by the National Veterinary Services Laboratories (NVSLs) of the United States Department of Agriculture (USDA). This tiger was examined right away after exhibiting respiratory disease symptoms. This was the first instance of SARS-CoV being transmitted by people to a wild animal. According to reports of SARS-CoV-2 infection in domestic and wild animals, this Malayan tiger is thought to have contracted the disease from an asymptomatic SARS-CoV-2-positive zookeeper. (USDA, 2020).

Ferrets

Ferrets are incredibly vulnerable to SARS-CoV-2, with effective virus replication starting as early as two days after infection in the upper respiratory tract (nasal turbinates, soft palate, and tonsils). Nasal washes had the highest viral titres. (Kim *et al.*, 2020).

Although viral RNA was found in rectal swabs of infected ferrets, replication does not seem to occur in the lower respiratory tract, even in intra-tracheal inoculation animals. Replication may, however, occur in the digestive tract. Low levels of antibodies were detected significantly more. Direct contact and the respiratory droplet pathway are the most efficient ways to spread the virus to other ferrets who are close. (Shi *et al.*, 2020).

Increased body temperatures, hunger loss, decreased activity, and sporadic coughing were seen. The clinical disease picture in infected ferrets and people is similar, and SARS-CoV-2 replicates effectively in the upper respiratory tract of ferrets, making them an excellent animal model for testing COVID-19 vaccine or antiviral medication candidates. (Richard *et al.*, 2020).

Cats

Cats are also susceptible to SARS-CoV-2 infection; after nasal inoculation, virus replication occurs in the upper respiratory tract (Shi et al., 2020). Peak oral and nasal virus shedding was observed 3 days after direct injection (dpi) in three cats and 7 days after exposure in two infected animals. Both direct contact and indirect transmission via aerosols take place. Juvenile cats (70 to 100 days old) are allegedly more vulnerable to severe clinical disease and death due to experimental exposure, leading to subclinical and symptomatic infections. Cats that were experimentally infected and those in contact had antibody titres recorded. (Shi et al., 2020).

Significant neutralising antibody titres that increased or stabilised from 14 dpi to 42 dpi were generated in infected cats. A slight rise in antibodies was seen after the cats were re-challenged with SARS-CoV-2 at 28 days post-infection, and no cats shed any virus during the following 14 days (Bosco-Lauth et al., 2020).

Cats have a high frequency of ACE2-expressing cells and a high proportion of cells that co-express ACE2 and TMPRSS2, two targets for SARS-CoV-2 entrance. Additionally, these target cells are widely distributed throughout cats' digestive, respiratory, and urinary systems, indicating that they may be vulnerable to infection and transmission through various channels (Chen et al., 2020).

Dogs

Five beagles were intranasally infected with SARS-CoV-2, and samples were collected over two weeks for analysis. Three of the dogs' rectal swabs between 2 and 6 dpi showed viral RNA. During the study period, no virus was found in any oropharyngeal swabs obtained from the dogs, and no virus was found in any organs or tissues upon autopsy. Attempts at virus isolation also came up empty-handed. Although neither of the two beagles was kept in close quarters, antibodies were found in the serum of 2/4 experimentally afflicted dogs (Shi *et al.*, 2020). The reduced vulnerability of dogs to SARS-CoV-2 infection may be brought on by deficient levels of co-expression of ACE2 and TMPRSS2 target receptors in canine lung cells and changes in crucial amino acid sequences in ACE2 receptors. (Chen *et al.*, 2020)

Syrian golden hamsters

With viral replication starting in the epithelial cells of the digestive and respiratory tracts after intranasal injection, SARS-CoV-2 infections in Syrian golden hamsters appear to have traits with moderate conditions in human patients. Around 2 to 3 days post-infection, the lungs showed a peak viral load of 105–107, and high viral RNA copy numbers were still detectable. Syrian hamsters experienced modest clinical symptoms such as weight loss, fast breathing, and postural alterations; older hamsters (32–24 weeks) showed more dramatic and consistent weight loss than younger hamsters (6 months) (Osterrieder *et al.*,2020).

Non-human primates

A variety of non-human primate species, such as Rhesus macaques (Macacamulatta), cynomolgus or crab-eating macaques (Macacafascicularis), common marmosets (Callithrixjacchus), and African green or vervet monkeys (Chlorocebusaethiops), have been the subject of experimental infection research. The most vulnerable species to SARS-CoV-2 infection were rhesus macaques (Macacamulatta), next cynomolgus or crab-eating macaques (Macacafascicularis), and finally, common marmosets (Callithrixjacchus). (Lu et al., 2020).

SARS-CoV-2, shed from the upper respiratory tract, was found in blood, nasal, throat, and anal swabs, as well as in all three monkey species. According to Denis et al. (2020), infections in all investigated monkey species varied from asymptomatic to slight nasal discharge and periodic or sporadic elevations in body temperature. Anorexia, postural alterations, weight loss, moderate respiratory illness with coughing, and some radiographic chest abnormalities were identical to those seen in human COVID-19 patients. (Rockxet al., 2020).

In seriously injured animals, a temporary drop in lung tidal capacity was accompanied by severe gross pathology in the heart, stomach, and lower respiratory tract, including diffuse interstitial pneumonia. However, ileum and tracheobronchial lymph nodes were also shown to contain viral replication, which was most prominent in lung tissue. One study noted a second recrudescent period of viral shedding from the respiratory and digestive tracts in all infected macaques, including subclinical animals, between 14-21 dpi. Viral shedding in oropharyngeal swabs peaked between 1 and 5 dpi and decreased below detectable levels by day 9. (Hartman *et al.*, 2020).

Some animals tested positive for anal and rectal swabs up to 11- and 20-days post-inoculation. Oldercynomolgus macaques had higher viral RNA levels in their nasal swabs than younger ones. Antibodies against the S1 domain and nucleocapsid proteins of SARS-CoV-2 were found in peripheral blood and could be detected by RT-PCR. (Rockx *et al.*, 2020).

Fruit bats

The upper and lower respiratory tracts of fruit bats (Rousettusaegyptiacus) intra-nasally infected with SARSCoV developed transitory infections, and virus replication was found in the nasal epithelium, trachea, lung, and lung-associated lymphatic tissue. At 4 dpi days following the illness of the experimentally inoculated bats, an infectious virus was found inoculated from the nasal epithelium and trachea of one bat. None of the bats showed any clinical symptoms, high body temperatures, weight loss, or mortality; these traits are compatible with those of a reservoir host. (Schlottau *et al.*, 2020).

Tree shrews

Given their genetic similarity to primates and their employment in biomedical research as animal models for viral diseases such as hepatitis B, influenza, and Zika viruses, tree shrews (Tupaiabelangeris) were evaluated as prospective animal models for SARS-CoV-2 infection. The one study that did restrict virus replication in tree shrews used intra-nasal SARS-CoV-2 inoculations. Swabs from the nose, throat, and anal regions contained SARS-CoV-2 RNA. In the early stages of viral infection, viral shedding was highest in young animals, and it lasted the longest in adults and older animals, especially in the males of these groups. Except for one adult animal with significant lung disease, all organs were morphologically normal, and histological alterations were often modest. (Zhou *et al.*, 2020).

Pigs

Pigs could not contract SARS-CoV-2 in an experiment and were thought to be immune to the virus (Shi et al., 2020). SARS-CoV-2 targets cells that co-express ACE2 and TMPRSS2 receptors for viral entry and these receptors are broadly expressed in a range of swine kidney and lung cells. Pigs may be able to serve as intermediate hosts for SARS-CoV-2, according to the authors (Chen *et al.*, 2020).

Animal models

There are currently no animal model studies for SARS-CoV-2. A recent study investigated the use of non-human primates, Rhesus macaques, as a model for SARS-CoV-2 investigations. The effectiveness of MERS-CoV vaccinations and antivirals was examined in non-human primates. Rhesus macaques were used to research SARS-CoV-2, and oral-nasal and rectal swabs were found to contain significant amounts of the virus (Wit *et al*., 2020).

The model's usefulness in examining the pathophysiology of this illness and assisting in developing and testing vaccines and antivirals was demonstrated by apparent disease lesions in lung radiographs and clinical symptoms lasting up to 16 days.SARS-CoV-2 isolation from dogs is also reported. (Munster *et al.*, 2020).

SARSCoV-2 replicates ineffectively in dogs, pigs, chickens, and ducks but successfully in ferrets and cats. Cats can spread disease using droplets. Specific animal models are required for reliable research, especially those with ACE2 receptors comparable to those in humans. (Shi *et al.*, 2020).

Developing effective animal models will aid in developing medicines and prophylactics, in addition to assisting in the study of the disease process. Non-human primates are regarded as the best animal models for studying the etiopathogenesis of human diseases, while other animal models are favoured for studying the immune response. (Andersen *et al.*, 2020).

Animal models for SARS and MERS are employed in non-human primates, mice, and hamsters; some may carry SARS-CoV-2. Golden Syrian hamsters have been studied for vaccine protection tests against SARS-CoV strains, and they have been proposed as a suitable animal model for exposing CoV pathology and pathogenesis, as well as vaccine efficacy to be assessed. Since there are structural changes between ACE 2 receptors in different animal species, to which the receptor binding domain of the spike protein of SARS-CoV-2 interacts, transgenic animals have a higher relevance for imitating SARS-CoV-2 (Roberts et al., 2008). Since mice and rabbits are readily available, inexpensive, and simple to handle, they are frequently chosen as small animal models. Mice first seemed difficult because of the different ACE2 receptor usage patterns. However, transgenic mice are now considered applicable to SARS-CoV models (Wang, 2020).

CONCLUSION

The present review has highlighted that the emergence of the Zoonotic disease SARS CoV and its geographical spread is complex and that the multiple factors involved at various levels play a critical role in its emergence, which includes the pathogen, environment, animals and humans. The host source of SARS-CoV is not yet confirmed. However, some analyses suggest that bats are the key reservoir. Environmental changes may be the reason for the coronavirus spill from animals to humans.

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