Animal coronaviruses and coronavirus disease 2019: Lesson for One Health approach

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Abstract

Coronaviruses are a group of enveloped, single-stranded, positive-sense RNA viruses that are broadly classified into alpha, beta, gamma, and delta coronavirus genera based on the viral genome. Coronavirus was not thought to be a significant problem in humans until the outbreak of severe acute respiratory syndrome in 2002, but infections in animals, including pigs, cats, dogs, and poultry, have been problematic for a long time. The outbreak of coronavirus disease 2019 in December 2019 in Wuhan, China, drew special attention towards this virus once again. The intermediate host of this novel coronavirus, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), is yet to be determined, but it has a very close genomic relationship with the bat coronavirus (Bat-CoV), RaTG13 strain, and the pangolin coronaviruses. As veterinary medicine has a long-term experience dealing with coronaviruses, this could be helpful in better understanding and detecting the origin of SARS-CoV-2 and drive human medicine towards the development of vaccines and antiviral drugs through the collaborative and transdisciplinary approaches of One Health.

Keywords: Animal Coronaviruses, COVID-19, One Health, SARS-CoV-2.

Introduction

Coronaviruses (CoVs) (Subfamily Orthocoronavirinae, family Coronaviridae, order Nidovirales) are a group of large, enveloped, single-stranded, positive-sense RNA viruses having exceptional genetic variations (Masters, 2006). Due to mutations and various viral recombination events that have led to the continuous emergence of new viral strains with higher virulence property, the ability to spillover and expand to multiple host range exists (Buonavoglia et al., 2006; Masters, 2006). The structural morphology of virus appears to be moderately pleomorphic or roughly spherical with club-like projections formed by the spike protein and helically symmetrical nucleocapsid that encloses the single-stranded RNA when viewed under the electron microscope (Kolesnikova *et al*., 2003). The viral genome is linear and monopartite, consisting of 26–32 Kilobases with 51 terminal cap structures and 31 poly-A tails which act as the initial RNA for the infectious cycle, the template for viral replication and viral transcription, and also as a substrate for packaging of progeny virus (Masters, 2006; Pradesh *et al*., 2020). Based on the comparisons on the sequence of entire viral genomes, the International Committee for Taxonomy of Viruses (ICTV) classified CoVs into four main genera: Alphacoronavirus, Betacoronavirus, Gammacoronavirus, and Deltacoronavirus (Gorbalenya *et al*., 2004).

During the early weeks of December 2019, several fatal cases of pneumonia with an unknown origin were reported in the city of Wuhan, Hubei Province of China, among those who had visited the wet seafood market which is the center for trade and marketing of other wild species (Lu *et al*., 2020). The suspected patients exhibited signs of respiratory illness, sneezing, coughing, dyspnea, severe chest pain, nausea, and diarrhea, and death was reported in comparatively older people (Gao, 2020; Lu *et al*., 2020). Genetic and molecular analysis revealed that the causative agent was the coronavirus, which was different from the previous human CoVs, and hence was provisionally named as novel CoV of 2019 (2019-nCov) by the World Health Organization (WHO) and the disease associated with it was called as coronavirus disease 2019 (COVID-19) (Du Toit, 2020). Later on, ICTV named the virus as severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) (Gorbalenya *et al*., 2020).

Considering the rapid outbreak of COVID-19, on 30 January 2020, the disease was declared as a Public Health Emergency of International Concern (WHO, 2020a), which was ultimately declared as a global pandemic by the WHO on 11 March 2020 (WHO, 2020b). The rapid spread and high severity of the disease caused 11.87 million infections across 216 reported countries, where more than 545,000 people died as of 9 July 2020 (WHO, 2020c). The origin of the disease is supposed to be from the bat and the intermediate hosts

are yet to be confirmed. With the potential chance of reverse spillover from humans to animals and pets, it is necessary to summon the representatives from different fields and counteract the situation with the collaborative One Health approach. This article highlights about CoVs in different animals, COVID-19 in animals and need of One Health approach for prevention and control of zoonotic infectious diseases.

Previous experiences with animal CoVs

The spread of different zoonotic and vector-borne diseases to humans and the reverse spillover of pathogens, like West Nile virus and Chikungunya virus, depend on various environmental factors, like climate change, deforestation, and rapid urbanization (McMahon *et al*., 2018). The destruction of natural habitats of the disease reservoir animals maximizes their close association with humans which can lead to the emergence of new zoonotic diseases, like Ebola virus, Hendra virus, Nipah Virus, Hanta virus, and SARS-CoV-2 (Lorusso *et al*., 2020).

CoVs have the ability to infect different animals that may include humans, farm animals, companion animals, bats, laboratory animals, wild animals, and marine whales (Salata *et al*., 2020). Alphacoronaviruses and betacoronaviruses infect bats and other mammals only, whereas gammacoronaviruses and deltacoronaviruses infect birds, but some of them can also infect mammals and fishes as well (Table 1) (Cui *et al*., 2019).

Infectious bronchitis virus (IBV), a member of gammacoronavirus, is the most common avian coronavirus that causes avian infectious bronchitis (IB) disease (Dhama *et al*., 2014). IB is responsible for significant morbidity and mortality in the poultry population, including pheasants, turkeys, and guinea fowls of all ages (Smith *et al*., 2015). Especially birds of younger age groups are highly susceptible, causing massive economic losses to the global poultry industry (Dhama *et al*., 2014; Smith *et al*., 2015). After the introduction of the virus in the birds through different routes, like feco–oral route and airborne transmission,

Table 1. Coronaviruses that affect different animal species.

S. No.	Susceptible species	CoV genus	Strain of virus	References
1.	Avian	Gamma Coronavirus	IBV	(Dhama *et al*., 2014)
		Delta Coronavirus	Bulbul coronavirus HKU11	(Paim *et al*., 2019)
			Wigeon coronavirus HKU20	
			White-eye coronavirus HKU16	
			Common moorhen coronavirus HKU21	
			Munia coronavirus HKU13	
			Night-heron coronavirus HKU19	
2.	Swine	Alpha Coronavirus	PRCoV	(Saif, 2004; Wang *et al*., 2019)
			TGEV	(Schwegmann-Weßels and Herrler, 2006; Wang *et al*., 2019)
			PEDV	(Banerjee *et al*., 2019; Lee, 2015)
			SADS-CoV	(Zhou *et al*., 2018)
		Beta Coronavirus	Porcine hemagglutinating PHEV	(Mora-Díaz *et al*., 2019)
		Delta Coronavirus	PDCoV	(Jung *et al*., 2016)
3.	Ruminants and wild animals	Beta Coronavirus	BCoVs	(Decaro *et al*., 2008; Suzuki *et al*., 2020)
			Bovine-like coronaviruses	
4.	Horse	Beta Coronavirus	ECoVs	(Guy *et al*., 2000; Sanz *et al*., 2019)
5.	Donkey and dromedary camel	Beta Coronavirus	MERS-CoV	(Kandeil *et al*., 2019; Meyer *et al*., 2015)
6.	Canine	Alpha Coronavirus	CCoV-I	(Escutenaire *et al*., 2007; Licitra *et al*., 2014)
			CCoV-II	
		Beta Coronavirus	CRCoV	
7.	Feline	Alpha Coronavirus	FIPV	(Rottier *et al*., 2005; Tekes and Thiel, 2016)
			FECV	

the virus usually replicates in ciliated epithelial cells of the respiratory tract and causes severe respiratory infections, like coughing, nasal discharge, rales, gasping, swollen sinus, and also affects the digestive, reproductive, and urogenital tract, resulting in nephritis and egg drop syndrome (Weiss and Navas-Martin, 2005; Fan *et al*., 2018). Other CoVs from the deltacoronavirus genus include Bulbul coronavirus HKU11, Wigeon coronavirus HKU20, White-eye coronavirus HKU16, Common moorhen coronavirus HKU21, Munia coronavirus HKU13, and Night-heron coronavirus HKU19 that can severely infect birds with more complications (Paim *et al*., 2019). Even though there were different attempts for effective vaccine development against the CoVs, the rapid mutations and antigenic variations created a hindrance to successfully trigger the local immune response and cure infections (Saif, 2020; Zhang *et al*., 2020b).

Viruses from alphacoronavirus, betacoronavirus, and deltacoronavirus affect the porcine population. Currently, six CoVs are circulating in the swine population. Alphacoronavirus infection in pigs includes four CoVs: porcine respiratory coronavirus (PRCoV), transmissible gastroenteritis virus (TGEV), porcine epidemic diarrhea virus (PEDV), and swine acute diarrhea syndrome coronavirus (SADS-CoV). Deltacoronavirus infection in pigs includes porcine deltacoronavirus (PDCoV), and betacoronavirus responsible for pig disease is porcine hemagglutinating encephalomyelitis virus (PHEV) (Wang *et al*., 2019). PRCoVs cause respiratory infections; TGEV, PEDV, SADS-CoVs, and PDCoVs cause acute gastroenteritis; and PHEV results in severe neurological and digestive disorders (Mora-Díaz *et al*., 2019; Wang *et al*., 2019). TGEV is a highly contagious, economically significant, and the oldest known swine CoV, mostly spread by feco–oral route affecting young pigs. TGEV virus targets the absorptive epithelial cells of villi causing its atrophy, leading to severe diarrhea, vomition, rapid weight loss, and death (Doyle and Hutchings, 1946; Weiss and Navas-Martin, 2005; Schwegmann-Weßels and Herrler, 2006). Currently, live attenuated and inactivated vaccines are available for the pregnant sow. PRCoV, an attenuated variant of TGEV, originated by the deletion of large 5' region in the spike gene of the virus, is an example of the evolution of CoVs with altered virulence property and tropism (Saif, 2004). PEDV is an important enteric virus of swine which was introduced in a pig population in the early 1970s, mostly affecting growing and fattening pigs and is believed to be the consequence of spillover from bats, causing tremendous economic losses to the American, European and Asian pork industries (Lee, 2015; Banerjee *et al*., 2019). More than 8 million piglets died due to PEDV in 2013 in the USA, Canada, and Mexico (Lee, 2015). PEDV, mainly transmitted by the respiratory route, uses the same receptor as TGEV for entry in host cells and it is also closely related to *Scotophilus* bat coronavirus

512, human alphacoronaviruses HCoV-299E, and HCoV-NL63, which are likely to have common evolutionary precursors (Banerjee *et al*., 2019). Various vaccines are designed to cope with PEDV in swine populations (Lee, 2015; Hsueh *et al*., 2020). Digestive and nervous systems in pigs of all age groups are affected by PHEV, which was first isolated in 1962 and the virus was identified as a neurotropic virus, which showed subclinical presence worldwide (Mora-Díaz *et al*., 2019). SADS-CoV, having more than 86% and 96% sequence identity with bat alphacoronavirus HKU2-CoV and *Rhinolophus* spp., respectively, is another virulent swine alphacoronavirus causing enteritis in the small piglets, which indicates that SADS-CoV and HKU2-CoV descended from a common ancestor (Zhou *et al*., 2018). Recently, in 2012, PDCoV, which caused a mild infection to the pigs, was detected in Hong Kong in the porcine population, which is closely related with quail deltacoronavirus UAE-HKU30, and it was proposed that the virus originated from the recombination between sparrow CoV HKU15 and Bulbul CoV HKU11 by host switching activity between avian and mammalian CoVs (Jung *et al*., 2016). In the experimental infection, swines were found to be infected with Middle East respiratory syndrome coronavirus (MERS-CoV) and SARS-CoV, but not with SARS-CoV-2 (Wang *et al*., 2005; Vergara-Alert *et al*., 2017; Shi *et al*., 2020).

Ruminants and wild animals are known to be infected by the number of CoVs. Bovine coronavirus (BCoV) is the oldest known ruminant CoV of betacoronavirus genus having the ability to cause severe clinical complications, including enteric diseases, like calf diarrhea in neonates and bloody diarrhea in adult cattle, and a respiratory form known as shipping fever in cattle of all age groups (Decaro *et al*., 2008; Suzuki *et al*., 2020). BCoVs are thought to be evolved from rodent CoVs and transmitted by the feco–oral route, mainly causing villous atrophy of small and large intestines leading to severe bloody diarrhea (Carman and Hazlett, 1992; Corman *et al*., 2018). Various bovine-like CoVs have been reported from domesticated animals, such as sheep and goats, water buffalo, llamas, alpacas, and some wild ruminants, such as sambar deer, white-tailed deer, sika deer, water deer, caribou, and elk (Jin *et al*., 2007; Kim *et al*., 2018). Similar type of viruses are also found in various species of antelopes, bisons, giraffes, and dromedary camels (Hasoksuz *et al*., 2007; Jin *et al*., 2007; Kim *et al*., 2018).

Equine CoVs (ECoVs), first reported from the fecal samples in 1999 in North Carolina (USA), are the only CoVs that have been reported in horses, especially in foals of less than 2 weeks of age (Guy *et al*., 2000; Sanz *et al*., 2019). ECoVs are thought to be descendants of BCoVs, and are responsible for causing self-limiting enteritis in the horse population (Pusterla *et al*., 2018; Sanz *et al*., 2019). Horses are not naturally infected by MERS-CoVs; however, research in Egypt showed

that 3 out of 42 donkeys were detected with MERS-CoV RNA in their respiratory specimen (Meyer *et al*., 2015; Kandeil *et al*., 2019). Canines are also infected by CoVs, two from alphacoronaviruses: canine enteric coronaviruses (CCoV-I and CCoV-II), and one from betacoronavirus genus: canine respiratory coronavirus (CRCoV) (Escutenaire *et al*., 2007; Licitra *et al*., 2014). Both CCoV-I and II affect the gastrointestinal tracts of dogs of all ages, but puppies are known to be affected more severely and simultaneous infection of both the virus may favor the recombination of the viral genome. TGEV is more analogous with CCoV and it is believed that TGEV originated from CCoV-II (Perlman and Netland, 2009). CRCoV, which causes severe respiratory infections, known as kennel cough, is more related to BCoVs (Erles *et al*., 2007).

Feline populations can be infected with two CoVs from alphacoronavirus genus, viz. feline infectious peritonitis virus (FIPV) and feline enteric coronavirus (FECV), which mainly affect the respiratory tract, abdominal cavity, and central nervous system, leading to severe enteritis and infectious peritonitis mainly in very young and old animals with suppressed immunity for both domestic and wild felines (Tekes and Thiel, 2016). It is believed that FIPV originated from FECV due to mutation of the *S* gene (Rottier *et al*., 2005; Pradesh *et al*., 2020).

Before the epidemic outbreak of SARS-CoV, bats were not considered as the natural host of CoVs. After that, many CoVs in bats have been identified and they are now considered as a natural reservoir of alphacoronavirus and betacoronavirus, and to date, more than 200 novel CoVs have been identified in bats (Poon *et al*., 2005; Chen *et al*., 2017). CoVs in bats have been reported from all continents, where the alphacoronavirus was found to be more widespread than betacoronavirus (Wong *et al*., 2019). Bats remain as an asymptomatic carrier and harbor CoVs persistently while searching for food and might shed virus in extensive areas close to humans by direct and indirect contacts (Fan *et al*., 2019). Also, in various countries, including China, bats are used as a source of food and in traditional Chinese medicine that increases the risk of transfer of novel zoonotic CoVs risking the human lives (Fan *et al*., 2019; Wong *et al*., 2019).

Previous experiences with human CoVs
Before the outbreak of SARS in 2002 in Guangdong Province, China, CoVs were not considered as a highly pathogenic virus to the humans (Zhong *et al*., 2003). SARS-CoV shocked the entire world becoming the first epidemic of the 21st century with high virulence property and efficient transmissibility among human populations, infecting more than 8,000 peoples from 26 different countries and resulting in 774 deaths (WHO, 2004). The virus is mainly transferred through respiratory droplets and by the feco–oral route, and each positive person can infect two to four healthy

individuals (Lee *et al*., 2003; Peiris *et al*., 2003a, 2003b). Although the incubation period is 4–7 days, viral load reaches peak on the 10th day, infecting all age groups and developing pneumonia with fever, myalgia, malaise, respiratory complications, pleurisy, and diarrhea as late symptoms (Peiris *et al*., 2003a; Scales *et al*., 2003). The outbreak of SARS not only affected human health but also heavily affected the global economy, with restrictions in travels and trade making a global loss of 40 billion dollars (To *et al*., 2013). After a decade of emergence of SARS-CoV, another highly pathogenic coronavirus, MERS-CoV, emerged in Saudi Arabia and other Middle Eastern countries (Zaki *et al*., 2012). MERS spread to 27 countries where a total of 2,494 positive cases had been reported with a case fatality of 34.4% globally, while Saudi Arabia alone had 2,102 cases with 780 deaths, 37.1% death rate, till the end of November 2019 (WHO, 2020d). The viral sequence obtained from infected humans and dromedary camels was found to be almost identical, which concludes that human infection with MERS originated from camels (Raj *et al*., 2014; Gautam *et al*., 2020).

Majority of CoVs associated with humans cause many respiratory diseases, like nasal discharge, common cold, cough, pneumonia, and bronchitis and enteric and neurological problems, especially affecting the elderly, children, and immunocompromised patients (Pene *et al*., 2003; Walsh *et al*., 2013). Human CoVs (HCoVs) are recognized as one of the most rapidly evolving viruses, with the capacity to jump the species barrier and having found the new ecological niche with the novel epidemiologic phenomenon (Vijgen *et al*., 2005). Rapid urbanization and modern farming systems favor the emergence of novel HCoVs by frequent mixing of species, facilitating genomic recombination of the virus (Jones *et al*., 2013). Seven HCoVs have been identified till date which can infect humans, two belonging to the alphacoronavirus genus and five belonging to the gammacoronavirus genus (Table 2). Four HCoVs, namely HCoV-NL63, HCoV-229E, HCoV-OC43, and HCoV-HKU1, were known to infect humans before the emergence of SARS-CoV (2002), MERS-CoV (2012), and SARS-CoV-2 (2019). Including novel SARS-CoV-2, four HCoVs, HCoV-229E, HCoV-NL63, HCoV-OC43, and HCoV-HKU1, are globally circulating in human populations and are contributing to a majority of common cold infections in humans (Lorusso *et al*., 2020). It has been postulated that the natural hosts for HCoV-NL63 and HCoV-229E are bats and rodents for HCoV-OC43 and HKU1 CoVs. Some CoVs require intermediate hosts before infecting humans, like cattle for HCoV-OC43, alpacas for HCoV-229E, masked Palm civets for SARS-CoV, and dromedary camels for MERS-CoV (Hu *et al*., 2017; Cui *et al*., 2019). SARS-CoV and MERS-CoV have been transmitted to human by masked palm civets

Table 2. Coronaviruses in humans.

Coronavirus genus	Strains	Cellular receptors	References
Alpha coronavirus	HCoV-229E	Human aminopeptidase N (CD13)	(Pene *et al.*, 2003)
	HCoV-NL63	ACE2	(Jones *et al.*, 2013)
Beta coronavirus	HCoV-OC43	9-O-acetylated sialic acid	(Walsh *et al.*, 2013)
	HCoV-HKU1	9-O-acetylated sialic acid	(Arbour *et al.*, 2000)
	SARS-CoV	ACE2	(Arbour *et al.*, 1999)
	MERS-CoV	DPP4	(Ramadan and Shaib, 2019)
	SARS-CoV-2	ACE2	(Tu *et al.*, 2020)

and dromedary camels, respectively (Zhong *et al.*, 2003). Both of these viruses originated in bats, and this concludes the hypothesis that SARS-CoV-2 may also involve an intermediate animal host (Hu *et al.*, 2017).

Coronavirus disease 2019 in animals
The waves of COVID-19 from the Hubei province of Wuhan, China, have caused ripples all around the world and have created havoc with several thousand human deaths and infections across the world except Antarctica. Alongside humans, a number of animals, including dogs and cats (small and large), are also reported to be infected with the disease where transmissions might have occurred from pet owners and zookeepers (Rodriguez-Morales *et al.*, 2020). SARS-CoV-2 has the ability to cross the species barrier, which makes it possible to infect humans, whereas COVID-19-positive humans facilitate the reverse zoonotic transmission of the virus from human to animals (Fig. 1) (Parry, 2020; Zhang *et al.*, 2020b).

Among the reported animals, an infected dog did not show any clinical signs, unlike cats. In March 2020, a Pomeranian and later a German Shepherd were found positive for COVID-19 infection in Hong Kong, whose owners were also the victims of the disease (Parry, 2020). The infected cats, wherein the transmission occurred from humans, were from Belgium, Hong Kong, and New York, that got infected in late March and April 2020 showed variations in the degrees of clinical signs, like mild respiratory illnesses (Parry, 2020). A tiger in a zoo in New York was also tested positive for the disease due to the association with a COVID-19-positive zoo employee (Parry, 2020). Positive cases of COVID-19 in domestic cats have also been reported in France, Spain, Germany, and Russia (Parry, 2020). COVID-19 has also been detected in two mink farms in The Netherlands where minks are supposed to transmit CoV to human (CDC, 2020; Yoo and Yoo, 2020). World Organization for Animal Health (OIE) has reported that, so far, there exists no relevant evidence of animal's role in the spread of the SARS-CoV-2 in the human population (OIE – World Organization for Animal Health, 2020).

One Health perspective
Throughout history, including the current COVID-19 pandemic, human civilizations have been blighted with subtle and impervious emerging and reemerging zoonoses that cost millions of lives and a ruined global economy. The egress and growth of avian and swine influenza viruses, such as Zika virus, Ebola virus, SARS, MERS, and COVID-19, have caused panic around the world and demonstrated how difficult it is to counteract and respond to these changing dynamics of the outbreaks (Streinu-Cercel, 2014; Boeuf *et al.*, 2016; Liu *et al.*, 2020). The emerging diseases are shared between both animals and humans, where about 60% of the emerging pathogens have an animal origin (Jones *et al.*, 2008). Emerging infectious diseases have always been considered as an economic threat, and to prevent the origin and spread of such diseases is of global importance (World Economic Forum, 2010; Morse *et al.*, 2012). Scientists have been warning about the possibility of pandemics, but the world was not prepared in responding to them (Ogawa *et al.*, 2009). Since 1940, more than two-third of the recorded 400 emerging infectious diseases have proved to be zoonotic in nature (Jones *et al.*, 2008; Morse *et al.*, 2012). The close interactions between the people, wildlife, livestock, and favorable environments are one of the major sources of recently emerging infectious diseases, and wildlife accounts for 71.8% of total zoonotic emerging infectious diseases (Caron *et al.*, 2012). Even though the identification and realization of zoonotic diseases are of huge importance, the underlying causes of origin and spread of those diseases have not been given the attention they require (Murray and Daszak, 2013). Veterinarians and epidemiologists have often advocated about the holistic approach of One World One Health to shorten the knowledge gap on disease origin and transmission, but this has not been materialized yet to the extent needed.

Animals and humans encounter each other on daily basis in similar ecological conditions for food, safety, companionships, and aesthetic purposes which create an opportunity for the spillover of viruses from their reservoirs (Taylor *et al.*, 2001). It appears very important to constantly maintain the ecological and biological barrier to intervene in the zoonotic transmission of the disease, which is only possible with the 'One Health' concept. The recent COVID-19 pandemic is
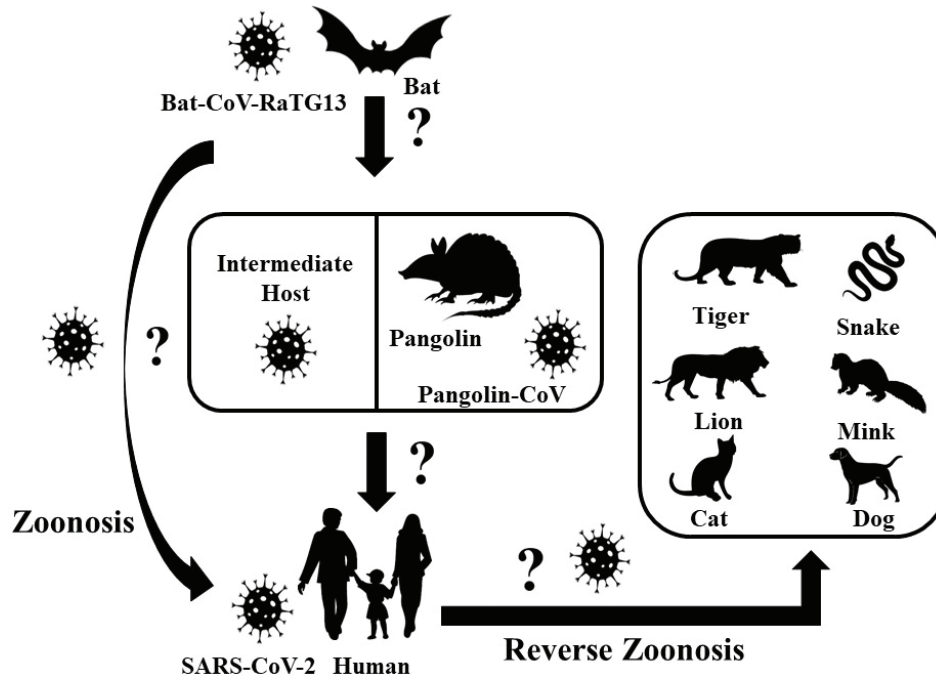
Fig. 1. Possible origin of SARS-CoV-2, and zoonotic and reverse zoonotic transmission possibility. SARS-CoV-2 = severe acute respiratory syndrome coronavirus-2; Bat-CoV = bat coronavirus; Pangolin-CoV = pangolin coronavirus.

also thought to be the result of such close associations between humans and animals (Fig. 2) (Lorusso *et al*., 2020). In order to intervene in the transmission chain of the disease, it is extremely crucial to understand the nature of pathogen transmission and identify the range of reservoirs, hosts, and susceptible animals. During the infection, the receptor-binding domain (RBD) of the virus spike protein identifies the angiotensin-converting enzyme 2 (ACE2) of the host tissues mainly in the pneumocytes of lungs, heart, and kidneys (Tai *et al*., 2020). Therefore, the various species that have ACE2 receptors identical to humans can harbor the disease and get infected. After 96% resemblance of the full-length genome sequence of SARS-CoV-2, obtained from five infected patients, with bat CoV isolate RaTG13, bats were considered as the natural reservoirs (Zhou *et al*., 2020). It is still the matter of concern if the transmission occurs directly from the bats or there are some intermediate hosts involved (Jin *et al*., 2020). In the light of research on intermediate hosts, Ji *et al*. (2020) mentioned the probability of snakes as wildlife animal reservoir based on the relative synonymous codon usage bias. Similarly, Guo et al. (2020), through the introduction of virus host prediction using deep learning algorithm, predicted the infectivity pattern of SARS-CoV-2 and found closeness to minks. Malayan pangolins are the recent discoveries as the intermediate hosts. Pangolin CoVs are believed to be the second closest relative to SARS-CoV-2, after

bat CoV RaTG13, with 91.02% identical genome and 97.1% RDB similarity (Zhang *et al*., 2020a).

Apart from humans, different wild and domestic animals have been diagnosed with infections. The experimental inoculation of the virus on four rhesus macaques by Bao *et al*. (2020) showed weight loss by about 200–400 gm, reduced appetite, transient period increased respiration, and hunched posture without change in rectal temperature. In the necropsy of the same experiment, lung lesions, like interstitial pneumonia, alveolar epithelium degeneration, and inflammatory cells infiltration, were observed in HE staining along with opacity of lungs and interstitial markings observed in X-ray 7 days post-inoculation. *Panthera tigris*, *Felis catus*, and *Canis lupus* with ACE2 similarity of 85.70%, 85.22%, and 84.01%, respectively, also showed the infection and clinical signs (Canrong *et al*., 2020). Although many researches on non-human primates are yet to be carried out, it has been reported by Canrong *et al*. (2020) that the primates like *Gorilla gorilla*, *Macaca nemestina*, *Papio Anubis*, and *Macaca fascicularis* have ACE2 similarity of 99.01%, 95.34%, 95.34%, and 95.21%, respectively, when compared to humans. In the same experiment, they found that the free binding energy of SARS-CoV-2 to ACE2, which also defines the affinity of RBD to ACE2, in the above-listed animals is nearly -51.5 KJmol^{-1} which is very close to free binding energy of SARS-CoV-2 RBD in humans'ACE2 (-50.13 KJmol^{-1}) (Canrong *et al*., 2020).
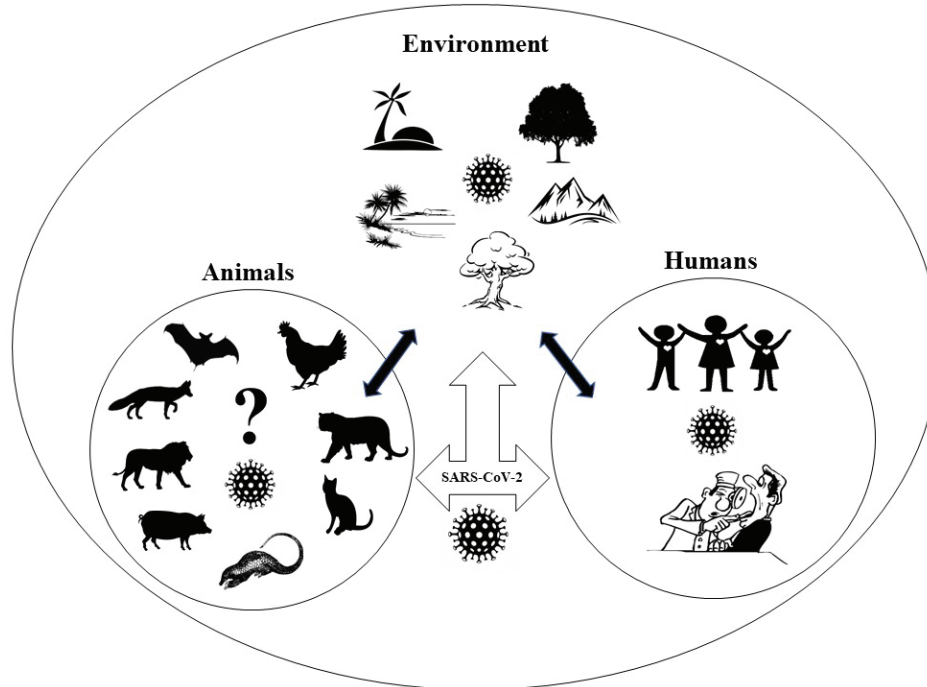
Fig. 2. One Health triad between animals, humans, and environment in the context of COVID-19.

Considering the very similar ACE2 receptor and close free binding energy of these primates when compared to humans, the possibility of the transmission of SARS-CoV-2 to those primates cannot be overlooked.

It is reported that the virus has been transmitted between several animals in nature (Lam *et al*., 2020). Therefore, veterinarians may be very important in identifying the disease dynamics of the CoVs because the virus is not novel for those veterinary virologists who have been working for a long time on the origin, infection, and transmission of CoVs on different animals, like cats, dogs, and pigs (Decaro and Lorusso, 2020). So far, there have been some shreds of evidence of COVID-19 transmission from humans to cats, as well where the veterinary perspective appears to be useful.

One Health approach focuses on the interrelationship between human, animals, and environment for the benefits of all the associated factors (Fig. 2) (Zinsstag *et al*., 2011). Considering the recent global SARS-COV-2 pandemic, there are several areas where One Health approach must be taken into consideration. SARS-COV-2 is a coronavirus of bat origin, transmitted to humans either by spillover from the bats itself or from the intermediate hosts yet to be confirmed (El Zowalaty and Järhult, 2020). It seems very important to identify non-human hosts that may include wild and domestic animals in the concerned seafood market of the epicenter. Only after the identification of the possible intermediate hosts of COVID-19 by effective genetic analysis, a proper One Health approach can be applicable to break the chain of transmission from a reservoir to intermediate hosts, from intermediate hosts to humans and reverse spillover. If the intermediate hosts remain unrevealed, there is a possibility of new disease outbreaks in the near future. So, it is necessary to include representatives from all the disciplines, like epidemiologists, veterinarians, human health professionals, and environmentalists to break the transmission chain of the disease by a collaborative One Health approach (Kelly *et al*., 2017). Only through this approach, all the responsible factors, like humans, hosts animals, reservoirs, environmental situations, can be thought of as a single unit. By maintaining ecological barriers between the animals and humans in their respective habitats, controlling the unmanaged slaughter, and consumption of animals we can reduce the zoonotic risks. Furthermore, it is the role of the veterinarians to inspect the animals in their respective field to reduce the animal to animal transmission, and human health professionals should always be conscious about the possibility of reverse zoonosis. Only when all the concerned authorities work with a common vision and strong mentality, the world can progress as one for the development of effective vaccinations, control of current disease, and prevention of future pandemics.

Conclusion

It is not a novel fact that different families of CoVs have affected different wild and domestic animals for several decades. But only after the first zoonotic incidence of SARS-CoV, at the beginning of this century, major attention was deviated toward CoVs.

MERS-CoV in 2012 and the recent COVID-19 pandemic have once again proved how difficult it is to cope with the emergence of new diseases. Learning from the experiences of veterinary virologists dealing with several coronavirus infections in the past could be an important aspect for not only understanding the SARS-CoV-2 transmission dynamics but also for the development of vaccines and therapeutics. Likewise, environmental factors, like continuous deforestation and unmanaged modernization, have disturbed the ecological niche and broken the natural barriers of humans and animals creating more opportunity for pathogen spillover. Therefore, representatives from human, animal, and environmental sectors should come together to advance the One Health approach and to effectively manage the ongoing COVID-19 pandemic and any pandemics in the future.

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