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Susceptibility to SARS, MERS, and COVID-19 from animal health perspective

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Abstract

Viruses are having great time as they seem to have bogged humans down. Severe acute respiratory syndrome (SARS), Middle East respiratory syndrome (MERS), and novel coronavirus (COVID-19) are the three major coronaviruses of present-day global human and animal health concern. COVID-19 caused by SARS-CoV-2 is identified as the newest disease, presumably of bat origin. Different theories on the evolution of viruses are in circulation, yet there is no denying the fact that the animal source is the skeleton. The whole world is witnessing the terror of the COVID-19 pandemic that is following the same path of SARS and MERS, and seems to be more severe. In addition to humans, several species of animals are reported to have been infected with these life-threatening viruses. The possible routes of transmission and their zoonotic potentialities are the subjects of intense research. This review article aims to overview the link of all these three deadly coronaviruses among animals along with their phylogenic evolution and cross-species transmission. This is essential since animals as pets or food are said to pose some risk, and their better understanding is a must in order to prepare a possible plan for future havoc in both human and animal health. Although COVID-19 is causing a human health hazard globally, its reporting in animals are limited compared to SARS and MERS. Non-human primates and carnivores are most susceptible to SARS-coronavirus and SARS-CoV-2, respectively, whereas the dromedary camel is susceptible to MERS-coronavirus. Phylogenetically, the trio viruses are reported to have originated from bats and have special capacity to undergo mutation and genomic recombination in order to infect humans through its reservoir or replication host. However, it is difficult to analyze how the genomic pattern of coronaviruses occurs. Thus, increased possibility of new virus-variants infecting humans and animals in the upcoming days seems to be the biggest challenge for the future of the world. One health approach is portrayed as our best way ahead, and understanding the animal dimension will go a long way in formulating such preparedness plans.

Keywords: Animal health, COVID-19, Cross-species, One health, Trio coronaviruses.

Introduction

Newer coronaviruses (CoVs) continue to be detected from various wildlife species, most notably the bat (Valitutto *et al*., 2020). It is a fact that humans and their interaction with wildlife is on an increasing frequency. CoVs infect a variety of animal species causing respiratory, hepatic, enteric, and neurological diseases of varying degrees (Woo *et al*., 2012). These are traditionally divided into three groups (groups I, II, and III) based on their serological and genomic characterization (Brian and Baric, 2005). The International Committee on Taxonomy of Viruses proposed replacing the genera for these traditional groups, namely α-coronavirus, β-coronavirus, and γ-coronavirus for group I, II, and III, respectively (Woo *et al*., 2012). Currently, the new genera δ-coronavirus is also grouped; hence, coronaviruses are grouped under four different genera, including severe acute respiratory syndrome (SARS) and Middle East respiratory syndrome (MERS; Xu *et al*., 2016). These genera and viruses possess special characteristics to undergo mutation in order to infect a new host and have the capacity to adapt to a new ecological niche (Woo *et al*., 2012). Thus, understanding these viruses in animals, the eco niche, the mechanism of mutation, and how they spread to other species will be crucial in managing pandemic risks. Research studies have been narrowed down to α- and β-coronaviruses that have originated from the host bats serving as an ancestral origin for mammalian CoVs (Woo *et al*., 2012). In November 2002, a new type of virus was identified in Guangdong Province of Southern China named SARS-CoV. By the end of the epidemic, around 8,437 human cases with case fatality of 9% was detected (Peeri *et al*., 2020; Fig. 1). These viruses were isolated from the palm civet and other game–food mammals in June, 2003 with 98.8% nucleotide similarity to SARS-CoV (Cheng *et al*., 2007). Subsequently, research studies identified the SARS-like coronavirus (SL-CoV) in horseshoe bats acting as a reservoir host and SARS-CoV in several carnivores (civet and raccoon dog) from the Chinese wet market (Bolles *et al*., 2011; Ge *et al*., 2013) acting as a replication host (Guan *et al*., 2003). After SARS, MERS reportedly evolved causing a global health threat in 2012 originating from Saudi Arabia (Mackay and Arden, 2015). Various studies have shown bats as a reservoir host for MERS-CoV since the HKU4 of

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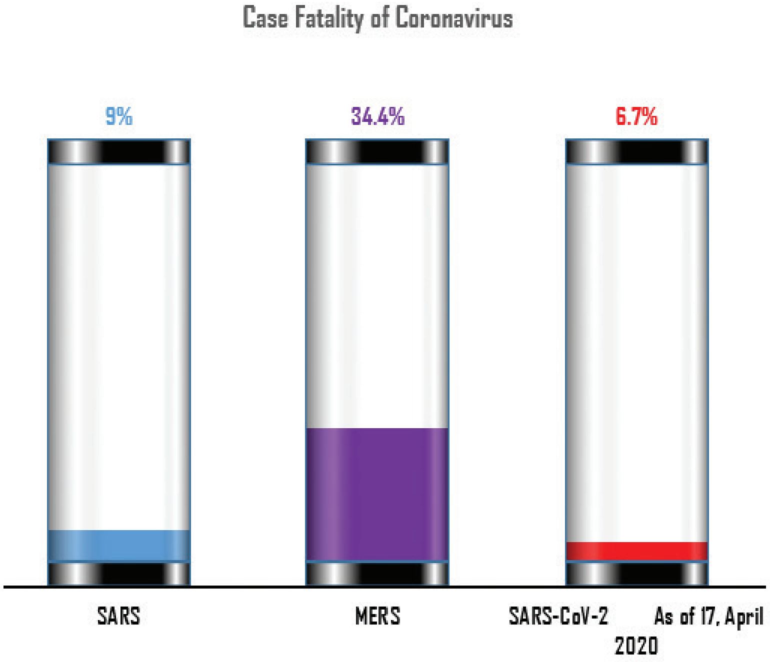

Fig. 1. Comparison of case fatalities in SARS, MERS, and SARS-CoV-2 as of 17 April 2020. It shows highest case fatality for MERS-CoV.

bats resembeled MERS-CoV genetically (Annan *et al*., 2013), but alpacas can also act as a potential reservoir for MERS (Mohd *et al*., 2016). Hemida *et al*., (2013) reported the genome of human origin MERS-CoV being 99.9% similar to the genome of MERS-CoV affecting dromedaries. It is still unclear how the dromedary camels got infected by MERS-CoV; however, a recent study also supports that MERS-CoV jumped from bats to camels in Africa some 20 years ago and these camels were reportedly imported to the Arabian Peninsula (Corman *et al*., 2014). Since 2012, around 2,494 health cases of MERS have been reported with 34.4% case fatality (Al-Omari *et al*., 2019; Fig. 1).

The novel coronavirus (COVID-19) epidemic is the current concern and is reported to have been detected in later part of the year 2019, hence, named from the wet market in Wuhan city in China. Various opinions on the origin of the virus is in discussion, including the theory of engineered virus spillage. The etiological agent for COVID-19 is SARS-CoV-2 (Tang *et al*., 2020). The virus is phylogenetically originated from bats (Cui *et al*., 2019; Li *et al*., 2020). The recent findings postulated that the SARS-CoV was genetically similar to bat-CoV of subgenus Sarbecovirus (Wu *et al*., 2020; Xu *et al*., 2020). Thus, the identified genome of COVID-19 has a 96.2% genomic similarity to bat-CoV (RaTG13) in China (Zhou *et al.*, 2020), but has around 79% and 50% genomic similarity to SARS-CoV and MERS-CoV, respectively (Lu *et al*., 2020). Anteaters and snakes are also reported to be possible reservoirs for COVID-19 (Ji *et al*., 2020). COVID-19's spread is happening globally at this moment, and around 2.2 million counting humans have tested positive with fatality of 6.7% detected since its outbreak until April 17, 2020 (WHO, 2020; Fig. 1). In addition to humans, several animals like cats, dogs, and tigers also tested positive, but no animal to animal or animal to human transmission is reported. The objective of this review article is to summarize all the deadly coronaviruses reported from animals and their possible cross-species transmission pattern along with phylogenetic modification. The objective is to present a concise and updated article for the growing attention on, interest in, and focus on this topic.

Phylogenic Modification

SARS-CoV

SARS appeared for the first time in 2002 in Guangdong Province, Southern China (Hu *et al*., 2015). After its emergence, SARS-CoV was confirmed in palm civets and horseshoe bats from the wet market in Guangdong Province, as reservoirs of SARS-CoV (Luk *et al*., 2019). Before the appearance of SARS, around 10 CoVs genome sequences were available and placed into three groups, namely groups I, II, and III. However, later the International Committee on Taxonomy of Viruses announced three genera for these groups, namely alphacoronavirus, betacoronavirus, and gammacoronavirus (de Groot *et al*., 2011). The discovery of SARS-CoV in 2003 and its phylogenic evidence placed SARS-CoV into the betacoronavirus, and subsequently, into the subgenus Sarbecovirus (Luk *et al*., 2019). Among these coronaviruses, the alpha and beta mainly infect mammals, and the assigned species (almost 7 out of 15) of viruses were reported in bats (de Groot *et al*., 2011). Hence, it is proposed that bats are an important source in the evolutionary analysis (Woo *et al*., 2012). Phylogenic modification of 16BO133 strain of the bat coronavirus is placed in beta-CoV lineage which is closely related to the JTMC15 strain of the horseshoe bat (*Rhinolophus ferrumequinum*) isolated in China (Kim *et al*., 2019).

MERS-CoV

Middle East respiratory syndrome (MERS) was classified into the family coronaviridae, subfamily coronavirinae, and genus *betacoronavirus* (Bayrakdar *et al*., 2015). The closest ancestors of MERS-CoV, namely SARS-CoV and human CoV-229E, phylogenetically evolved through the Vespertilionidae (insectivorous bat) family and belong to *Neoromicia* and *Pipistrellus* (Annan *et al*., 2013). The *Tylonycteris* bat coronavirus HKU4 (Ty-BatCoV HKU4) and *Pipistrellus* bat coronavirus (Pi-BatCoV HKU5) genomes of bat resemble with MERS-CoV, hence, considered as a reservoir host, but alpacas also act as a potential reservoir for MERS-CoV (Mohd *et al*.,2016. The first report of MERS identified it as a novel betacoronavirus (MERS-CoV) (Zaki *et al*., 2012). The evolutionary history of MERS-CoV reported its evolution through a genetic recombination of MERS-CoV clade A and B (Wang *et al*., 2015). This genomic recombination occurred in two groups (groups III and V) among the five phylogenic groups of clade B (Wang *et al*., 2015).

SARS-CoV-2

Belonging to family *Coronaviridae* and genus *β-coronavirus*, SARS-CoV-2 shares a similar genetic make-up with Bat-CoV (RaTG13/Beta-CoV) and an almost similar make-up with snakes; hence, considered as a reservoir for COVID-19 (nCoV; Ji *et al*., 2020; Zhang *et al*., 2020). Convergent evolution through homologous recombination between this virus and a virus of unknown origin makes it different from the coronavirus of human origin (Ji *et al*., 2020; Sun *et al*., 2020). SARS-CoV-2 shares almost a 91.02% character similarity to pangolin-CoV and 90.55% with RaTG13 (Zhang *et al*., 2020). But the difference in the neutral site of RaTG13 and SARS-CoV-2 is almost 17%, suggesting a much larger divergence between these two viruses than previous estimated study (Tang *et al*., 2020). The developing variation is due to the variation raised in the Ras-binding domain of the glycoprotein spike, which acts as an angiotensin-converting enzyme-2 (ACE-2), and the genetic mutation of pangolin SARS-CoV is most likely a genetic recombination (Tang *et al*., 2020). The evolutionary tree indicates that SARS-CoV-2 is closer to RaTG13, followed by the pangolin SARS-CoV (Tang *et al*., 2020).

Susceptibility in Animal Species

SARS-CoV

In addition to reservoir (horseshoe bat) and replication intermediate (Himalayan palm civet and raccoon dog) hosts, various non-human primates are liable to be infected, causing a fever and quite, mildly labored breathing in aged animals (Smits *et al*., 2010). The susceptibility of various species with SARS-CoV is shown Table 1.

MERS-CoV

The life-threatening diseases of humans somehow have possible links with the animal species. MERS, although recognized as a disease of the dromedary camels, causes asymptomatic or mild respiratory distress (Hemida *et al*., 2014), mild fever, and rhinorrhea (Adney *et al*., 2014). Various other animal species are also found susceptible to MERS-CoV (Table 2). The virus causes mild respiratory problems (respiratory discharges, coughing, sneezing), fever, and loss of appetite in animals (Hemida *et al*., 2014).

COVID-19 (SARS-CoV-2)

The following questions were unknown to scientists during the SARS-CoV-2 pandemic: Does the virus infect animals as well as humans? If yes, what types of animals are more susceptible? Does the virus transmit from animals to humans? At the same time, a report from Hong Kong showed that one Pomeranian tested weakly positive, after which one German shepherd tested positive to SARS-CoV-2 (Cohut, 2020). A report from Belgium also reported SARS-CoV-2 in cats (Jeanna, 2020a). These reports suggest the chance of transmission of SARS-CoV-2 from humans to animals. Because of the contradictory information regarding the possibility of transmission of SARS-CoV-2 in animals, scientists from Harbin Veterinary Research Institute, Chinese Academy of Agricultural Sciences, and the National High Containment Laboratory for Animal Diseases Control and Prevention gathered together and analyzed its susceptibility in different animals. They concluded that cats and ferrets are the most susceptible to SARS-CoV-2 infections, but virus multiplication in dogs, pigs, chickens, and ducks are poor, and there was no intraspecies and interspecies transmission of SARS-CoV-2 from dogs, pigs, chickens, and ducks (Shi et al., 2020; Table 3). Wild animals are also susceptible to SARS-CoV-2. The US Wildlife Conservation Society announced on April 5, 2020, cases in a 4-year-old female Malayan tiger together with her sister, two Amur tigers, and three African lions (Jeanna, 2020b).

Bats are supposed to be the natural reservoir for the SARS-CoV-2 because the virus shares a 96% genomic identity to the bat coronavirus and their protein sequence shares a similarity to SARS-CoV (Zhou et al., 2020). Recent findings that analyze the probable animal reservoir to COVID-19 suggest the snake as a reservoir, based on relative synonymous codon usage (RSCU) bias (Ji et al., 2020). The missing link or intermediate link for animal to human transmission of SARS-CoV-2 from a recent study suggests the DNA and protein sequence of Malayan pangolins (Zhang et al., 2020).

Table 1. Susceptibility of various animal species to SARS-CoV.

Order	Family	Animals category	Species	Detection methods	Prevalence	References
Primates	*Cercopithecidae*	Rhesus macaque^{c}	*Macaca mulatta*	Histopathology and radiography	6/6	(Munster *et al.*, 2013)
		Cynomolgus macaque^{c}	*Macaca fascicularis*	Histopathology	12/12	(Smits *et al.*, 2011)
	Canidae	Raccoon dog^{b}	*Nyctereutes procyonoides*	RT-PCR	15/15	(Kan *et al.*, 2005)
				RT-PCR and viral isolation	1/1	(Guan *et al.*, 2003)
		Red fox^{c}	*Vulpes vulpes*	Real-time RT-PCR	3/5	(Wang *et al.*, 2005)
		Chinese ferret-badger^{c}	*Melogale moschata*	Western blot	1/2	(Guan *et al.*, 2003)
Carnivora	*Mustelidae*	Hog-badger	*Arctonyx collaris*	RT-PCR	0/3	(Guan *et al.*, 2003)
		Mink	*Mustela vison*	Real-time RT-PCR	0/1	(Wang *et al.*, 2005)
	Viverridae	Himalayan palm civet^{b}	*Paguma larvata*	Viral isolation	4/5	(Guan *et al.*, 2003)
	Felidae	Domestic cat	*Felis catus*	Real-time RT-PCR	0/13	(Wang *et al.*, 2005)
	Canidae	Domestic dog	*Canis familiaris*	ELISA, RT- PCR	0/20	(Chen *et al.*, 2005)
Artiodactyla	*Suidae*	Pig^{c}	*Sus scrofa domesticus*	RT-PCR, ELISA, Western blotting	2/108	(Chen *et al.*, 2005)
		Wild pig^{c}	*S. scrofa*	Real-time RT-PCR	1/19	(Wang *et al.*, 2005)
	Bovidae	Goat	*Capra hircus*	Real-time RT-PCR	0/3	(Wang *et al.*, 2005)
		Cattle	*Bos Taurus*	RT-PCR, ELISA	0/60	(Chen *et al.*, 2005)
Rhodentia	*Muridae*	Lesser rice-field rat^{c}	*Rattus losea*	Real-time RT-PCR	1/6	(Wang *et al.*, 2005)
Chiroptera	*Rhinolophidae*	Horseshoe bat^{a}	*R. ferrumequinum*	RT-PCR	2/348	(Lau *et al.*, 2015)
Galliformes	*Phasianidae*	Chicken	*Gallus domesticus*	RT-PCR, ELISA	0/11	(Chen *et al.*, 2005)
		Red jungle fowl	*Gallus gallus*	Real-time RT-PCR	0/46	(Wang *et al.*, 2005)
		Green peafowl	*Pavo muticus*	Real-time RT-PCR	0/2	(Wang *et al.*, 2005)
		Common pheasant	*Phasianus colchicus*	Real-time RT-PCR	0/8	(Wang *et al.*, 2005)
		Chinese francolin	*Francolinus pintadeanus*	Real-time RT-PCR	0/2	(Wang *et al.*, 2005)
Anseriformes	*Anatidae*	Spot-billed Duck	*Anas platyrhynchos*	Real-time RT-PCR	0/13	(Wang *et al.*, 2005)
		Greylag goose	*Anser anser*	Real-time RT-PCR	0/12	(Wang *et al.*, 2005)
		Duck	*A. platyrhynchos Domesticus*	RT-PCR, ELISA	0/30	(Chen *et al.*, 2005)

RT-PCR = reverse transcription polymerase chain reaction; ELISA = enzyme-linked immunosorbent assay.

[a] SL-CoV acts as a reservoir host.

[b] SARS-CoV in several carnivores (civet and raccoon dog) acts as a replication host for SARS-CoV.

[c] Other animals susceptible to SARS-CoV.

Table 2. Susceptibility of various animal species to MERS CoV.

Order	Family	Animal category	Species	Detection method	Prevalence	References
Primates	*Cercopithecidae*	Rhesus macaque^{c}	*M. mulatta*	Quantitative RT-PCR	6/6	(de Wit *et al.*, 2013)
Artiodactyla+	*Camelidae*	Llamas^{c}	*Lama glama*	Immunohistochemistry, *in situ* hybridization	3/4	(Vergara-Alert *et al.*, 2017a)
		Dromedary camel^{b}	*Camelus dromedaries*	RT-qPCR, RT-PCR	5/76	(Nowotny and Kolodziejek, 2014)
				RT-PCR	2/14	(Haagmans *et al.*, 2014)
				RT-qPCR	126/131	(Chu *et al.*, 2015)
				MERS-CoV S1 ELISA	502/570	(Falzarano *et al.*, 2017)
				Viral neutralization assay	65/155	(Reusken *et al.*, 2013)
		Alpaca^{a}	*Vicugna pacos*	ELISA, VNT	35/102	(David *et al.*, 2018)
	Suidae	Pig^{c}	*S. scorfa domesticus*	Immunohistochemistry, *in situ* hybridization	2/4	(Vergara-Alert *et al.*, 2017a)
				Viral neutralization assay	4/5	(Vergara-Alert *et al.*, 2017b)
	Bovidae	Cattle^{c}	*B. taurus*	Plate reduction neutralization test (PRNT), RT-PCR	1/53	(Kandeil *et al.*, 2019)
		Sheep^{c}	*Ovis aries*	Viral neutralization assay	0/40	(Reusken *et al.*, 2013)
				Plate reduction neutralization test (PRNT), RT-PCR	35/63	(Kandeil *et al.*, 2019)
		Goat^{c}	*C. hircus*	Viral neutralization assay	0/50	(Reusken *et al.*, 2013)
				Plate reduction neutralization test (PRNT), RT-PCR	5/121	(Kandeil *et al.*, 2019)
Lagomorpha	*Leporidae*	Rabbit	*Oryctolagus cuniculus*	RT-qPCR	0/12	(Widagdo *et al.*, 2019)
Chiroptera	*Emballonuridae*	Bat^{a}	*Taphozous perforatus*	PCR	1/94	(Memish *et al.*, 2013)
			Eidolon helvum	PCR	1/82	(Memish *et al.*, 2013)
	Vespertilionidae	Common wing-bent bat^{c}	*Miniopterus schreibersii*	RT-PCR	4/53	(Luo *et al.*, 2018)
		Japanese pipistrelle^{c}	*Pipistrellus abramus*		15/75	(Luo *et al.*, 2018)
		Asian particolored bat^{c}	*Vespertilio superans*		34/159	(Luo *et al.*, 2018)

Continued

Order	Family	Animal category	Species	Detection method	Prevalence	References
Perissodactyla	*Equidae*	Donkey[c]	*Equus africanus*	Plate reduction neutralization test (PRNT), RT-PCR	3/42	(Kandeil *et al*., 2019)
		Horse[c]	*Equus ferus*	VMN	1/2	(Kandeil *et al*., 2019)
Galliformes	*Phasianidae*	Chicken	*G. domesticus*	pseudoparticle neutralization test (ppNT)	0/240	(Hemida *et al*., 2013)

RT-PCR = reverse transcription polymerase chain reaction; ELISA = enzyme-linked immunosorbent assay; RT qPCR = quantitative reverse transcription polymerase chain reaction; VNT = virus neutralization test; VMN = virus microneutralization.

[a] Bat and alpacas are considered as a reservoir host for MERS-CoV.

[b] Dromedary camel acting as an animal host to transmit virus to animals.

[c] Other animals susceptible to MERS-CoV.

Table 3. Susceptibility of various animal species to SARS-CoV-2[a]

Order	Family	Animals category	Species	Sample	Detection methods	Prevalence	References
Carnivore	*Mustelidae*	Ferrets	Mustela putorius	Nasal swab	qPCR, ELISA	6/6	(Shi *et al*., 2020)
				Nasal turbinate, soft palate, and tonsils		4/4	
	Felidae	Cat	*F. catus*	Nasal turbinate, soft palate, tonsil, and trachea	qPCR, ELISA	5/5	(Shi *et al*., 2020)
	Canidae	Dog	*C. familiaris*	Rectal and esophageal swab	qPCR, ELISA	2/5	(Shi *et al*., 2020)
Artiodactyla	*Suidae*	Pig	*S. scorfa domesticus*	Rectal and esophageal swab	qPCR, ELISA	0/5	(Shi *et al*., 2020)
Anseriformes	*Anatidae*	Duck	*A. platyrhynchos domesticus*	Rectal and esophageal swab	qPCR, ELISA	0/5	(Shi *et al*., 2020)
Galliformes	*Phasianidae*	Chicken	*G. domesticus*	Rectal and esophageal swab	qPCR, ELISA	0/5	(Shi *et al*., 2020)

qPCR = quantitative polymerase chain reaction; ELISA = enzyme-linked immunosorbent assay.

[a] This table does not include bat and pangolin.

Cross-Species Transmission

SARS-CoV

A unique virus was isolated from the palm civet and other game–food mammals in June, 2003, with 98.8% nucleotide similarity to SARS-CoV (Cheng *et al*., 2007). Subsequently, research studies have identified SL-CoV in horseshoe bat acting as a reservoir host, and SARS-CoV in several carnivores (civet and raccoon dog) from the Chinese wet market (Bolles *et al*., 2011; Ge *et al*., 2013) acting as a replication host (Guan *et al*., 2003; Fig. 2). Later, one asymptomatic and four symptomatic cases of SARS were reported from December 16, 2003 to January 8, 2004 in Guangdong Province, China, which were similar to SARS-CoV of animal origin (Cheng *et al*., 2007). Chen *et al*. (2005) reported the transmission of SARS-CoV of human origin to pigs. Ge *et al*. (2013) provided the solid evidence of horseshoe bats acting as a reservior host and the virus acting as a cellular receptor ACE-2 in both bats and humans. The analysis of spike glycoprotein for receptor ACE-2 indicated that amino acid 487 was responsible for the spike ACE-2 interaction. Its mutation appeared to be responsible for the human to human transmission of SARS-CoV (Li *et al*., 2005).

MERS-CoV

Various studies have shown bats as a reservior host for MERS-CoV since the HKU4 of bats resembeled MERS-CoV genetically (Annan *et al*., 2013), but alpacas also act as a potential reservior for MERS (Mohd *et al*., 2016). Humans get infected when MERS-CoV spike attaches to the dipeptidyl peptidase 4 (DPP4) of the human receptor. Both HKU4 and MERS-CoV are attached to the DPP4 receptor, but the HKU4 requires the host endogenous protesase for activation in humans, and only MERS-CoV can mediate its entry into the human cell (Yang *et al*., 2014). But the mutation of HKU4 in S246R and N762A possesses a special capacity to enter inside the human cell receptor (Yang *et al*., 2015). A two-fold mutation of HKU4 adaptive for its attachement to the endogenous cellular protease supports the role of bats in the transmission cycle either directly or by amplyfying the host in humans (Yang *et al*., 2015). Hemida *et al*. (2014) reported that the genome of human origin MERS-CoV is 99.9% similar to the genome of MERS-CoV afffecting the dromedary camels. It is still unclear how the dromedary camels got infected with MERS-CoV; but a recent study supports that MERS-CoV jumped to the camel from bat-CoV in Africa 20 years ago and these camels from Africa were imported to the Arabian Peninsula (Corman *et al*., 2014). The evidence of the transmission of MERS-CoV from dromedary camels to humans was reported in October 2013 in Qatar (Haagmans *et al*., 2014) and in November 2013 in Saudi Arabia (Azhar *et al*., 2014). These findings also support the possible infection in humans through dromedary camels (Fig. 3).

SARS-CoV-2

Bats are supposed to be the natural reservoir of the SARS-CoV-2 since they share a 96% genomic identity with bat coronavirus and their protein sequence shares a similarity to SARS-CoV (Zhou *et al*., 2020). However,

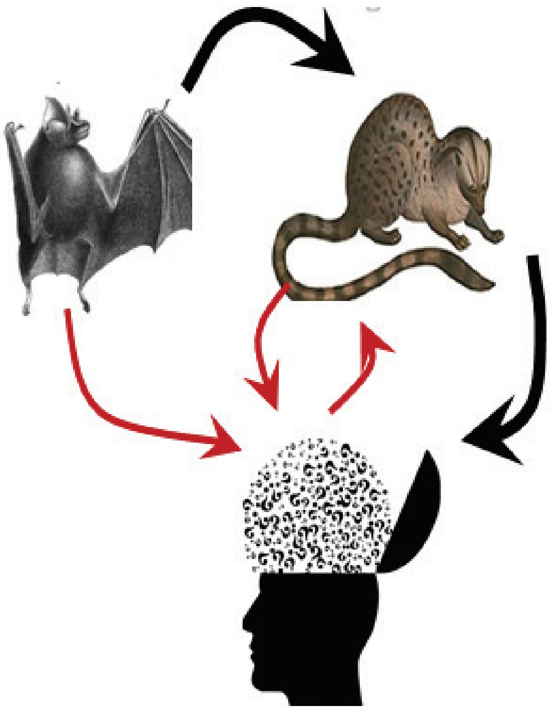

Fig. 2. The summarized information suggests that bats acted as a reservoir host for SARS-CoV, and initially jumped to palm civet and subsequently into humans (black arrows). Phylogenetic study suggested direct transmission from bats to humans and possible cross-transmission between palm civet and humans (red arrows).

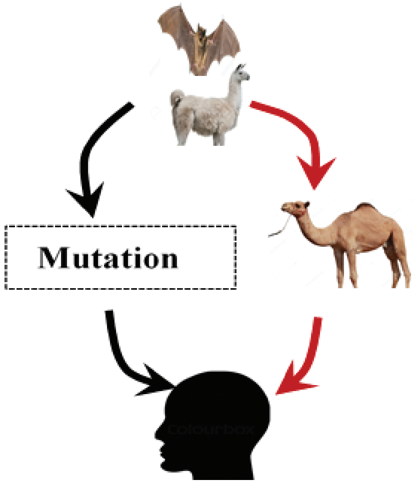

Fig. 3. Bat and alpacas are considered as a reservoir host for MERS-CoV. Dromedary camel acting as an animal host to transmit virus to animals (red arrows). But recent studies show the mutation of the MERS-CoV spike of reservoir host in bat to human transmission (black arrows).

snakes are the recently reported possible reservoirs for COVID-19 (Ji *et al*., 2020). In humans, COVID-19 is developed from a homologous recombination of cell surface receptors recognizing the glycoprotein spike of the bat virus and a new virus of unknown origin (Ji *et al*., 2020). This homologous recombination of the glycoprotein spike in bats and snakes contributes to the cross-species transmission from animals to humans (Ji *et al*., 2020) (Fig. 4). A recent study reported that the DNA and protein sequence of Malayan pangolins share a 91.02% similarity to SARS-CoV-2, acting as an intermediate link or missing link for cross-species transmission (Zhang *et al*., 2020). Cats are also susceptible to SARS-CoV-2, since the cellular receptor ACE2 protein for entry of SARS-CoV-2 in humans resembles the feline homologue ACE2 (Jeanna, 2020a). The information on the cross-transmission model of SARS CoV-2 is still contradictory; however, a previous study on SARS-CoV showed possible transmission of SARS-virus from infected cats to humans (Martina *et al*., 2003). A team of virologist, led by Bu Zhigao, reported on intraspecies transmission of SARS-CoV-2 in cats through respiratory droplets, but the actual mode of transmission in those cats is unclear; however, it could be through the virus secreted in the urine or feces (Mallapaty, 2020a, 2020b). Steven Van Gucht, a virologist from Belgium, told Live Science the possible interspecies transmission of COVID-19 from humans to cats because a week after the owner got sick the cat tested positive (Jeanna, 2020a). Virologist Linda Saif says there is no direct evidence that the coronavirus in the secretion of cats infects humans (Mallapaty, 2020b). Shi *et al*. (2020) reported no intraspecies and interspecies transmission of COVID-19 from dogs, pigs, chickens, and ducks.

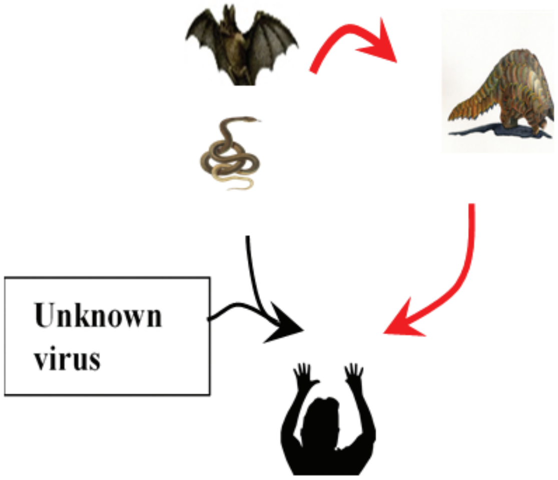

Fig. 4. A recent report showed bats and snakes acting as reservoirs for SARS-CoV-2 and Malayan pangolin as a jumping link (red arrows). Humans get infected either from the recombination of the reservoir host virus with an unknown virus (black arrows) or from the intermediate link (red arrows).

Conclusion

Bats cause various life-threatening diseases in both animal- and human-like SARS (SARS-CoV), MERS (MERS-CoV), Ebola virus, Nipah virus, Hendra virus, and Murburg virus (Han *et al*., 2015). Recently, COVID-19 caused by SARS-CoV-2 was identified as a newest disease of bat origin (Zhou *et al*., 2020). Research studies have identified SL-CoV in horseshoe bats and palm civets from the Chinese wet market named SARS-CoV (Bolles *et al*., 2011; Ge *et al*., 2013). Horseshoe bats act as a reservoir for this virus, but it is difficult to understand this characteristic properly in wild animals because of their genetic diversity. Moreover, other animals, like the red fox, Chinese ferret-badger, pig, wild pig, and lesser field rats, are also susceptible to SARS-CoV (Table 1 and Fig. 5). MERS caused by MERS-CoV originated in Saudi Arabia, a direct ancestor of SARS-CoV, also originated from bats (Annan *et al*., 2013). In addition to bats, alpacas also act as a potential reservoir for MERS-CoV, and the dromedary camels act as a host to transmit virus to humans (Table 2), since MERS-CoV spike is attached to the DPP4 human receptor (Yang *et al*., 2014). Other animals, like the rhesus macaque, llamas, pig, cattle, sheep, goat, donkey, and horse, are also susceptible to MERS-CoV (Table 2 and Fig. 5).

The novel outbreak causing respiratory illness in global human health is caused by COVID-19 (SARS-CoV-2; Peeri *et al*., 2020). Bats are common ancestors

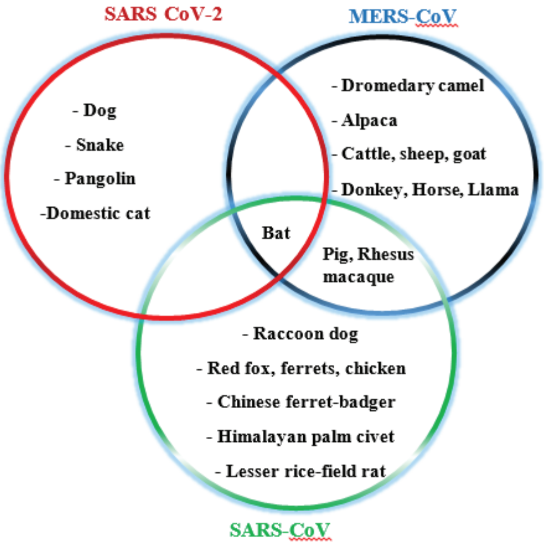

Fig. 5. Various animal species susceptible to coronaviruses. It shows that bats are common for all, acting as a reservoir host.

Table 4. Clinical presentation of SARS-CoV-2, SARS-CoV, and MERS-CoV infections in animals according to published series.

Virus	**SARS-CoV-2**	**SARS-CoV**	**MERS-CoV**
Clinical presentation	Cat: loss of appetite, vomition, diarrhea, respiratory problem (Jeanna, 2020a) conjunctivitis, and severe ocular implication (Seah and Agrawal, 2020) Tiger, Lions: cough and loss of appetite (Jeanna, 2020b) Ferrets: fever and loss of appetite (Shi *et al*., 2020).	Non-human primates: fever, quite, mildly labored breathing in aged animals (Smits *et al*., 2010).	Dromedary camels: asymptomatic with mild respiratory distress (Hemida *et al*., 2014), mild fever, and rhinorrhea (Adney *et al*., 2014). Calves: mild respiratory problems (respiratory discharges, coughing, sneezing), fever, appetite loss (Hemida *et al*., 2014).
Laboratory findings	Ferrets: vasculitis and perivasculitis of alveolar lumen (Shi *et al*., 2020).	Cat: Mild to severe interstitial pneumonitis (Roberts *et al*., 2008)	Dromedary camels: intraepithelial and submucosal inflammation with multifocal necrosis of respiratory of URT and LRT (Adney *et al*., 2014).
Histopathology	Ferrets: type II neutrophils, macrophages, pneumocytes in respiratory mucosa, and alveolar septa (Shi *et al*., 2020). Cat: loss of cilia with lymphocytic infiltration in respiratory mucosa and alveolar wall (Shi *et al*., 2020).	Cat: Perivascular and peribronchiolar mononuclear infiltration, intraluminal necrotic debris in trachea, and interstitial pneumonia (Roberts *et al*., 2008)	Dromedary camels: multifocal squamous and pseudostratified degeneration with metaplasia of nasal turbinate, trachea, and bronchus with neutrophilic infiltration, absence of goblet cells, and nuclear regimentation (Adney *et al*., 2014).
Detection method	Real-time RT-PCR (Corman *et al*., 2020)	RT-PCR (Martina *et al*., 2003)	qRT-PCR (de Wit *et al*., 2013)

URT = upper respiratory tract; LRT = lower respiratory tract; RT-PCR = reverse transcription polymerase chain reaction; qRT-PCR = quantitative reverse transcription polymerase chain reaction.

for all the deadly coronaviruses. SARS-CoV-2 also shares a 96% genomic similarity to bat-CoV (Ji *et al*., 2020). Hence, bats act as a reservoir for COVID-19. The virus also has characteristics to undergo genomic recombination as SARS-CoV between glycoprotein spike of the bat virus and a virus of unknown origin. The recombinant virus of SARS-CoV-2 and SARS-CoV acts on the ACE-2 receptor of humans (Jeanna, 2020a). In addition to humans, animals, like cats and ferrets, are also most susceptible to SARS-CoV-2, but its multiplication in dogs, pigs, chickens, and ducks are poor (Shi *et al*., 2020; Table 3 and Fig. 5). Clinical presentation, laboratory findings, histopathology, and detection methods of SARS-CoV-2, SARS-CoV, and MERS-CoV infections in animals according to the published series are presented in Table 4. It is very difficult to understand how the genomic pattern occurs among these coronaviruses, in order to make an effective plan for control and prevention. There is increased possibility of new virus-variants infecting animals and humans in the upcoming days which seems to be the biggest challenge for the future of the world.

Conflict of interest

The authors declare that there is no conflict of interest.

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