



Mini Review Article

Aspects of zoonosis of Covid-19 in animals: A Review

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Summary

In late 2019, covid-19 was initiated in Wuhan (Hubei province, China) due to a new severe acute respiratory syndrome coronavirus-2 or SARS-CoV-2). Covid-19 not only has claimed four million lives and influenced millions of people but also has confined the movement of the population in most of the world. Until now, covid-19 is the leading challenge in terms of economic, health, and humanitarian in the 21 century. Various animal infections of SARS-CoV-2 have been reported (dog, cat, tiger, lion, and mink) along with the significant covid-19 cases, deaths, and hospitalizations in humans. Therefore, this increased the concern of pet keepers. Furthermore, further explanation is required for the disease dynamics, mainly regarding the human-animal transmission of the virus and vice versa. Thus, this study's is to collect data from reported cases of covid-19 transmission in animals by reviewing published articles. Despite the numerous SARS-CoV-2 transmission instances, further and cautious studies are essential for avoiding the maltreatment incidence in animals. Hence, a better comprehension is obtained of the disease dynamics in the environment, animals, and humans. This article lists corona reports in various animals. More studies on the animal-human interface can be effective in formulating and implementing preventive measures for combating the further covid-19 transmission.

Keywords: Coronavirus, Pandemic, Animals, Epidemiology

Introduction

There is evidence indicates that the Huanan Seafood Wholesale Market in Wuhan, Hubei province, China, is where the first case of Coronavirus disease-2019 (covid-19) was infected (Lu et al., 2020; Wang et al., 2020). The new pathogen was named severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). It was called covid-19 (Lai et al., 2020). It is the third coronavirus appeared in the last 20 years. The Middle East respiratory syndrome coronavirus (MERS-CoV) and severe acute respiratory syndrome coronavirus (SARS-CoV) are other

diseases that occurred over 2012 and 2002, respectively (Wang et al., 2020; Munster et al., 2020). Compared to MERS-CoV and SARS-CoV, the highest number of deaths and infections and the most significant economic loss are caused by SARS-CoV-2 (Shi et al., 2020). The covid-19 infected about 200 million cases and claimed more than four million lives until August 2021. SARS-CoV-2 is related to the suborder Coronavirineae, order Nidovirales, and Coronaviridae family. Two subfamilies of Coronaviridae family are Orthocoronavirinae and Lentovirinae. Orthocoronavirinae contains four genera of

Betacoronavirus (β CoV), Alphacoronavirus (α CoV), Deltacoronavirus (δ CoV), and Gammacoronavirus (γ CoV). The δ CoVs and γ CoVs lead to infections in birds. On the other hand, α CoVs and β CoVs primarily infected mammals (e.g., bats, civets, rodents, horses, pigs, and cattle), including humans (Lau et al., 2015; Helmy et al., 2020; Woo et al., 2005; Woo et al., 2012).

SARS-CoV-2 clusters with lineage β CoV along with MERS-CoV and SARS-CoV (Woo et al., 2005) are originated from bats (Chen, 2020; Liu et al., 2020; Lu et al., 2020). Genome size Coronaviruses and stranded positive-sense RNA (+ss) are enclosed viruses with a single length of between 26 and 32 kb (Su et al., 2016; Pradesh et al., 2014). These viruses have four essential structural proteins, including an envelope protein (E), spike glycoprotein (S), nucleocapsid protein (N), and matrix protein (M) (Pradesh et al., 2014; Mortola and Roy, 2004; Wang et al., 2017; Junejo et al., 2020). According to the genomic analysis, the identity between SARS-CoV-2 and genome of bat CoV was 96.2%, which shows that bats may be a possible source (Malik et al., 2020; Lai et al., 2020). According to numerous studies, pangolin can be the potential intermediate host included in the virus's progression owing to the exclusive receptor-binding domain (RBD) configuration (Shafique et al., 2020; Kelley et al., 2015; Andersen et al., 2020; Junejo et al., 2020).

The first human to animal transmission was reported in Hong Kong, on a 17-years-old Pomeranian dog, within the global panic caused by the fast expansion of the virus and lack of a vaccine or treatment (Tazerji et al., 2020). This raised worries about the possibility of SARS-CoV-2 human-animal transmission and contrariwise represented the difficulties in significant fighting against the virus. Nevertheless, other authors assumed an immunological cross-protection between canine respiratory coronavirus (CRCoV) and SARS-CoV-2 owing to the more significant homology within the spike protein (SP) epitopes of the two coronaviruses associated taxonomically (Tilocca et al., 2020a).

The current work was aimed to collect, present information, and discuss the recorded animal cases of covid-19 while concentrating on pets and performing phylogenetic and genomic analyses of SARS-CoV-2 isolated from animal hosts. More investigations are essential on the diseases' dynamics for adopting appropriate control measures and reducing the virus transmission.

Discussing the source of SARS-CoV-2 requires analyzing the origin of other coronaviruses like MERS-CoV and SARS-CoV (Junejo et al., 2020). In November 2002, SARS-CoV was developed in Southern China, Guangdong province, and characterized as humans' contagious respiratory disease (Junejo et al., 2020; Organization, 2003). According to the studies, the existence of various coronaviruses in horseshoe bats species (genus *Rhinolophus*) is evolutionarily associated with SARS-CoV in their genome sequence and organization (Lau et al., 2005; Li et al., 2005). The initial outbreak of SARS-CoV in 2002 was further investigated in Hong Kong, indicating that SARS-CoV can also infect ferrets (*Mustela furo*) and cats (*Felis domesticus*) (Martina et al., 2003).

In Saudi Arabia, another coronavirus was first reported leading to severe acute respiratory syndrome in humans, termed the MERS-CoV later (Zaki et al., 2012). MERS-CoV is β CoV of the C lineage with a genotype the same as bats in the same line, like BtCoVHKU5 and BtCoV-HKU4 (van Boheemen et al., 2012). In these animals, the MERS-CoV-dromedaries transmission was recognized by detecting definite antibodies against the virus (Reusken et al., 2013). Corman et al. indicated that MERS-CoV has circulated in dromedaries for over two decades (Corman et al., 2014). Thus, bats are presumed reservoirs for various coronaviruses like MERS-CoV, SARS-CoV-2, and SARS-CoV (Li et al., 2005; Annan et al., 2013; Hampton, 2005).

Reports indicated a close relation between SARS-CoV and SARS-CoV-2 (Kim et al., 2020; Petrosillo et al., 2020). Moreover, the similarity of about 80% was also reported between the genomes (Lai et al., 2020, Malik et al., 2020). SARS-CoV-2 was the most possibly initiated from

bats; however, it is not yet well-known the animal contributed to the progress of the virus and served as an intermediate host before occurring the spillover to humans (Junejo et al., 2020).

SARS-CoV-2 was demonstrated as a chimerical virus among the coronavirus of unknown origin and a bat coronavirus in another study (Ji et al., 2020b). RmYN02 bat-derived coronavirus was also found via a metagenomics study. In that study, 227 bats were gathered from Yunnan province in China within May-October 2019 (Zhou et al., 2020). Remarkably, RmYN02 is 93.3% similar to SARS-CoV-2 at the complete genome scale and 97.2% in the ORF1ab gene. Thus, it can be regarded as the nearest relative of SARS-CoV-2 identified so far. However, RmYN02 represented a lower sequence identity of 61.3% with SARS-CoV-2 in the RBD, indicating that RmYN02 may not connect to angiotensin-converting enzyme 2 (ACE2). By administering multiple amino acids at the junction site of the S1 and S2 subunits of the spike (S) protein as SARS-CoV-2, RmYN02 was critically characterized. Hence, there is strong evidence regarding the possibility of such natural insertion animal β CoV (Zhou et al., 2020; Khailany et al., 2020).

The nucleotide identity between tiger SARS-CoV-2 and the human type was 99.96% at the whole genome-scale after mink SARS-CoV-2 (99.90%), cat SARS-CoV-2 (99.85%), mouse SARS-CoV-2 (99.87%), and dog SARS-CoV-2 (99.51%). A higher level of nucleotide identity was observed between isolates obtained from humans and animals.

Considering the percentage of SP nucleotide identity, SARS-CoV-2 of cat, tiger, and dog share 99.97% with the human type. A 99.92% similarity is reported between the spike protein's amino acid identity between SARS-CoV-2 of tiger, dog, and cat with SARS-CoV-2. Nevertheless, the nucleotide identity and SP amino acid among SARS-CoV-2 of dog, cat, and tiger was 100%. Such a finding appears to be associated with human-to-animal transmission of SARS-CoV-2 (cat, dog, and tiger, initially). Transmission to humans no longer seems likely, though

transmission between animals seems possible considering the identity between amino acids and nucleotides of the spike protein. SARS-CoV-2 may experience nucleotide mutation while transmitting to animals due to the genome similar to other animal coronaviruses, which expresses amino acids, increasing its pathogenicity in animals, particularly those associated with SP (Khailany et al., 2020; Wan et al., 2020).

The SARS-CoV-2 spike protein's RBD laying in the S1 domain is of crucial importance to determine the vulnerability of the novel host species. Investigating the interaction between the ACE2 and viral RBD, pangolins, turtles, and snakes were represented as the potential intermediate hosts (Liu et al., 2020a). Turtles are preferred animals in the Huanan Seafood Wholesale Market, along with other animals. Though, prolonged studies are scientifically required for proving their associations (Liu et al., 2020b).

A pangolin is a possible intermediate host for the virus. Pangolin-CoV possesses the identity of 90.55% and 91.02% to Bat-CoV and SARS-CoV-2, respectively (Kim et al., 2020). Moreover, Malayan pangolin-CoV (Pangolin-CoV) is closely resembled by the SARS-CoV-2 spike proteins RBD (Liu et al., 2020a). Such results suggested pangolins as the intermediate host for transmission of SARS-CoV-2. More studies are required to prove the SARS-CoV-2 origin dynamics and transmission.

The probable protective effects of pet rights against coronaviruses warrant consideration about the high coronavirus prevalence within the pet groups. Canine respiratory coronaviruses are common among dogs. The viruses can be transmitted from animals to humans by ownership of an infected animal. There is no comprehensive understanding of possible protection resultant from the possession of a pet. However, the frequent existence of coronavirus in canines could be effective for developing a better response of the human immune system against the covid-19 (Jurgiel et al., 2020). When initiating the covid-19 outbreak, it was thought that pets are not vulnerable to the SARS-

CoV-2. Though, in Belgium, reports were provided on the natural infection of a cat, with the virus traces recognized in the gathered specimens by PCR. Diarrhea, respiratory difficulty, vomiting were found in this cat representing the virus's active replication (Jurgiel et al., 2020; Chini, 2020). Nevertheless, the cat was not assessed by a veterinarian. Hence, more assessment was essential, like serology. Shi et al. also reported natural infection of cats with covid-19 and virus-inoculated adolescent cats artificially provided severe histological lesions and died (Kelley et al., 2015). However, dogs exhibited seroconversion in other studies, but not isolated virus. The ferret's and cats' susceptibility to covid-19 can be associated with the ACE2 (SARS-CoV-2 receptors) (Lai et al., 2020; Hoffmann et al., 2020). In tracheobronchial submucosal glands' type 2 pneumocytes serous epithelial cells in ferrets, these receptors are expressed (Tazerji et al., 2020). Both ferrets and cats involved the SARS-CoV-2 spike-contacting regions of ACE2, which were different only based on two amino acids (Shi et al., 2020). Former reports revealed that cats and ferrets could be infected by SARS-CoV (Shi et al., 2020), indicating that cats and ferrets might be vulnerable to covid-19, which may be related to the SARS-CoV-2 transmission to animals. Bats possess considerable similarities among their genotypes, along with possibly sharing the same origin (Lai et al., 2020; Li et al., 2005; Annan et al., 2013; Hampton, 2005; Ji et al., 2020b). SARS-CoV epidemiology revealed that the covid-19 pandemic alarms that animals can also be infected while potentially transmitting the virus to humans. Numerous animal abandonments have been created by the panic of possible animal-human transmission and the force on most residents to leave their animals owing to quarantine and evacuation while thinking they would be returned soon (Kim, 2020). Authorities in Zhejiang and Hunan provinces in China also declared that they avoid the virus transmission by killing the pets found outside. In late February 2020, this concern was intensified when the tests of dogs in Hong Kong were positive

for the novel coronavirus. It was regarded as the first known case of human-animal transmission of covid-19 later by felines (Khailany et al., 2020; Mallapaty, 2020). The present work deals with investigating the possible protection based on individuals' former exposure to animals infected naturally with coronaviruses taxonomically associated with the circulating SARS-CoV-2 (Tilocca et al., 2020a; Jurgiel et al., 2020; Decaro and Lorusso, 2020; Tilocca et al., 2020b; Tilocca et al., 2020c). The animals were exposed to SARS-CoV-2 infection experimentally through the intranasal route and the receptor ACE2 (Sun et al., 2020). The use of ACE2 was reported in various studies by the new SARS-COV as its receptor for cell entry (Hoffmann et al., 2020; Lai et al., 2020). Dogs were also vaccinated, and no virus could be isolated from the uninoculated and inoculated contacts despite the seroconversion. Furthermore, ferrets represented equivalent susceptibility to cats, while chickens, ducks, and pigs were vulnerable (Shi et al., 2020).

The probability of involvement of rabbits, mice, and rats in the SARS-CoV-2 cycle was ruled out by studies oriented by RBD domain analysis (Lutz et al., 2020). The results on orangutans, monkeys, and ferrets represented a greater affinity of ACE2 with the SARS-CoV-2 S protein RBD domain (Wan et al., 2020). In an analysis based on using codon, snakes were pointed as a probable host, though these results were denied by the consequent studies (Ji et al., 2020a).

Some studies indicated the possibility of natural infection of cats with the rest of coronaviruses like feline coronavirus and canine coronavirus can cause infection in canines (Buonavoglia et al., 2006; Jaimes et al., 2020). The infection of these animals probably starts by binding the virus to the receptor, ACE2 (Sun et al., 2020). A retrospective serological survey has investigated cats suffering from covid-19 in Wuhan, China. In this work, 102 isolates were collected after the covid-19 outbreak, and 39 were included before the outbreak. The ELISA test showed that of 102 serum samples gathered after the outbreak, 15 (14.7%) were positive for antibodies against the SARS-CoV-2

receptor-binding domain (RBD). Neutralizing antibodies to SARS-CoV-2 were found among the positive samples in 11 samples with a titer within the range of 1/20 to 1/1080. According to the findings, 29 (out of 39) serum samples gathered before the disease emergence were negative. No clinical signs were found in any cat with a positive result on serological tests. There was no serological cross-reactivity between type 1 or 2 of the feline infectious peritonitis virus and SARS-CoV-2. According to the authors, the covid-19 infection was found in the cat population investigated in Wuhan after starting the outbreak (Zhang et al., 2020). The spread of the new coronavirus was investigated on nine cats and 12 dogs by 18 veterinary students in France. The symptoms compatible with covid-19 were found in 11 cases; however, only two were positive for the new coronavirus. The clinical symbols of gastrointestinal or respiratory disease were found in 3 cats, while positive RT-PCR or the presence of definite antibodies to SARS-CoV-2 was found in no animal (Sun et al., 2020).

The possibility of transmission through the intranasal route is also reported by experimental studies on cats, dogs, and ferrets (Liu et al., 2020a). According to numerous studies, the same receptor, ACE2, is utilized by the SARS-CoV-2 for entering the respiratory mucosa (Hoffmann et al., 2020, Lai et al., 2020, Shi et al., 2020). Hence, the possibility of human-animal covid-19 transmission is indicated. It has been experimentally found that the virus can be transmitted by SARS-CoV-2 infected cats to naïve cats and contact them (Halfmann et al., 2020). Nevertheless, it is unknown if humans can convey the virus to other animals or pets.

Moreover, the first report on the SARS-CoV-2 transmission on the non-domesticated animal case was related to a big cat (Nadia) and a Malayan tiger (4-year-old), infected by infected workers at the Bronx Zoo, New York, the US, which is the first identified case of human-to-animal transmission to a tiger in the US and all over the world. The US Centers for Disease Control and Prevention, the US Department of Agriculture, Wildlife Conservation Society, and the National Veterinary Services

Laboratories confirmed this case (Ji et al., 2020a; Law and Leung, 2020). Thus, covid-19 was found in three lions and four tigers. In two pet cats, mild respiratory distress infection was reported in the US (Tazerji et al., 2020).

In Moskva (Moskovskaya Oblast, Russia), a 5-year-old cat was reported as the new case of covid-19 infection. Nasal and throat samples were used for virus detection. RT-PCR was conducted with the electrophoretic discovery of amplification products in real-time. The selected primers flanking a 232 bp N gene fragment (ORF1ab) of the SARS-CoV-2 were used to sequence the amplification reaction product. According to the tests, an identity of 100% was found for the examined fragment of the N gene ORF1ab of the SARS-CoV-2. Then, the animals were isolated (Tazerji et al., 2020).

It was revealed that SARS-CoV causes no infection in poultry. Since the SARS-CoV is related to a group similar to SARS-CoV, it uses a similar ACE2 host cell receptor. It is greatly improbable that poultry is vulnerable to SARS-CoV and should be confirmed systematically yet (Jackwood, 2020). SARS-CoV-2 human-animal transmission is not entirely comprehended, but it is possible to transmit by contact of hands defiled with saliva or respiratory droplets with mouth or noses (Chen, 2020). The essential factors in the virus transmission of humans to animals are coughing, sneezing, or even talking, respiratory droplets by the infected humans (Ozaslan et al., 2020). However, the other possible ways of transmission should be concerned, like kissing, licking, petting, or hugging pets facilitate the virus transmission from affected people (Leroy et al., 2020). The Netherlands government, in a letter delivered by the Ministry of Agriculture, Nature and Food Quality, stated the possibility of SARS-CoV-2 infection of an employee working on a mink farm, which has already been recovered from the disease. Moreover, according to, minks can be asymptomatic, and cats have critical roles in the potential viruses transfer within assessed farms (Tazerji et al., 2020).

According to the findings, covid-19 can infect domestic cats, which indicates the necessity of assessing its potential risk for SARS-CoV-2 transmission, particularly regarding their close contact with humans. Such assessment would be helpful for quantification of humans-to-cats transmission and cats-to-cats and from the cats-to-humans transmission. The potential role of cats in the transmission and maintenance of covid-19 is undeniable. Still, some questions remain to be answered, including the risk of human-to-cat, and vice versa, transmission (Gonzales et al., 2021).

Conclusions

Numerous studies exist on the source of coronaviruses and their zoonotic potential. Some animals infecting coronaviruses can infect humans, similar to the SARS and MERS. This is also the same as the virus causing the present covid-19 outbreak. Though, the exact origination of this virus is not still apparent. Scientifically numerous efforts are made to identify the origin of the virus. To date, bats have been suggested as the origin based on genetic evidence. The first infection was associated with a live animal market in Wuhan, which offered a zoonotic source. SARS-COV-2, with the rapid spread from individual to individual, has caused one of the most recent significant pandemics. Experimental inoculations and molecular and serological analyses reported covid-19 infection in various animals. Though human-to-animal transmission, and vice versa, is not shown. It is essential for designated public health and veterinary officials to further work on testing animals for covid-19 when placed in the same setting as the infected owners through a One Health method. According to existing data, the likelihood of animal-to-human transmission is lower. As the animal-to-human transmission and contrariwise is shown, effective and cautious communication with those in close contact with pets is essential to avoid the extensive death and abandonment of animals. While only a case of animal-human transmission has already been reported, further studies are required before declaring the transmission of the new coronavirus to humans by animals. More studies are needed to comprehend the transmission

dynamics and origination of the virus. This will help train people and prevent unessential discrimination against animals.

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Conflict of interest statement

There is no conflict of interest.

Ethical approval

Not applicable

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