REVIEW ARTICLE

Risks of Coronavirus Infectious Disease 19 (SARS-CoV-2) in Companion Animals

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Abstract

The epidemiological situation of Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) in humans and animals is continually evolving. Given the probable animal origin of SARS-CoV-2 and the recent case reports in pets, especially cats and dogs, and their close contact with humans, it is critical to comprehend how sensitive SARS-CoV-2 is to humans and vice versa in order to control the coronavirus infectious disease 19 (COVID-19) pandemic. The most susceptible companion animals to contract SARS-CoV-2 infection include cats, ferrets, and hamsters. The virus SARS-CoV-2 that is carried from pets to humans is generally thought to have little to no effect on the viral transmission across the broader community, and there is little evidence of mutations. Thus, there is no requisite for specialized surveillance programmes for SARS-CoV-2 infection in pets; in most cases, testing should only be done on pet owners or veterinarians who interact with these animals. It is recommended to properly dispose of human waste in order to lower the probability of SARS-CoV-2 spreading to animals. Additionally, it is best to avoid contact with pets, particularly if they are ill or deceased. In addition to evaluating animals exhibiting clinical indications, monitoring is advised for household pets.

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Introduction

In December 2019, an outbreak of pneumonia in the human population of unknown cause occurred in Wuhan, China, and rapidly spread worldwide. The pathogen was soon identified as SARS-CoV-2, and the disease was called COVID-19 by the World Health Organization[1][2]. The newly identified SARS-CoV-2, the virus responsible for COVID-19, is a betacoronavirus genetically linked to Severe Acute Respiratory Syndrome (SARS) CoV and only distantly connected with Middle East Respiratory Syndrome (MERS-CoV)[3]. The RNA viruses known as coronaviruses (CoVs) are made up of positive-sense, single-stranded RNA that is around 27–32 kb in length. They have the ability to infect a large number of species, including people and pets. As the name suggests, under an electron microscope, the spherical external spike protein has a distinctive crown form[4]. All CoVs share similarities in the organization and genomic expression with 16 nonstructural proteins and at least 4 structural proteins. Coronaviruses are four genera that include alpha, beta, gamma, and delta coronaviruses, with 40 species and 22 subspecies[5]. There has always been interspecies transmission of the Coronaviridae. To facilitate easier transmission and result in more serious illnesses, the virus may evolve[6]. The information now available indicates that SARS-CoV-2 may have been indirectly transferred to humans through another species that serves as a reservoir or intermediate host, even though it is theoretically possible for the virus to spread straight from bats to people. Furthermore, no transitional animal species has been discovered so far. It has been established that SARS-CoV-2 belongs to the same viral family as MERS-CoV, also known as the Middle East respiratory disease coronavirus. Due to their animal-to-human transmission, these viruses have historically caused serious illnesses in people (MERS-CoV was linked to dromedary camels, while SARS-CoV was linked to civet cats)[7]. Zoonotic transmission of SARS-CoV-2 from animals, especially pets, to people may be the source of the outbreak[8]. The SARS-CoV-2 virus's animal origins sparked discussion on the disease's potential animal-to-human transmission. It is concerning that infected animals might potentially spread the virus to people and that studying the intermediate host and the reservoir of SARS-CoV-2 can aid in comprehending the dynamics and epidemiology of the COVID-19 pandemic. Due to their popularity as household pets, cats and dogs are included in this study. It focuses on potential transmission channels, preventative and control strategies based on the One-Health approach, and hazards associated with SARS-CoV-2 infection in dogs and cats.

Coronavirus diseases in dogs and cats

It is often recognized that having a pet animal, such as a dog or cat, has significant positive effects on an owner's social, emotional, and general health. However, social fear and the psychological fallout from anecdotal media stories about pets' involvement in the spread of SARS-CoV-2 to humans during the early stages of the COVID-19 pandemic resulted in a sharp rise in pet abandonment[9]. Numerous animal species have been discovered to be vulnerable to SARS-CoV-2 infection since the beginning of the COVID-19 epidemic. Given the close proximity of people and pets, the role of pets deserves particular consideration[10]. It is important to understand that even if there is a slight chance of SARS-CoV-2 spread to humans, these situations can still happen while making the decision to buy and keep a pet. Pets are believed to be significantly exposed to human infections, such as SARS-CoV-2, given that they are animals of close interaction with

humans, namely dogs and cats[11]. There is still a dearth of information on its pathogenicity, modes of transmission, and methods of removal. Dogs are infected with two unrelated coronaviruses: an alphacoronavirus, Canine coronavirus (CCoV), which causes enteric disease[12], and a betacoronavirus (Canine respiratory coronavirus, CRCoV), which causes a mild self-limiting respiratory disease[13]. A brief review of the findings from the studies reveals that most dog illnesses had no symptoms and that reported viral (genome) findings in dogs are less common than in cats. Research including the sampling of both dogs and cats revealed that cats had a greater percentage of positive results than dogs, with one research in particular showing that cats had higher probabilities of infection than dogs[14].

Feline coronavirus, or FCoV, is predominantly a pathogen of domestic cats worldwide. It replicates in the intestines and is disseminated by faecal-oral transmission from cats who are either temporarily or continuously infected[15][16]. FCoV infections are frequently asymptomatic, although they can cause both acute and chronic diarrhoea, stunting in kittens, temporary upper respiratory symptoms in newly infected cats and kittens, and faecal incontinence in carrier cats that have been infected for a long time[17]. Five out of fourteen cats with chronic caecocolic illness had FCoV, albeit it was not obvious if FCoV was the source of the lesions[18]. A lethal immune-mediated illness called feline infectious peritonitis is commonly experienced by certain cats that get the infection[19]. Feline cases have generally been linked to mild to moderate gastrointestinal, respiratory, or general non-specific symptoms. According to clinical signs or links to SARS-CoV-2 infections in the population, 51 references have been found to identify 725 probable cases of cats worldwide. A number of these investigations included case studies of cats that had been shown to be sick, linked to contaminated households, and exhibiting clinical symptoms. Seventy cases (out of 124 analysed cases) had clear data on clinical presentation, according to a systematic study on the clinical manifestation of infection in cats[20]. When the presence of the virus was confirmed by virus isolation or genome identification from respiratory and/or anal samples, high viral loads were found, especially in some symptomatic individuals[21][22]. Several studies explored the incidence of SARS-CoV-2 in cats and dogs (Table 1).

Table 1. SARS-CoV-2 natural infection in cats and dogs worldwide.

Sr. No.	Pet Species	Number of Tested Pets	COVID-19 Positive Pets	Country/Area	Reference
1	Cats	22	1	France	[23]
	Dogs	12	0		
2	Dogs	15	2	Hong Kong, China	[24]
3	Cats	1	1	Spain	[25]
4	Cats	10	2	Wuhan, China	[26]
	Dogs	9	1		
5	Cats	1	1	France	[27]
6	Cats	4	3	United Kingdom	[28]
7	Dogs	13	2	France	[29]
	Cats	34	8		
8	Cats	920	6	Germany	[30]
9	Cats	15	3	Wuhan, China	[31]
10	Cats	191	11	Italy	[32]
	Dogs	451	15		
11	Cats	50	6	Hong Kong, China	[33]
12	Cats	1	1	Italy	[34]
13	Cats	17	3	Brazos, Texas, USA	[35]
	Dogs	59	1		
14	Dogs	15	2	Hong Kong, China	[36]
15	Cats	8	1	Spain	[37]
	Dogs	12	0		
16	Cats	4	3	Chile	[38]
17	Cats	1	1	Latin America	[39]
18	Cats	2	2	Argentina	[40]
	Dogs	4	4		
19	Cats	2	2	The Switzerland	[41]
20	Cats	1	1	Italy	[42]
21	Dogs	29	9	Rio de Janeiro, Brazil	[43]
	Cats	10	4		
22	Dogs	1	1	Hong Kong, China	[44]
23	Dogs	2	2	New York State, USA	[45]
24	Cats	131	1	Croatia	[46]
	Dogs	654	2		
25	Dogs	2113	35	Thailand	[47]
	Cats	1112	4		

Risks of COVCID -19 (SARS-COV-2) in Pets

In addition to spreading from people to other humans, SARS-CoV-2 may also spread from animals to other animals and from animals back to humans. It has been documented that certain animal species are not capable of contracting the virus or transferring it back to humans[48]. The possibility exists that SARS-CoV-2 might spread from people to animals and infect a large number of them. This might allow the virus to continue evolving and adapting in its new hosts and potentially spread to people in the form of new viral strains[49]. During the COVID-19 pandemic, there have been cases of pets harbouring the coronavirus (SARS-CoV-2) worldwide, including dogs and cats. More people are fostering or adopting cats and dogs, becoming wondering and worrying about the risks of the novel coronavirus to their pets. In almost all cases of reported infected pets, the pet owners were also ill and tested positive for SARS-CoV-2. Therefore, there is a risk that pets can be infected by their owners. Infected pets might get sick, or they might not have any symptoms. There have been two recorded cases of spontaneous infection in dogs in Hong Kong that showed no symptoms[36]. Thus, as of yet, only four naturally infected cats have been documented[50]. Two of them had a cough, and one of them had some minor stomach and respiratory symptoms. It was the first instance of symptomatic SARS-CoV-2 infection in pets when two cats in the United States tested positive for the virus. They both experienced respiratory infections lasting eight and ten days. Sneezing, coughing, watery discharge from the nose, clear ocular discharge, lethargy, and appetite loss were the respiratory symptoms that the infected cats experienced[51]. There was also a report of a natural infection with SARS-CoV-2 in a cat in France (near Paris), most likely from its owners. This cat had little evidence of digestive and respiratory disorder[23]. Recently, another study showed that SARS-CoV-2 can be effectively disseminated in cats[52]. Cats are able to communicate infection to animals that are housed in their cages. Although cats may get airborne disease, the younger cats are more vulnerable to SARS-CoV-2[24]. Previous findings have demonstrated that cats may contract SARS-CoV, suggesting that cats may also be susceptible to SARS-CoV-2[53]. The serological frequency of SARS-CoV-2 in domestic cats was examined by Chinese researchers using an indirect enzyme-linked immunosorbent assay (ELISA) and a viral neutralisation test subsequent to the epidemic. According to the findings, SARS-CoV-2-specific antibodies were detected in 14.7% of the cat blood samples collected during the pandemic. The greatest amounts of antibodies were found in three cats kept by COVID-19 patients[31].

Dogs are also less sensitive to SARS-CoV-2[24][54]. Dogs were shown to be less susceptible to SARS-CoV-2 infection based on x-ray structures of the human host receptor, angiotensin-converting enzyme 2 (ACE2), linked to the SARS-CoV-2 spike protein's receptor-binding region; dogs' respiratory tracts showed comparatively low amounts of ACE2[55]. Out of the 22 stray dogs and cats, 14 (63.6%) showed a positive COVID-19 molecular test result. Seven (31.8%) of those tested had signs of sneezing and coughing[56]. Dogs can become infected; if they do, the illness is usually asymptomatic, and they may excrete minimal amounts of the virus, which could prevent the virus from spreading between dogs[57]. The virus that causes COVID-19 is still unknown to us, but it appears that there are situations in which animals can get the disease from humans and vice versa. According to a study, household cats may easily spread SARS-CoV-2 to one another. Felines are shedding, dropping their droppings into homes, shelters, and human civilizations, and there's a chance that humans may come into contact with the virus[38].

In general, cats are thought to be very susceptible to the virus and may even excrete it at levels similar to those observed

in humans, which might result in effective direct cat-to-cat transmission[58][59][21] and possible incidents of cat-to-human spread[21][22]. The greatest risk of infection is seen in cats living with sick individuals. If these cats are let to wander outside, they may pose a threat to other cats. The study's primary author, Peter Halfmann, a research professor at the University of Wisconsin, wrote a letter that was published in the New England Journal of Medicine, saying that people should be aware of this. The researchers advised people to keep cats away from anyone in a household who may be ill with Covid-19 and to be mindful of the risk of SARS-CoV-2 transmission from cats to people[60]. It is imperative to acknowledge and do more research on the plausible human-cat-human transmission cycle.

SARS-CoV-2 may evolve in animals and experience evolutionary events that develop viral features that might harm public wellness, though it hasn't been shown yet. These mutations peculiar to individual animal species may be found in distinct or comparable genomic locations in relation to humans[61]. Another concern is the development of a reservoir in animals; for example, marginally altered virus variants tailored to animals might co-circulate while sharing similarities with the SARS-CoV-2 viruses that are concurrently occurring among people[62]. On the other hand, a SARS-CoV-2 variant may potentially proliferate in animals over an extended period of time that has little to no relation to the corresponding human viral variation. The animal host of such variants would likewise go through evolutionary processes, which may result in the developed variants being reintroduced into the general population and infecting a more susceptible human population[63][62]. Cross-species transmission of SARS-CoV-2 may result in the introduction of various mutations and processes linked to evolution and species, which may modify the genetic and antigenic profile of the virus. However, a sizable vulnerable population may be required to sustain the infectious disease over an extended period of time in order to take into account ongoing animal-to-animal transmission[64][62]. A particular vulnerable species could not function as a reservoir but rather as an intermediary host or vector in the transmission pathway[65]. Animals carrying the SARS-CoV-2 virus do provide a risk to people who have intimate, unprotected access to them. This hazard may pertain to lone members of the community, such as housemates, or certain occupationally vulnerable groups in the pet animal industry. A greater number of individuals, as well as a single person, may be regarded as having occupational exposure to the pet animals that has been recognized as a potential source of transmission[62].

Role of Pet Animals in Zoonotic Transmission of SARS-CoV-2

The possibility that people may get SARS-CoV-2 originating from animals depends on the particular kind of animals to which the individual comes into contact, the duration and degree of contact, and the likelihood that the animal would contract the infection and spread it to others[66]. Certain animal species are more vulnerable than others and can spread the virus to members of their own or different species. Furthermore, the likelihood of infection is determined by the animal species' level of infectiousness, which is connected with viral load, as well as the length of infection. It was revealed that SARS-CoV-2 replicates poorly in dogs, ducks, and chickens, but that infection can spread to ferrets and cats. Furthermore, cats can get diseases through the air[24]. The possibility of exposure depends on the environment (such as a home, office, etc.), the degree, and the quality of exposure, which are established by the type and degree of human protection, the quantity and regularity of exposure episodes throughout time, and the length of exposure. People who are

repeatedly exposed to diseased animals over an extended period of time are more likely to get the virus[53].

Pathogen transmission from animals to humans and vice versa probably follows the same patterns as the known routes between humans and animals, for example, through aerosols or droplets near infected animals, tainted hands, surfaces, or other objects, as well as the surroundings[67]. It is thought that among pets, cats, ferrets, and hamsters have the greatest potential risk of contracting the virus and passing it on to other animals in their species as well as humans[24]. Since the Omicron variant first appeared, it has also been shown that rats and mice may get the virus and may be able to disseminate it further. Dogs can contract the virus, but they seldom spread it to other animals, suggesting that they have a lesser risk than other animals. The only place where an epidemic involving people and a larger cluster among pet animals has been seen is at a Hong Kong pet store with hamsters[68]. Few viruses with different evolutionary histories peculiar to each species have been shown to exhibit limited clustering and infrequent transmission to humans in companion animals[69].

It is incredibly unlikely that a human will get an infection from a cat that is able to go outside and was previously infected by another cat. For occupationally exposed groups like veterinarians who have a larger number of intimate encounters with various cats from different houses, this likelihood is higher. According to estimates, the severity of the associated illness is comparable to that of human-to-human transmission[70]. Comparably, it is anticipated that the risk is larger for groups that are occupationally exposed to hamsters and extremely low in cases of non-occupational exposure to the animals. Likewise, the risk is assumed to be higher for groups that are exposed to hamsters at work and to be very low for individuals who are not exposed at work but have close interaction with the animals. Pets have a none to very low probability of influencing the viral transmission among the broader population, despite the fact that there have been smaller hamster outbreaks. The severity of the associated disease is projected to be comparable in relation to the condition of human-to-human spread, meaning that the overall threat is quite low[71].

Measures to prevent and control SARS-CoV-2 at the animal–human interface

Preventive strategies against SARS-CoV-2 have an effect on the spread of other respiratory infections. Widespread SARS-CoV-2 testing at public testing centres hinders surveillance within the network of general practitioners. In order to inform control strategies and lessen the effects of COVID-19, the methods for monitoring respiratory viruses must be able to track the extent and severity of SARS-CoV-2 spread. In addition to keeping an eye out for potential novel varieties, respiratory virus integrated surveillance systems should also keep tabs on other pertinent occurrences[72].

Therefore, it is inevitable that diseased owners and companion animals may cohabit a home. In order to validate the SARS-CoV-2 infection and, if required, to provide the right treatment, testing the household's animals in this instance, especially the ones exhibiting significant clinical symptoms, might be pertinent. To minimize the potential danger of additional transmission, cats should have restricted or no outside access when living with sick individuals in the same household[73]. Furthermore, if positive samples from these animals are sequenced, genome sequencing could be helpful, particularly if the owner's samples did not yield the sequences or if additional epidemiological conditions (such as an

unusual clinical picture) point to the need for a more thorough analysis of the implicated virus. A crucial component of SARS-CoV-2 surveillance is genomic monitoring, which aims to track the distribution, emergence, and widespread presence of both established and newly discovered virus variants in the population, characterize significant mutations and pertinent locations during processes of evolution, provide information for the composition of vaccines or epidemic analyses, and detect newly emerging SARS-CoV-2 variants in advance[74]. A One Health approach should be used to analyse viruses originating from animals and how they relate to human viruses that are currently circulating. The national respiratory virus surveillance plans must incorporate genetic surveillance[75].

Wastewater monitoring has proved helpful in identifying increases in infections and is a promising technique for tracking the general status of SARS-CoV-2 in the inhabitants without requiring individual testing. It is possible to discover new or emerging viruses as well as the variety that is now in circulation by sequencing viruses from wastewater monitoring. Although wastewater surveillance is still monitored in many parts of the world and acts as an early "warning signal," several of its shortcomings have also been found[76].

Public health initiatives known as non-pharmaceutical interventions (NPI) are intended to halt the spread of infectious illnesses such as respiratory viral infections like SARS-CoV-2 in the population. Though the best method to decrease the influence on health is definitely COVID-19 immunization, NPIs are more successful at reducing transmission than vaccination[77]. It is advised in all situations to practise good cough and sneezing hygiene, wash your hands often with soap and water for at least 20 seconds, and use hand hygiene products such as gels or rubs with alcohol. These are easy ways to lessen exposure and the transmission of infection[78].

In order to determine incidents of transmission at the interface between humans and animals and prevent further spread, strong cooperation and exchange of information between the animal and public health departments, workplace safety, and health authorities are essential components of a One Health strategy[79]. Understanding aspects associated with transmission and evolutionary host-driven mechanisms requires combining testing methods with the genetic surveillance of viral samples from both animal sources and individuals in close proximity to animals with proven SARS-CoV-2 disease[80]. Gathering representative samples from both animals affected with SARS-CoV-2 and the general population is crucial for further characterizing viruses. It is imperative to use personal protective equipment (PPE) as a safety precaution for employees to avoid contact with animals or polluted work environments that harbour SARS-CoV-2[81]. Information on outbreaks should be quickly shared with public health authorities in order to provide appropriate follow-up with those exposed to the epidemic and the implementation of control measures.

Recent developments in SARS-CoV-2 diagnosis in animals

A variety of testing methods, such as viral nucleic acid detection and serological tests, must be taken into consideration depending on the diverse monitoring aims[82]. Respiratory tract samples, including those from the tonsils, soft palate, and nasal turbinate, are essential for viral analysis[7].

Particular care must be exercised if novel variations appear that might not show up in previously validated testing. It is

important to consider the limits of diagnostic testing. Among animals, especially in wild groups, very few diagnostic methods have been proven to be reliable. The most reliable method for identifying SARS-CoV-2 in animals is real-time reverse transcription polymerase chain reaction (RT-PCR)[83][84]. Additional techniques for identifying SARS-CoV-2 in animals include sequencing the viral genome, isolating the virus in a cultured cell, and using different molecular assays such as reverse transcription loop-mediated isothermal amplification (RT-LAMP)[85]. Antigen tests intended for humans should not be used on animals due to uncertain sensitivity and specificity[62].

Low specificity can have a significant impact on serological tests (such as neutralisation tests or ELISAs), which are crucial for both prospective and retroactive epidemiological investigations[86]. This is because low specificity might result in cross-reactions with antibodies against other coronaviruses that are often found in animals. Remarkably, several animals are able to generate antibodies against coronaviruses that do not harm them. For surveillance research, it is also possible to gather samples from the surroundings of animals. This could involve surface, air, or water sample collection for data related to the environment associated with SARS-CoV-2.

Diagnostic tests are only as useful when the community is completely involved, people participate in and adhere to confinement policies, and people wear personal protective equipment as prescribed. To effectively address the present and next pandemics, there has to be international unity over test accessibility. More significantly, infection control and diagnostic treatments need to be closely linked. The choice of therapy and how well it is working should be guided by the results of the diagnostic process[82].

Treatment and pharmaceutical prophylaxis of COVID-19

A variety of pharmaceuticals have been investigated to evaluate their safety and effectiveness as possible medicines for COVID-19 therapy or pharmacological prophylaxis. Among them are COVID-19 convalescent plasma, monoclonal antibodies, corticosteroids, immunomodulatory drugs, antivirals, and other medicinal substances[87]. Short- and medium-term COVID-19 treatment with therapeutic neutralising antibodies is thought to be successful[88]. Post-exposure prophylaxis (PEP) has been studied for a few antiviral monoclonal antibodies (casirivimab/imdevimab, amlanivimab/etesevimab), although none has been advised as of yet since they are not very effective against Omicron[89]. SARS-CoV-2 mutations and newly developing variants are among the most significant therapeutic problems, despite the large range of therapeutic alternatives offered for the treatment of COVID-19[87].

Conclusion

The novel coronavirus (SARS-CoV-2) may transmit through pet animals such as dogs and cats. It is known that in cats, ferrets, hamsters, and mice, SARS-CoV-2 may be directly transmitted from an animal donor to an animal receiver belonging to the same species; however, there is no proof that the virus can spread between dogs. Most likely, a human infection is the source of the SARS-CoV-2 infection in pet animals. Humans who often come into contact with companion animals from other households, such as veterinarians, are at a very low to low risk of contracting an infection from one of

these animals. So, avoid contact and separate them if any infection activities like diarrhea, cold, and fever are observed. The frequency of reports of COVID-19 detections in pets is steadily rising globally. The possibility of pets acting as effective reservoir hosts and changing the dynamics of human-to-human transmission has to be investigated further. To evaluate and pinpoint potential risk factors of animal-to-human transmission, epidemiologists are increasingly working in tandem with veterinary and wildlife professionals in their research. Effective management methods for newly developing zoonotic illnesses will be developed with the use of such collaboration. Since SARS-CoV-2 may communicate a disease to both humans and animals, it is strongly advised to avoid or restrict contact with animals. Those who must take care of their pets ought to practise excellent hygiene. Animals owned by people who have contracted SARS-CoV-2 should be confined indoors in accordance with local or national lockdown guidelines for people.

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