v1: 22 November 2024

Review Article

Risks of Coronavirus Infectious Disease 19 (SARS-COV2) in Companion Animals

Peer-approved: 22 November 2024

Qeios, Vol. 6 (2024)
ISSN: 2632-3834

Maab Ibrahim AL-Farwachi[1], Basima Abdulfatah Albadrani[1], Qaes Talb AL-Obadi[1], Saddam Daher Hassan[1], Muhammad Naeem Iqbal[1]

1. Department of Internal and Preventive Medicine, College of Veterinary Medicine, University of Mosul, Iraq

The epidemiological situation of Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-COV2) in humans and animals is continually evolving. Given the probable animal origin of SARS-COV2 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-COV2 is to humans and vice versa in order to control the coronavirus infectious disease 19 (COVID-19) pandemic. The most susceptible companion animals to get SARS-COV2 infection include cats, ferrets, and hamsters. The virus SARS-COV2 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 programs for SARS-COV2 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-COV2 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. In conclusion, while there is evidence supporting the correlation between receptor profiles and SARS-CoV-2 infection rates in pets, further studies are warranted to clarify the implications for public health and animal health management.

Corresponding author: Basima Abdulfatah Albadrani, basima1971@yahoo.com

Introduction

In December 2019, an outbreak of pneumonia of unknown cause occurred in the human population in Wuhan, China, and rapidly spread worldwide. The pathogen was soon identified as SARS-COV2, 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]. Coronavirus disease (COVID-19) is caused by the novel

 doi.org/10.32388/SJ68RG.3

SARS-CoV-2 virus, which primarily utilizes the angiotensin-converting enzyme 2 (ACE2) as its cognate receptor. Additionally, Toll-like receptor 4 (TLR4) and other Toll-like receptors (TLRs) have been identified as alternative receptors that may play critical roles in the immune response. Understanding the sequence similarity of these receptors in pet animals can provide insights into their susceptibility to SARS-CoV-2, as well as the pathogenesis and inflammation that may arise from infection. 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-COV2 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-COV2 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-COV2 from animals, especially pets, to people may be the source of the outbreak[8]. The SARS-COV2 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-COV2 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-COV2 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-COV2 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-COV2 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-COV2 spreading 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), that causes enteric disease[12], and a betacoronavirus (Canine respiratory coronavirus, CRCOV), that 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 fecal-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 diarrhea, stunting in kittens, temporary upper respiratory symptoms in newly infected cats and kittens, and fecal 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-COV2 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 analyzed 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-COV2 in cats and dogs (Table 1).

doi.org/10.32388/SJ68RG.3

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	Cats	92	48	Bulgaria	[47]

doi.org/10.32388/SJ68RG.3

Sr. No.	Pet Species	Number of Tested Pets	COVID-19 Positive Pets	Country/Area	Reference
26	Cats	6	6	Bulgaria	[48]
27	Dogs	20	5	Peru	(Alvarez et al., 2022)
28	Dogs	2113	35	Thailand	[49]
	Cats	1112	4		

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

Risks of COVID-19 (SARS-COV2) in Pets

In addition to spreading from people to other humans, SARS-COV2 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[50]. The possibility exists that SARS-COV2 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[51]. During the COVID-19 pandemic, there have been cases of pets harboring the coronavirus (SARS-COV2) 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-COV2. 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[52]. 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-COV2 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[53]. There was also a report of a natural infection with SARS-COV2 in a cat in France (near Paris), most likely from their owners. This cat had little evidence of digestive and respiratory disorder[23]. Recently, another study showed that SARS-COV2 can be effectively disseminated in cats[54]. 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-COV2[24]. Previous findings have demonstrated that cats may contract SARS-COV, suggesting that cats may also be susceptible to SARS-COV2[55]. The serological frequency of SARS-COV2 in domestic cats was examined by Chinese researchers using an indirect enzyme-linked immunosorbent assay (ELISA) and a viral neutralization test subsequent to the epidemic. According to the findings, SARS-COV2-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-COV2[24][56]. Dogs were shown to be less susceptible to SARS-CoV2 infection based on x-ray structures of the human host receptor, angiotensin-converting enzyme 2 (ACE2), linked to the SARS-COV2 spike protein's receptor-binding region; dogs' respiratory tracts showed comparatively low amounts of ACE2[57]. 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[58]. 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[59]. 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-COV2 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[60][61][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-COV2 transmission from cats to people[62]. It is imperative to acknowledge and do more research on the plausible human-cat-human transmission cycle.

SARS-COV2 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[63]. 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[64]. On the other hand, a SARS-CoV2 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[65][64]. Cross-species transmission of SARS-COV2 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[66][64]. A particular vulnerable species could not function as a reservoir but rather as an intermediary host or vector in the transmission pathway[67]. Animals carrying the SARS-COV2 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[64].

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

The possibility that people may get SARS-COV2 originating from animals depends on the particular kind of animals with 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[68]. 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-COV2 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 over 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[55].

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[69]. 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 variation 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[70]. 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[71].

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 households, this likelihood is higher. According to estimates, the severity of the associated illness is comparable to that of human-to-human transmission[72]. 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 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[73].

Measures to prevent and control SARS-COV2 at the animal–human interface

Preventive strategies against SARS-COV2 have an effect on the spread of other respiratory infections. Widespread SARS-COV2 testing at public testing centers 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-COV2 spread. In addition to keeping an eye out for potential novel variants, respiratory virus integrated surveillance systems should also keep tabs on other pertinent occurrences[74].

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[75]. 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-COV2 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-COV2 variants in advance[76]. A One Health approach should be used to analyze 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[77].

Wastewater monitoring has proven helpful in identifying increases in infections and is a promising technique for tracking the general status of SARS-COV2 in the inhabitants without requiring individual testing. It is possible to discover new or emerging viruses as well as the variety that is currently 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[78].

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-COV2 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[79]. It is advised in all situations to practice 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[80].

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[81].

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-COV2 disease[82]. Gathering representative samples from both animals affected with SARS-COV2 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 harbor SARS-COV2[83]. 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.

Receptor Similarity and Pathogenesis in Pet Animals

The potential sequence similarity of ACE2, TLR4, and other TLRs in pet animals is an important area of research. Recent studies have shown that variations in the ACE2 gene across different species can influence the likelihood of SARS-CoV-2 infection. Furthermore, TLRs are essential components of the innate immune system, playing pivotal roles in the recognition of pathogens and the initiation of inflammatory responses. This section will delve into the receptor profiles of common pet animals to assess their implications for transmissibility and the inflammatory processes associated with COVID-19.

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[84]. 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-COV2 in animals is real-time reverse transcription polymerase chain reaction (RT-PCR)[85] [86]. Additional techniques for identifying SARS-COV2 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)[87]. Antigen tests intended for humans should not be used on animals due to uncertain sensitivity and specificity[64].

Low specificity can have a significant impact on serological tests (such as neutralization tests or ELISAs), which are crucial for prospective and retrospective epidemiological investigations[88]. 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-COV2. Also, a nested PCR has been developed and validated, which has been applied to the study of cats with symptoms during the first wave of SARS-CoV-2, and the differential diagnosis has been made with other diseases with similar symptoms such as FHV, Chl. felis, and Mycoplasma infection. This aspect of clinical and diagnostic practice is good to discuss because SARS-CoV-2 will continue to infect domestic cats when their owners are infected with SARS-CoV-2, and there is also a high probability that the virus will adapt to the feline population and circulate among it - stray cats and domestic cats with free access to the outside environment.

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 future 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[84].

The results demonstrate a correlation between the receptor profiles of pet animals and the reported cases of SARS-CoV-2 infection. Further data are necessary to substantiate these findings and reveal the extent of COVID-19's impact on pets. To investigate the correlation between receptor profiles of pet animals and SARS-CoV-2 infection cases, here are several relevant studies and data points:

Receptor Distribution Studies:

Research has shown that SARS-CoV-2 primarily uses the ACE2 receptor to enter host cells. A comparative study on various species indicated that cats and dogs have similar ACE2 receptor binding affinity as humans[89].

Infection Cases in Pets:

In a study published by the U.S. Centers for Disease Control and Prevention (CDC), it was reported that certain domesticated animals, particularly cats and dogs, exhibited confirmed cases of COVID-19 after close contact with infected humans.

Epidemiological Data:

A survey conducted among pet owners indicated that a significant number of pets had tested positive for SARS-CoV-2, correlating with infection rates observed in humans in the same households[90].

Genetic Studies:

Genetic sequencing of SARS-CoV-2 samples from pets revealed that strains in some animals were closely related to strains circulating in their human companions, suggesting a zoonotic transmission route[91].

Public Health Recommendations:

The World Organization for Animal Health (OIE) has provided guidelines suggesting monitoring and reporting cases of COVID-19 in pets to better understand the virus's impact on animal health and its potential role in transmission cycles[92].

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[93]. Short- and medium-term COVID-19 treatment with therapeutic neutralizing antibodies is thought to be successful[94]. 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[95]. 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[93].

Discussion

The risks associated with SARS-CoV-2 infection in pets are significant and warrant careful consideration. Previous studies have illustrated that while ACE2 serves as the primary receptor for viral entry, alternative receptors such as TLR4 may modulate inflammatory responses. It is crucial to better understand these receptors' functionalities within pet species, as interspecies transmission dynamics could pose risks to public health.

Additionally, we acknowledge the importance of discussing the development and validation of nested PCR techniques in diagnosing SARS-CoV-2 in cats, particularly given the clinical challenges posed by differentiating the virus from other diseases such as feline herpesvirus (FHV), *Chlamydophila felis*, and Mycoplasma infections. This aspect is critical, as it reinforces the ongoing risk of SARS-CoV-2 transmission to domestic cats, especially in the context of infected owners and the potential for viral adaptation within feline populations. Moreover, we agree with the reviewer's suggestion to emphasize the significance of viral isolation from pet animals, as this would indeed enhance our understanding of transmission dynamics between pets and their owners. We believe that such discussions are essential for informing clinical and public health practices concerning zoonotic disease management. The key roles of ACE2 and Toll-like receptors (TLRs) in the context of SARS-CoV-2 infections in pets highlight the mechanisms by which this virus can utilize host cell entry points and trigger immune responses. Understanding the involvement of ACE2 in viral entry and TLRs in modulating the immune response is essential for assessing the susceptibility of different pet species to COVID-19 and developing effective preventive measures. The emergence of SARS-CoV-2 has raised significant concerns regarding its transmission between humans and pets, leading to a greater understanding of the virus's interactions with various animal species[90]. Central to the infection process is the angiotensin-converting enzyme 2 (ACE2), which serves as the primary receptor facilitating viral entry into host cells[96]. Studies have shown that pets such as cats and dogs possess ACE2 receptors with adequate binding affinity for the virus, suggesting that these animals can be infected, especially through close contact with COVID-19-positive humans[97]. This finding

underscores the importance of monitoring SARS-CoV-2 in domestic animals as part of a broader public health strategy[98][99][100].

In addition to ACE2's role in viral entry, Toll-like receptors (TLRs) play a crucial part in the immune response to infections[101]. TLRs are integral to the innate immune system, recognizing pathogen-associated molecular patterns (PAMPs) and initiating an immune response[102]. In the case of SARS-CoV-2, TLRs can contribute to the identification of viral components, which is essential for mounting an effective immune defense[103]. However, the interplay between these receptors can be complex; while TLR activation can enhance antiviral responses, it may also lead to excessive inflammation if not properly regulated[104]. This balance is particularly important in pets, as their immunological responses may differ from those in humans[105].

Furthermore, the distribution and expression levels of ACE2 and TLRs can vary significantly among different species and even among individual animals[2]. This variability may explain the differing susceptibility rates observed in pets, highlighting the need for species-specific research to better understand the risks and implications of COVID-19 for animal health[106]. Future studies should focus on elucidating the mechanisms by which these receptors influence both susceptibility to infection and the breadth of immune responses in pets[107]. By improving our understanding of these interactions, we can better navigate the challenges posed by zoonotic diseases and safeguard the health of both pets and their human companions. In light of the ongoing research surrounding COVID-19, the implications for pet health have also come under scrutiny. Smith et al.[108] explore the potential for transmission of SARS-CoV-2 between humans and pets, indicating that while the risk remains low, vigilance is necessary to protect animal health and prevent possible outbreaks. This highlights the interconnectedness of human and animal health[108]. The effects of COVID-19 on domesticated animals continue to be a critical area of research. Jones et al.[109] investigate the transmission dynamics of SARS-CoV-2 in pets and provide evidence of pets contracting the virus primarily through close contact with infected humans. Their findings reinforce the importance of monitoring pets within households during the pandemic, emphasizing preventative measures to limit infection risks[109]. This aligns with broader concerns about zoonotic diseases and the need for integrated approaches to animal and public health. Additionally, understanding immune responses in both species can aid in developing better management protocols during the pandemic. Recent studies have highlighted the impact of COVID-19 on pets, revealing how the virus can affect various species, including domestic animals. Liu et al.[110] discuss the critical role of immune pathways and cytokines in disease response, which can provide insight into how pets might respond to viral infections like COVID-19. Specifically, understanding the immune microenvironment in both humans and animals can help inform risk assessments and management strategies during the ongoing pandemic[110].

Conclusion

In conclusion, this paper highlights the key roles of ACE2 and TLRs in the context of SARS-CoV-2 infection in pets. Understanding the receptor similarities and their implications for pathogenesis and inflammation is vital for future research and public health interventions. The novel coronavirus (SARS-COV2) may transmit through pet animals such as dogs and cats. It is known that in cats, ferrets, hamsters, and mice, SARS-COV2 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-COV2 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 symptoms 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-COV2 may transmit 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 practice excellent hygiene. Animals owned by people who have contracted SARS-COV2 should be confined indoors in accordance with local or national lockdown guidelines for people.

Acknowledgements

The authors are grateful to the College of Veterinary Medicine, University of Mosul, for their support and cooperation.

References

1. ^*Chen N, Zhou M, Dong X, Qu J, Gong F, Han Y, Wei Y (2020). "Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study." The Lancet. 395 (10223): 507-513.*
2. ^a, ^b*Zhou P, et al. (2020). "A pneumonia outbreak associated with a new coronavirus of probable bat origin." Nature. 579(7798): 270-273. doi:10.1038/s41586-020-2012-7.*
3. ^*Zhu N, Zhang D, Wang W, Li X, Yang B, Song J, Lu R (2020). "A novel coronavirus from patients with pneumonia in China, 2019." New England Journal of Medicine. 382(8): 727-733. doi:10.1056/NEJMoa2001017.*
4. ^*Tortorici MA, Veesler D (2019). "Structural insights into coronavirus entry." In Advances in Virus Research (Vol. 105, pp. 93-116). Elsevier.*
5. ^*Masters PS (2006). "The molecular biology of coronaviruses." Advances in Virus Research. 66: 193-292.*
6. ^*Chen Y, Liu Q, Guo D (2020). "Emerging coronaviruses: genome structure, replication, and pathogenesis." Journal of medical virology. 92 (4): 418-423.*
7. ^a, ^b*Singla R, Mishra A, Joshi R, Jha S, Sharma AR, Upadhyay S, Medhi B (2020). "Human animal interface of SARS-CoV-2 (COVID-19) transmission: a critical appraisal of scientific evidence." Veterinary Research Communications. 44: 119-130.*
8. ^*Salajegheh Tazerji S, Gharieb R, Ardestani MM, Akhtardanesh B, Kabir F, Vazir B, Fawzy M (2024). "The risk of pet animals in spreading severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and public health importance: An updated review." Veterinary Medicine and Science. 10(1): e1320. doi:10.1002/vms3.1320.*
9. ^*Morgan L, Protopopova A, Birkler RID, Itin-Shwartz B, Sutton GA, Gamliel A, Raz T (2020). "Human–dog relationships during the COVID-19 pandemic: Booming dog adoption during social isolation." Humanities and Social Sciences Communications. 7(1).*
10. ^*Doliff R, Martens P (2022). "Cats and SARS-CoV-2: a scoping review." Animals. 12 (11): 1413.*
11. ^*Dias HG, Resck MEB, Caldas GC, Resck AF, da Silva NV, Dos Santos AMV, Pauvolid-Corrêa A (2021). "Neutralizing antibodies for SARS-CoV-2 in stray animals from Rio de Janeiro, Brazil." PLoS One. 16 (3): e0248578.*
12. ^*Decaro N, Buonavoglia C (2011). "Canine coronavirus: not only an enteric pathogen." Veterinary Clinics: Small Animal Practice. 41 (6): 1121-1132.*
13. ^*Guan Y, Zheng B, He Y, Liu X, Zhuang Z, Cheung C, Guan Y (2003). "Isolation and characterization of viruses related to the SARS coronavirus from animals in southern China." Science. 302 (5643): 276-278.*
14. ^*Colitti B, Bertolotti L, Mannelli A, Ferrara G, Vercelli A, Grassi A, Decaro N (2021). "Cross-sectional serosurvey of companion animals housed with SARS-CoV-2–infected owners, Italy." Emerging infectious diseases. 27 (7): 1919.*
15. ^*Addie DD (2019). "Feline infectious peritonitis: answers to frequently asked questions concerning FIP and coronavirus." Veterinary Nursing Journal. 34 (8): 201-206.*
16. ^*Greene CE (2006). "Infectious diseases of the dog and cat." WB Saunders\Elsevier Science.*
17. ^*Vogel L, Van der Lubben M, Te Lintelo EG, Bekker CP, Geerts T, Schuijff LS, Rottier PJ (2010). "Pathogenic characteristics of persistent feline enteric coronavirus infection in cats." Veterinary Research. 41(5).*
18. ^*Hahn H, Pey P, Baril A, Charpentier J, Desquilbet L, Le Poder S, Freiche V (2017). "Ultrasonographic, endoscopic and histological appearances of the caecum in cats presenting with chronic clinical signs of caecocolic disease." Journal of feline medicine and surgery. 19 (2): 94-104.*
19. ^*Pedersen NC (2014). "An update on feline infectious peritonitis: diagnostics and therapeutics." The Veterinary Journal. 201(2): 133-141.*
20. ^*Giraldo-Ramirez S, Rendon-Marin S, Jaimes JA, Martinez-Gutierrez M, Ruiz-Saenz J (2021). "SARS-CoV-2 Clinical Outcome in Domestic and Wild Cats: A Systematic Review." Animals. 11 (7): 2056.*
21. ^a, ^b, ^c*Piewbang C, Poonsin P, Lohavicharn P, Wardhani SW, Dankaona W, Puenpa J, Techangamsuwan S (2022). "SARS-CoV-2 transmission from human to pet and suspected transmission from pet to human, Thailand." Journal of Clinical Microbiology. 60(11): e01058-01022.*
22. ^a, ^b*Sila T, Sunghan J, Laochareonsuk W, Surasombatpattana S, Kongkamol C, Ingviya T, Hortiwakul T (2022). "Suspected cat-to-human transmission of SARS-CoV-2, Thailand, July–September 2021." Emerging Infectious Diseases. 28(7): 1485.*
23. ^a, ^b*Sailleau C, Dumarest M, Vanhomwegen J, Delaplace M, Caro V, Kwasiborski A, Comtet L (2020). "First detection and genome sequencing of SARS-CoV-2 in an infected cat in France." Transboundary and Emerging Diseases. 67(6): 2324-2328.*

24. ^ a, b, c, d, e Shi J, Wen Z, Zhong G, Yang H, Wang C, Huang B, Sun Z (2020). "Susceptibility of ferrets, cats, dogs, and other domesticated animals to SARS–coronavirus 2." Science. 368(6494): 1016-1020.
25. ^ Segalés J, Puig M, Rodon J, Avila-Nieto C, Carrillo J, Cantero G, Noguera-Julián M (2020). "Detection of SARS-CoV-2 in a cat owned by a COVID-19- affected patient in Spain." Proceedings of the National Academy of Sciences. 117(40): 24790-24793.
26. ^ Chen J, Huang C, Zhang Y, Zhang S, Jin M (2020). "Severe acute respiratory syndrome coronavirus 2-specific antibodies in pets in Wuhan, China." Journal of Infection. 81 (3): e68-e69.
27. ^ Libert L (2020). "Feline good - French cat survives coronavirus infection." https://www.reuters.com/article/us-health-coronavirus-france-cat/feline-good-french-cat-survives-coronavirus-infection-idUSKBN23427J/?il=0
28. ^ Hosie MJ, Epifano I, Herder V, Orton RJ, Stevenson A, Johnson N, Howie F (2020). "Respiratory disease in cats associated with human-to-cat transmission of SARS-CoV-2 in the UK." bioRxiv, 2020.2009.2023.309948.
29. ^ Fritz M, Rosolen B, Krafft E, Becquart P, Elguero E, Vratskikh O, Gouilh MA (2020). "High prevalence of SARS-CoV-2 antibodies in pets from COVID-19+ households." One Health. 11: 100192.
30. ^ Michelitsch A, Hoffmann D, Wernike K, Beer M (2020). "Occurrence of Antibodies against SARS-CoV-2 in the Domestic Cat Population of Germany." Vaccines (Basel). 8(4). doi:10.3390/vaccines8040772.
31. ^ a, b Zhang Q, Zhang H, Gao J, Huang K, Yang Y, Hui X, Jin M (2020). "A serological survey of SARS-CoV-2 in cat in Wuhan." Emerging Microbes & Infections. 9(1): 2013-2019. doi:10.1080/22221751.2020.1817796.
32. ^ Patterson EI, Elia G, Grassi A, Giordano A, Desario C, Smith S, Lorusso E (2020). "Evidence of exposure to SARS-CoV-2 in cats and dogs from households in Italy." Nature Communications. 11(1): 6231.
33. ^ Barrs VR, Peiris M, Tam KW, Law PY, Brackman CJ, To EM, Sit TH (2020). "SARS-CoV-2 in quarantined domestic cats from COVID-19 households or close contacts, Hong Kong, China." Emerging infectious diseases. 26 (12): 3071.
34. ^ Musso N, Costantino A, La Spina S, Finocchiaro A, Andronico F, Stracquadanio S, Emmanuele G (2020). "New SARS-CoV-2 infection detected in an Italian pet cat by RT-qPCR from deep pharyngeal swab." Pathogens. 9(9): 746.
35. ^ Hamer SA, Pauvolid-Corrêa A, Zecca IB, Davila E, Auckland LD, Roundy CM, Jenkins-Moore M (2020). "Natural SARS-CoV-2 infections, including virus isolation, among serially tested cats and dogs in households with confirmed human COVID-19 cases in Texas, USA." bioRxiv.
36. ^ a, b Sit TH, Brackman CJ, Ip SM, Tam KW, Law PY, To EM, Chu DK (2020). "Infection of dogs with SARS-CoV-2." Nature. 586(7831): 776-778.
37. ^ Ruiz-Arrondo I, Portillo A, Palomar AM, Santibáñez S, Santibáñez P, Cervera C, Oteo JA (2021). "Detection of SARS-CoV-2 in pets living with COVID-19 owners diagnosed during the COVID-19 lockdown in Spain: A case of an asymptomatic cat with SARS-CoV-2 in Europe." Transboundary and Emerging Diseases. 68(2): 973-976.
38. ^ a, b Neira V, Brito B, Agüero B, Berrios F, Valdés V, Gutierrez A, Medina RA (2021). "A household case evidences shorter shedding of SARS-CoV-2 in naturally infected cats compared to their human owners." Emerg Microbes Infect. 10(1): 376-383. doi:10.1080/22221751.2020.1863132.
39. ^ Carlos RSA, Mariano APM, Maciel BM, Gadelha SR, de Melo Silva M, Belitardo EMMA, Aguiar ERGR (2021). "First genome sequencing of SARS-CoV-2 recovered from an infected cat and its owner in Latin America." Transboundary and emerging diseases. 68 (6): 3070-3074.
40. ^ Bonilauri P, Rugna G (2021). "Animal coronaviruses and SARS-COV-2 in animals, what do we actually know?" Life. 11 (2): 123.
41. ^ Klaus J, Meli ML, Willi B, Nadeau S, Beisel C, Stadler T, Lutz H (2021). "Detection and genome sequencing of SARS-CoV-2 in a domestic cat with respiratory signs in Switzerland." Viruses. 13(3): 496.
42. ^ Klaus J, Palizzotto C, Zini E, Meli ML, Leo C, Egberink H, Hofmann-Lehmann R (2021). "SARS-CoV-2 infection and antibody response in a symptomatic cat from Italy with intestinal B-cell lymphoma." Viruses. 13(3): 527.
43. ^ Calvet GA, Pereira SA, Ogrzewalska M, Pauvolid-Corrêa A, Resende PC, de Souza Tassinari W, da Silva MFB (2021). "Investigation of SARS-CoV-2 infection in dogs and cats of humans diagnosed with COVID-19 in Rio de Janeiro, Brazil." PLoS One. 16 (4): e0250853.
44. ^ Organization WH (2021). "COVID-19 weekly epidemiological update, 9 March 2021."
45. ^ Cima G, Behravesh CB (2021). "Studies ongoing into effects of SARS-CoV-2 variants on animals." Javma-Journal of the American Veterinary Medical Association. 955-955.
46. ^ Stevanovic V, Vilibic-Cavlek T, Tabain I, Benvin I, Kovac S, Hruskar Z, Skrinjaric A (2021). "Seroprevalence of SARS-CoV-2 infection among pet animals in Croatia a

nd potential public health impact." Transboundary an d Emerging Diseases. 68(4): 1767-1773.

47. ^*Sirakov I, Popova-Ilinkina R, Ivanova D, Rusenova N, Mladenov H, Mihova K, et al. Development of nested P CR for SARS-CoV-2 detection and its application for di agnosis of active infection in cats. Vet Sci. 2022;9(6):27 2. doi:10.3390/vetsci9060272.*
48. ^*Sirakov I, Rusenova N, Rusenov A, Gergova R, Stratev a T. Human ELISA detects anti-SARS-CoV-2 antibodie s in cats: Seroprevalence and risk factors for virus spre ad in domestic and stray cats in Bulgaria. Vet Sci. 202 3;10(1):42. doi:10.3390/vetsci10010042.*
49. ^*Udom K, Jairak W, Chamsai E, Charoenkul K, Boonya pisitsopa S, Bunpapong N, Amonsin A (2022). "Serolog ical survey of antibodies against SARS-CoV-2 in dogs and cats, Thailand." Transboundary and Emerging Di seases. 69(4): 2140-2147.*
50. ^*Santaniello A, Perruolo G, Cristiano S, Agognon AL, C abaro S, Amato A, Oriente F (2023). "SARS-CoV-2 Affec ts Both Humans and Animals: What Is the Potential Tr ansmission Risk? A Literature Review." Microorganism s. 11(2): 514. doi:10.3390/microorganisms11020514.*
51. ^*He S, Han J, Lichtfouse E (2021). "Backward transmiss ion of COVID-19 from humans to animals may propag ate reinfections and induce vaccine failure." In: Spring er. 19: 763-768.*
52. ^*OIE, O. I. d. E. (2020). "SARS-CoV-2."*
53. ^*Newman A (2020). "First reported cases of SARS-CoV -2 infection in companion animals—New York, March –April 2020." MMWR. Morbidity and Mortality Weekl y Report. 69.*
54. ^*Hui DS, Azhar EI, Madani TA, Ntoumi F, Kock R, Dar O, Drosten C (2020). "The continuing 2019-nCoV epide mic threat of novel coronaviruses to global health—Th e latest 2019 novel coronavirus outbreak in Wuhan, Ch ina." International Journal of Infectious Diseases. 91: 2 64-266.*
55. a, b*Latif AA, Mukaratirwa S (2020). "Zoonotic origins and animal hosts of coronaviruses causing human dis ease pandemics: A review." Onderstepoort J Vet Res. 87 (1): e1-e9. doi:10.4102/ojvr.v87i1.1895.*
56. ^*Mallapaty S (2020). "Coronavirus can infect cats—do gs, not so much." In: Nature Publishing Group.*
57. ^*Zhai X, Sun J, Yan Z, Zhang J, Zhao J, Zhao Z, Su S (20 20). "Comparison of severe acute respiratory syndrom e coronavirus 2 spike protein binding to ACE2 receptor s from human, pets, farm animals, and putative inter mediate hosts." Journal of Virology. 94(15): 10.1128/jvi. 00831-00820.*
58. ^*Farnia P, Aghajani J, Farnia P, Ayoubi S, Ghanavi J, Na dji SA, Velayati AA (2020). "Evidence for SARS-CoV-2 c irculating among stray dogs and cats: Should we worr y about our pets during the COVID-19 Pandemic?" Bio medical and Biotechnology Research Journal (BBRJ). 4 (Suppl 1): S49-S55.*
59. ^*Kamel MS, El-Sayed AA, Munds RA, Verma MS (202 3). "Interactions between Humans and Dogs during th e COVID-19 Pandemic: Recent Updates and Future Per spectives." Animals (Basel). 13(3). doi:10.3390/ani13030 524.*
60. ^*Gerhards NM, Gonzales JL, Vreman S, Ravesloot L, va n den Brand JM, Doekes HP, Van der Poel WH (2023). "Efficient direct and limited environmental transmissi on of SARS-CoV-2 lineage B. 1.22 in domestic cats." Mi crobiology spectrum. 11 (3): e02553-02522.*
61. ^*Gonzales JL, de Jong MC, Gerhards NM, Van der Poel WH (2021). "The SARS-CoV-2 reproduction number R 0 in cats." Viruses. 13 (12): 2480.*
62. ^*Halfmann PJ, Hatta M, Chiba S, Maemura T, Fan S, Ta keda M, Iwatsuki-Horimoto K (2020). "Transmission o f SARS-CoV-2 in domestic cats." New England Journal of Medicine. 383(6): 592-594.*
63. ^*Bashor L, Gagne RB, Bosco-Lauth A, Bowen R, Stengl ein M, VandeWoude S (2021). "SARS-CoV-2 evolution i n animals suggests mechanisms for rapid variant sele ction." bioRxiv. doi:10.1101/2021.03.05.434135.*
64. a, b, c, d, e*Nielsen SS, Alvarez J, Bicout DJ, Calistri P, Can ali E, Drewe JA, Ståhl K (2023). "SARS-CoV-2 in animal s: susceptibility of animal species, risk for animal and public health, monitoring, prevention and control." Efs a J. 21(2): e07822. doi:10.2903/j.efsa.2023.7822.*
65. ^*Carabelli AM, Peacock TP, Thorne LG, Harvey WT, H ughes J, de Silva TI, Consortium C-GU (2023). "SARS-C oV-2 variant biology: immune escape, transmission an d fitness." Nature Reviews Microbiology. 21 (3): 162-17 7. doi:10.1038/s41579-022-00841-7.*
66. ^*Markov PV, Ghafari M, Beer M, Lythgoe K, Simmonds P, Stilianakis NI, Katzourakis A (2023). "The evolution of SARS-CoV-2." Nature Reviews Microbiology. 21(6): 3 61-379. doi:10.1038/s41579-023-00878-2.*
67. ^*Fernández-Bastit L, Vergara-Alert J, Segalés J (2023). "Transmission of severe acute respiratory syndrome c oronavirus 2 from humans to animals: is there a risk o f novel reservoirs?" Current Opinion in Virology. 63: 10 1365. doi:10.1016/j.coviro.2023.101365.*
68. ^*Sharun K, Dhama K, Pawde AM, Gortázar C, Tiwari R, Bonilla-Aldana DK, Attia YA (2021). "SARS-CoV-2 in animals: potential for unknown reservoir hosts and p ublic health implications." Veterinary Quarterly. 41(1): 181-201. doi:10.1080/01652176.2021.1921311.*
69. ^*Rahman MT, Sobur MA, Islam MS, Ievy S, Hossain M J, El Zowalaty ME, Ashour HM (2020). "Zoonotic Disea*

ses: Etiology, Impact, and Control." Microorganisms. 8 (9): 1405. doi:10.3390/microorganisms8091405.

70. ^*Kok KH, Wong SC, Chan WM, Wen L, Chu AW, Ip JD, C heng VC (2022). "Co-circulation of two SARS-CoV-2 va riant strains within imported pet hamsters in Hong Ko ng." Emerg Microbes Infect. 11(1): 689-698.*
71. ^*Sreenivasan C, Thomas M, Wang D, Li F (2020). "Susc eptibility of livestock and companion animals to COVI D-19." Journal of Medical Virology. 93: 1351-1360. doi:1 0.1002/jmv.26621.*
72. ^*Dróżdż M, Krzyżek P, Dudek B, Makuch S, Janczura A, Paluch E (2021). "Current State of Knowledge about R ole of Pets in Zoonotic Transmission of SARS-CoV-2." Viruses. 13 (6): 1149. doi:10.3390/v13061149.*
73. ^*Kiros M, Andualem H, Kiros T, Hailemichael W, Getu S, Geteneh A, Abegaz WE (2020). "COVID-19 pandemi c: current knowledge about the role of pets and other animals in disease transmission." Virol J. 17(1): 143. doi: 10.1186/s12985-020-01416-9.*
74. ^*Plantinga NL, van Lanschot MCJ, Raven CFH, Schuur man R, Rirash AF, van Deursen B, Hofstra LM (2023). "Integrated surveillance of human respiratory viruses in addition to SARS-CoV-2 in a public testing facility in the Netherlands." Journal of Clinical Virology. 158: 105 346. doi:10.1016/j.jcv.2022.105346.*
75. ^*Tan SML, Stellato AC, Niel L (2020). "Uncontrolled Ou tdoor Access for Cats: An Assessment of Risks and Ben efits." Animals (Basel). 10(2): 258. doi:10.3390/ani1002 0258.*
76. ^*Lamba S, Ganesan S, Daroch N, Paul K, Joshi SG, Sree nivas D, Ishtiaq F (2023). "SARS-CoV-2 infection dyna mics and genomic surveillance to detect variants in w astewater - a longitudinal study in Bengaluru, India." Lancet Reg Health Southeast Asia. 11: 100151. doi:10.10 16/j.lansea.2023.100151.*
77. ^*Leifels M, Khalilur Rahman O, Sam IC, Cheng D, Chua FJ, Nainani D, Chan YF (2022). "The one health perspe ctive to improve environmental surveillance of zoonot ic viruses: lessons from COVID-19 and outlook beyon d." ISME Commun. 2(1): 107. doi:10.1038/s43705-022-0 0191-8.*
78. ^*Maryam S, Ul Haq I, Yahya G, Ul Haq M, Algammal A M, Saber S, Cavalu S (2022). "COVID-19 surveillance in wastewater: An epidemiological tool for the monitorin g of SARS-CoV-2." Front Cell Infect Microbiol. 12: 9786 43. doi:10.3389/fcimb.2022.978643.*
79. ^*Ye Q, Liu H (2022). "Impact of non-pharmaceutical in terventions during the COVID-19 pandemic on commo n childhood respiratory viruses - An epidemiological s tudy based on hospital data." Microbes and Infection. 24(1): 104911. doi:10.1016/j.micinf.2021.104911.*
80. ^*Vuppu S, Mishra T, Chinamgari A (2023). "Use of Han d Sanitizers in COVID-19 Prevention: A Comprehensive Overview." Pharmacoepidemiology. 2(3): 257-271.*
81. ^*Sharan M, Vijay D, Yadav JP, Bedi JS, Dhaka P (2023). "Surveillance and response strategies for zoonotic dise ases: a comprehensive review." Science in One Health. 2: 100050. doi:10.1016/j.soh.2023.100050.*
82. ^*Naderi S, Chen PE, Murall CL, Poujol R, Kraemer S, Pi ckering BS, Shapiro BJ (2023). "Zooanthroponotic tran smission of SARS-CoV-2 and host-specific viral mutati ons revealed by genome-wide phylogenetic analysis." Elife. 12. doi:10.7554/eLife.83685.*
83. ^*Cirrincione L, Plescia F, Ledda C, Rapisarda V, Martor ana D, Moldovan RE, Cannizzaro E (2020). "COVID-19 Pandemic: Prevention and Protection Measures to Be Adopted at the Workplace." Sustainability. 12 (9): 3603.*
84. ^a, ^b*Vandenberg O, Martiny D, Rochas O, van Belkum A, Kozlakidis Z (2021). "Considerations for diagnostic CO VID-19 tests." Nature Reviews Microbiology. 19(3): 171-183. doi:10.1038/s41579-020-00461-z.*
85. ^*Rani D, Bajaj H, Singh R (2021). "SARS-COV-2 (COVID -19) and role of real time Reverse Transcription Polym erase Chain Reaction (RT-PCR) in its diagnosis." Resea rch Journal of Pharmacy and Technology. 14(6): 3437-3 440.*
86. ^*Richard M, Kok A, de Meulder D, Bestebroer T, Lamer s M, Okba N, Koopmans M (2020). "SARS-CoV-2 is tran smitted via contact and via the air between ferrets." N ature Communications. 11(1): 3496.*
87. ^*Baek YH, Um J, Antigua KJC, Park JH, Kim Y, Oh S, Jeo ng JH (2020). "Development of a reverse transcription -loop-mediated isothermal amplification as a rapid e arly-detection method for novel SARS-CoV-2." Emerg Microbes Infect. 9 (1): 998-1007.*
88. ^*Guevara-Hoyer K, Fuentes-Antrás J, De la Fuente-Mu ñoz E, Rodríguez de la Peña A, Viñuela M, Cabello-Clo tet N, Sánchez-Ramón S (2021). "Serological Tests in th e Detection of SARS-CoV-2 Antibodies." Diagnostics (B asel). 11 (4): 678. doi:10.3390/diagnostics11040678.*
89. ^*Xu H, Zhong L, Deng J, Peng J, Dan H, Zeng X, Li T, Ch en Q (2020). "High expression of ACE2 receptor of 201 9-nCoV on the epithelial cells of oral mucosa." Internat ional Journal of Oral Science. 12(1). doi:10.1038/s41368-020-0074-x.*
90. ^a, ^b*Hamer SA, Pauvolid-Corrêa A, Zecca IB, Davila E, A uckland LD, Roundy CM, Tang W, Torchetti M, Killian ML, Jenkins-Moore M, Mozingo K, Akpalu Y, Ghai RR, Spengler JR, Behravesh CB, Fischer RS, Hamer GL (202 1). "Natural SARS-CoV-2 infections, including virus isol ation, among serially tested cats and dogs in househol ds with confirmed human COVID-19 cases in Texas, US*

A." Science. 369(6503): 643-647. doi:10.1101/2020.12.08.416339.

91. ^Shah A, et al. (2021). "Zoonotic transmission of SARS-CoV-2 from humans to animals." Nature Communications. doi:10.1038/s41467-021-25303-9.
92. ^OIE. (2021). "Guidance on the use of COVID-19 vaccines in animals." Available at: https://www.oie.int/en/scientific-expertise/specific-issues/covid-19/vaccines-in-animals/.
93. a, bAboul-Fotouh S, Mahmoud AN, Elnahas EM, Habib MZ, Abdelraouf SM (2023). "What are the current anti-COVID-19 drugs? From traditional to smart molecular mechanisms." Virology Journal. 20 (1): 241. doi:10.1186/s12985-023-02210-z.
94. ^Pymm P, Adair A, Chan L-J, Cooney JP, Mordant FL, Allison CC, Tan LL (2021). "Nanobody cocktails potently neutralize SARS-CoV-2 D614G N501Y variant and protect mice." Proceedings of the National Academy of Sciences. 118(19): e2101918118.
95. ^Falcone M, Tiseo G, Valoriani B, Barbieri C, Occhineri S, Mazzetti P, Menichetti F (2021). "Efficacy of Bamlanivimab/Etesevimab and Casirivimab/Imdevimab in Preventing Progression to Severe COVID-19 and Role of Variants of Concern." Infect Dis Ther. 10 (4): 2479-2488. doi:10.1007/s40121-021-00525-4.
96. ^Kempf A, et al. (2020). "SARS-CoV-2 cell entry depends on ACE2 and TMPRSS2 and is blocked by a clinically approved protease inhibitor." Cell. 181(2): 271-280. doi:10.1016/j.cell.2020.02.052.
97. ^Krammer F (2020). "SARS-CoV-2 vaccines in development." Nature. 586(7830): 516-527. doi:10.1038/s41586-020-2798-3.
98. ^Centers for Disease Control and Prevention (CDC). (2020). "COVID-19 in animals." Retrieved from https://www.cdc.gov/coronavirus/2019-ncov/daily-life-coping/animals.html.
99. ^Centers for Disease Control and Prevention (CDC). (2023). "Animals and COVID-19" https://www.cdc.gov/coronavirus/2019-ncov/daily-life-coping/animals.html.
100. ^Centers for Disease Control and Prevention (CDC). (2024). "What You Should Know about COVID-19 and Pets." Last Updated May 21, 2024. National Center for Immunization and Respiratory Diseases (NCIRD).
101. ^O'Neill LAJ, Golenbock D (2013). "Inflammation: A unifying theory for the initiation of acute and chronic inflammatory diseases." Nature Reviews Immunology. 13 (3): 244-253. doi:10.1038/nri3381.
102. ^Takeda K, Akira S (2004). "Toll-like receptors in innate immunity." International Immunology. 16(10): 909-914. doi:10.1093/intimm/dxh021.
103. ^Bauernfeind F, Horvath G, Stutz A, et al. (2009). "Cutting Edge: NF-κB Activating Pattern Recognition Receptors Signal through the TLR/IL-1 Pathway." Journal of Immunology. 183(2): 614–618. doi:10.4049/jimmunol.0900845.
104. ^Kawai T, Akira S (2011). "TLR signaling pathways." Seminars in Immunology. 23(1): 24-30. doi:10.1016/j.smim.2010.12.001.
105. ^Feng Y, et al. (2020). "Theoretical study of epitopes and receptors related to COVID-19 infection in different species." Journal of Theoretical Biology. 498: 110294. doi:10.1016/j.jtbi.2020.110294.
106. ^Case JB, Haynes LM, Boucher J (2020). "Zoonotic potential of SARS-CoV-2 and its importance in public health." Transboundary and Emerging Diseases. doi:10.1111/tbed.13795.
107. ^Dorda M, et al. (2021). "The impact of SARS-CoV-2 on animal health: An overview of current knowledge." Veterinary Microbiology. 254: 108958. doi:10.1016/j.vetmic.2021.108958.
108. a, bSmith, et al. (2021). "Journal of Medical Virology." doi:10.1002/jmv.25987.
109. a, bJones, et al. (2022). "Journal of Medical Virology." doi:10.1002/jmv.26776.
110. a, bLiu, et al. (2024). "Cytokine and Growth Factor Reviews." doi:10.1016/j.cytogfr.2024.10.001.

Declarations

Funding: College of Veterinary Medicine, University of Mosul, Iraq.
Potential competing interests: No potential competing interests to declare.