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Current Evidence About the Role of Animals in the Transmission of Sars-Cov-2: Implications for Public Health[1]

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Abstract

Introduction: The SARS-CoV-2 is the denomination of the new betacoronavirus, which was discovered and isolated for the first time in Wuhan, China, at the end of December 2019, and it is the causal agent of the sanitary emergency of the COVID-19 pandemic. Experimental studies have shown susceptibility to infection in pets (dogs and cats). **Objective:** To present the current information available on SARS-CoV-2 in animals under the care of humans that have been officially reported in the sanitary registries of the World

1 Article research-derived thinking from the research project molecular epidemiology of betacoronavirus in wildlife species and pets in the Department of Antioquia, of Unilasallista Corporación Universitaria, executed between August 2020 and August 2021, Veterinary Clinical Diagnostic Laboratory, Laboratory Center, Caldas, Antioquia, Colombia, financed by Sistema General de Regalías (SGR), Fondo de Ciencia, Tecnología e Innovación (FCTeI). Macro-project BPIN 2020000100131: "Strengthening of installed Science and Technology capacities, through a Regional Network of Laboratories, to address problems associated with high-risk biological agents for human health in the Department of Antioquia".

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Animal Health Information System (WAHIS) of the World Organization for Animal Health. **Materials and methods:** We conducted a narrative review using Medline/ PubMed, Scopus, and Web of Sciences, and official documents of the World Organisation for Animal Health. The search terms used were as follows: "coronavirus", "SARS coronavirus 2019", "SARS-CoV", "SARS-CoV-2 in dog and/or cat" "pets SARS-CoV-2". **Results:** The studies reviewed in this manuscript highlight those positive cases in cats and dogs for SARS-CoV-2 have been associated with an exposure to positive COVID-19 people. In the available evidence, 55.17 % of the total cases of animals that were positive for SARS-CoV-2 were associated with people with COVID-19 who had the disease at home, possibly due to maintaining a longer exposure to the humans. **Conclusion:** Regarding the zoonotic aspects, it is important to clarify that although several animal species have been infected by SARS-CoV-2, none of them has been scientifically proven to represent a risk of direct transmission between positive animals and other humans or to play an epidemiological role in the disease.

Keywords: Virus, COVID-19, pandemics, pets, SARS-CoV-2.

Evidencia Actual sobre el Papel de los Animales en la Transmisión del Sars-Cov-2: Implicaciones para la Salud Pública

Resumen

Introducción: El SARS-CoV-2 es el nombre para el nuevo betacoronavirus, que fue descubierto y aislado por primera vez en Wuhan, China, a fines de diciembre de 2019, y es el agente causal de la emergencia sanitaria del COVID-19. Estudios experimentales han demostrado susceptibilidad a la infección en mascotas (perros y gatos). **Objetivo:** Presentar la información actual sobre el SARS-CoV-2 en animales bajo el cuidado de humanos que han sido oficialmente reportados en los registros sanitarios del Sistema Mundial de Información Sanitaria Animal (WAHIS) de la Organización Mundial de Sanidad Animal. **Materiales y métodos:** Se realizó una revisión narrativa utilizando Medline/PubMed, Scopus y Web of Sciences, y documentos oficiales de la Organización Mundial de Sanidad Animal. Los términos de búsqueda utilizados fueron los siguientes: "coronavirus", "SARS coronavirus 2019", "SARS-CoV", "SARS-CoV-2 en perro y/o gato" "mascotas SARS-CoV-2". **Resultados:** Los estudios revisados en este manuscrito destacan que los casos positivos en gatos y perros para SARS-CoV-2 se han asociado con una exposición a personas positivas para COVID-19. En la evidencia disponible, el 55,17 % del total de casos de animales positivos para SARS-CoV-2 estaban asociados a personas con COVID-19 que tenían la enfermedad en casa, posiblemente por mantener una mayor exposición a los humanos. **Conclusión:** En cuanto a los aspectos zoonóticos, es importante aclarar que si bien varias especies animales han sido infectadas por el SARS-CoV-2, ninguna de ellas ha demostrado científicamente que represente un riesgo de transmisión directa entre animales positivos y otros humanos o que juegue un papel epidemiológico en la enfermedad.

Palabras clave: Virus, COVID-19, pandemia, mascotas, SARS-CoV-2.

Evidências Atuais sobre o Papel dos Animais na Transmissão do Sars-Cov-2: Implicações para a Saúde Pública

Resumo

Introdução: SARS-CoV-2 é o nome do novo betacoronavírus, que foi descoberto e isolado pela primeira vez em Wuhan, China, no final de dezembro de 2019, e é o agente causal da emergência sanitária COVID-19. Estudos experimentais mostraram suscetibilidade à infecção em animais de estimação (cães e gatos). **Objetivo:** Apresentar as informações atuais sobre SARS-CoV-2 em animais sob cuidados humanos que foram oficialmente notificados nos registros sanitários do World Animal Health Information System (WAHIS) da Organização Mundial de Saúde Animal. **Materiais e métodos:** Foi realizada uma revisão narrativa utilizando Medline/PubMed, Scopus e Web of Sciences e documentos oficiais da Organização Mundial de Saúde Animal. Os termos de pesquisa utilizados foram os seguintes: "coronavírus", "SARS coronavirus 2019", "SARS-CoV", "SARS-CoV-2 in dogs and/or cats" "SARS-CoV-2 pets". **Resultados:** Os estudos revisados neste manuscrito destacam que casos positivos em gatos e cães para SARS-CoV-2 foram associados à exposição a pessoas positivas para COVID-19. Nas evidências disponíveis, 55,17 % do total de casos animais positivos para SARS-CoV-2 foram associados a pessoas com COVID-19 que tiveram a doença em casa, possivelmente devido à maior exposição a humanos. **Conclusão:** Em relação aos aspectos zoonóticos, é importante esclarecer que, embora várias espécies animais tenham sido infectadas pelo SARS-CoV-2, nenhuma de las foi cientificamente comprovada como representando risco de transmissão direta entre animais positivos e outros humanos ou que desempenhe um papel papel epidemiológico da doença.

Palavras-chave: Vírus, COVID-19, pandemia, animais de estimação, SARS-CoV-2.

Introduction

The SARS-CoV-2 pandemic has led to incomparable challenges, related to the prevention and control of viral diseases, around the world. The appearance of this novel virus has led to the global deployment of technology and human talent, which has produced an amount of information in record time. However, Important questions about the disease's transmissibility in human populations remain unanswered.

In recent publications, SARS-CoV-2 has been reported to infect animals, including dogs, cats, ferrets, tigers, and lions (Temmam et al., 2020). In several countries, such as Colombia, the transmission to animals in the care of humans has not been documented. It has been suggested that coronaviruses' ability to quickly traverse species barriers is related to certain biological and virological properties. (Sharun et al., 2020). Beta-coronavirus infections in humans have previously been reported as SARS-CoV and MERS-CoV in the province of Guangdong province of China in November 2002 and Saudi Arabia in 2012, respectively. SARS-CoV-2 is the third zoonotic beta-coronavirus to be identified in the twenty-first century, with its origins in Wuhan, Hubei Province, China. (Dhama et al., 2020).

The complete SARS-CoV-2 genome was reported by Zhou et al.,2020 They found that there is a 96 % identity with the BatCoV RaTG13 bat coronavirus, indicating that it is the most likely common ancestors of SARS-CoV-2;

however, the most likely hypothesis is that there is an intermediate host. Furthermore, the same authors also confirmed that SARS-CoV-2 enters human cells using the angiotensin-converting enzyme 2 (ACE2), which is also the entry receptor for SARS-CoV (Muralidar et al., 2020) and which has a high percentage of identity with the ACE2 protein of cats and dogs.

Currently, the actual susceptibility of animals to exposure to SARS-CoV-2 is uncertain, including the role of the inoculum and the transmission channel, among other Considerations. In the current context, significant person-to-person transmission appears to be the main aspect to be addressed and the participation of animals is being seen as a negligible factor, but this merits an integral strategy and evaluation to better understand the epidemiology and the evolution of the disease. It is also needed to understand the endemic role of infection in reverse zoonotic scenarios in which pets may carry the virus or be vehicles for SARS-CoV-2 (Temmam et al., 2020). In the case of multiple countries, there have been no instances of transmission from humans to animals, including Colombia, until now, however, in addition to lions, tigers, dogs and cats, there may be concern about infection in South American mustelids, but it has not yet been seen or documented (Bonilla-Aldana et al., 2020).

In this scenario of interactions between animal, human and environmental health, it is once again essential to return to the concept of One Health; it is an integrate and unifying approach that acknowledges that the health of people is closely related to the health of animals and our wider environment (Lorusso et al., 2020). Research and surveillance of COVID-19 in animals under the care of humans, as well as in their caregivers, veterinarians, and owners must be improved during the pandemic, which would help to implement better health strategies and to develop preventive and mitigation measures to effectively counter the SARS-CoV-2 infection (Lorusso et al., 2020).

This manuscript aims to present the current information available on SARS-CoV-2 in animals under the care of humans that have been officially reported in the sanitary registries of the World Animal Health Information System (WAHIS) of the World Organization for Animal Health, as well as the perspectives in the scientific community regarding its implications and impacts on animal health.

Materials and Methods

We conducted a narrative review using Medline/ PubMed, Scopus, and Web of Sciences, and official documents of the World Organisation for Animal Health. The search terms used were as follows: "coronavirus", "SARS coronavirus 2019", "SARS-CoV", "SARS-CoV-2 in dog and/or cat" "pets SARS-CoV-2". The searches were concluded by February 1, 2020, to November 21, 2020. Data extraction forms, including information on the type of publication, the publishing institution, country, and date of publication, as well as the number of infected animals assessed by molecular tests.

Results

Coronaviruses

Coronaviruses (CoV) are viruses whose origin dates back to immemorial times and their evolutionary processes of recombination and high mutation rates have enabled them to adapt to new hosts of ecological niches over time (Higgs & Lehman, 2015). The current classification of the *Coronaviridae* Study Group (CSG) of the International Committee on Taxonomy of Viruses (ICTV) recognizes

39 species in 27 genera within the family *Coronaviridae* in the order *Nidovirales*. CoVs of the *Coronavirinae* subfamily are classified into four known genera: Alpha, Beta, Gamma, and Deltacoronavirus (ICTV, 2011).

The study of protein structures has long been useful for understanding biological functions and developing therapies against emerging viruses (Johnson et al., 2018; Shi & Hu, 2008). In particular, CoV research pioneered this type of study in the context of an emerging virus outbreak (Wang et al., 2018), with structural models of the SARS-CoV Spike (S) protein that provided information about its transition to new hosts and their neutralization (Cotten et al., 2013).

CoVs are positive-sense, enveloped, single-stranded RNA viruses (ssRNA+) (ICTV, 2011), their genomes (between ~26-32 kb) have been recognized as the largest genomes, in comparison with other known RNA viruses (Cui et al., 2019a). The CoV genome encompasses a variable number of small open reading frames (ORF), interspersed between different structural genes (ORF1ab, spicula, envelope, membrane, and nucleocapsid) (Woo et al., 2010), which is the basis of the classification into several lineages (Cui et al., 2019b). The complete CoV genome contains five major open reading frames (ORFs) that encode replicase polyproteins (ORF1ab), spike glycoprotein (S), membrane protein (M), and nucleocapsid protein (N), flanked by a 5′–untranslated region (UTR) and a 3′- UTR (Sola et al., 2015).

The genomic sequence of CoVs is divided into two ORF segments, the first encoding non-structural proteins and the four structural ones: spike (S), envelope (E), membrane (M), and nucleocapsid (N) (Woo et al., 2010). The molecular detection of beta-CoVs is mainly based on three regions with highly conserved sequences: the first corresponds to the RdRp gene (RNA-dependent RNA polymerase gene) in the ORF1ab region, the second is the gene E (gene envelope protein), and finally the molecular product of gene N (nucleocapsid protein gene) (Ramírez, Muñoz, et al., 2020). For the new SARS-CoV-2, the markers for the RdRP and E gene have been recognized for their high analytical sensitivity for detection (technical limit of detection of 3.6 and 3.9 copies per reaction of transcribed RNA *in vitro*) (Corman et al., 2020); however, recent studies for the SARS-CoV-2 indicate that the RdRP gene and the N gene lack specificity as they are affected by various mutations evidenced in massive nucleotide variations within the primer binding sites, while the virus has been distributed in different geographical areas (Ramírez, Muñoz, et al., 2020).

Natural Transmission in Domestic Animals

Given the epidemiological, biological, and virological characteristics of coronaviruses, and in particular their demonstrated ability to easily cross species barriers, it has been suggested that contamination of pets by infected owners is highly likely to occur (Tiwari et al., 2020). Currently, some animals, such as dogs, cats, ferrets, lions, and tigers have been reported as been infected with the virus after having close contact with infected humans (Goumenou et al., 2020). However, so far, the transmission of the virus from pets to humans or between pets has not been reported, because the viral load found in the animals does not seem sufficient to infect other members of the family or other animals found during regular pet walks. The latency period for SARS-CoV-2 is similar in humans and animals; on average it ranges from 3-7 days to 14 days and in very rare cases the animals have presented a dry cough (Singla et al., 2020).

The virus's replication rate in dogs is low, however the virus's replication rate in cats and ferrets is higher, suggesting that the virus could be transmitted to other animals of the same species. (Fernández-raga et al., 2020). SARS-CoV-2 has been detected

in several cats and dogs, however none have shown any symptoms or died as a result of COVID-19 (Leroy et al., 2020). A 17-year-old positive dog died in Hong Kong apparently due to heart and kidney failure (Patterson et al., 2020). In Spain, a SARS-CoV-2 positive cat with cardiomyopathy was euthanized and the autopsy did not evidence COVID-19 related injuries (Ansede, 2020). Moreover, in Belgium, a cat was positive, presenting some intestinal dysfunctions that caused vomiting; however, after nine days it fully recovered (Singla et al., 2020). In all reported cases, pet owners have previously exhibited symptoms of COVID-19. As a result, the animals were determined to have been infected by their owners. Furthermore, the animals had a low virus load and were not considered contagious (Fernández-Raga et al., 2020).

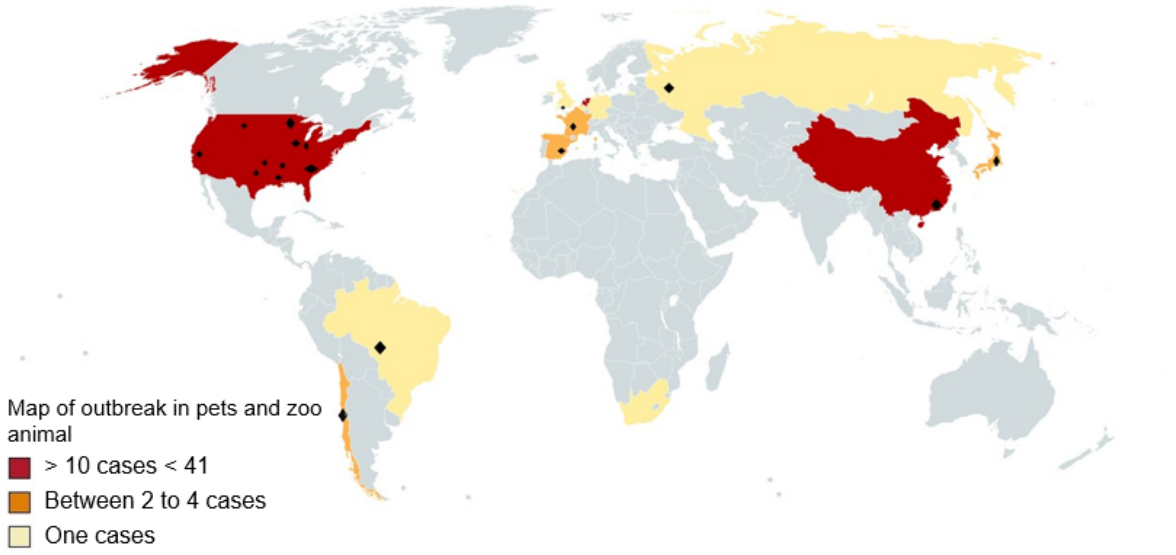

Figure 1. Map of the outbreak of the SARS-CoV-2 report in World Zoosanitary Information System (WAHIS) as of October 30th. 2020.

Source: OIE-WAHIS, 2020

On October 30th, 2020, there have been 84 reported cases of animals in human care that have tested positive for SARS-CoV-2; out of 138 animals evaluated between February 29 to October 22; of which 52.4 % and 28.6 % correspond to cats and dogs, respectively (Table 1), according to data taken from the sanitary registries of the World Animal Health Information System (WAHIS) of the World Organization for Animal Health. The United States was the country with the highest number of reported cases, representing 51.25 % of the cases (Figure 1). Owners were classified as negative, asymptomatic, active at home, hospitalized, observed at the Intensive Care Unit, and deceased. A Fisher's exact test showed, for the 58 cases that reported this information, that there are differences in the proportions of positive cases in pets, depending on the classification of the disease category presented by the owner (p-value <0.001), being the active at home those that reported the

highest number of infected pets (55.17 %), of which cats and dogs represented 59.4 % and 40.6 %, respectively (Table 2). According to the clinical symptoms reported in the cases, 19 animals had some respiratory signs, such as cough (5), sneezing (2) and nasal discharge (1), three animals respectively had fever and lethargy; while other isolated cases, for one or two animals, presented haemolytic anaemia, diarrhoea, vomiting, hypothermia, and conjunctivitis. The animals reported as positive were kept in mandatory quarantine in 78.87 % of the cases and in 21.13 % the veterinary medical decision was made to apply euthanasia, due to the severity of the clinical picture related to pre-existing pathologies in dogs and cats, and as a sanitary measure in the eight American minks from the U.S. farms where infection outbreaks occurred. From the reported cases, 39.39 % finally recovered and were negative to the diagnostic test, for which the health care was closed, on the contrary, 9.09 % continued with the open case. Nine animals, for which the health decision was euthanasia, were defined as death associated with SARS-CoV-2 as the outcome of the cases, and it represented 27.27 %. On the other hand, deaths from other pathologies represented 24.24 %.

Table 1. Cases of animals reported by SARS-CoV-2 of the World Zoosanitary Information System (WAHIS) as of October 30th, 2020.

N°	Official report	City / Country	Animal	Epidemiological unit	Susceptible	Cases	Clinical signs	Measures applied
1	28/02/2020	Hong Kong, China	Dog	Urban	1	1	No clinical signs	Quarantine
2	18/03/2020	Belgium*	Cat	Urban	1	1	Respiratory with other clinical signs	Quarantine
3	20/03/2020	Hong Kong, China	Dog	Urban	2	1	No clinical signs	Quarantine
4	31/03/2020	Hong Kong, China	Cat	Urban	1	1	No clinical signs	Quarantine
5	04/04/2020	Bronx, USA	Lion	Zoo	3	3	Other clinical signs	Quarantine
6	04/04/2020	Bronx, USA	Tigre	Zoo	5	4	Other clinical signs	Quarantine
7	04/04/2020	Nassau, USA	Cat	Urban	3	2	Other clinical signs	Quarantine
8	04/04/2020	Richmond, USA	Dog	Urban	2	1	Other clinical signs	Euthanasia
9	04/04/2020	Minnesota, USA	Cat	Urban	1	1	Respiratory with other clinical signs	Quarantine
10	04/04/2020	Illinois, USA	Cat	Urban	1	1	Respiratory with other clinical signs	Quarantine
11	04/04/2020	Berrien, USA	Dog	Urban	3	2	Other clinical signs	Euthanasia
12	04/04/2020	Orange, USA	Cat	Urban	2	1	Respiratory with other clinical signs	Quarantine
13	04/04/2020	Tarrant, USA	Dog	Urban	1	1	No clinical signs	Quarantine
14	04/04/2020	Charleston, USA	Dog	Urban	3	1	Respiratory	Euthanasia
15	04/04/2020	Brazos, USA	Cat	Urban	1	1	No clinical signs	Quarantine

Nº	Official report	City / Country	Animal	Epidemiological unit	Susceptible	Cases	Clinical signs	Measures applied
16	04/04/2020	Brazos, USA	Dog	Urban	2	0	No clinical signs	Quarantine
17	04/04/2020	Livingstone, USA	Dog	Urban	2	1	No clinical signs	Euthanasia
18	04/04/2020	Brazos, USA	Dog	Urban	5	5	No clinical signs	Quarantine
19	04/04/2020	Brazos, USA	Cat	Urban	5	5	No clinical signs	Quarantine
20	04/04/2020	Moore, USA	Dog	Urban	2	1	Respiratory with other clinical signs	Quarantine
21	04/04/2020	Coweta, USA	Cat	Urban	1	1	Respiratory	Quarantine
22	04/04/2020	Maryland, USA	Cat	Urban	5	1	Respiratory	Quarantine
23	04/04/2020	Maryland, USA	Dog	Urban	1	1	No clinical signs	Quarantine
24	04/04/2020	Contra Costa, USA	Cat	Urban	1	1	Respiratory	Quarantine
25	04/04/2020	Rapides, USA	Cat	Urban	2	1	Respiratory	Quarantine
26	04/04/2020	Brazos, USA	Dog	Urban	1	1	Respiratory with other clinical signs	Quarantine
27	04/04/2020	Somervell, USA	Cat	Urban	9	1	No clinical signs	Quarantine
28	04/04/2020	Brazos, USA	Cat	Urban	1	1	No clinical signs	Quarantine
29	04/04/2020	Brazos, USA	Cat	Urban	1	1	No clinical signs	Quarantine
30	04/04/2020	Brazos, USA	Dog	Urban	1	1	No clinical signs	Quarantine
31	04/04/2020	Fayette, USA	Cat	Urban	3	1	Respiratory with other clinical signs	Quarantine
32	26/04/2020	Netherlands	American Mink	Rural	8	8	Respiratory with other clinical signs	Euthanasia
33	01/05/2020	France*	Cat	Urban	12	1	No clinical signs	Quarantine
34	08/05/2020	Barcelona, Spain*	Cat	Urban	1	1	No clinical signs	Euthanasia
35	12/05/2020	Bordeaux, France*	Cat	Urban	1	1	Respiratory with other clinical signs	Not intervened
36	13/05/2020	Insel Riems, France*	Cat	Urban	3	1	No clinical signs	Quarantine
37	15/05/2020	Netherlands**	Dog	Urban	1	1	Respiratory	Euthanasia
38	15/05/2020	Netherlands**	Cat	Rural	11	7	No clinical signs	Not intervened
39	21/05/2020	Spain*	Cat	Urban	8	1	No clinical signs	Not intervened
40	22/05/2020	Moskovskaya, Russia	Cat	Urban	1	1	No clinical signs	Quarantine
41	20/07/2020	London, UK	Cat	Urban	2	1	Respiratory	Quarantine
42	23/07/2020	Hong Kong, China	Cat	Urban	5	5	No clinical signs	Quarantine

N°	Official report	City / Country	Animal	Epidemiological unit	Susceptible	Cases	Clinical signs	Measures applied
43	23/07/2020	Hong Kong, China	Dog	Urban	2	2	No clinical signs	Quarantine
44	31/07/2020	Pretoria, South África	Puma	Zoo	2	1	No clinical signs	Quarantine
45	03/08/2020	Tokyo, Japan	Dog	Urban	5	4	No clinical signs	Quarantine
46	16/10/2020	Brazil	Cat	Urban	1	1	No clinical signs	Quarantine
47	22/10/2020	Santiago de Chile	Cat	Urban	3	3	Respiratory	Quarantine

* Report retrieved from another source (bioRxiv).
** Report retrieved from internal government entities of the country.

Source: Elaborated and adapted by the authors

Table 2. SARS-CoV-2 positive animal cases according to the clinical picture of COVID-19 positive people.

Affected animals		Clinical case of the COVID-19 patient						Total	P†
		Active at home	Hospitalized	ICU	Deaths				
American mink	Cases	8	0	0	0	0	0	8	< 0.001
	%	100.0 %	0.0 %	0.0 %	0.0 %	0.0 %	0.0 %	12.9 %	
Cat	Cases	0	1	23	1	1	2	28	
	%	0.0 %	12.5 %	63.9 %	14.3 %	100.0 %	100.0 %	45.2 %	
Dog	Cases	0	0	13	6	0	0	19	
	%	0.0 %	0.0 %	36.1 %	85.7 %	0.0 %	0.0 %	30.6 %	
Lion	Cases	0	3	0	0	0	0	3	
	%	0.0 %	37.5 %	0.0 %	0.0 %	0.0 %	0.0 %	4.8 %	
Tigre	Cases	0	4	0	0	0	0	4	
	%	0.0 %	50.0 %	0.0 %	0.0 %	0.0 %	0.0 %	6.5 %	
Total	Cases	8	8	32	7	1	2	62	

ICU: Intensive Care Unit.
†Fisher's exact test.

Source: Elaborated and adapted by the authors

Each of the 80 animals suspected of being infected underwent the RT-qPCR diagnostic test, using different samples for the analysis, such as feces (5 %), nasopharyngeal smear (33.8 %), oropharyngeal smear (33.8 %), and rectal swab (27.5 %), according to the criteria stipulated by the guide "Evaluation for SARS-CoV-2 tests in animals" of the CDC (2020) for the United States and the guide "Considerations for sampling, tests and the report of SARS-

CoV-2 in animals "of the World Organization for Animal Health. The results of the available data showed that, out of a total of 80 infected individuals (thus defined by the cases reported in WAHIS), the oropharyngeal samples had the best sensitivity ratio: 25/27 = 0.93 (93 %). Of the stool samples, nasopharyngeal smear, and rectal smear, 50 %, 60 %, and 50 % respectively, were correctly diagnosed (true positives), while 2, 10, and 2 samples respectively, were incorrectly diagnosed as healthy (false negatives). In the data reported, only in some cases the days between the first positive confirmatory test for SARS-CoV-2 and the closure of the case with a negative confirmatory test were reported. In the available data, it was found that the average was 16 days, with one case presented for only 10 days and the maximum time reported was 26 days (Table 3).

Table 3. RT-qPCR diagnostic tests in animals suspected of infection for SARS-CoV-2.

	RT-qPCR diagnostic test result			P†	Sensitivity ratio
Type of sample	Positive	Negative	Total		
Feces	2	2	4	0.008	0.5
	3.6 %	8.0 %	5.0 %		
Nasal swabs	17	10	27		0.63
	30.9 %	40.0 %	33.8 %		
Oral swabs	25	2	27		0.93
	45.5 %	8.0 %	33.8 %		
Rectal swabs	11	11	22		0.5
	20.0 %	44.0 %	27.5 %		
Total	**55**	**25**	**80**		**0.68**

†Fisher's exact test.

Source: Elaborated and adapted by the authors

Discussion

Experimental Animals for Sars-Cov-2

The need for the development of vaccines and antiviral drugs against SARS-CoV-2 has highlighted the role of the animal models in the preclinical phases, in the context of the COVID-19 pandemic. The need for the development of infection models for SARS-CoV-2 in animals has led to experimentation with several species, such as dogs, domestic cats, poultry, pigs, transgenic mice, fruit bats, ferrets, hamsters, and some primate species (Segalés et al., 2020).

Studies have revealed that dogs have a low susceptibility to the virus, however, there may be some clinical respiratory signs and the susceptibility is increased when they suffer from comorbidities, which can trigger serious signs (Sharun et al., 2020). On the contrary, domestic cats have a high susceptibility to SARS-CoV-2, this is since the ACE-2 receptor of felines differs only by three amino acids

from the ACE-2 of humans (Guo et al., 2008). Their clinical signs maybe none or mild, such as sneezing, clear eye discharge, and lethargy; the presence of other respiratory pathogens or comorbidities can aggravate the health of the animal. Transmission can be cat to cat as they excrete the virus in their faeces or in their nasal secretions (Leroy et al., 2020; Musso et al., 2020; Patterson et al., 2020).

On the other hand, macaques (*Macaca fascicularis* and *Macaca mulatta*), Syrian golden hamsters, and ferrets are highly susceptible to experimental infection with SARS-CoV-2, and it was shown that they could transmit the infection to their cage mates. Nasal discharge, feces, saliva, and airborne transfer are all possible modes of transmission. In terms of clinical indicators, macaques exhibit moderate respiratory symptoms that are remarkably comparable to those seen in COVID-19 patients (decreased appetite, hunched posture, irregular breathing patterns, dehydration, pale appearance, and weight loss among others). In ferrets and Syrian golden hamsters, the virus causes neonatal respiratory signs, in addition to progressive weight loss, ruffled skin, lethargy, and hunched-back posture, among others (Chan et al., 2020; Melin et al., 2020; J. Shi et al., 2020).

Cats, ferrets, macaques, and Syrian hamsters could be suitable models to simulate the clinical, pathological, virological, and immunological characteristics of COVID-19 induced by SARS-CoV-2, facilitating experimental platforms for the evaluation of possible vaccines and antiviral drugs.

Status of the Pandemic in the National Context and the Population of Domestic Pets in Colombia

As an example of the need for studies in developed countries, we highlight some information about Colombia. On March 6, 2020, the first case of COVID-19 was identified in Colombia, in a traveller returning from Milan, Italy. So, early control efforts were implemented by the Colombian government to avoid transmission. (Ramírez, Florez, et al., 2020). However, as of November 17th, 2020, 1,211,128 cases of SARS-CoV-2 have been reported in Colombia, occupying the third position in Latin America and the tenth position worldwide. The territories that have been most affected have been Bogotá D.C, Antioquia, Valle del Cauca and Santander, and the national death toll has reached 34,381.

Colombia is the home of many dogs and cats. According to the 2019 population census of the Subdirection of Environmental Health of the Vice Ministry of Public Health, the total population of dogs and cats in the care of Colombian families is 44,564 dogs and 15,112 cats, per 10,000 inhabitants. The main regions are Bogotá D.C., (16.0 %), Antioquia (12.7 %), and Cundinamarca (6.3 %) with the highest number of pets to the total population of 7,572,883 dogs and cats. It has been estimated that there are 170 pets (dogs or cats) for every 1,000 inhabitants in the country.

In addition, the COVID-19 cases reported until October 10 in the country had several 50 to 350 infected people per 10,000 inhabitants in the 32 departments of the country, with Bogotá D.C. having more than above 325 cases per 10,000 inhabitants, and a population of dogs and cats had several 1,600 and 450 respectively for every 10,000 people (figure 2). This panorama highlights the close relationship between humans and pets, and it has been hypothesized that pets may be potential sources of urban transmission of the virus (Leroy et al., 2020). Besides that, it has been reported that the modes of transmission of SARS-CoV-2 from humans to dogs and cats might arise through respiratory droplets emitted by coughing, sneezing, talking, or breathing (Nature, 2020). In addition to this, sharing common environments, licking, and kissing are additional risk factors that facilitate

the transmission of the virus between infected people and their pets (Chen, 2020). Although there are reports at the international level, in countries such as the United States, in Colombia and other developing countries there are no reported studies about the role of animals in the pandemic.

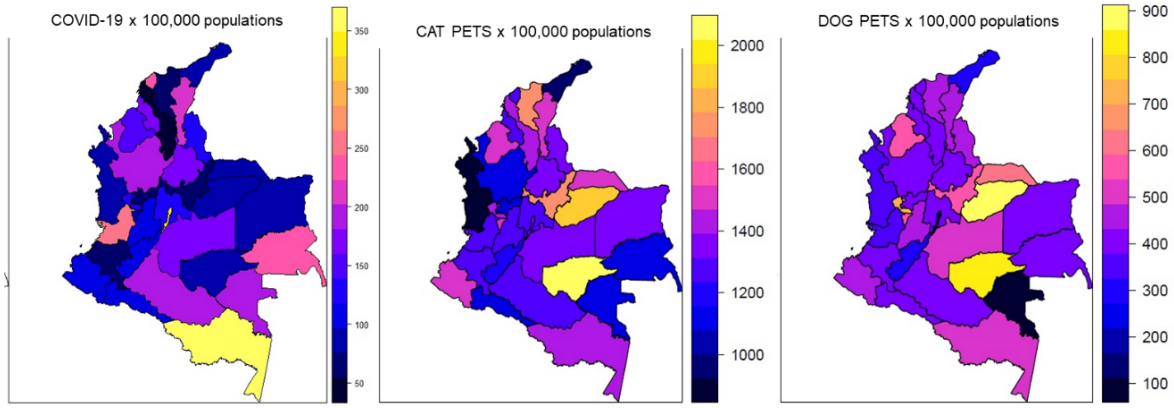

Figure 2. Heat map of the distribution per 10,000 inhabitants for the COVID-19 cases reported in the country as of the cut-off date of October 10th. 2020. and the population of dogs and cats according to the 2019 population census.

Source: Elaborated and adapted by the authors

Conclusions

Conclusion and Perspectives about Possible Zooanthroponosis

The studies reviewed in this manuscript highlight those positive cases in dogs and cats for SARS-CoV-2 have been associated with an exposure to positive COVID-19 people. In the available evidence, 55.17 % of the total cases of animals that were positive for SARS-CoV-2 were associated with people with COVID-19 who had the disease at home, possibly due to maintaining a longer exposure to the humans. The health emergency due to COVID-19 reveals a scenario in which natural or accidental infection in companion animals can have consequences for human and animal health, as well as for biomedical research (Nature, 2020). Cats (domestic and big cats), minks, and dogs have been officially reported as positive cases for SARS-CoV-2 in the official health notification for the World Organization for Animal Health. Although the complete physiological and pathological processes of the new coronavirus in animals are unknown, results of laboratory studies and reported cases suggest that, for the animal species investigated so far, cats are the most susceptible species to SARS-CoV-2 and can be affected with clinical manifestations, including respiratory and gastrointestinal signs (Munir et al., 2020); However, until now, there are no therapeutic alternatives. On the other hand, the SARS-CoV-2 infection in farmed minks has indicated that the infection can lead to respiratory disease with a high rate of morbidity and mortality among this species of animal (Leroy et al., 2020).

Regarding the zoonotic aspects, it is important to clarify that although several animal species have been infected by SARS-CoV-2, none of them has been scientifically proven to represent a risk of direct transmission between positive animals and other humans or

to play an epidemiological role in the disease. In this context, the World Health Organization has confirmed that the current spread of COVID-19 is the result of human-to-human transmission. However, in the context of the study of a new virus and its biological complexity, several studies are being carried out to provide a better understanding of the susceptibility of different animal species to SARS-CoV-2 and to evaluate the health implications in susceptible animal species (Leroy et al., 2020). These studies, as well as the handling of information on the subject, must be adequately discussed with the public opinion to avoid taking inappropriate measures that compromise the integrity and well-being of domestic or wild animals.

In order to evaluate the pharmacological effects of treatments or the effectiveness of vaccine candidates, biomedical research might use ferrets as a useful model for future studies (Dhama et al., 2020). On the other hand, golden hamsters, macaques, and Rhesus macaques can be constantly infected without showing clinical signs.

Preventive Measures

Due to the reported cases, the World Organization for Animal Health has considered SARS-CoV-2 in animals as an emerging infection with mandatory reporting. Therefore, as a result, any event of SARS-CoV-2 infection in animals should be reported to the World Organization for Animal Health using their Terrestrial Animal Health Code, which requires information on the species, diagnostic tests, and epidemiological data.

Although a sanitary plan has not been established, the entity's recommendations are focused to minimize the close contact of infected people with animals, including farm animals, zoo animals or other captive animals, wild fauna, particularly those species that have demonstrated susceptibility to SARS-CoV-2 infection (Decaro et al., 2020). Multiple health authorities promote that, as a preventive management in humans, animal owners or caregivers must adopt effective biosecurity measures, such as hand washing, use of masks, and daily disinfection of mobile phones and the space that is shared with animals. The isolation and quarantine of people who are infected by SARS-CoV-2 are also applicable to their companion animals (Munir et al., 2020).

In the face of such a health emergency of public and animal health, the interdisciplinary cooperation in epidemiological monitoring and accurate communication of risk factors has a vital role for the activities of public human and animal health entities and academic centres.

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Data Availability Statement

Data available on request from the authors.

Ethics Statement

The authors confirm that the ethical policies of the journal, as noted on the journal's author guidelines page, have been adhered to. No ethical approval was required as this is a review article with no original research data.

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