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What does the evidence for COVID-19 in dogs and cats point to? An Investigation in the literature

In view of the current COVID-19 pandemic scenario, uncertainties still remains around the role of domestic animals on COVID-19 epidemiology, this systematic review aims to present the scientific evidence available, so far, on dogs and cats' epidemiological role in the COVID-19 pandemic. The systematic review was conducted in accordance with the recommendations of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses – PRISMA. Selected studies report negative results of dogs and cats both in serological tests, for the detection of neutralizing antibodies, and in tests that investigated the presence of the SARS-CoV-2 RNA. We verified the lack of national studies, which serves as a motivation for more research to be carried out in Brazil. In Brazil, in the animals tested, 5.4 and 6.2% of cats and dogs were positive, respectively. Few studies, so far, have been carried out with stray animals or animals belonging to shelters. This absence of broad conducted studies on animal interface enphasizes the need for more research with animals in vulnerable conditions, since they can contribute to the spread of the disease if they are confirmed as positive for SARS-CoV-2. The compilation of data, through this systematic review of the literature, to date suggests that dogs and cats are not factors of viral spread to humans. However, further studies are still recommended.

Keywords: SARS-COV2; Zoonoses; Domestic animals; Systematic review.

Para que apontam as evidências do COVID-19 em cães e gatos? Uma Investigação na Literatura

Tendo em vista o atual cenário de pandemia do COVID-19, ainda permanecem incertezas em torno do papel dos animais domésticos na epidemiologia do COVID-19, esta revisão sistemática visa apresentar as evidências científicas disponíveis, até o momento, sobre o papel epidemiológico de cães e gatos no COVID-19 -19 pandemia. A revisão sistemática foi conduzida de acordo com as recomendações do Preferred Reporting Items for Systematic Reviews and Meta-Analyses – PRISMA. Estudos selecionados relatam resultados negativos de cães e gatos tanto em testes sorológicos, para detecção de anticorpos neutralizantes, quanto em testes que investigaram a presença do RNA do SARS-CoV-2. Verificamos a carência de estudos nacionais, o que serve de motivação para que mais pesquisas sejam realizadas no Brasil. No Brasil, nos animais testados, 5,4 e 6,2% de gatos e cães foram positivos, respectivamente. Poucos estudos, até o momento, foram realizados com animais errantes ou animais pertencentes a abrigos. Essa ausência de estudos amplos realizados sobre interface animal reforça a necessidade de mais pesquisas com animais em condições vulneráveis, uma vez que podem contribuir para a disseminação da doença caso sejam confirmados como positivos para SARS-CoV-2. A compilação de dados, por meio desta revisão sistemática da literatura, até o momento sugere que cães e gatos não são fatores de disseminação viral para humanos. No entanto, mais estudos ainda são recomendados.

Palavras-chave: SARS-COV2; Zoonoses; Animais domésticos; Revisão sistemática.

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INTRODUCTION

In December 2019, some cases of pneumonia of unknown origin were reported in the Hubei province, China, in patients who had contact with a seafood and live animal market. After sequencing the genome of this new virus, it was shown that, still according to the Society of Pediatrics, it is 75% to 80% identical to SARS-CoV, a well known potential pandemic virus, and even more closely related to the bat. This virus is found in the blood circulation of *Rhinolophus* bat populations, being a possible intermediate transmitter of the virus. This virus of the *Coronaviridae* family was named SARS-CoV-2 or just novel coronavirus, causing the disease called COVID-19.

In view of the facts and the recurring association with bats, in addition to the recognition of the presence of coronavirus strains associated with domestic species (enteric symptomatology canine coronavirus - CCoV and feline infectious peritonitis - FIP), the common sense has raised doubts about the possibility that COVID-19 is a zoonosis, affecting animals, but potentially transmissible to humans (SCHRER et al., 2021).

Since the beginning of the pandemic, many studies have been developed to better elucidate this issue. Now that infections by COVID-19 are widely distributed in the human population, and that investigations of the occurrence of the disease in animals are already expressive, the present study proposes to compile and analyze the existing data so far.

It is hoped that this article will transmit reliable and scientific information to people, seeking to resolve any doubts and explain the directions of science in the midst of this public health crisis. In addition, it is worth emphasizing the need to address a theme that, in the midst of scientific uncertainties, opens the door to the network of information disseminated by common sense, whose absence of veracity and reliable sources can cause panic and often lead the tutor to abandonment. of your animal or the poor execution of preventive measures. Communications from international non-governmental organizations (NGOs) working with animal protection and welfare point out that cases of dog and cat abandonment and mistreatment increased after the onset of the pandemic, especially in Latin America and Asia. Furthermore, it seeks to collaborate to enrich the literary repertoire of the scientific community.

In view of this current pandemic scenario, and the uncertainties still generated around the involvement of domestic animals by COVID-19, this systematic review aims to present the scientific evidence available, so far, on the epidemiological role of dogs and cats in COVID-19 pandemic.

MATERIALS AND METHODS

Research characterization and search strategies

The systematic review was conducted according to the recommendations of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses – PRISMA (MOHER et al., 2015). Searches for scientific articles were conducted by two independent researchers in the electronic databases MEDLINE (Pubmed)[1]

[1] http://www.ncbi.nlm.nih.gov/pubmed/

and LILACS[2] without language and location restriction, from March 2020 to June 2021. The survey was structured and organized in the form PICOS, which represents an acronym for Target Population, Intervention, Control, 'Outcomes', 'Study' (Table 1).

Table 1: Definition of PICOS components.

Acronym	Definition
P	Dogs and cats
I	Covid-19
C	Epidemiology
O	Human beings
S	Descriptive study Cross-sectional study Observational study Laboratory study

The descriptors were selected from the Dictionary Descriptors in Health Sciences (DeCS) and Medical Subject Heading Terms (MeSH). The following Boolean descriptors and operators were proposed for the searches: 'Domestic animals' AND Covid-19 OR Coronavirus disease OR SARS-COV-2; Dog AND Covid-19 OR Coronavirus disease OR SARS-COV-2; Cat AND Covid-19 OR Coronavirus disease OR SARS-COV-2. The use of descriptors and Boolean operators was adequate according to the databases researched. In addition, a manual search was performed in the references of the articles included in the search and a search for gray literature on Google Scholar.

Selection criteria

Inclusion criteria

The selected study designs consisted of a descriptive study, randomized or non-randomized controlled clinical trials, cross-sectional study, cohort study, case study and laboratory study. Studies without language and location restrictions were included, with publication from March 2020 to June 2021 to search for articles.

Exclusion criteria

Studies published in the format of Letters to the Editor, guidelines, literature reviews, systematic reviews, meta-analyses, abstracts, studies with other domestic animals (other than dogs and cats) were excluded. Table 2 represents the inclusion and exclusion criteria developed in this study.

Table 2: Summary of article selection criteria.

Inclusion criteria	
Kind of study	Case reports Case and control studies Controlled clinical trials Cohort studies Triage studies Observational studies Laboratory studies
Localization	Without restriction

[2] http://lilacs.bvsalud.org/

Language	Without restriction
Exclusion criteria	
Kind of study	Letters to the editor Guidelines Literature reviews Systematic reviews Meta-analysis Studies in other animal models only
Studies	Unclear studies Misdescribed or inappropriate Not available in full With insufficient data for analysis
Publication form	Summary only

Data analysis

The extraction of data for the eligibility process of the studies was carried out using a specific form for systematic review prepared by the researchers in Excel@ Program, in which the extracted data were initially added by one of the researchers and then checked by the other researcher. For the data obtained from the eligible studies, they were also transported to a spreadsheet in the same program, in order to organize the results.

The data extracted from the studies were analyzed in a descriptive way, being extracted: year of publication, place of research, type of study design, evaluations and tests performed, as well as the methods used and the results found. These studies obtained scores greater than six in the modified protocol by Pithon et al. (2015) to assess their quality.

RESULTS AND DISCUSSION

Initially, 625 articles were identified, of which 145 were qualified and passed to the abstract evaluation phase. Of these, 81 were excluded for not answering the guiding question. Sixty-four articles were fully evaluated, and of these 19 were excluded, after a detailed evaluation, as they did not meet all the inclusion criteria. Of the 50 articles that were entered in the spreadsheet for data extraction, 5 were excluded because they did not contain enough adequate data. Thus, 45 articles became eligible according to the PRISMA criteria (MOHER et al., 2015) used for the development of this review. A careful reading of the entire study was carried out and after applying the eligibility criteria, studies on the investigation of COVID-19 in dogs and cats were the objects of this analysis.

The studies admitted for this systematic review contemplated both natural and experimental infection of dogs and cats by SARS-COV2. The search and analysis strategy for the articles can be seen in Figure 1.

In the articles selected for analysis, we found, in total, a sample of 11,780 dogs and 6,615 cats. Most of the selected studies used both species, dogs and cats, in the analyzes (Figure 2A), including domestic animals, laboratory animals and street animals, submitted to natural or experimental infection. Taking into account the sample numbers of the analyzed articles, it was observed that the prevalence of COVID-10 was higher in cats, being close to 3% (Figure 2B). Although the sampling is still small and the recruitment is random, the findings indicate that cats can act as sentinels for human cases, particularly sharing households

with asymptomatic human cases (EPIFANIO et al., 2021).

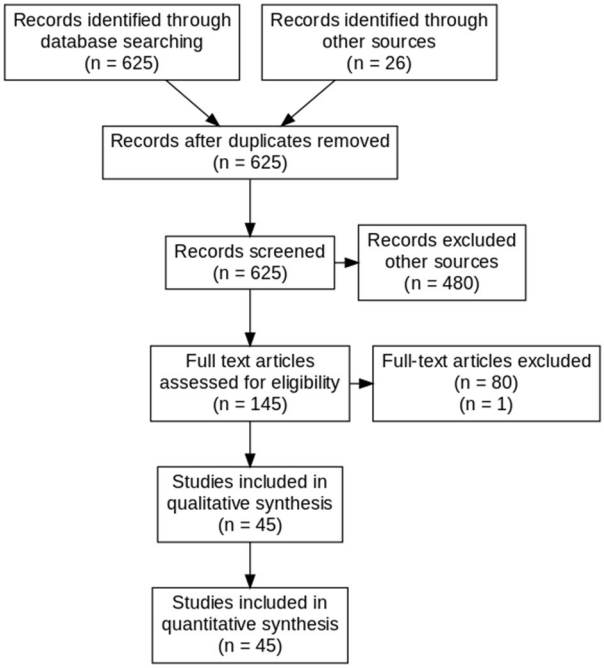

Figure 1: Article search and analysis flowchart.

More than half of the selected studies performed one or more serological tests in addition to one or more tests for the identification of the SARS-COV2 virus (Figure 2C). This diversification in the quantity and quality of the tests used gives greater reliability to the results.

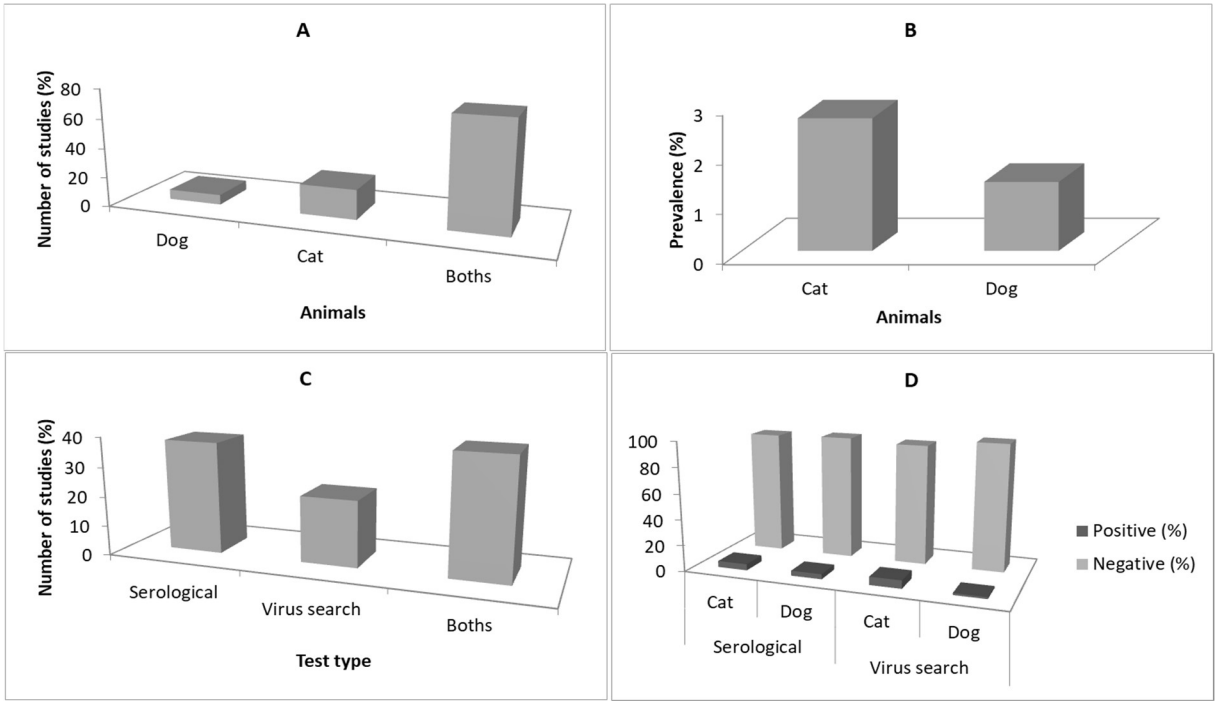

Figure 2: Information about sampling (dogs and cats) and tests performed in selected studies. A – Number of studies that performed tests on dogs, cats or both. B – Prevalence of COVID-19 in dogs and cats based on sample numbers of selected studies. C – Number of studies that performed serological tests, SARS-COV2 research or both. D – Percentage of animals that had positive and negative results in the tests performed by the selected studies.

Figure 2D shows that in the studies selected for analysis, the vast majority of dogs and cats had negative results both in serological tests aiming detection of neutralizing antibodies, and in tests that

investigated the presence of the SARS-COV2 virus. Proportionally, reiterating the prevalence results, the number of cats that tested positive was greater than the number of positive dogs in the different types of tests. Apparently, the primary source of infection for cats is related to contact with infected people, however, there is still no evidence that transmissibility to humans has emerged (SHI et al., 2020; DAVIDSON, 2020a; DAVIDSON, 2020b; NVSB, 2020; WOAH, 2020). Previous studies for SARS-CoV-1 have already demonstrated in cats exactly what is now being discovered for SARS-CoV-2 (MARTINA, 2020).

Studies carried out in 15 countries were selected, with Italy and the United States having the largest number of published studies (Figure 3A). We verified the lack of national studies (Figure 3B), which serves as a motivation for further research to be carried out in Brazil. The highest prevalences, based on the sample size of each country, were observed in Peru and the United Kingdom. Although the largest sample numbers were observed in the United States, Thailand and Germany. In Brazil, in the animals tested, 5.4 and 6.2% of cats and dogs were positive, respectively (Figure 3C).

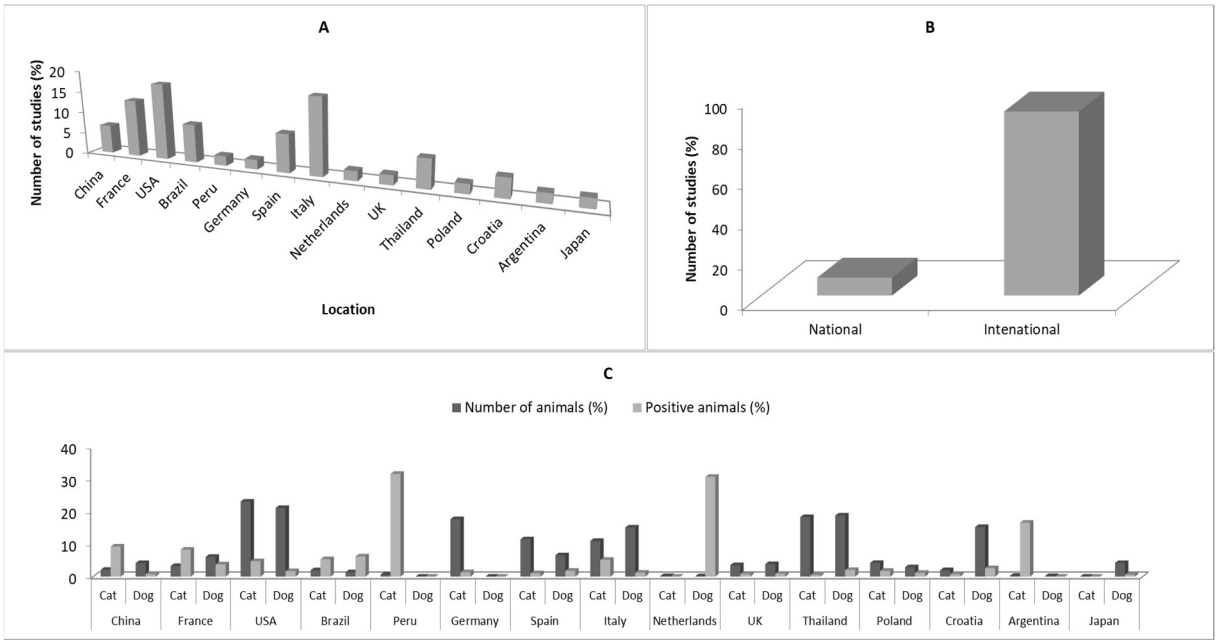

Figure 3: Information about the situation in each country where the selected studies were carried out. A – Countries involved in the selected studies. B – Discrimination of national and international studies. C – Number of animals used in the studies in each country, as well as the number of positive animals in percentage.

Most of the studies were carried out with animals that acquired the infection naturally (Figure 4A), which could possibly have happened with close contact with infected humans. Reports show that seroprevalence was higher among animals living in close contact with SARS-CoV-2 positive owners (COLITTI et al., 2021).

Few studies, so far, have been carried out with stray animals or animals belonging to shelters (Figure 4B). This shows the need for more research with animals in these abandoned conditions, since they can contribute to the spread of the disease if they are confirmed as positive for SARS-COV-2. Although a study has pointed out a low probability of human-animal transmission events in cats and dogs in shelter environments with early implementation of infection prevention interventions (COSSABOOM et al., 2021). And in a study using stray animals, there was also no evidence of cases of positivity among those tested

(DENG et al., 2020). However, a study carried out in Brazil showed that a stray cat and dog had neutralizing antibodies to SARS-CoV-2 (DIAS et al., 2021). The authors suggested that not only pets from families with COVID19 cases, but also stray animals are being exposed to SARS-CoV-2 during the COVID-19 pandemic.

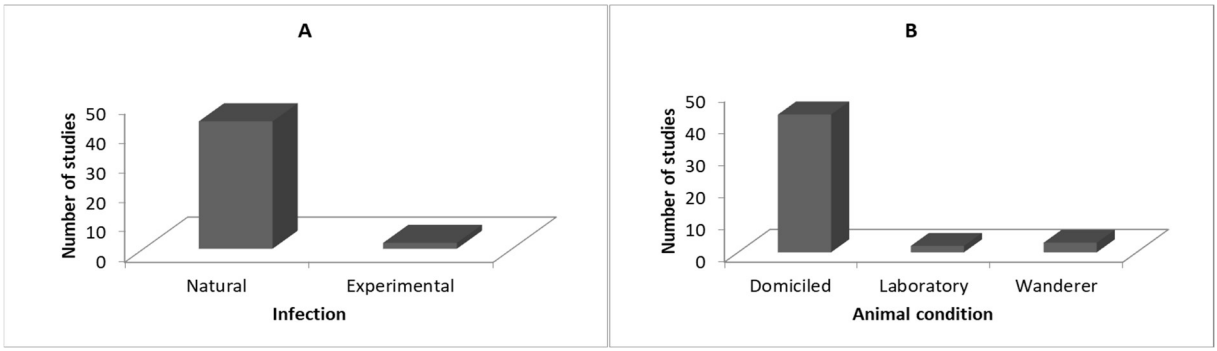

Figure 4: A – Form of animal infection by SARS-COV-2 in selected studies. B – Shelter conditions in which the animals were at the time of the studies.

The compilation of data, through this systematic review of the literature, to date suggests that dogs and cats are not factors of viral spread to humans. As there is no epidemiological support yet that justifies the inclusion of dogs and cats in the chain of transmission of the virus, at the moment the risk can be considered very low.

Still, people suspected or confirmed for COVID-19 should minimize direct contact with their pets to avoid any potential transmission. The main reason is that the virus can be indirectly carried by the animal to an uninfected person. In this sense, dogs and cats can function as fomites, that is, they can behave like a handkerchief, a cup or an object contaminated with the virus. This is an unlikely episode, but not impossible (RISTOW et al., 2020).

Although the current evidence points to an insignificant participation of dogs and cats in the epidemiology of COVID-19, we need further and better-designed studies that prove the hypothesis that pets, such as dogs and cats, can be important sources of infection to humans and vice versa. Thus, the guideline is that we must be vigilant regarding the infection of both humans and pets, aiming to control the COVID-19 pandemic (Figure 5).

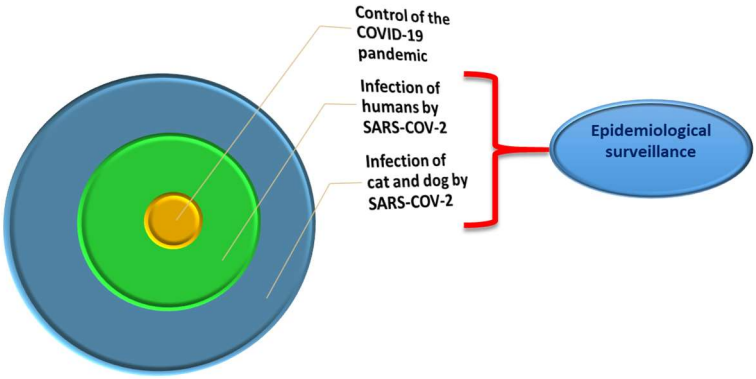

Figure 5: Schematic representation of the importance of epidemiological surveillance on humans and pets for effective control of the COVID-19 pandemic.

CONCLUSIONS

Although medical entities and researchers have increased their attention to the occurrence of COVID-

19 in dogs and cats, more detailed descriptions of the clinical course of this population are still needed, especially with regard to the potential for transmission of the virus to humans. Although some studies have detected the presence of the virus in dogs and cats, the data compiled here show that these animals are unlikely to play an important epidemiological role in the COVID-19 pandemic. Thus, it is recommended to carry out further studies, with samples of larger sizes, in order to solve once and for all the uncertainties at a delicate moment and without further threatening the well-being of pets, as well as public health.

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