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Epidemiological aspects of leptospirosis in the Brazilian population (2007-2022) and its relationship with companion animals

Aspectos epidemiológicos da leptospirose na população brasileira (2007-2022) e sua relação com animais de estimação

Vinícius José de Oliveira[1]
Thiago Alves de Jesus[2]
Maria Vitória Gilvan da Silva[3]
Lucas Maurício Lopes Navasquez[4]
Laís de Deus Sousa[5]
Heitor Leocádio de Souza Rodrigues[6]
Andrezza Brigato Siqueira[7]
Gabriella Dinair Mendonça de Assis[8]
Guilherme Gonçalves de Faria[9]
Matheus Henrique Silva Sampaio[10]

ABSTRACT

Objective: The aim of this article was to analyze the epidemiological variables of cases (2007-2022) and deaths (2007-2021) of human leptospirosis in Brazil, and to correlate the data on this zoonosis with the contact between humans and companion animals. **Methods:** This is

[1] Doctoral Student in the Post-graduation Program in Applied Immunology and Parasitology. dr.vinicius.oliveiras@gmail.com, https://orcid.org/0000-0003-2632-4129, Specialist in Zoonosis and Public Health; Coordinator of the Interdisciplinary Research Group on Public Health; College Professor at Faculdade ZARNS (Faculdade de Medicina de Itumbiara). Itumbiara, Goiás – Brazil.
[2] Biomedicine Undergraduate. thiago498.tadj@ufu.br, https://orcid.org/0000-0002-4967-4175. Universidade Federal de Uberlândia, Uberlândia, Minas Gerais – Brazil.
[3] Veterinary Medicine Undergraduate. mariavitoriags02@gmail.com, https://orcid.org/0000-0002-5869-1145, Member of the Programa de Educação Tutorial (PET) of the Veterinary Medicine course at Universidade Federal de Uberlândia. Uberlândia, Minas Gerais – Brazil.
[4] Veterinary Medicine Undergraduate. lucas.navasquez@gmail.com, https://orcid.org/0000-0001-5891-5586, Universidade Federal de Uberlândia, Uberlândia, Minas Gerais – Brazil.
[5] Veterinary Medicine Undergraduate. laisdedeussousa@gmail.com, https://orcid.org/0000-0002-6911-5282, Universidade Federal de Uberlândia, Uberlândia, Minas Gerais – Brazil.
[6] Veterinary Medicine Undergraduate. heitor1605@hotmail.com, https://orcid.org/0000-0002-7855-8640, Universidade Federal de Uberlândia, Uberlândia, Minas Gerais – Brazil.
[7] Resident Veterinarian in Small Animal Surgery. andrezza.brigato@gmail.com, https://orcid.org/0000-0001-5887-8252, UNIUBE Veterinary Hospital. Uberaba, Minas Gerais – Brazil.
[8] Veterinary Medicine Undergraduate. gabidinairassis@gmail.com, https://orcid.org/0000-0001-8703-7452, Universidade Federal de Uberlândia, Uberlândia, Minas Gerais – Brazil.
[9] Veterinary Medicine Undergraduate. guilherme.faria1@ufu.br, https://orcid.org/0000-0001-6597-2650, Universidade Federal de Uberlândia, Uberlândia, Minas Gerais – Brazil.
[10] Bachelor's degree in Biological Sciences. theus.hss@gmail.com, https://orcid.org/0000-0002-8472-4019, Veterinary Medicine Undergraduate at Universidade Federal de Uberlândia. Uberlândia, Minas Gerais – Brazil.

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an epidemiological, ecological, cross-sectional, quantitative, and descriptive study. Data from the *Sistema de Informação de Agravos de Notificação* (Sinan) and the *Sistema de Informações sobre Mortalidade* (SIM) were analyzed. **Results:** 55,779 cases of leptospirosis were reported. It was observed that the regions with the highest number of notifications were the Southeast, South and North regions, with 2011 being the year with the highest prevalence of the disease. Men, white, those aged between 20 and 39 years old, and with incomplete schooling from 5th to 8th grade of elementary school were the most affected by the infection. We identified 304 cases of infection in pregnant women of various gestational ages. Leptospirosis killed 8.37% of those infected. The victims were male, between 50 and 59 years old, white, single and with less education. **Final considerations**: It is concluded that conducting epidemiological surveys on leptospirosis in Brazil is crucial to understand the burden of this disease, identify risk factors, and develop effective prevention, and control strategies.

Keywords: Access to Health Information; Measurements in Epidemiologic; Leptospirosis; Brazil.

RESUMO

Objetivo: O objetivo deste artigo foi analisar as variáveis epidemiológicas dos casos (2007-2022) e óbitos (2007-2021) de leptospirose humana no Brasil, e correlacionar os dados desta zoonose com o contato entre humanos e animais de estimação. **Métodos:** Trata-se de um estudo epidemiológico, ecológico, transversal, quantitativo e descritivo. Foram analisados dados do Sistema de Informação de Agravos de Notificação (Sinan) e do Sistema de Informações sobre Mortalidade (SIM). **Resultados:** Foram notificados 55.779 casos de leptospirose. Observou-se que as regiões com maior número de notificações foram as regiões Sudeste, Sul e Norte, e 2011 foi o ano com maior prevalência da doença. Indivíduos do sexo masculino, raça branca, faixa etária de 20 a 39 anos e com escolaridade entre 5ª a 8ª série do ensino fundamental incompleto foram os mais acometidos pela infecção. Foram identificados 304 casos de infecção em gestantes de diversas idades gestacionais. A leptospirose matou 8.37% dos infectados. As vítimas eram do sexo masculino, com idade entre 50 e 59 anos, de cor branca, solteiras e com menor nível de escolaridade. **Considerações Finais:** Conclui-se que a realização de inquéritos epidemiológicos sobre a leptospirose no Brasil é fundamental para

entender a carga dessa doença, identificar fatores de risco e desenvolver estratégias eficazes de prevenção e controle.

Palavras-chave: Acesso à Informação de Saúde; Brasil; Leptospirose; Medidas em Epidemiologia.

INTRODUCTION

Leptospirosis is a zoonotic bacterial disease caused by a group of spirochetes belonging to the genus *Leptospira*, which can be transmitted directly or indirectly to humans[1]. Many mammals, although asymptomatic, can carry the bacteria in their renal tubules and shed them in the urine. Therefore, the most common form of transmission is through contact with contaminated soil and water or biological material from infected animals[2].

In tropical regions, the humid and hot climate predominates, which contributes to the persistence of the bacteria in the environment[3]. In addition, in developing countries, flooding is frequent and basic sanitation is precarious, which favors the transmission of the disease, such that the highest incidence of leptospirosis is found in Southeast Asia, South America, and sub-Saharan Africa[4]. Brazil is a country located in a tropical region of South America, and its climate, territorial extension, and social inequality make it conducive to the spread of *Leptospira* spp.[5]

Rats remain the most common vector of infection in urban areas. However, dogs, as the main predators of rodents and due to their close relationship with humans, play an important role in disease transmission by acting as a conduit between rats and humans[6].

After entering the host through the mucosal or skin barrier, *Leptospira* migrate through the blood and become established, causing multisystem disease affecting multiple organs, including the kidneys, liver, lungs, meninges, and spleen[7]. Thus, the clinical manifestations are quite variable, such as kidney damage, fever, muscle pain, headache, tachypnea, and jaundice[8]. On the other hand, carrier animals usually do not show symptoms except for some dogs that may show human-like symptoms depending on the infecting serovar[9]. In some cases, leptospirosis can even be fatal for dogs[8].

Despite being neglected, leptospirosis has been classified by the World Health Organization (WHO) as one of the main emerging and reemerging diseases[6]. Worldwide,

approximately one million people are infected and more than 58,000 die each year[10]. In this sense, measures aimed at reducing the incidence of the disease can be adopted based on epidemiological surveillance, which allows obtaining regional and demographic data to understand the profile of the infected population, modes of transmission, and endemic regions, to guide control and prevention actions from leptospirosis[1].

Brazil has a mandatory reporting system for new cases of the disease, which allows for agile but timely control measures. However, more comprehensive, up-to-date analyses that aggregate the different regions and provide temporal trends are still scarce. Such assessments are necessary to understand the context of the disease and to guide projects to control leptospirosis in the medium and long term[10].

Therefore, the aim of this article was to analyze the epidemiological variables of cases (2007-2022) and deaths (2007-2021) of human leptospirosis in Brazil, and to correlate the data on this zoonosis with the contact between humans and companion animals.

METHODOLOGY

This is an epidemiological, ecological, cross-sectional, quantitative, and descriptive study. Its subject is the notification of cases (2007-2022) and deaths (2007-2021) due to leptospirosis in Brazil.

Brazil is the largest country in South America and the fifth largest in the world, with a total area of 8,515,767 square kilometers. Brazil's population is approximately 213 million, concentrated in urban areas, with an annual growth rate of about 0.7%, making it the sixth most populous country in the world[11]. Brazil has a federal system of government consisting of 26 states and one federal district. The largest cities in Brazil are São Paulo, Rio de Janeiro, and Brasília, with populations of 12.3 million, 6.7 million, and 3.1 million, respectively. The Brazilian population is relatively young, with an average age of 33. However, there is a significant gender imbalance, with women representing approximately 51% of the population[11].

Brazil has a diverse demographic profile, with a mix of ethnicities and cultures, including indigenous peoples, Europeans, Africans, and Asians. The majority of the population speaks Portuguese, and the country is predominantly Catholic[12]. The country is known for its rich biodiversity, including the Amazon rainforest, which is the largest in the world[11]. These

ecosystems support a rich and diverse biodiversity, and Brazil is home to approximately 13% of the world's species[13].

The methodological strategy involved the analysis of raw data provided by the *Sistema de Informação de Agravos de Notificação* (Sinan)[14] and the *Sistema de Informações sobre Mortalidade* (SIM)[15]. Data collected on June 12, 2023. Data collection took place from January 2007 to December 2022 for Sinan and from January 2007 to December 2021 for SIM. Research using only publicly available data that does not identify participants does not require approval from Brazilian research ethics committees.

For the epidemiological characterization of cases reported on Sinan, gross sociodemographic characteristics were analyzed, such as gender (male and female), race (white, black, yellow, brown, and indigenous), education **(**illiterate**,** 1st to 4th incomplete elementary school, 4th year of elementary school completed, 5th to 8th incomplete elementary school, complete elementary school, incomplete secondary education, complete secondary education, complete higher education, and incomplete higher education), age group (<1, 1-4, division into 5-year age periods, 70-79, and ≥80 years), and region of residence (north, northeast, southeast, south, and midwest).

The reports in pregnant women were studied according to the gestational period (1st, 2nd, and 3rd trimester). In addition, variables related to the criteria for case confirmation (clinical-laboratory and clinical-epidemiological) and the evolution of the cases (cure, death from the reported disease and death from another cause) were analyzed. Ignored or blank information was considered for all analyzed variables.

Variables were transferred and analyzed using TabWin 4.15®, Excel®, and GraphPad Prism 6® and presented in figure and table formats. The map of the spatial distribution of deaths was generated using TabWin 4.15®.

To calculate the annual prevalence, the number of cases in each year was used as the numerator and the Brazilian population per year, according to the Brazilian Demographic Census projection[11], as the denominator. The results of the division were multiplied by one hundred thousand inhabitants, adapted from Oliveira & collaborators[16].

Statistical analysis of the number of leptospirosis cases during the study period was performed on GraphPad Prism 6. The normality of the data was assessed by Kolmogorov-Smirnov and a non-parametric distribution was found. They were submitted to the Kruskal-

Wallis's test and Dunn's multiple comparison test for comparison between groups. P values <0.05 were considered significant.

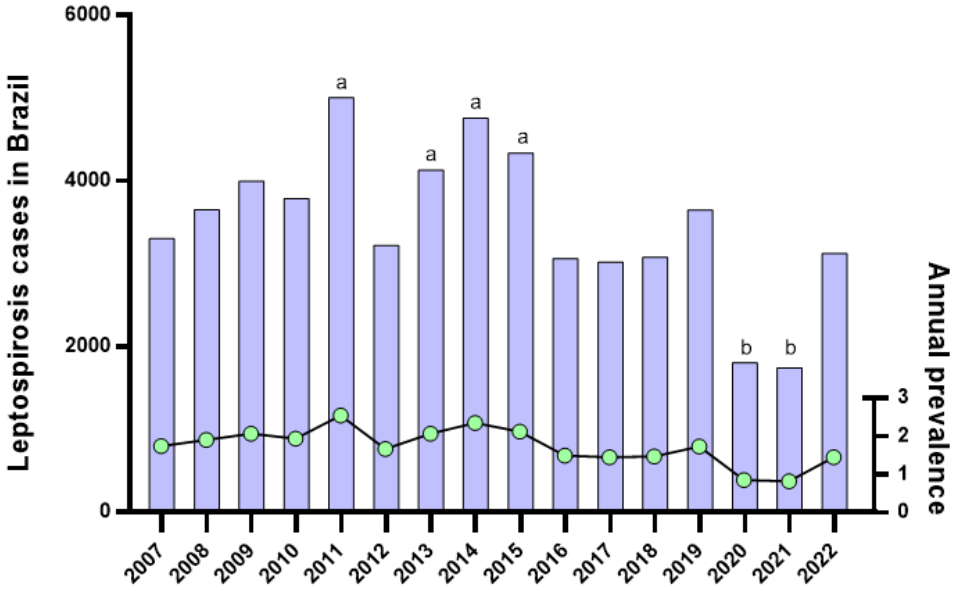
A brief integrative literature review was conducted to facilitate the discussion of the data collected. The bibliographic review was carried out in the databases of scientific articles Medline (Pubmed) and Google Scholar. Scientific articles that addressed leptospirosis in pets in the context of public health were reviewed. The descriptors used were "*leptospirose*/ leptospirosis", "*saúde pública*/public health", and "*animais de companhia*/pet animals OR companion animals". Articles with topics related to the detection of leptospirosis in companion animals (dogs and cats) were selected to contribute to the knowledge and enhance the discussion. Articles that did not fit the main topic were excluded. The most recent articles were selected rather than a specific publication period.

RESULTS

From the year of 2007 to the year of 2022, 55.779 cases of leptospirosis were confirmed in Brazil. Among the years studied, 2011 presented the highest number of leptospirosis notifications in Brazil, with 5,011 cases, with a significant decrease in cases until 2022. Consequently, the year presented the highest annual prevalence rate of infection, with 5.24 cases/100,000 inhabitants.

The number of notifications per year and their annual prevalence rate are shown in Figure 1. The column chart represents the number of cases and should be analyzed with the Y-axis on the left. The line graph with circle symbols represents the annual prevalence rate in the period studied and should be analyzed with the Y-axis on the right side of the figure.

Figure 1 - Number of reported cases and annual prevalence of leptospirosis in Brazil (2007-2022)



Legend: The letter "a" above the columns represents the statistical difference (p=0.0019) between the number of reports from the years 2011, 2013, 2014, and 2015 (a) compared to the year 2020 and 2021 (b). Different letters indicate significance. The other years showed no statistical difference when compared to each other.

Source: Author's elaboration with data from Sinan[14].

Table 1 shows the description of the infection notifications registered in each Brazilian region during the period studied. It was observed that the regions with the highest number of notifications were Southeast, South, and North.

Table 1 - Leptospirosis notifications registered by region of Brazil (2007-2022)

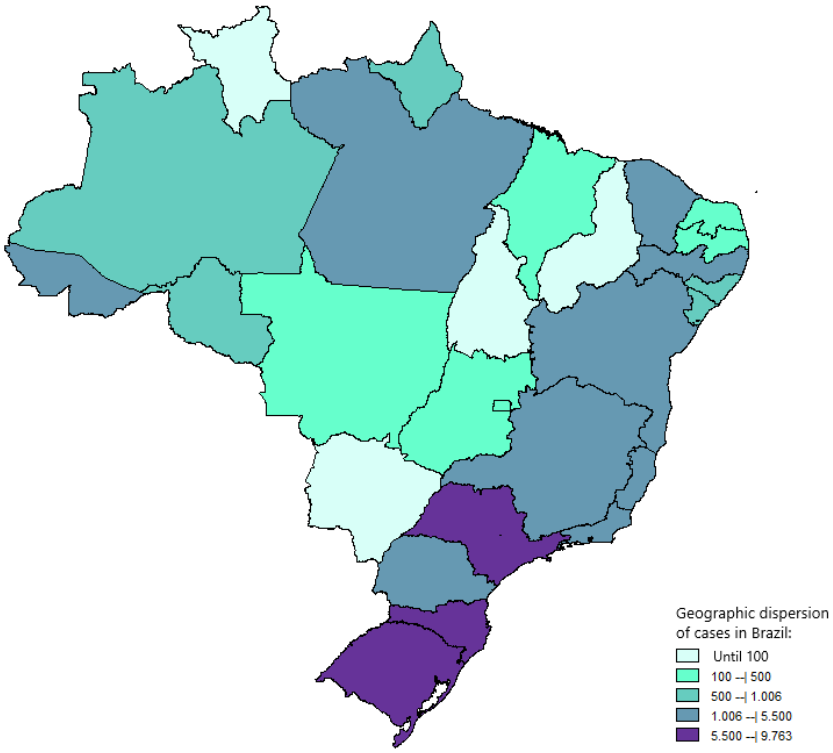
	Brazilian regions				
Year	***North***	***Northeast***	***Center-west***	***Southeast***	***South***
2007	241	566	39	1221	1235
2008	334	643	50	1066	1561
2009	365	929	49	1532	1121
2010	258	717	47	1538	1225
2011	494	930	24	1836	1725
2012	529	414	55	1314	909
2013	931	521	66	1502	1111
2014	1718	573	62	1328	1076
2015	1312	424	80	948	1573
2016	480	324	74	973	1213
2017	517	463	54	919	1066
2018	499	468	71	1021	1020

2019	493	619	75	1058	1401
2020	296	247	58	664	537
2021	288	324	38	552	542
2022	309	971	53	1012	777

Source: Author's elaboration with data from Sinan[14].

Figure 2 shows the geographical distribution of leptospirosis cases during the period studied. The states with the highest number of cases were São Paulo (19.21%), Rio Grande do Sul (12.6%), Santa Catarina (11.63%), Paraná (8.79%) and Acre (8.3%).

Figure 2 - Geographical distribution of leptospirosis cases reported in each Brazilian state (2007 and 2022)



Source: Author's elaboration with data from Sinan[14].

Table 2 presents the sociodemographic profile of Brazilian individuals who contracted leptospirosis between 2007 and 2022. It was possible to verify that the males, white, aged between 20 and 39 years old, and with schooling from 5th to 8th grade of incomplete elementary school are the most affected individuals by the infection.

Table 2 - Sociodemographic profile of people with leptospirosis in Brazil (2007 and 2022)

Sex	**N**
Male	44,702
Female	11,073
Ignored/blank	4
Race	N
White	25,052
Black	3,147
Yellow	349
Brown	20,918
Indigenous	174
Ignored/blank	6,139
Schooling	N
Illiterate	816
1st to 4th incomplete elementary school	5,218
4th complete grade of elementary School	3,195
5th to 8th incomplete elementary school	8,743
Complete elementary school	3,940
Incomplete secondary education	3,833
Complete secondary education	6,413
Complete higher education	1,133
Incomplete higher education	715
Ignored/blank	21,773
Age group	N
Less than 1 year	329
1-4 years	278
5-9 years	1,268
10-14 years old	3,031
15-19 years old	5,049
20-39 years old	22,376
40-59 years old	18,204
60-64 years old	2,324
65-69 years old	1,416
70-79 years old	1,253
80 years or older	239
Ignored/blank	12

Legend: N is the raw number of messages related to the described resource.

Source: Author's elaboration with data from Sinan[14].

Regarding leptospirosis diagnosed in pregnant women, 304 cases were reported, 77 in the 1st trimester, 108 in the 2nd trimester, and 81 of them in the 3rd trimester. In addition, there were 38 reports in which the gestational age was not reported (ignored/blank).

Regarding clinical information, 47,917 (85.9%) cases were diagnosed using the clinical-laboratory criterion, while 7,183 (12.87%) cases were diagnosed using the clinical-epidemiological criterion; in addition, 679 (1.23%) notifications ignored the diagnostic criterion when filling out the notification form (ignored/blank).

As for the clinical features, 45,924 (82.33%) progressed to cure and 496 (0.88%) died of another cause. However, 4,327 (7.77%) notifications did not complete this table in the notification procedure (ignored/blank).

The sociodemographic profile of infection victims (n = 4,669)[15] was male (81.77%), between 50 and 59 years old (42.1%), white (42.81%), single (45.81%), and less educated (28.76%). 92.8% of deaths occurred in a hospital.

DISCUSSION

Leptospirosis is a zoonosis with a wide geographical distribution, reported throughout the Brazilian territory[17,18]. Our data confirmed that the regions with the highest prevalence of leptospirosis are the Southeast, South, and North. The main factor associated with the increase in the number of cases in these regions is the increase in rainfall rates in areas subject to flooding[19]. In addition, the highest incidence rates of leptospirosis are found in coastal areas, low altitudes, and predominantly agricultural use associated with irrigated agriculture[20].

Although leptospirosis is prevalent in tropical regions due to high rainfall, it has recently been diagnosed in temperate and even semi-arid areas, such as the southwestern United States[21]. Sri Lanka is also the country with the highest incidence of infection in the world, with more than 700 deaths per year. This high prevalence is due to the high concentration of workers in rice fields and is known as "rice field fever"[21].

The data presented in this study suggest that the increase in cases of leptospirosis in 2014 is related to an increase in temperature and humidity, a fact that has contributed to an increase in the population of urban rodents and, consequently, their proximity to humans, a fact supported by data from the Netherlands[22].

In 2015, the Pan American Health Organization (PAHO) included human cases of leptospirosis in its Regional Core Health Data Initiative[23]. Among the 28 countries with reported cases of leptospirosis were Brazil (40.2%), Peru (23.6%), Colombia (8.8%), and

Ecuador (7.2%)[23]. On average, 65.1% of cases were male[20], which is consistent with the epidemiological profile found in this study.

However, with the advent of COVID-19, these numbers are believed to be higher because the clinical signs are non-specific and similar to those of leptospirosis. Therefore, it is believed that SARS-CoV-2 infection will contribute to the misdiagnosis of leptospirosis as COVID-19, further spreading the disease due to the lack of treatment and prevention strategies[21].

Regarding the gender variable, our study found a prevalence of cases of infection in men, in line with studies by Martins and Spink[17] and Gonçalves et al.[24]. A justification for this fact is the greater exposure of men to risk factors, as they spend more time away from home, develop unhealthy occupational activities in informality, low-skilled work on the streets or open fairs, with situations or practices that facilitate contagion[25,26].

Martins and Spink[17] found that most people with leptospirosis did not complete the 8th grade, which is consistent with the data described in this study. Thus, it is understood that low education may be a critical risk factor for exposing people to infection.

Studies agree that people who become infected and develop leptospirosis tend to live in areas without sanitation, such as slums and precarious settlements, and/or have work or leisure activities that may expose them to rat urine[24,25]. These people are characterized by poverty, racial segregation, and low levels of education.

In this study, the laboratory diagnostic criterion was used in 86.4% of cases, followed by the clinical-epidemiologic criterion based on the history of other affected humans or animals. Similar data have been described by Martins and Spink[17] and Lara et al.[28]. Considering the confusion between the symptoms of leptospirosis and diseases such as dengue, influenza, rickettsiosis, among others, it is necessary to investigate risk factors at the time of the patient's anamnesis to broaden the clinical suspicion. Leptospirosis should be included in the differential diagnosis and the use of specific protocols in the case of icterohemorrhagic fevers syndromes, valuing the disease as a public health problem[29].

In leptospirosis, the main immunity is humoral, and immunoglobulins are produced from two to ten days after infection according to the species, host immunity and infecting serovar. High IgG and IgM antibody activity can be observed in serological tests after natural infection or immunization, evidencing the humoral immune response[30].

Most antibodies produced by the host are against the lipopolysaccharides (LPS) of the bacteria. An important difference in this disease is the fact that LPS from Leptospira spp. is recognized by human cells by Toll-Like receptor-2 and not by Toll-Like 4, which is a receptor that recognizes LPS from gram-negative bacteria[31].

The diagnosis of leptospirosis in pregnant women is common, according to data collected in this study. It is important to emphasize that pregnant women are more likely to develop severe cases of leptospirosis, especially in the third trimester of pregnancy. In these cases, they may present with myocarditis, acute kidney injury, coagulopathy, acute respiratory distress syndrome, and liver dysfunction[32]. In addition, there is a significant risk for fetal development in which, in addition to the high probability of miscarriage and prematurity, there may be alterations in the development of the cardiorespiratory apparatus, making it essential to monitor these newborns[33].

According to Costa et al.[20] the regions of South and Southeast Asia, Oceania, Caribbean, Andean, Central, and Tropical Latin America, and East Sub-Saharan Africa have the highest estimates of morbidity and mortality from leptospirosis. The relative risk of infection is between 20 and 39 years of age, while the relative risk of death is between 40 and 69 years of age[20].

It was found that the prevalence of deaths from leptospirosis increases with age. The history of the disease (chronic pattern) is propably responsible for this, as well as the prevalent immune and physiological characteristics of the population and the frequent co-morbidities, such as persistent illnesses that are common in the elderly, according to the pattern found in schistosomiasis deaths[34].

The interaction of animals with humans appears strong since primitive times. In the current scenario, pets are used not only as companions, but also for hunting, protection, and assistance to people with physical disabilities[35]. In combination with the many risk factors that predispose humans to infection with strains of *Leptospira* spp. close contact with domesticated animals may contribute to humans contracting leptospirosis.

Domestic dogs get infected primarily by *Leptospira interrogans* and *Leptospira kirschneri* and disseminate this serovar into the environment[36]. In contrast, clinical disease in cats is rarely reported, even in the face of serological evidence of cat exposure to *Leptospira*. In this species, the serovars Canicola, Grippotyphosa, and Pomona have been isolated[37].

Thus, the veterinarian is of great importance in the control and prevention of this disease, to reduce the risk of disease transmission to the population, especially to the most vulnerable groups, such as inhabitants of rural areas and areas with precarious basic sanitation, garbage collectors, animal caretakers, firefighters, among other professions[38].

Therefore, the veterinarian has a fundamental role in taking preventive measures, informing the owners of pets and livestock about vaccination, basic hygiene and sanitation measures, and the correct way to dispose of animal excreta, in addition to warning about how the environment can favor the presence of rodents due to the presence of available feed that is improperly stored and ends up as food for these animals[38].

In a retrospective study by Jorge et al.[39] with human and animal exposure to leptospirosis in Southern Brazil they found the highest seroreactivity in humans to *Leptospira kirschneri* serovar Butembo (serogroup Autumnalis) and high interspecies association between canine and human exposure to leptospirosis.

Unfortunately, the true extent of leptospirosis in the world is not known because it is an underreported disease; many countries do not have efficient surveillance and statistical systems, and it is also difficult to distinguish it from other diseases with similar symptoms[40].

Completing the information on disease notification forms in the *Sistema de Informação de Agravos de Notificação* (Sinan) is crucial for effective disease surveillance and control. The information collected enables health authorities to identify and monitor the spread of infectious diseases, track trends, and develop appropriate control measures to prevent further spread of the disease[41]. In addition, data is used to inform policy decisions, allocate resources, and prioritize interventions. By accurately and promptly filling out the disease notification forms, health professionals can help ensure that diseases are detected and managed in a timely and efficient manner, ultimately contributing to better public health outcomes.

FINAL CONSIDERATIONS

Leptospirosis remains a major public health concern in Brazil due to its high prevalence. The best conditions for infection are populations with lower socioeconomic status living in homes that are easily flooded and in contact with water contaminated with rodent urine, especially during the rainy season. Despite efforts to control the disease through vaccination

campaigns, improved hygiene and sanitation, and early diagnosis and treatment, challenges remain in ensuring adequate access to health services and implementing effective prevention strategies.

Reducing the burden of leptospirosis in Brazil will require a comprehensive approach that integrates public health interventions, environmental management, and community participation. This includes strengthening surveillance systems to monitor the disease and its risk factors, improving the quality and accessibility of health services, promoting health education and behavior change, and implementing environmental and infrastructure interventions that reduce exposure to bacteria. By addressing the root causes of leptospirosis and working with communities, policymakers and health professionals can make significant progress in reducing the impact of this neglected tropical disease on the health and well-being of the Brazilian population.

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