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Influence of Environmental Factors on Occurrence of Leptospirosis in Humans and Animals in Brazil-A Review

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Review Article

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Abstract

Leptospirosis is an infectious, zoonotic and neglected disease, distributed worldwide and endemic in America and in several states of Brazil. It is a disease that causes significant social, economic and health impact. Pathogenic species can survive in the environment for relatively long periods. Some environmental conditions favor the survival and maintenance of the bacteria in the environment, such as characteristics of the soil to be alkaline and humid, type of agricultural production and proximity to farm Animals. Animals play an important role in environmental contamination, especially rodents. The findings in this review reinforce the need for an integrated approach from a one health perspective so that prevention actions are more effective.

Keywords: One Health; Risk factors; Zoonosis; Public Health; Epidemiology

Introduction

Leptospirosis is an infectious, zoonotic and neglected disease, distributed worldwide and endemic in America and in several states of Brazil [1]. The etiological agent of this disease is a bacterium of the genus Leptospitospira, which has as reservoir several animal species, and the environment is fundamental for the analysis of risk factors in a multidisciplinary approach, as in single [1-3]. In America, out of 52 countries and territories, 28 reported the presence of human cases. A total of 10.433 human cases of leptospirosis were reported in the Region of the Americas. The regional cumulative incidence rate was of 2.11 per 100,000 inhabitants. Brazil reported 38% of human cases in the Region of the Americas in the same period [4]. However, leptospirosis remains a silent disease, mainly due to the scarcity of data in many countries [5].

The diversity of reservoir animals represents a significant challenge for prevention and control [6], and synanthropic rodents and dogs play the role of the main reservoirs of the disease. Exposure to water and soil contaminated by the urine of infected animals is the most common route of transmission of people and domestic animals [7]. In addition, geological and geographic characteristics together with demographic, agricultural and livestock factors are also determinant for transmission [8]. Understanding the factors that influence the strong occurrence of leptospirosis in Brazil is essential for the elaboration of public policies directed to the control and prevention of the disease [8]. It is also important to extrapolate the understanding of these factors in other territories of the world. Thus, this study aims to understand the influence of environmental factors in the occurrence of leptospirosis in humans in Brazil through a literature review.

Social Impacts of Leptospirosis

Leptospirosis is a zoonosis of worldwide distribution, caused by bacteria of the genus *Leptospira*. The disease may present with nonspecific signs such as fever, myalgia, abdominal pain, vomiting, and evolving to hematuria and

petechiae. Some patients develop the most severe form of the disease, known as Weil syndrome, in which the patient may have intravascular hemolysis, hemorrhagic manifestations, renal and hepatic involvement [9]. Infected animals may be asymptomatic, capable of releasing Leptospiras for months, years or throughout life continuously and intermittently, depending on the serovar involved and the species of the infected animal [10]. Worldwide, around 1.3 million and 300,000 cases of leptospirosis are recorded in humans, with incidence rates ranging from 0.1 to 975.0 cases per 100,000 inhabitants [11]. In Brazil, the highest incidence per 100,000 inhabitants was observed in the southern region, in 2011 (4.46), followed by the North (2.27), Southeast (1.73), Northeast (1.34) and Midwest (0.39) regions [12].

It is a disease that causes significant social, economic and health impact. According to the Ministry of Health (MS), the disease has great social and economic importance due high incidence and significant percentage of hospitalizations, high hospital costs and loss of working days, as well as its lethality [2]. Pereira C [13] concluded that 3,492 cases of leptospirosis occurred in 2008 generated an approximate cost of R$ 1,542,526 and 10,664 potential years of life lost to the Brazilian health system. In addition, the sick people presented loss of productivity, which ranged between R$ 278,481.60 to R$ 979,317. After a partial economic evaluation of the cost-illness type from the economic and social perspective, authors pointed out that the disease produces a financial impact on society due to the high number of potential years of life lost and salaries that are not received by the patient [2]. Similarly, in this other study, the authors identify that, in 2007, the age group that lost the most years of life, belonged to the group of 20 to 49 years, a phase of life of high creativity and productivity [2].

In humans, leptospirosis has been related to a low level of education [2]. The sociodemographic profile of individuals with leptospirosis coincides with the incidence in poor areas, poor sanitation, in addition to regions where flooding occurs [11,14]. The presence of rodents in areas with these characteristics has been described previously and is the main factor associated with [15]. In several studies the higher prevalence of affected individuals is male [14,16]. This is due to the fact that men are at the forefront of activities involving risk situations [14], such as animal management, agricultural work, maintenance of sewage network, among other occupations [17].

Pathogenic Species in the Environment

Transmission of leptospirosis can occur through the direct route; which occurs through the host's contact with blood, urine, or other reservoir fluid, which contains leptospiras; and the indirect route, in which contact with leptospiras occurs through contaminated soil or water [18,19]. The indirect route highlights the importance of studies of environmental factors, for a better understanding of this link of transmission [20,21].

Leptospires are mobile bacteria, 6 to 20 μm long and helically coiled. They are spirochetes belonging to the family Leptospiraceae [22]. The genus Leptospira is traditionally divided into two groups, the saprophytes*, Leptospira biflexa sensu lato*, and the pathogenic, *Leptospira interrogans sensu lato*. After a phylogenetic analysis, it was revealed that leptospira can be divided into three strains correlated with the pathogenicity level of the species: saprophyte, intermediate and pathogenic [23]. Intermediate species share an almost common ancestor with pathogenic species, exhibiting moderate pathogenicity in humans and animals. Different serovars of leptospira have been isolated from environmental sources as they are able to survive in humid soil and fresh water for several weeks [24,25]. Leptospira's ability to occupy several ecological niches is undoubtedly due to a diversity of mechanisms, such as signal transduction systems encoded by its large genome and that allow it to adapt and resist adverse conditions [26,27].

The discovery of new species of leptospira, including species belonging to the pathogen and intermediate strains is fundamental for the development of robust detection and diagnostic tools that are necessary to treat infected hosts more quickly and appropriately. The characterization of leptospira populations in soil and water is also important for prevention and control actions aimed at reducing the risk of infection by bacteria in the environment [28]. Thus, recent studies have isolated new species of leptospira in the soil [29,30], leading to an important expansion of taxonomy, with currently 35 species named [30,31]. It is believed that virulent pathogenic leptospiras cannot multiply in the environment [32]. However, although the survivability of most species outside a host is not questionable, little is known about the environmental factors and determinants that condition this survival [33]. Leptospira's ability to adapt to parameters such as osmolarity within a host or in nature also showed to be species-specific and related to genome size [34].

Viability of Bacteria in the Environment

Knowledge about the biology and survival mechanisms of pathogenic leptospiras in the environment is still scarce, and the ability of different strains to survive in environmental conditions remains largely unexplored. However, the understanding of these factors is of paramount importance for a better understanding of the epidemiology of the disease and a better control and prevention of human leptospirosis [35].

Recognizing this importance, some studies to evaluate the viability of leptospira in environment have been conducted. Although the real-time PCR technique detects leptospiras in environmental samples, it does not provide information regarding the viability of these cells. For this, studies have combined PCR methods with the use of propidium monoazide to reduce the detection of dead or membrane-compromised cells. This technique, known as PCR-feasibility, provides leptospira's viability indications in environmental samples [25,36]. Recently, some researchers have optimized procedures for the molecular detection of pathogenic leptospiras from environmental water sources [37], increasing the possibilities of further studies on environmental leptospirosis and opening up pathways for one health studies of this complex zoonosis [35].

Saprophyte species, common inhabitants of the environment, are abundant and grow faster, are the most often isolated from soil and water samples [38,39]. But pathogenic species such as *L. interrogans* have already been detected in surface waters and from rice planting [40]. In a systematic review, strong evidence was found that virulent pathogenic leptospiras may remain viable and have the potential to infect people and/or animals in the environment for months, especially in soils [35]. In addition, they were isolated more frequently in the soil than in standing waters, currents or springs [35,41,42].

Associated Environmental Factors

Not only is leptospirosis a public health issue in developing countries, like Brasil, it has become an urban health problem in developed and industrialized countries, especially during periods of seasonal reinfall and flooding in unsanitary environments. The disease is also occurring in countries that natural disasters like hurricanes, typhoons and floods, is relatively common [15]. In urban areas in Brazil, especially in poor conditions of basic sanitation and paving, such as slums in large centers, associated with floods, soil contamination is a relevant risk factor for the population. In this setting, it is described that contact with the remaining mud of floods has a strong association with the occurrence of the disease in humans when compared to people's contact with the water itself [43].

Some environmental components have been related to the occurrence of the disease, including soil type and use, as well as vegetation cover and predominant climate. It is suspected that alkaline and neutral soil promotes a longer survival of the bacterium, especially in young and unstructured soils, such as those of volcanic origin [44]. Added to these, soil temperature and proximity to water bodies have also been reported as potential facilitators for bacterial survival [41]. In addition, the incidence of leptospirosis is seasonal, usually peaking in summer and autumn, in temperate climate countries and during the rainy seasons in tropical climates [45]. Lower altitudes are associated with the higher occurrence of leptospirosis. They are places with a greater propensity for flooding. Low altitudes also usually have higher temperatures and this type of environment have favored the maintenance of the bacteria [8,46]. Rainfall is another important factor for maintaining moisture [47].

Leptospirosis is endemic in rural and urban regions [48]. In southern Brazil, the rural population has an eight-fold higher risk of acquiring the disease compared to the urban population. In addition, the largest number of cases in these areas is concentrated in places where tobacco and rice are cultivated, due to the characteristic of Schneider MC, et al. [49]. Other types of production, such as grains, have their harvest and storage, attractive factors for rodents, favoring environmental contamination [50,51]. Brazil is a major grain producer, and this may be a risk factor for rural populations [47]. Spatial analysis studies have shown the association of leptospirosis with the territory. They have also associated the disease with various aspects and characteristics belonging to the studied environment [8,47,52].

Farm Animals and the Environment

In addition to rodents, domestic animals have participated in the epidemiological chain of leptospirosis, because they act as carriers and potential transmitters of the disease [17]. Dogs, serovar maintenance hosts Canicola, but which can also bear other serovars such *as Pyrogenes, Castellonis, Autumnalis, Icterohaemorrhagiae* [53-57], live close to humans, especially in urban areas. Animais de produção também possuem participação na manutenção da leptospira no ambiente. Recentemente, 17 sorovares da bactéria foram encontrados em bovinos, equinos, ovinos e suínos, sendo que as mais frequentes foram Celledoni, e Icteroheamorrhagiae e sorogrupo Serjoe. As suas últimas também foram encontradas em humanos na mesma região [50]. Em bovinos, a soroprevalência é relativamente alta no sul do Brasil (44,69%) e os fatores de risco mais relevantes são a baixa altitude e a elevada temperatura [58]. Alguns fatores de risco para a doença em suínos é a presença de bebedouros do tipo canaleta, a presença de áreas alagadiças próximas às instalações dos animais e a falta de higienização dos reservatórios de água [59].

Embora as espécies animais mencionadas possam ter participação na contaminação ambiental, o principal transmissor de leptospiras patogênicas são os ratos. Desses, o *R. norvegicus e R. rattus, apresentam a maior*

prevalência de leptospira em diversas partes do mundo [15], sendo o R. novergicus, o hospedeiro definitivo do sorovar Icterohaemorrhagiae, o mais patogênico ao homem [60]. Leptospirosis is an excellent example of one health, as it is a disease that integrates human medicine, veterinary medicine and environmental health, due to the diversity of species and serovars, hosts and conditions of survival in the environment [50]. Thus, the one health approach is essential for the development of control and prevention measures, which need to be multidisciplinary and multisectoral [3].

Conclusion

Leptospirosis is a disease of wide distribution in Brazil that has social and economic impacts. The survival of pathogenic strains in the environment depends on soil conditions and their use. Alkaline soils with fewer nutrients favor the maintenance of the bacterium in the environment. The disease occurs more in rural areas in some regions of Brazil, when the conditions of some plantations such as rice, tobacco and grains are attractive to rodents, in addition to the greater proximity of humans to other susceptible animals. In urban areas, the occurrence of leptospirosis is associated with large centers, floods and precarious basic sanitation, associated with the presence of mud, more than the water itself. Those exposed in this review reinforce the importance of an integrated approach to the prevention of leptospirosis in humans.

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