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Leptospirosis: A re-emerging zoonosis

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ABSTRACT

Leptospirosis is a zoonotic disease caused by a bacteria of the genus *Leptospira*, which attacks people and domestic and wild animals. The bacteria can live and reproduce in rivers, streams, lakes, ponds and swamps. The risk of transmission increases in the rainy and flood seasons due to the characteristics of the survival of the bacteria, which can survive in water and even in stagnant water. Reservoirs are mainly rodents and dogs that eliminate *Leptospira* through urine, thus contaminating the environment inside and outside homes. In the documented epidemics, weather, health and environmental conditions in the geographical region could cause the disease. In this review, risk factors related to the disease in different epidemiological scenarios are analysed.

1. Introduction

Leptospirosis is an acute and generalized disease, which is characterized by an infectious vasculitis that causes changes in several organs such as lungs, livers and kidneys. The causal agent of this disease is a spirochete of the genus *Leptospira*, especially the pathogenic *Leptospira interrogans* for humans. Different serogroups and serovars have been identified for this genus. They are not specific for any specie[1].

Leptospirosis is a zoonosis of broad geographic distribution. The bacterium is excreted in the urine of domestic and wild animals, thus contaminating water sources. It prevails in underdeveloped countries. In these countries, it is an important public health problem. It appears as sporadic cases or there are seasonal outbreaks mainly in the rain and floods seasons. The number of cases increases with high temperature and rainfall, although it may occur throughout the year. Outbreaks of leptospirosis usually appear after natural disasters such as floods, hurricanes or periods of heavy rain[2].

The ideal environment for the emergence of cases is uncontrolled urbanization with poor environmental sanitation, presence of rubbish

and proliferation of rodents. And if we add the presence of stray dogs, animals without health control, we will have the proper conditions for a serious public health problem. In each specific region, the risk of human infection will vary depending on direct or indirect contact opportunities. While all people are susceptible regardless of sex and age, it is more common among young men. This would be explained by their higher exposure to risks[3].

Humans can become infected by contact with the urine of infected animals. That is the reason why the infection is related to living conditions as well as to recreational or work activities that promote contact with infected animals, water or soil contaminated by the urine from reservoirs[4].

Leptospirosis reservoir in rural areas is made of the livestock, cattle, pigs, goats, horses and wild rodents. In urban areas, reservoirs are mainly rodents and dogs. As regards rodents, the sewer rats or mice (*Rattus norvegicus*) and black rats or roof rats (*Rattus rattus*) are considered the most relevant ecological reservoirs of leptospirosis. In South America, leptospirosis mainly affects young adult males (20–30 years old), especially in hot and rainy seasons. The prevalence of this zoonosis is increasing because life and work conditions of most of the population are getting worse. Thus, it should not be only related to people's work, but also associated with environmental conditions[5].

2. Microbiology

It is considered one of the most widespread and underdiagnosed zoonosis of cosmopolitan distribution. This is partly due to the nonspecific clinical presentation of the disease, as well as the

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survival capacity of *Leptospira interrogans* both in infected animals and in the environment. Leptospirosis remains in nature by chronic kidney infection of asymptomatic carrier animals, which eliminate the microorganism in urine, thus contaminating the environment. Rodents excrete *Leptospira* in the environment intermittently throughout their whole life. Moreover, domestic and wild animals excrete *Leptospira* in their urine for long periods and in large quantities[6].

This bacterium has the ability to live in the convoluted tubules of Henle's loop in animals which are completely asymptomatic, and it can survive up to six months in the environment after its urinary excretion. *Leptospira* can survive several days in warm or cold water as well as in wet soil[7,8].

The survival period of pathogenic *Leptospira* in water and soil varies according to temperature, pH, salinity or the degree of contamination. They die with desiccation and tolerate low temperatures but not higher than 40 °C. The optimum pH for multiplication is 7.2–7.4 and they are destroyed in acidic media or alkalinity above pH 8. They do not survive in salt water, but they can stay for weeks in fresh water with favourable physicochemical conditions. Ultraviolet radiation inactivates them[9,10].

3. Transmission

Leptospirosis is a zoonosis of broad geographical distribution, and it is more common in tropical and subtropical regions where it has an endemic nature. Epidemics occur after natural disasters such as hurricanes and floods[11]. The urine of infected animals contaminates water, soil, vegetation and food. The most important reservoirs in urban environments are rats (*Rattus* spp.) and dogs. In rural areas, farm animals such as cattle, pigs, sheep and horses are also reservoirs[12].

Infection in humans occurs when *Leptospira* penetrate through the skin, nasal mucous membrane and upper digestive tract, and conjunctiva. Moreover, skin and mucosal lesions facilitate transmission[13]. The transmission occurs when there is contact with urine, water or soil contaminated with urine of infected animals. *Leptospira* can also be acquired by consumption of liquids or food that are stored in warehouses or cupboards where rodents have access. Leptospirosis has also been associated with inhalation of liquids contaminated with spray[9].

The most favourable conditions for *Leptospira* to survive outside the reservoir are stagnant or slow-moving water, which have neutral or slightly alkaline reaction with temperatures between 22 °C and 30 °C and no sunlight. Under these conditions, *Leptospira* can maintain their virulence for several weeks, especially in swampy or marshy areas, streams and ditches[14].

Therefore, the greatest opportunity to acquire the disease occurs in hot countries, and especially during rainy seasons when agricultural work is done and people are working in sewage systems, ditches, canals, dams and wells. It can also be transmitted by immersion or swimming in contaminated water[6].

Indirect transmission, especially by contact with contaminated water, is the most common mechanism and it determines the epidemiological characteristics of the disease. Most of the cases and epidemics of this disease are associated with floods and recreational activities in aquatic environments. In temperate countries, the peak incidence occurs from late summer to early fall, and the number of cases and epidemics increase after periods of excessive rain[15].

There are risk groups, such as people exposed to contaminated environments or animal reservoirs, due to leisure or work such as slaughterhouse workers, people exposed to sewage, agricultural workers and military personnel[16].

On the other hand, in areas of tropical weather, more reservoirs can be found, and besides occupational exposure, there may be infections which are not related to labour[17]. For example, in the context of floods, there are favourable environmental conditions for disease transmission, especially when they occur close in time to massive recreational or sports activities. A third model of transmission in urban areas is caused by exposure to the urine of rodents or other pets, especially dogs[18,19].

4. Risk groups

In Latin America and Southeast Asia, the most common source of infection is exposure to rats[20]. These are the ubiquitous reservoir of *Leptospira* in both urban and rural areas. The conditions of poor environmental sanitation, such as overcrowding, accumulation of rubbish and poor sanitation, favour the proliferation of rodents[21]. The rate of infection in rodents can reach 50% of the population. The presence of stray dogs and the proliferation of rats in large human clusters are the scene of urban leptospirosis[22]. On the other hand, flood areas are sometimes used for recreational activities. In addition, they usually build shanties near rivers or streams[23].

In underdeveloped countries, floods are the most important risk factor of epidemics. After floods, recreational activities in contaminated water are the most important source of leptospirosis in these countries. In rural areas, the infection may be associated with exposure to livestock and pets, such as dogs[24].

Leptospirosis can occur as an occupational disease in vets, rubbish collectors or people responsible for cleaning sewers[25]. For these reasons, there are different models of disease transmission, with specific risk factors in each of them, and different epidemiological situations[26,27]. There is a rural occupational transmission, which occurs mainly in temperate climates, affecting workers in contact with infected livestock[28-30].

5. Occupational and rural transmission

Campagnolo *et al.* analysed an outbreak of leptospirosis which occurred in staff exposed to infected pigs in slaughterhouses at the University of Missouri. It was determined that 30% of the staff did not use eye protection or gloves during exposure or did not wash their hands after being in contact with pigs or handling animal tissues. Also, it was found that smoking or drinking during working activity was a significant risk factor. The main gates were the oral and conjunctival mucosa and skin wounds[31].

Lo *et al.* reported two patients who acquired leptospirosis as an occupational disease. One patient was in charge of raising horses, goats and chickens on his farm. He also worked in derattization in an auto part warehouse. Another similar case was a patient who worked at a farm with pigs, chickens and goats and usually performed tasks of rodent control[32].

Brown *et al.* wanted to determine the risk factors for acquiring leptospirosis in Jamaica, so he carried out a study in slaughterers. Slaughterhouses are the proper environment for the survival of the microorganism and a critical factor for the maintenance of infection and transmission to human hosts. Most of the affected population

belonged to agricultural or farming communities or were workers at slaughterhouse. Traditionally, these tasks are mostly performed by men, about 40% of which, according to data collected by Brown, were under 40 years old[33]. With this study, it was found that workers were constantly exposed to blood, faeces and other waste fluids of slaughtered animals without proper personal protective elements. At the time of inspection, stray dogs in or near the facilities were observed. The proximity of these animals could make humans acquire leptospirosis. Alive rodents were found in 5% of slaughterhouses, where solid wastes of animals are used as food. The risk of transmission of leptospirosis increases even more when there are no adequate facilities for the collection and storage of waste.

Katz *et al.* gathered information from reports made by the State of Hawaii. During the period of 25 years, between 1974 and 1998, 752 cases were reported. In 41% of the cases, transmission was related to labour, 77% of these people were performing agricultural tasks[34]. Most cases were sporadic and unrelated, although six outbreaks were confirmed by laboratory during the period of 25 years, and two to eight people were involved. Three outbreaks were associated with occupational exposure, and three to recreational activities. In 207 out of 353 cases, there were data about the presence or absence of skin lesions during the incubation period with 82% of patients (179 people) reported that they had skin wounds.

6. Transmission related to recreational activities

Lo *et al.*[32] reported a case of leptospirosis in a patient who had swum in a stream near his home ten days before the onset of symptoms. Morgan *et al.* investigated an epidemic of leptospirosis associated with a triathlon that was held in Springfield, Illinois on June 21st, 1998. The first cases were 3 athletes who were hospitalized with headache, myalgia, increased serum level of liver enzymes and haematuria. He contacted 834 of the 876 participating athletes; 98 of them (12%) reported being sick. Serum samples were obtained from 474 athletes, of which 52 (11%) were positive for leptospirosis. Accidental ingestion of water from Lake Springfield and the exposure time while they were swimming for more than 42 min were the predominant risk factors for getting the disease. Among residents, there also were cases of the disease. In some cases, they had been exposed to water of the lake or its surroundings, where the triathlon was held, in recreational activities such as swimming or jet ski[35].

In an analysis of Katz *et al.*, which was performed on reports of 353 confirmed cases over a period of 25 years in Hawaii, it can be seen that there is a change as regards the exposure mode from occupational to recreational. This reflects the change in economic activity, with a decrease in agricultural activities, most notably in sugar and pineapple industries, and greater emphasis on activities related to tourism. Therefore, in 43% of documented cases, leptospirosis infection was associated with recreational exposure. Swimming was reported in 59% of cases, hiking or camping in 19%, fishing in 15% and hunting in 10%[34].

Stern *et al.* investigated an outbreak of leptospirosis which occurred after a sporting event in Florida through information obtained from interviews with 192 (96%) out of 200 participants of the competition. On November 21st, 2005, a 32-year-old man from New York was hospitalized after a consultation due to a sudden onset of fever accompanied by headache and myalgia. The patient had participated in the National Championship, carried out

by the association of adventure racing in the United States. The event was held at a State Park nearby Hillsborough River in Tampa, Florida. The National Championship in 2005 was developed as a sport endurance competition in a bog, covering a distance of 100 miles in a 24-hour period, and included four components: rowing, cycling, hiking and orientation. Two hundred athletes from the United States and Canada took part in the event. Two weeks before the competition, Hurricane Wilma crossed the western region of Florida and caused heavy rains and floods in the region of Tampa and the Hillsborough River State Park. During the journey, the athletes had a long exposure to the surface of the river, streams and marshes nearby. It was found that the intake of water from the river or marshes and wet food, as well as prolonged immersion were significantly associated with an increased risk of acquiring leptospirosis. Two variables suspected of risk were analysed, as well as the presence of skin lesions in lower limbs and the fact of wearing shorts, but it was not found a statistically significant association with the infection risk[36].

Potential zoonotic sources for the development of leptospirosis in the park included several mammals, such as pigs, possums, armadillo, raccoons, rodents and cattle, some of which were seen in the areas where the sporting event took place[14].

7. Transmission related to weather events

Pereira *et al.* reported an outbreak with 177 confirmed cases. It happened in January 2011 after floods in Nova Friburgo, in the state of Rio de Janeiro. Uncontrolled urban growth, soil compaction and deficiency of basic health services contributed to the epidemics[37].

Moreover, Melo *et al.* analysed the geographical distribution of 329 cases of leptospirosis in Aracaju, Sergipe, Brazil between 2001 and 2007 and the differences between periods of rain and drought. The author noted that there were some houses where waste collection was not good or there were no rubbish bins. In these areas, the highest number of cases of leptospirosis was recorded. Under these conditions, in which rubbish accumulate at floor level, the presence of dogs and rodents is favoured. Also, when rubbish is dumped to the ground, drainage systems and culverts are blocked, thus contributing to floods during rainy season. On the other hand, local people did not know about the risks of acquiring leptospirosis related to swimming in the canals where rubbish was thrown. It is worth to highlight that the city of Aracaju is below sea level, so when levels of rainfall rise, accumulated rubbish goes into streams and canals that run through the neighbourhoods. The drainage system of the city was saturated, so even in periods of low rainfall people who were close to the sewage system were exposed to leptospirosis[38].

In the study carried out by Morgan *et al.* on a leptospirosis outbreak which occurred among athletes and residents after a triathlon in Springfield, Illinois in 1998, rainfall records were analysed in Springfield in the period 1994–1998. The average annual rainfall between 1994 and 1997 was much lower than the one recorded in 1998. This was the largest outbreak of leptospirosis reported in the United States, in which a massive sporting activity and changes in rainfall patterns during that period came together[35].

In the analysis carried out by Stern *et al.* as regards the outbreak occurred after a water sporting event developed in a public park near Hillsborough River in Tampa, Florida, it was also shown that a precise weather situation, which occurred two weeks before the competition, was a key element for the outbreak development. At

that time, Hurricane Wilma crossed the western region of Florida, and caused heavy rains and floods in the region[36].

8. Leptospirosis as traveler's disease

An epidemic of leptospirosis occurred among travellers returning from a white-water rafting trip in Costa Rica[39]. Another case involved a traveller from China[40]. Moreover, a Japanese traveller developed leptospirosis after a trip to the Bali Islands, Indonesia[41]. In the USA, a serious case of leptospirosis was reported in a traveller who returned from a trip in Southeast Asia[42].

International travellers who are in contact with water from canals, lakes and rivers may be exposed to the infection. Particularly, vulnerable people are the ones who practice water sports such as kayaking, adventure racing, white-water rafting, triathlon or marathon events. Also, swallowing, swimming or fording in potentially contaminated waters including canals, ponds, rivers, streams and swamps increase the risk of acquiring *Leptospira*. During such activities, travellers should use barrier methods such as protective clothing, especially footwear[19].

9. Conclusions

Leptospirosis is a zoonosis of broad geographic distribution (except for the polar regions) and it is endemic[18,25]. It is common in tropical and subtropical regions. Its wide distribution is related to the diversity of hosts and environmental factors that facilitate intra and interspecies transmission. It is transmitted to humans through contact with the urine of infected animals, either direct or indirectly, and by environmental pollution. It has been reported as isolated cases or outbreaks, but its real incidence is unknown due to underreporting[43].

Recently, this disease has been recognized as a major public health problem due to the increase in both morbidity and mortality. *Leptospira* usually produces a chronic infection in mammals because of the colonization of the renal tubules, thus becoming the main source of infection for humans, as this bacterium is excreted through the urine and it contaminates the environment as irrigation water, which is the way people become infected. Sometimes other products or tissues derived from infected or diseased animals can cause infection in humans by direct contact with skin or mucous membranes. Animals may have asymptomatic infections as well as severe disease, similar to humans, except from rodents, which do not get sick[44,45]. It is considered as an occupational disease because it occurs mainly in people who are related to agriculture or pest control, vets, sewer cleaners, and slaughterhouse workers[46,47].

But it has also been related to recreational activities such as submersion in contaminated irrigation water. Outbreaks or epidemics may be associated with changes in human behaviour, water pollution, changes in the density of animal reservoirs or as a result of natural disasters such as floods[48,49].

Some of the identified risk factors among workers include people who perform agricultural tasks related to irrigation water and who clean closed places with rodents. Furthermore, recreational activities like swimming, outdoor sports in contact with contaminated water or soil also expose people to the risk of the disease[23]. Multiple risk factors were identified such as lack of proper rubbish disposal, lack of sewage, inadequate methods to protect workers in contact with irrigation water and high murine infestation. This review

showed that the existence of leptospirosis in urban or rural areas is associated with risk factors that are known for this disease and its diagnosis depends on having a high level of clinical suspicion[29].

People should take into account the following prevention measures: improving the socioeconomic conditions and the use of barrier methods that protect skin and mucous membranes when an activity with risk of contamination is carried out. The population should be alerted that adventure sports such as kayaking, rafting and swimming may expose you to the risk of this zoonosis[31-33]. As prophylaxis in exposure periods, doxycycline (200 mg/week) is recommended to eliminate the risk, for example, in workers during floods[19]. Finally, as leptospirosis is a disease of zoonotic origin and of interest in public health, it is required that the competent authorities at the national level devote more attention and strengthen actions of coordination among sectors to carry out health promotion, risk management and public health management[15,21].

Conflict of interest statement

We declare that we have no conflict of interest.

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