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EPIDEMIOLOGICAL PROFILE OF LEPTOSPIROSIS IN THE STATE OF RONDÔNIA BETWEEN 2012 TO 2019

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Abstract: Leptospirosis affects more than one million people and causes almost 60 thousand deaths every year, making it one of the most significant zoonoses worldwide. Currently, there is an annual average of more than 3,600 cases in the country, with, on average, 375 deaths per year. Although there are efficient medications to treat leptospirosis and prevent its progression, in some cases, late diagnosis can lead to the patient's death. Because it is a disease associated with poverty, social disinterest and eventually the need for costly treatments after infection, it has become, internationally, a neglected tropical disease (NTD). The consequences of the incidence of leptospirosis can last for long periods and generate worrying impacts on the affected communities. This study aims to observe and portray the epidemiological profile of leptospirosis in the state of Rondônia, so that it is possible to understand the disposition of the disease and the outcome of cases. This is a cross-sectional, descriptive, retrospective and quantitative study, carried out in April 2021. The data used in the present study were collected from information available on government websites TABNET/DATASUS. As demonstrated by this study, leptospirosis still causes deaths, despite being an easily treated disease. It is important that public health bodies develop more emphatic policies for the control and correct diagnosis of leptospirosis, just as the private network must also pay attention to the disease as a differential diagnosis, even in non-endemic periods.
Keywords: Leptospirosis. Rondônia. Negligence. Epidemiological profile.

INTRODUCTION

Leptospirosis affects more than one million people and causes almost 60,000 deaths every year, making it one of the most significant zoonoses worldwide. It is also one of the biggest public health problems and is directly linked to socioeconomic and climatic conditions, especially in tropical and developing countries. Cattle are also affected by leptospirosis, damaging developing economies by millions of dollars each year and affecting subsistence farmers (SANTOS, 2016; GOARANT, 2019).

It is a zoonotic disease caused by Leptospira, a helical spirochete. There are more than 20 species of leptospira, classified into more than 300 serovars grouped into more than 24 serogroups. An important pathogenic species of leptospirosis is *Leptospira interrogans.* In addition, there are 12 more pathogenic species, 6 of which are *L. santarosai, L. weilli, L. alexanderi, L. kirschneri, L. Borgpetersenii* and *L. noguchii.* While *L.biflexa* covers some of the saprophytic serotypes. Leptospira is classified, according to its degree of virulence, into three phylogenetic lineages, which are saprophytic, intermediate and pathogenic. Intermediate and pathogenic species share a common ancestor, however intermediate species have low virulence in animals and humans (SOO, 2020).

There are many reports that Leptospira was first mentioned by DJ Larrey, in 1812 in Cairo, among Napoleon's troops. However, in 1886, Adolph Weil was the one who described, using kidney tissue, the disease that became known as Weil's disease. In 1907, Arthur Stimson differentiated *Leptospira interrogans* from other spirochetes such as *Spirochaeta interrogans* from the kidney lumen of patients with yellow fever. In 1915, Hubener, Uhlenhuth and Fromme in Germany and Noguchi and Inada in Japan transmitted leptospirosis to a guinea pig and isolated Leptospira from the

guinea pig. Ido et al, in 1917, discovered that rats carry leptospires (KARPAGAM, 2020).

In Brazil, Leptospirosis was first described by BEAUREPAIRE DE ARAGÃO in 1917, he demonstrated the presence of the microorganism in rats, and it was from then about that the country devoted more attention to the disease (ENRIETTI 2001).

It is assumed that the bacteria arrived in Brazil on slave ships with rodents. The first outbreaks mentioned in Rio de Janeiro occurred in the 1960s, always coinciding with summer storms (MARTELI, 2020).

In 1940, Leptospira were found as the etiological agent of bovine yellow fever. In the 1980s, leptospirosis was reported as a veterinary disease in dogs, pigs, cattle, horses and perhaps sheep of extreme economic importance. At that time, a lot of research was carried out on Leptospira and leptospirosis and still continues (KARPAGAM, 2020).

The disease is concentrated in the wettest and hottest regions of the world, such as Central and South America, the Caribbean, Oceania and Southeast Asia (RODRIGUES, 2016). **The** HealthMap database revealed that between 2007 and 2013 more than half of the 787 global alerts occurred in the Americas (63%), mainly in Brazil (18%), Nicaragua (6%) and Argentina (YANG, 2018).

It was registered from the Information Technology Department of the Ministry of Health (DATASUS), in the years 2001 to 2017, more than 62,000 cases in Brazil, with a mortality rate of 10%. The disease is endemic in the country, occurring every month of the year, and has an average incidence rate of 2 cases/100,000 inhabitants (PINNA 2018; CERVEIRA 2020).

The fatality rate varies between countries, being estimated between 5 and 40%. The Ministry of Health estimates that, in Brazil, around 10% of serious cases are accompanied by deaths, however, in cases of associated severe pulmonary hemorrhage, this figure can reach up to 50% (RODRIGUES, 2016). Currently, there is an annual average of more than 3,600 cases in the country, with, on average, 375 deaths per year. Farmers and practitioners of aquatic activities are the most exposed to contamination (MARQUEZ, 2017; MARTELI, 2020).

The main risk factor for the occurrence of leptospirosis outbreaks in urban areas is flooding, through which the urine of rats present in sewers and drains mixes with runoff and mud from floods. In the northern region, discussions about deaths from leptospirosis are still scarce. Studies that analyze deaths and describe their occurrence in situations of seasonal outbreaks and the occurrence of floods are insufficient, which has implications for the epidemiological surveillance of the disease (PINNA, 2018).

The Ministry of Health established through Ordinance No. 204 that leptospirosis is an immediately notifiable disease by the Municipal Health Departments (SMS), therefore it is required that notification of suspected cases be carried out within 24 hours.

Every suspected case must be registered in SINAN (Notifiable Diseases Information System), respecting the criteria and standards defined by the Health Surveillance Secretariat of the Ministry of Health (SVS/MS). (PINNA, 2018).

It is transmitted mainly through direct contact with the urine of infected animals, such as rodents, dogs, cattle and pigs; but indirect infection can also occur through water containing spirochetes (CERVEIRA, 2020).

Domestic and wild animals can serve as a reservoir; however, the most important source of spread is the brown rat (RATTUS NORVEGICUS). Individuals who live in environments such as urban slums, with inadequate basic sanitation or precarious

housing are at the highest risk of exposure to rats and consequently leptospirosis. Infection occurs after direct or indirect exposure to infected hosts, who carry the pathogen in their renal tubules and shed pathogenic leptospires in their urine. In the proximal tubules of reservoirs, the bacteria colonize the brush border for a long period, producing no adverse effects on the host, but acting to disseminate the microorganism (HAAKE 2015; BRITO, 2018).

Leptospirosis is a zoonosis that has humans as accidental hosts, but it is important to highlight that the transient elimination of leptospires occurs during human infections and person-to-person infections; although it is rare, it can occur through sexual intercourse (DOELEMAN, 1932; HARRISON AND FITZGERALD, 1988), during lactation (BOLIN AND KOELLNER, 1988), through transplacental transmission it can occur if the infection occurs during pregnancy, resulting in miscarriage (CHUNG ET AL.1963) or still born (COGHLAN AND BAIN 1969; FAINE ET AL. 1984; HAAKE, 2015).

Due to the existence of several types of serovars, humans can be infected more than once, presenting only specific antibodies to the serovar causing previous infections. Leptospirosis presents variable clinical manifestations, from asymptomatic and oligosymptomatic to severe conditions that can be fatal. More serious cases probably depend on three factors: pathogen virulence, host susceptibility and epidemiological conditions. Mortality increases with age, especially in elderly patients (HAAKE, 2015; PAULA, 2019).

Leptospirosis has three clinical forms: asymptomatic, anicteric and icteric. In the asymptomatic form, the patient becomes infected, but shows no signs or symptoms.

In the anicteric form, there may be meningitis or hemorrhage or interstitial pneumonitis. In general, leptospirosis is biphasic, beginning with flu-like symptoms, fever and malaise, then begins a brief period of defervescence and recrudescence of fever and other symptoms. The icteric form, known as Weil syndrome, presents the same signs and symptoms as the anicteric form, but also presents with jaundice and multiple organ failure, such as hemorrhagic pneumonitis, acute renal failure, cardiac arrhythmias, coagulopathy and shock (MARTELI, 2020).

In leptospirosis, when the central nervous system (CNS) is affected, aseptic meningitis or, more rarely, encephalitis are evident and in the peripheral nervous system it can present as neuritis, polyneuritis and polyradiculoneuritis. Prudent clinical suspicion and early diagnosis are essential for effective management of these rare presentations of neuroleptospirosis (BHATT, 2018).

Diagnosis is the fundamental step in the management of a suspected case of leptospirosis. The disease must be evaluated in the differential diagnosis when there is a history of recent travel to regions known to be endemic, or that have had an outbreak, being accompanied by signs and symptoms of an undifferentiated febrile illness, for example, a flu-like illness, or in conjunction with fever, jaundice and renal failure (RODRIGUES, 2016).

Throughout the acute phase, it is recommended that the patient undergo a leptospira culture and PCR. Leptospires can be cultured in the Ellinghausen - McCullough -Johnson-Harris (EMJH) method from urine, blood and cerebrospinal fluid samples. The doctor must also request the IgM -ELISA method, as it is often difficult to establish which phase of the disease the patient is in, giving a positive result between the end of the phase and the beginning of the immunological phase. In the immunological phase, the serodiagnosis method is the most

appropriate, as leptospires begin to leave the blood. The microscopic agglutination test (MAT) is important for diagnosis in the immunological phase, as it identifies the presence of antibodies specific to leptospires (FRAGA, 2015).

A simple latex agglutination test for the serodiagnosis of acute human leptospirosis was evaluated by Pradutkanchana and Nakarin (2005). The study showed that the sensitivity of the test for acute infection was only 17.6%, when focused on the first sera obtained from patients. Therefore, the authors concluded that the latex agglutination test is easy to perform as it does not require training or the use of special equipment, has good sensitivity and specificity, and is an attractive alternative for the serological diagnosis of acute human leptospirosis. (ADLER B. 2015)

Pointing out the treatment of Leptospirosis, according to the research analyzed on the most used treatments, Baracho, Lima and Costa (2017) point out that the most used drugs in the acute phase of the disease are doxycycline, ampicillin and amoxicillin, already for the advanced disease, indicate the use of Penicillin G and ampicillin. Similar to these collaborators, Ribeiro et al. (2018) instruct the use of doxycycline and ampicillin in the acute phase of the disease for more effective treatment (GUEDES 2020).

Specifying further, Rodrigues et al (2019) and Rocha (2019) detail the use of amoxicillin 500 mg orally in adults every 8 hours, or every 6 hours, for up to 7 days; Medeiros (2020) recommended for use in children of just 50 mg every 6 to 8 hours for a period of up to 7 days. According to Rocha (2019), in moderate cases, the most correct treatment would be the use of crystalline penicillin 1,500,000 IU, IV every 6 hours; as well as Magalhães and Acosta (2019) and Filho et al. (2020) talked about the need for correct hydration and the use of antibiotics until the 4th day of the disease, these precautions can prevent its progression. (GUEDES, 2020).

Although there are efficient medications to treat leptospirosis and prevent its progression, in some cases, late diagnosis can lead to the patient's death. Some facts contribute to the underreporting of the disease, among them it is possible to report medical conduct with difficulties in diagnosing cases, meaning there is no notification or transfer to other professionals in the field, this all occurs as a consequence of the professional's training., the fact that patients need to return to care to undergo tests that confirm the disease, the structure of the work environment and the quality of care (GUEDES, 2020).

Leptospirosis, as it is a disease associated with poverty, social disinterest and eventually the need for costly treatments after infection, has become, internationally, a neglected tropical disease (NTD). Brazil has a high percentage of NTDs, such as leptospirosis (around 90% of cases), leprosy, dengue fever, schistosomiasis, trachoma, malaria, cutaneous and visceral leishmaniasis and Chagas disease, directly relating the country's social and economic inequalities.

Faced with this problem, the nation has been investing in notices for NTDs through the research and development program for neglected diseases, which aims to stimulate the development of medicines for public health programs. Although leptospirosis is internationally recognized as an NTD, the national notices do not mention investments in research and interventions for the disease, as seven other priority diseases that constitute the disease program were established through demographic, epidemiological and impact data. neglect in Brazil. In relation to direct government investment, human leptospirosis is not classified as an NTD in the country and was not favored with its own or joint notice (MARTINS, 2020).

The global burden of leptospirosis was considered to be largely underestimated for a number of reasons, including the fact that the vast majority of countries do not have a reporting system for the disease, or reporting is not mandatory (Ahmed et al. 2012). In an attempt to resolve this situation, the WHO established the Leptospirosis Burden Epidemiology Reference Group (LERG), (Abela-Ridder et al. 2010). The LERG met in 2009 and 2010. The objectives established at the 2010 meeting were: (1) Review and evaluate systematic reviews of mortality, morbidity and disability from human leptospirosis. (2) Review a draft transmission model for leptospirosis and provide technical input for the future; (3) Create preliminary estimates of the global burden of the disease. (4) identify knowledge and research gaps, and (5) advise WHO on next steps for estimating the burden of human leptospirosis and implications for policy (HAAKE, 2015).

The consequences of the incidence of leptospirosis can last for long periods, and generate worrying impacts on the affected communities. Oliveira et al. (2009) reported that leptospirosis is a zoonosis with a high lethality rate (9%), lacking public prevention policies in the health sector. According to Santos et al. (2012), leptospirosis affects the economy due to the high financial cost of hospital admissions and the fact that it impacts commercial transactions involving products of animal origin, as well as the fact that it harms the productive lives of infected individuals. In Brazil, there has been little research on the subject, considering that 63,302 cases of this zoonosis were recorded between 2000 and 2016, resulting in around 4000 cases/year (MINISTRY OF HEALTH, 2017). In these 17 years, the disease was responsible for the deaths of 6,064 people. The states with the highest number of confirmed deaths from the disease were São Paulo (1,554), Rio de Janeiro (793), Pernambuco (563), Rio Grande do Sul (449) and Bahia (331). The highest number of cases was recorded in the Southeast (21,633) and South (20,343) regions, followed by the Northeast (11,198), North (9,198) and Central-West (930) regions (PORTELA, 2020).

The Brazilian Ministry of Health has been making efforts to qualify the diagnosis and treatment of leptospirosis, but this does not trigger an increase in the number of notifications of suspects. In view of this, the Matrix of the Vicious Circle of Leptospirosis Neglect in Brazil was proposed, which serves to estimate different aspects inherent to the lack of an earlier and more accurate diagnosis of the disease, in order to avoid underreporting of cases and the lack of data on the real incidence of the global burden of leptospirosis. This data would directly impact health management planning, demonstrated by opinion research with experts who defend the view of negligence regarding health information in Brazil (PORTELA, 2020).

It is important to impose measures to control leptospirosis reservoirs, but strategies that aim to improve sanitary conditions and public knowledge regarding the case also deserve attention, especially in high-risk areas. For this to occur, the areas where the occurrence of leptospirosis is highest must be identified, justifying the need for techniques in spatial statistical analysis. Carrying out a joint analysis of space-time variation allows for better identification of affected areas and the spread of leptospirosis over time (CERVEIRA, 2020).

This study aims to observe and portray the epidemiological profile of leptospirosis in the state of Rondônia, so that it is possible to understand the disposition of the disease and the outcome of cases. We collected and observed data on the incidence and distribution of leptospirosis in the state of

Rondônia and discussed the clinical features of the disease.

MATERIAL AND METHODS

This is a cross-sectional, descriptive, retrospective and quantitative study, carried out in April 2021. The data used in the present study were collected from information available on the government websites TABNET/DATASUS (http: //tabnet.datasus.gov.br/cgi/tabcgi.exe?sinannet/cnv/le ptoro def).

The sample was limited to the period from 2012 to 2019 and data analysis was carried out using simple descriptive statistics using Microsoft Excel ® software. The variables used were number of confirmed cases per year, sex, age group, race, confirmation criteria, area of residence and final classification of cases.

RESULTS AND DISCUSSION

According to the 8-year period (2012 to 2019) that was studied, it was observed that there were a total of 544 confirmed cases of leptospirosis in the state of Rondônia. The years 2013 and 2014 presented the highest numbers of confirmed cases among all other years, accounting for a total of 187 records in 2014 and 150 in 2013 as described in table 1.

Among all individuals with a confirmed diagnosis of leptospirosis, it was possible to observe that male individuals had a greater number of people affected, with a total of 372 confirmed cases, representing 68.4% of the population affected by the disease in the period studied, the number of women with a confirmed diagnosis was 172 (31.6%).

When evaluating the distribution of the disease according to age, it is noted that the age group with the highest prevalence of the disease is 20 to 39 years old, which presented a total of 243 (44.7%) of confirmed cases, followed by individuals aged 40 to 59 years with 141 (25.9%) of the cases.

The race classified as brown presented a total of 315 (57.9%) of the cases, followed by the white race with a total of 144 (26.5) of the cases.

According to the evolution of the cases, it was possible to observe that 487 (89.4%) progressed to curing the disease, especially 21 (3.9%) of the individuals died from the reported condition. The others affected by the disease either died for other reasons or did not have recorded information regarding the outcome of the disease.

Most confirmed cases of leptospirosis were confirmed by the clinical-laboratory method, representing 483 (88.7%) of the cases among the 544 confirmed cases, another 58 (10.7%) of the individuals had their cases confirmed by the clinical-epidemiological method and 3 (0.6%) of the confirmed cases did not contain records on how the pathology was confirmed.

Among the confirmed cases in the state of Rondônia, the area of residence with the highest number of confirmed cases was the urban area with a total of 314 (57.7%), the rural area was responsible for representing 220 (40.4%) of cases.

According to what was observed in the region of the state of Rondônia, men represented the majority of those affected by leptospirosis (68.4%). In relation to age group, people between 20 and 39 years old were most affected (44.7%). These results corroborate studies carried out in Alagoas, Pará and Roraima that indicated a greater incidence in males and in individuals between 20 and 39 years old (SOARES, 2017; RIBEIRO 2018; GUEDES 2021;).

During the period analyzed by this study, it was possible to observe that race described as brown represented the majority of cases (57.9%). In the state of Pernambuco, a study was carried out that demonstrated a higher incidence in brown people (52.6%). However, the study carried out in Paraná demonstrated

VARIABLE	Year								(N)	(%)
	2012	2013	2014	2015	2016	2017	2018	2019		
CASES CONFIRMED	9	150	187	87	38	22	27	24	544	-
GENDER										
Masculine	9	90	126	54	27	20	23	23	372	68.4
Feminine	-	60	61	33	11	2	4	1	172	31.6
AGE GROUP	-									
< 1 Year	-	1	1	2	1	1	1	-	7	1.3
1 to 4	-	2	2	1	-	1	-	-	6	1.1
5 to 9	-	12	5	2	1	-	1	1	22	4
10 to 14	1	10	12	3	2	1	-	1	30	5.5
15 to 19	2	14	17	8	1	3	5	4	54	9.9
20 to 39	4	71	83	42	20	9	7	7	243	44.7
40 to 59	1	32	52	21	11	6	8	10	141	25.9
60 to 64	-	2	5	1	2	-	2	1	13	2.4
65 to 69	1	3	4	4	-	-	2	-	14	2.6
70 to 79	-	1	4	2	-	1	1	-	9	1.7
80+	-	2	2	1	-	-	-	-	5	0.9
RACE										
Ign/White	-	25	11	5	3	-	1	2	47	8.6
White	3	31	57	26	12	2	9	4	144	26.5
Black	1	11	10	5	5	-	1	-	33	6.1
Yellow	-	-	4	-	1			-	5	0.9
brown	5	83	105	51	17	20	16	18	315	57.9
EVOLUTION OF CASES										
Ign/White	1	4	6	7	2	4	3	-	27	5
Cure	7	141	172	76	33	15	20	23	487	89.4
Death due to notified injury	1	5	4	3	1	3	3	1	21	3.9
Death from another cause	-	-	5	1	2	-	1	-	9	1.7
CONFIRMATION CRITERIA										
Ign/White	-	-	-	1	1	1	-	-	3	0.6
Clinical-Laboratory	9	120	174	84	37	19	18	22	483	88.7
Clinical-epidemiological	-	30	13	2	-	2	9	2	58	10.7
RESIDENCE AREA										
Ign/White	-	-	3	2	-	-	-	1	6	1.2
Urban	6	46	138	60	21	15	15	13	314	57.7
Rural	3	104	43	25	17	7	12	9	220	40.4
Periurban	-	-	3	-	-	-	-	1	4	0.7

Table 1 – Characterization of leptospirosis in the state of Rondônia between 2012 and 2019.

that the white race was the most affected (72.9%) (TAVARES, 2018; SUGUIURA, 2019).

Regarding the evolution of the disease, the majority of cases in the period evaluated by this study progressed to cure (89.4%) and a small proportion of individuals died from the reported condition (3.9%). A result similar to that found in Santa Catarina, in which 92.73% of cases resulted in a cure and 2.81% of them were fatal. However, a study carried out in Pará showed that 12.44% of those affected died (DA ROCHA, 2019; GUEDES, 2021).

The vast majority of cases were confirmed using the clinical-laboratory method (88.7%). Studies carried out in Paraná and Roraima demonstrated similar results (93.3% and 95.65% respectively). In the period evaluated in the state of Rondônia, the most affected area of residence was urban (57.7%), similar to what was found in the study carried out in the Federal District (SILVA 2013; RIBEIRO, 2018; SUGUIURA, 2019).

FINAL CONSIDERATIONS

In accordance with the objective of collecting and analyzing data on the incidence and distribution, as well as the outcome of leptospirosis cases in the state of Rondônia, it was possible to observe that, in the period in which this study was carried out, cases have been decreasing throughout of years. It is important to highlight that 2013 and 2014 were the years in which there were the most confirmed cases of leptospirosis, which may be related to the fact that there were several floods that hit the municipality of Porto Velho during this period, and thus, causing the outbreak.

As demonstrated by this study, leptospirosis still causes deaths, despite being an easily treated disease. This may be due to the fact that treatment of the disease is being delayed, due to the clinical signs and symptoms being similar to those of other diseases, being easily confused and, therefore, resulting in a delay in diagnosis. It is therefore suggested that research be carried out at national level and seek to find out whether there is negligence in the diagnosis of leptospirosis.

This work was limited to studying only the epidemiological profile of the state of Rondônia. Therefore, it is important that public health bodies develop more emphatic policies for the control and correct diagnosis of leptospirosis, just as the private network must also pay attention to the disease as a differential diagnosis, even in cases where the place of occurrence does not is in an endemic period.

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