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Leptospirosis in Campinas, São Paulo, Brazil: 2007-2014

Leptospirose no município de Campinas, São Paulo, Brasil: 2007 a 2014

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ABSTRACT: ***Objective*:** to analyze the distribution of leptospirosis according to sociodemographic, epidemiologic, and clinical characteristics, assistance time, rainfall and spatial distribution in Campinas/SP in the period from 2007 to 2014. ***Method*:** This is an ecological study using information from the confirmed cases. A descriptive analysis was carried out according to the selected variables. The relationship between the cases and rainfall was verified through the Spearman's correlation coefficient. The cases/deaths were georeferenced per areas classified according to socioenvironmental deprivation indexes in Campinas. ***Results*:** From the 264 cases, 76.1% occurred in men, 58,4% in the 20 to 49 years old age range. Approximately 55% were hospitalized, with a prevalence of clinical-laboratorial diagnoses of 89.4%, and the lethality was 10.6%. The urban area concentrated 74.2% of the cases, and 48,9% occurred in the household environment. The main risk factor was evidence of the presence of rodents at the site. There was strong correlation between the incidence of cases and rainfall ($p < 0.05$) in 2010 to 2012. A higher concentration of the cases was observed in the Center-Southwest region. Spatial distribution of cases/deaths showed clusters in regions classified at lower socioeconomic levels. ***Conclusions*:** The patterns of occurrence of leptospirosis in Campinas showed similarity with other Brazilian municipalities. The identification of areas with higher incidence of cases/deaths contributes to the adoption of strategies for intervention and prioritization of resources aiming at the reduction of the risk of infection and at early treatment for those affected.

Keywords: Leptospirosis. Incidence. Risk factor. Seasonality. Spatial analysis.

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RESUMO: ***Objetivo*:** Analisar a distribuição de casos e óbitos humanos por leptospirose, segundo características sociodemográficas, epidemiológicas, clínicas, tempo de atendimento, pluviosidade e distribuição espacial em Campinas, São Paulo, no período de 2007 a 2014. ***Método*:** Estudo ecológico utilizando informações dos casos confirmados de leptospirose. Realizou-se análise descritiva dos casos, segundo variáveis selecionadas. A relação entre casos autóctones e pluviosidade foi verificada pelo coeficiente de correlação de *Spearman*. Georreferenciaram-se casos/óbitos por áreas classificadas segundo indicadores socioambientais. ***Resultados*:** Dos 264 casos, 76,1% eram homens e 58,4% tinham entre 20 e 49 anos. Cerca de 55% foram hospitalizados. Prevaleceu o diagnóstico clínico-laboratorial (89,4%) e a letalidade foi de 10,6%. Na área urbana, ocorreram 74,2% dos casos e, 48,9%, no domicílio. O principal fator de risco foi o local com sinal de roedores. Houve forte correlação entre a incidência de casos e a pluviosidade ($p < 0,05$) nos anos de 2010 a 2012. Observou-se maior concentração de casos na região centro-sudoeste. A distribuição espacial dos casos/óbitos mostrou aglomerados em regiões classificadas como de menor nível socioeconômico. ***Conclusão*:** Os padrões de ocorrência de leptospirose em Campinas, São Paulo, mostraram similaridade com outras cidades brasileiras. A identificação de áreas com maior incidência de casos/óbitos contribui para a adoção de estratégias específicas de intervenção e priorização de recursos na redução do risco de infecção e tratamento precoce dos acometidos pela doença.

Palavras-chave: Leptospirose. Incidência. Fatores de risco. Análise espacial.

INTRODUCTION

Leptospirosis is a zoonotic disease with worldwide distribution. It has an important impact on public health[1], as well as social and economic relevance due to absenteeism in the workplace and high hospital costs in severe cases. An evaluation carried out in Brazil concluded that the 3,492 cases occurred in 2008 caused a cost of approximately R$ 1,542,526 to the Unified Health System (SUS), as well as 10,664 potential years of life lost and a decrease in productivity[2].

This disease is included in the Brazilian List of Causes of Death Avoidable by SUS Interventions[3]. According to the Brazilian Ministry of Health, in the period from 2001 to 2007, 91,948 suspected cases were reported, of which 23,628 were confirmed (26%). The mean incidence rate was 1.8/100,000 thousand inhabitants, with the occurrence of 2,679 deaths and the average lethality of 11.3%.[4]. In contexts of greater severity, lethality can reach 40%[5]. For Paploski[6], the incidence is underestimated due to medical conditions that can be confused with other diseases, which causes only severe cases to be reported.

The etiological agent are mandatory aerobic helix-shaped bacteria of the genus Leptospira, of which 14 pathogenic species are known today, with *L. interrogans* being the most important[5]. In outdoor environments, leptospires survive in water or muddy soil with slightly alkaline pH for up to six months. Synanthropic animals (mainly rodents), both domestic and wild, are reservoirs for the persistence of outbreaks. Humans are accidental and terminal hosts within the transmission chain. Human infection results from direct or indirect exposure to urine of infected animals. The penetration of the microorganism occurs through the skin with or without lesions and mucous membranes. Contact with contaminated water and mud demonstrates

the importance of the water link in transmission to humans. Although leptospirosis occurs during all months of the year, there is a higher incidence in the rainy season[5,7]. Usually there is a greater incidence of cases in urban areas, due to the high agglomeration of low income populations that live near stream channels, in places with insufficient sanitary infrastructure, and with rodent infestations, factors that predispose to the onset of the disease[6,8,9].

Analyzes of the disease's occurrence patterns may contribute to programs aimed at its prevention and control. The objective of this study was to assess the distribution of leptospirosis according to sociodemographic, epidemiological, clinical, and healthcare-related characteristics, as well as rainfall and spatial distribution, in Campinas, São Paulo, in the period from 2007 to 2014.

METHOD

This is an ecological study to analyze the incidence of confirmed cases of leptospirosis during the period 2007-2014 in Campinas, São Paulo. Data from the notifications contained in the National Notification System (SINAN), made available by the Municipal Health Department of Campinas (SMS/Campinas), were used. The study population consisted of total confirmed cases (n = 264), including those confirmed by Epidemiological Surveillance (ES) by clinical-epidemiological and laboratory criteria. Cases discarded and presenting inconsistencies were excluded.

The data of the municipality's population in the period were collected from the Brazilian Institute of Geography and Statistics (IBGE) and are available on the DATASUS website (1,080,113 inhabitants — 2010 Census). Information on rainfall was obtained from the Integrated Center for Agrometeorological Information (CIIAGRO), which provides a climatic monitoring of rainfall measured in millimeters (mm) of monthly rainwater.

The variables contained in the Leptospirosis Research Papers used in the study were:

- demographic variables: gender, age, race/color and schooling;
- clinical variables: date of medical treatment, date of first symptoms until diagnosis, sample collection, hospitalization, duration of hospitalization and evolution (death or cure);
- epidemiological variables: any risk situation occurred within 30 days prior to the first symptoms (contact with or cleaning of flooding water or mud, animal husbandry, water tank, cesspit, grease trap or sewage, place with evidence of presence of rodents, plantation or collection, river, stream channel, pond or dam, rodents directly, storage of grains and/or food, vacant lots, trash and/or debris and others); probable location of the source of infection (urban, rural, peri-urban and ignored), infection environment (household, workplace, leisure, other and ignored) and the evolution of the case;
- climatic variables: monthly precipitation.

Descriptive analysis was performed based on the distribution of absolute and relative frequencies of the cases, according to the variables selected independently of the outcome. To evaluate the correlation between confirmed autochthonous cases (n = 264) and the

mean monthly rainfall for each year of study, Spearman's correlation coefficient (RSp) was used, considering a significance level of 5%. The analyzes were performed in the Statistical Package for the Social Sciences (SPSS), version 21.

For spatial analysis, the addresses in the research records corresponding to the probable infection site (PIS) underwent georeferencing. The geographical coordinates were obtained in Google Maps and later plotted in the municipality's basemap. The addresses that did not present inconsistencies (n = 151) were georeferenced in the centroids of the coverage areas of Health Centers (HCs), Basic Health Units (BHUs), Emergency Care Units (ECUs), and public and private hospitals in the 56 areas of coverage of SMS/Campinas, obtaining approximate information on the spatial location of the cases.

The Kernel density estimation method, with a radius of influence of 1 kilometer, was used to analyze the spatial distribution of the cases. The Kernel estimation is a nonparametric, exploratory technique that allows the visualization of the cases' concentration areas of (hot spots). The map shows density levels of cases/deaths according to the observed tonality[10].

In this study, the spatial distribution map of the Socio-environmental Vulnerability Index (SEVI) was also used, according to socioeconomic and environmental classes per HC coverage area in Campinas, developed by Costa et al.[11] to allow comparison between the location of cases/deaths and the respective areas classified according to levels of vulnerability. This map considers three strata of socio-environmental vulnerability — low, moderate and high — , based on demographic and socio-environmental information with data from the 2010 IBGE Census. SEVI was obtained using the principal components statistical method with variables such as the proportions of persons responsible for household with income ≤ three minimum wages, households with inadequate sanitary sewage, and households with inadequate waste disposal. Higher values indicate a greater degree of socio-environmental vulnerability.

The study was submitted to SMS/Campinas for the use of the data in the Notification Reports. It was also presented to and approved by the Research Ethics Committee of the School of Medical Sciences of Universidade Estadual de Campinas (CEP/FCM/UNICAMP), under protocol no. 1.430.519.

RESULTS

Considering the sociodemographic distribution of the cases in the period, it was observed that 201 (76.1%) were men. Regarding the age group, there are cases at all ages, although the one with the highest number of occurrences is the 20-49 years group. Regarding race/color, there was a higher occurrence among whites (53.8%), followed by browns (18.2%). It should be noted that, for this variable, 19.6% of the information was absent (Table 1). In relation to schooling, it was verified that 64.4% of the files were not filled, compromising the evaluation of case distribution.

Regarding the clinical variables, 55% of the cases were hospitalized. The duration of the hospitalization was up to 10 days in 76% of them and about 5.6% were hospitalized for more

than 30 days. It should be noted that, for the length of hospitalization variable, there was also a high number of records ignored (35%). Regarding the diagnostic criteria, laboratorial diagnosis corresponded to the majority (89.4%), followed by the clinical-epidemiological (10.2%). About 83% of the cases evolved to cure and 10.6% evolved to death (Table 2). For most of them, the time elapsed from the first symptoms to the date of notification was five days.

The time between the onset of the first symptoms and the sample collection for laboratory tests was up to five days in 28.8% of the cases and, for about 49%, the time elapsed was 6-11 days. As for hospitalizations, 90% occurred within 10 days of the first symptoms. For the 28 deaths, it was observed that, in relation to the time elapsed since the first symptoms, 11 occurred between 5-11 days and, in 4 cases, deaths occurred with more than 22 days of the first symptoms. All individuals who died were hospitalized.

Table 1. Sociodemographic distribution and clinical characteristics of confirmed cases of leptospirosis. Campinas, SP, 2007–2014.

Variables	Number of cases	%
Sex		
Male	201	76.1
Female	63	23.9
Total	264	100.0
Age group (in years)		
0–9	8	3.0
10–19	39	14.8
20–29	47	17.8
30–39	53	20.1
40–49	54	20.5
50–59	35	13.3
60 and over	28	10.6
Total	264	100.0
Race/color		
White	142	53.8
Black	20	7.6
Yellow	2	0.8
Brown	48	18.2
Ignored	52	19.6
Total	264	100.0

Regarding the probable area of infection, there was a greater occurrence in the urban area (74.2%), but in 10.6% of the files, these data were not filled. Regarding the probable environment of infection, there were more cases with PIS in the household environment (48.9%), followed by the workplace (21.2%) and the peri-urban area (9.8%). It was verified that 21.6% (n = 57) of the records for this variable had no information (data not shown).

Of the risk situations occurred in the 30 days prior to the first symptoms, in order of importance, sites with evidence of the presence of rodents and contact with trash or debris, vacant lot, and mud are highlighted.

Table 2. Characterization of clinical and epidemiological variables of confirmed cases of leptospirosis. Campinas, SP, 2007-2014.

Variables	Number of cases	%
Hospitalization		
Yes	146	55.3
No	111	42.0
Ignored	7	2.7
Total	264	100.0
Hospitalization time (days)		
0–10	82	56.2
11–20	16	11.0
21–30	4	2.7
31–40	4	2.7
41 and over	2	1.4
Ignored	38	26.0
Total	146	100.0
Diagnostic criteria		
Clinical-laboratorial	236	89.4
Clinical-epidemiological	27	10.2
Ignored	1	0.4
Total	264	100.0
Evolution		
Death due to leptospirosis	28	10.6
Cure	220	83.4
Ignored	16	6
Total	264	100.0

Considering the study period, 2011 presented the highest incidence of confirmed cases (0.51 cases/10,000 inhabitants). Higher lethality coefficients were observed between 2009-2011. In 2010, lethality reached 17.6% despite the lower number of deaths.

Figure 1 shows the incidence of confirmed autochthonous cases and the average monthly rainfall in the period. The highest rainfall rates were observed in the years 2007, 2009 and 2011. The monthly average rainfall for January 2007 was 404.1 mm of water; in December 2009, it was 398.8 mm; and in January 2011, recorded rainfall was 403.6 mm. The correlation between precipitation and cases occurring immediately in the following month (30-day gap after infection) was verified. There was a strong statistically significant correlation ($p < 0.05$) in the years 2010, 2011 and 2012 ($RSp = 0.804$; $RSp = 0.741$; and $RSp = 0.714$, respectively).

Through the Kernel estimation, the areas of concentration of the cases can be visualized. Figure 2 shows all cases/deaths. It is possible to distinguish a highest concentration in the municipality's Center-Southeast region.

Figure 3 shows the spatial distribution of the cases ($n = 151$) per CS coverage area in Campinas, São Paulo, according to SEVI. In most reported cases, PISs are located in areas with higher SEVI. In about 36% of the HCs, the PIS of cases corresponds to the highest SEVI; about 32% correspond to areas with moderate vulnerability and 32%, with lower vulnerability. It was verified that 43.7% of the deaths happened in areas with moderate SEVI, 31.2% in areas with lower vulnerability, and the rest, in an area classified as having a higher SEVI.

DISCUSSION

The sociodemographic profile of individuals with leptospirosis in the period from 2007 to 2014 in Campinas, São Paulo, reveals similarities with other studies that relate incidence to poor areas, with precarious sanitation, as well as regions subject to flooding[6,12-14].

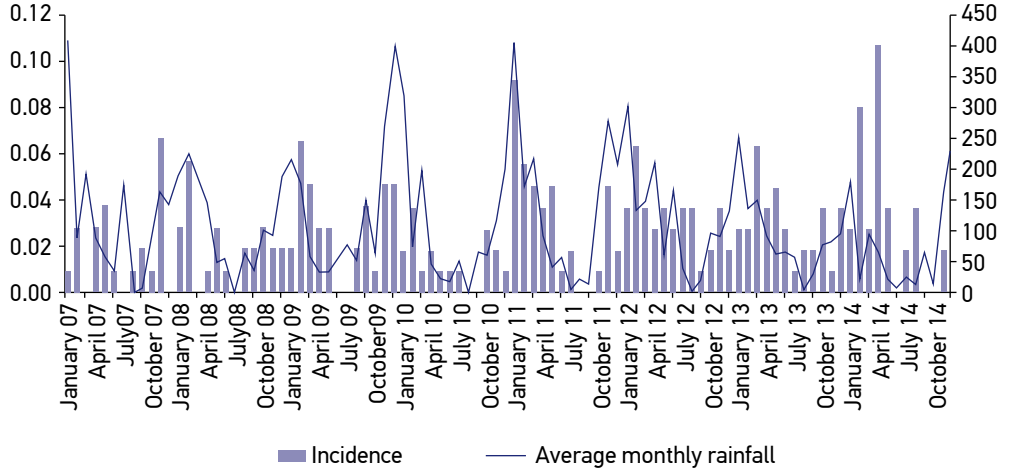

Figure 1. Incidence of autochthonous cases of confirmed leptospirosis and average monthly rainfall (in millimeters). Campinas, SP, 2007-2014.

The majority of cases occurred in men and aged between 20 and 49 years, an age group considered productive[15]. This situation can be explained by the fact that men usually participate more in activities that involve risk situations[13].

Studies indicate that leptospirosis is related to a low level of schooling[2,15]. In this study, the lack of information on this variable in more than 50% of the cases made comparisons impossible; the same happened for race / color. It is worth noting that, according to data from the Demographic Census of 2010, about 20-25% of the inhabitants of the municipality are black or brown.

It is noteworthy that 76% of the cases were hospitalized and stayed in hospital for up to 10 days. Leptospirosis is characterized by multiple forms of clinical presentation, ranging from subclinical to severe forms[16]. There is a high proportion of hospitalizations, suggesting that notification has occurred in severe cases. This is concerning, as many cases of the disease have been underreported, possibly due to presenting conditions similar to other diseases that are common in the municipality[6].

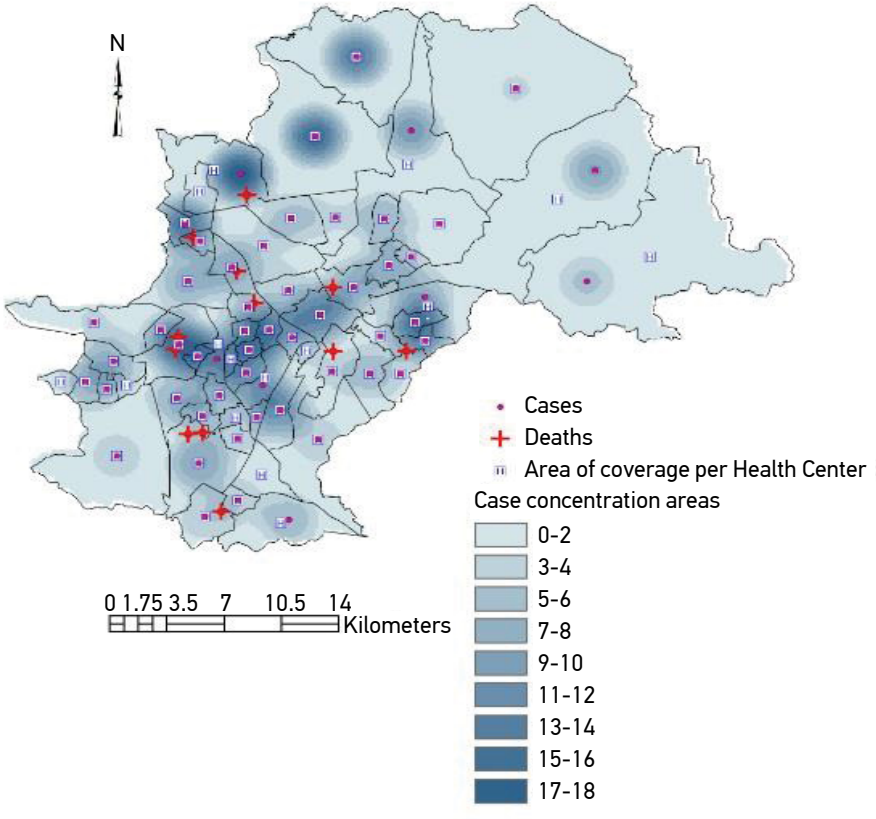

Figure 2. Spatial distribution of cases and deaths by leptospirosis per area of concentration. Campinas, SP, 2007–2014.

In Campinas, São Paulo, it was observed that the time elapsed between the first symptoms and hospitalization for most patients was 0-5 days, a short period that indicates the acute character of the cases, as well as time to implement appropriate treatment aiming to reduce complications.

Half of the notifications occurred with 15 days or more of the first symptoms, suggesting delay in acknowledging the case for ES and, consequently, in adopting intervention measures[17]. The time between the first symptoms and the notification date allows the decision-making process by ES to prevent the spread of the disease, allowing the prevention of other cases or the identification of undiagnosed cases in the transmission area. It is worth highlighting the importance of the quality of the information in the notification report for the analysis of the epidemiological situation[18].

The time elapsed between the first symptoms and the sample collection occurred within 6 days after the onset of symptoms for 50% of the notifications. It is emphasized that the choice of the laboratory method depends on the evolutionary phase in which the patient is. In an early stage, leptospires can be visualized in blood by direct examination, culture, or DNA

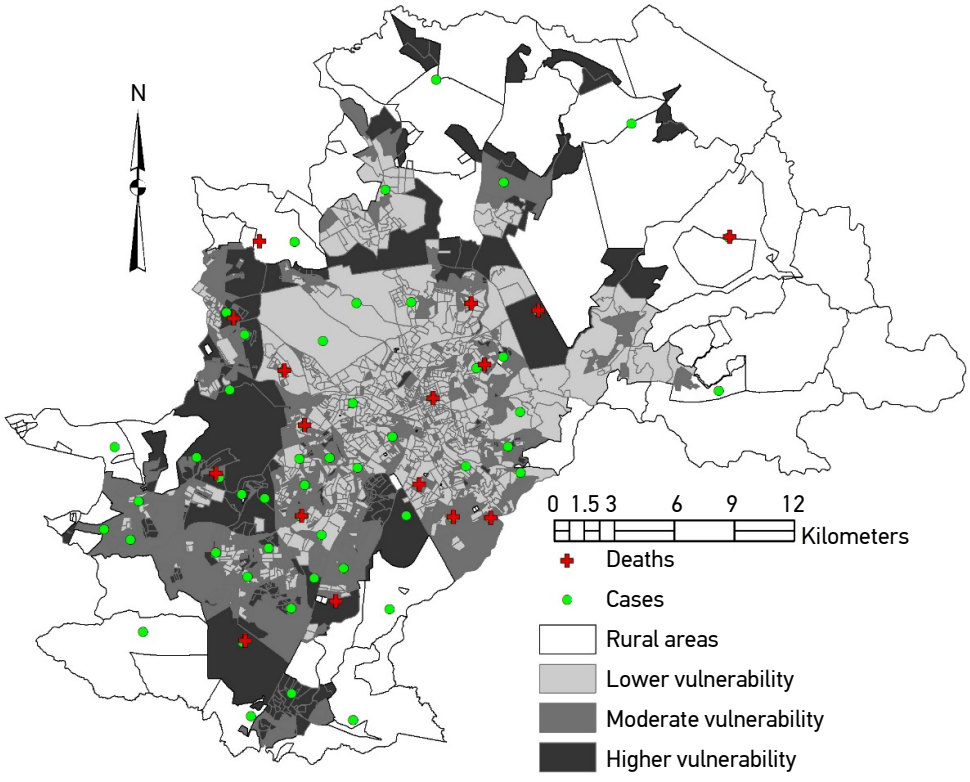

Figure 3. Spatial distribution of cases and deaths by leptospirosis (n = 151), according to socio-environmental vulnerability classes, per area of coverage of the Health Centers. Campinas, SP, 2007-2014.

detection by the polymerase chain reaction (PCR) technique[19]. However, due to the difficulties inherent to culture test, serological methods are chosen as a priority for diagnosis. The most commonly used are enzyme immunoassay (ELISA-IgM) and micro-agglutination (MAT), preferably after the seventh day of onset of symptoms. Laboratory confirmation is important for ratification of the diagnosis, but treatment should be initiated at the time the patient is classified as a probable suspect, and antibiotic medication is indicated prior to serological confirmation[7,20]. Some characteristics of the patient such as age (child or elderly) and clinical conditions (chronic diseases)[7], are often associated with the severity of the course of the disease and to the risk of death, even if medical treatment occurs in a timely manner. In Brazil, the serovars Icterohaemorrhagiae and Copenhageni are related to the most severe cases[5].

In this study, the laboratory diagnosis criterion was used for 90% of the cases and the rest was confirmed by clinical-epidemiological criteria, based on the antecedents of other affected individuals or animals[5]. In early stages, it can be confused with diseases like dengue, influenza, rickettsioses, among others. In late stages, it can be confused with acute hepatitis, severe dengue, pneumonia, among others[5,8]. Thus, it is necessary, at the time of the patient's anamnesis, to investigate risk factors to increase clinical suspicion. Leptospirosis should be included among the differential diagnoses and the use of specific protocols for ES in the case of syndromes of icterus hemorrhagic fever, highlighting the disease's importance as a public health problem[21].

The time elapsed between the first symptoms and death was, for the most part, 6-11 days. This data may suggest situations in which the clinical management was not timely, as leptospirosis, in its initial stages, presents similarity of symptoms with other diseases, causing late diagnosis and treatment with consequent worse prognosis[6,22].

The lethality observed for the period was 10.6%, and it was higher in 2010. This situation can be explained by the decrease in the number of confirmed cases in that year and, consequently, a higher percentage of severe cases. Soares[23], in a study of leptospirosis with data from São Paulo from 1998 to 2006, reported a lethality of 14%. A study of the disease in Belém, Pará, with data from the years 2006-2011, found lethality of 17% in 2007[24]. In Brazil, during the period from 1985 to 1997, lethality was of 12.5%[9].

Considering the PIS, the majority of reported cases became infected in the urban area and at home, as verified in the Federal District in 2011-2012[25]. In contrast to previous situations in which contact with farm animals and activities were factors related to infection, the literature currently emphasizes that socio-environmental changes, such as overpopulated areas with inadequate waste treatment, combined with climate changes, are the main risk factors[8,19].

Regarding the risk situations related to the 30 days prior to the first symptoms, a place with evidence of the presence of rodents and contact with garbage or debris and vacant lot and mud were the most reported. A study carried out in Pernambuco in the period from 2001 to 2009 by Vasconcelos et al[13] also highlights the risk factors in urban areas, such as contact of the skin or mucous membranes with contaminated mud in places with precarious sanitary infrastructure, which provide the adequate environment for the reproduction of rodents.

This study verified the correlation between rainfall and the incidence of leptospirosis for the years considered. It is known that the average incubation period of this disease is

5–14 days[5], and the cases do not occur concomitantly with the rains. Considering rainfall as a predisposing factor for eventual floods, a correlation was made between precipitation and cases occurring immediately in the following month. It was verified that there was a statistically significant ($p < 0.05$) correlation between the number of cases and the rainfall in the years 2010, 2011 and 2012. It should be noted that 2009 presented a high incidence with no significant correlation with rainfall, which can be explained by the set of socio-environmental factors that go beyond the climatic aspects involved in the causal chain of the disease, and which are not yet fully understood[26].

Although leptospirosis is considered an occupational disease[13,19], in Campinas, São Paulo, the highest incidence occurred in the household environment. One hypothesis for this is that there are large numbers of recyclable waste pickers who store them in their homes in this municipality.

Noting that not all addresses were available, spatial analysis contributed to a better understanding of the distribution of cases. The thematic maps showed a higher concentration of leptospirosis in areas with poor urban infrastructure, basic sanitation and water supply, classified as having the highest SEVI[11].

The comparison of the maps with the Kernel estimation (Figure 2) and with the SEVI (Figure 3) allowed the identification of areas where the cases share socioeconomic and environmental conditions. Their visualization facilitates the implementation of strategies to improve aspects such as adequate waste disposal, drainage of water for the prevention of floods in the rainy periods, and programs for rodent control, both in the rainy season and in the dry season.

Other authors also associate indicators of socioeconomic and environmental conditions, urban infrastructure, workplace and presence of rodents in the household that are associated with leptospira infection[13,23]. In general, everyone points out the relationship between leptospirosis and low socioeconomic levels, areas of poverty, and environmental degradation.

The main limitation of this study was the lack of information for some variables, such as schooling, hospitalization time and the PIS addresses of a vulnerable population that needs preventive measures — the absence of the latter makes some analyzes and comparisons with other locations impossible. In the correlation test, as well as for the georeferencing of cases/deaths according to SEVI, it should be considered that other variables may be related to the outcome, which were not considered, as this is an exploratory ecological study using secondary data.

It should be noted that the lack of filling in some fields of the notification reports compromises the quality of the information and limits the possibility of actions triggered by the ES. For Laguardia et al.[18], "despite technological innovation, standardization of routines and financial incentives, a health information system cannot be not sustained without information management policies and without training of its professionals." Thus, training and awareness for the professionals responsible for completing the records is of vital importance to improve the database and health statistics.

The data analyzed allowed the characterization of leptospirosis cases/deaths in Campinas, São Paulo, for the period 2007-2014, for a set of variables, as well as the recognition of areas

with a higher incidence of cases/deaths, contributing to the adoption of particular strategies of intervention and prioritization of resources in reducing the risk of infection and in the early treatment of individuals affected by the disease.

CONCLUSION

The patterns of occurrence of leptospirosis in Campinas, São Paulo, showed similarity with other Brazilian cities. The identification of areas with higher incidence of cases/deaths contributes to the adoption of specific strategies of intervention and prioritization of resources in reducing the risk of infection and in the early treatment of those affected by the disease.

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