Epidemiology of leptospirosis in Colombia between 2007 and 2015

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Epidemiologia da leptospirose na Colômbia entre 2007 e 2015

Clara Susana Arias-Monsalve[1], Daniela Salas-Botero[2], Maria Rita Donalisio[3]

[1] Doctora en Ecología, Médica Veterinaria.Corporación Universitaria Remington. Medellín, Colombia. csariasm@unal.edu.co. ORCID: https://orcid.org/0000-0003-3875-1566

[2] Especialista en Epidemiología, Médica Veterinaria. Instituto Nacional de Salud. dsalas@ins.gov.co

[3] Doctora en Ciencias Médicas, Médica. Universidade Estadual de Campinas. rita.donalisio@gmail.com. ORCID: https://orcid.org/0000-0003-4457-9897

Abstract

Leptospirosis is a zoonotic disease of global distribution caused by the bacterium *Leptospira*. In Colombia, it has been mandatory to report this disease since 2007. **Objective**: to perform an epidemiological analysis of human leptospirosis in Colombia at the national, departmental and municipal levels for the period between January 2007 and December 2015. **Methods**: A retrospective ecological study of the temporal trend and spatial distribution of leptospirosis cases reported between January 2007 and December 2015 was conducted. The variables of sex, age, municipality of residence, area of residence (urban, rural), date of onset of symptoms, and lethality were analyzed. Results: A total of 23,994 suspected cases were reported, of which 39.51% were confirmed; 82.4% came from urban areas; 68.87% presented in men; the lethality was 2.66% in men and 2.04% in women. The departments with the highest number of cases were Valle del Cauca (n=2032), Antioquia (n=1747), Atlántico (n=1159); the incidence varied between 2 (Arauca) and 465.4 (Guaviare) per 100,000 inhabitants. At the municipal level, Cali had the highest number of cases (n=682), followed by Barranquilla (n=612) and San José del Guaviare (n=448). The highest incidence was 1597.6 in Pueblo Rico (Risaralda), followed by Sabanas de San Ángel (Magdalena) with 883.4 and San José del Guaviare (Guaviare) with 742.5; the majority of municipalities had incidences between 0 and 50 per 100,000 inhabitants. **Conclusions**: Leptospirosis is distributed throughout Colombia with 85% of the cases concentrated in 10 of its 32 departments. At the municipal level there is a large degree of variation in annual incidences. Six hotspots for cases were also identified, indicating that there are areas of high risk for the disease.

----------*Keywords:* leptospirosis, zoonoses, epidemiology, Colombia, incidence.

Resumo

A leptospirose é uma doença zoonótica de distribuição global causada pela bactéria *Leptospira*. Na Colômbia, a notificação da doença é obrigatória desde 2007. **Objetivo**: realizar uma análise epidemiológica da leptospirose humana na Colômbia em escalas nacionais, departamentais e municipais no período entre janeiro de 2007 e dezembro de 2015. **Métodos**: Foi conduzido estudo ecológico retrospectivo da tendência temporal e distribuição espacial de casos de leptospirose no período. Variáveis demoráficas (sexo, idade, município de residência, área de residência urbana, rural), data de início dos sintomas e letalidade foram analisadas. Resultados: Foram relatados de 23 994 casos suspeitos, dos quais 39,51% foram confirmados; 82,4% vem de áreas urbanas; 68,87% dos casos em homens; letalidade de 2,66% nos homens e de 2,04% nas mulheres. Os departamentos com maior número de casos foram Valle del Cauca (n=2032), Antioquia (n=1747), Atlántico (n=1159); a incidência variou entre 2 (Arauca) e 465,4 (Guaviare) por 100 000 habitantes. No nível municipal, Cali tem o maior número de casos (n=682), seguido por Barranquilla (n=612) e San José del Guaviare (n=448). A maior incidência foi de 1597,6 por 100 mil em Pueblo Rico (Risaralda), seguida por Sabanas de San Ángel (Magdalena) com 883,4 e San José del Guaviare (Guaviare) com 742,5. A maioria dos municípios tinha incidências entre 0 e 50 por 100 mil habitantes. **Conclusões**: A leptospirose é distribuída em toda a Colômbia, com 85% dos casos concentrados em 10 dos 32 departamentos. Na escala municipal, há grande variação nas incidências anuais e foram identificados seis pontos quentes para os casos, indicando que existem área de alto risco para a doença.

----------*Palavras chave*: leptospirose, zoonoses, epidemiologia, Colômbia, incidência.

Resumen

La leptospirosis es una enfermedad zoonótica de distribución mundial causada por la bacteria *Leptospira*. En Colombia, su reporte es obligatorio desde 2007. **Objetivo**: realizar un análisis epidemiológico de la leptospirosis humana en Colombia a escala nacional, departamental y municipal en el período comprendido entre enero de 2007 y diciembre de 2015. **Métodos**: Se realizó un estudio ecológico retrospectivo de tendencia temporal y distribución espacial de los casos de leptospirosis reportados entre enero de 2007 y diciembre de 2015. Se analizaron las variables de sexo, edad, municipio de residencia, área de residencia (urbana, rural), fecha de inicio de síntomas y letalidad. Resultados: se reportaron un total de 23 994 casos sospechosos, de los cuales se confirmó el 39,51%; el 82,4% proviene de zonas urbanas; el 68.87% se presentaron en hombres; la letalidad fue del 2,66% en los hombres y del 2,04% en las mujeres. Los departamentos con mayor número de casos fueron Valle del Cauca (n=2032), Antioquia (n=1 747), Atlántico (n=1159); la incidencia varió entre 2 (Arauca) y 465,4 (Guaviare) por 100 000 habitantes. A nivel municipal, Cali tiene el mayor número de casos (682), seguido de Barranquilla (n=612) y San José del Guaviare (n=448); la incidencia más alta fue 1 597.6 en Pueblo Rico (Risaralda), seguida por Sabanas de San Ángel (Magdalena) con 883.4 y San José del Guaviare (Guaviare) con 742.5; la mayoría de los municipios tuvieron incidencias entre 0 y 50 por 100 000 habitantes. **Conclusiones**: la leptospirosis se distribuye en toda Colombia, con el 85% de los casos concentrados en 10 de los 32 departamentos. A escala municipal, existe una gran variación en las incidencias anuales y se identificaron seis puntos calientes para casos, lo que indica que existen área de alto riesgo para la enfermedad.

----------*Palabras clave*: leptospirosis, zoonosis, epidemiología, Colombia, incidencia.

Introduction

Leptospirosis is a disease of worldwide distribution caused by the bacteria *Leptospira*. Leptospirosis affects domestic animals, mainly dogs, cattle, sheep and pigs. It also affects wildlife, especially carnivores, rodents and marsupials in captivity. In humans, leptospirosis is acquired from an animal host. Rodents have been shown to play a key role in the transmission cycle [1]. The tropics and subtropics have characteristics such as soil moisture, temperature, rainfall, areas of potential flooding and areas with poor hygienic sanitary conditions that meet the perfect conditions for the presence of the bacteria, its maintenance and its transmission. Leptospirosis can manifest in humans as a simple cold, however, it can also be so severe that it leads to death [1,2]. In its typical form, it shows up as a non-specific systemic disease characterized by fever, myalgia and headaches.

It is often confused with other illnesses, such as influenza, dengue or malaria [3–5]. Because it does not have typical symptomatology, diagnosis by laboratory or epidemiological link is essential.

The average annual incidence for the Americas region is 12.5 per 100,000 people, ranging from 0.1 to 306.2 in the period between 1970 and 2009, with a mortality rate of over 10% [6]. In the Americas there are information gaps in relation to the disease's epidemiology and, therefore, the disease's real impact. In Colombia, leptospirosis has been mandatory to report to the System of Epidemiological Surveillance of the Colombian National Institute of Health (SIVIGILA by its Spanish acronym) since 2007. The first documented case of human leptospirosis occurred around 1957, while the first epidemic in Colombia occurred in the country's Atlántico department in 1995, with a case fatality rate of 17% among the confirmed cases [7]. In Colombia, the ELISA technique is used as a screening test. All cases that are indicated to be positive via this test are then sent to the National Institute of Health (INS) reference laboratory to be confirmed by a Microscopic Agglutination Test (MAT), which is the gold standard recommended by the World Health Organization [8,9].

Reports of leptospirosis in Colombia must be analyzed from an epidemiological perspective in order to have a better understanding of the disease's presentation. It is crucial to determine the distribution, incidence and lethality of the disease. Adding to work already done focusing on human leptospirosis from an epidemiological perspective in Colombia [10], our work presents an analysis from three different spatial scales with additional associations with variables of sex, age, place of origin and geographical region.

The objective of this study was to perform an epidemiological analysis of human leptospirosis in Colombia at the national, departmental and municipal level in the period between January 2007 and December 2015.

Methodology

An ecological study of temporal trend and spatial distribution of leptospirosis cases reported to SIVIGILA between January 2007 and December 2015 was conducted. The study was conducted in Colombia, a country located in the north-west of South America that has a population of 45.5 million people [11], according to the preliminary results of the census held by the National Administrative Department of Statistics (DANE) in 2018. Administratively, Colombia is divided into 32 departments and 1,032 municipalities. In the present study, data was grouped into 3 spatial scales: national, departmental and municipal.

The leptospirosis data for the years 2007 to 2015 [8] was obtained from the SIVIGILA databases, which contain all suspected cases as defined by the Public Health Surveillance Protocol. The epidemiological analysis of the disease included cases that were confirmed by laboratory and cases that were confirmed by epidemiological link. Confirmation by laboratory is done with the MAT technique with a result greater than 1:400 in single sample or seroconversion in paired samples with a 10 to 15 day period between them [8]. Confirmation by epidemiological nexus is done by taking cases confirmed by laboratory and linking people, a time and place to the source of the infection identified in the confirmed case [8].

Distribution of cases among sex, age groups, municipality of residence and area of residence (urban, rural) was obtained, and the disease's lethality was calculated. The symptom onset date was used for the temporal analysis of cases and the municipality of residence was used for the spatial analysis. The monthly annual cycle of cases for Colombia was estimated. To estimate the annual cycle, the monthly average cases was obtained and plotted with its respective standard error. The total and annual incidence rates per 100,000 inhabitants were calculated at the national, departmental and municipal level. In order to estimate the total incidence rate, the total number of cases of the study period and the average population of the study period were obtained. The incidence rate was calculated by taking the number of cases and dividing it by the population, then multiplying the result by 100,000. To calculate the annual incidence rate, the number of cases for each year and the average population of the same year were compiled. The population for each year and for each municipality of the country was obtained from DANE, with projected populations based on the census carried out in 2005 [12]. The case fatality rate was calculated at the national level by dividing number of deaths by number of confirmed cases for each year. The proportions according to variables of interest were compared using the Chi square test with Yates correction and with a significance level of 5%. Case distribution maps were developed at the municipal level. To identify areas of higher case concentration (hotspots), a kernel estimator was used [13].

The free software R version 3.5.0, from the R Foundation, was used to perform epidemiological data analysis. For spatial representation, ArcGis version 10.3 from ESRI was used. Data regarding leptospirosis cases were not acquired through interaction with individuals and contained no identifiable private information, so were therefore considered exempt from review by an Ethics Board (following the WMA Declaration of Helsinki ethical principles for medical research involving human subjects).

Results

For Colombia, 23,994 suspected cases of leptospirosis were identified during the period between 2007 and 2015, of which 9,449 (39.4%) were confirmed by laboratory or epidemiological link. The origin of the confirmed cases was mainly from urban areas (82.4%), showing that, over the years, the distribution of this disease has been significantly disproportionate (p value = 0) (see Supplemental material 1, Figure A). Regarding the distribution by sex, there were 6,505 confirmed cases in men (68.87%) and 2,943 in women (31.13%) (p ≤ 0.001) (see Supplemental material 1, Figure B). The lethality was higher in men than in women, with 2.66 and 2.04 respectively (see Supplemental material 1, Figure B). The age group with the most cases each year was 14 to 34 years in both sexes (p ≤ 0.001). For the period from 2007 to 2015, the incidence in Colombia varied between 1.62 and 3.06 per 100,000 inhabitants (2015 and 2011 respectively). A peak incidence can be observed between 2010 and 2012 (see Supplemental material 1, Figure C). In the annual cycle of the monthly total cases, the majority are concentrated in October and November and do not indicate a marked seasonal pattern (see Supplemental material 1, Figure D).

Kernel estimation identified four areas of concentrated cases in the national territory located on the Caribbean coast, in the north-west and center of the Antioquia department, Valle del Cauca, the Colombian coffee region and Guaviare (see Figure 1, right).

The department with the highest number of confirmed cases of leptospirosis in the study period was Valle del Cauca (21.5% of the total for the country), followed by Antioquia, Atlántico, Bolívar and Risaralda. Vichada was the department with the lowest number of confirmed cases (2 cases). The total incidence rate per 100,000 inhabitants at the departmental level ranged from two, for the department of Arauca, to 465.4, for the department of Guaviare. Results of the total number of cases and total incidence for each of Colombia's 32 departments are presented in Table 1. The annual incidences and annual number of cases at the departmental level are presented in Supplemental material 2.

At the municipal level, the highest number of cases occurred in the city of Cali, which had 682 confirmed cases during the study period. No cases were reported for some municipalities, while other municipalities had between one and two cases during the study period.

As for the total incidence per 100,000 inhabitants at the municipal level, the highest incidence occurred in Pueblo Rico (Risaralda), followed by Sabanas de San Ángel (Atlántico), San José del Guaviare (Guaviare) and Puerto Arica (Amazonas). Other incidences were found distributed as follows: two municipalities with incidences between 300 and 400; six municipalities between

Table 1. Total number of leptospirosis cases and total incidence per 100,000 people at the departmental level.

Number of cases and incidence of leptospirosis at the departmental level		
Department	Total number of cases	Total incidence per 100,000 people
Valle del Cauca	2032	45.87
Antioquia	1747	28.43
Atlántico	1159	49.45
Risaralda	680	73.08
Bolívar	683	34.07
Magdalena	551	45.41
Guaviare	488	465.41
Cundinamarca	314	12.47
Tolima	241	17.32
Cauca	200	15.02
Quindío	158	28.58
Cesar	134	13.69
Sucre	131	16
Córdoba	120	7.46
Huila	110	10.02
Santander	99	4.9
Chocó	98	20.37
Caldas	84	8.57
La Guajira	80	9.45
Nariño	71	4.27
San Andrés	44	59.49
Casanare	39	11.75
Norte de Santander	38	2.9
Boyacá	32	2.52
Meta	30	3.37
Putumayo	26	7.88
Caquetá	21	4.63
Amazonas	18	24.71
Vaupés	9	21.45
Guainía	7	17.97
Arauca	5	2
Vichada	2	3.06

200 and 300; 22 municipalities between 100 and 200; 47 municipalities between 50 and 100; 309 municipalities between 10 and 50; and 211 municipalities with less than 10. The annual incidence at the municipal level varied between 0 and 1599.7 per 100,000 people. The 30 municipalities with the highest number of cases of leptospirosis and with the highest incidences are shown in Tables 2 and 3, respectively.

Table 2. Total number of leptospirosis cases in selected municipalities.

Municipalities with the highest incidences of leptospirosis		
Municipality	Department	Total incidence per 100,000 people
Pueblo Rico	Risaralda	1 597.6
Sabanas De San Ángel	Cesar	883.41
San José Del Guaviare	Guaviare	742.51
Puerto Arica	Amazonas	432.1
El Cairo	Valle Del Cauca	349.75
Bolívar	Valle Del Cauca	323.92
Turbo	Antioquia	272.83
Guapi	Cauca	272.6
Roldanillo	Valle Del Cauca	232.6
Colosó	Sucre	217.15
Mistrató	Risaralda	209.82
Riofrío	Valle Del Cauca	203.74
Versalles	Valle Del Cauca	196.7
Apartadó	Antioquia	179.82
La Celia	Risaralda	161.66
El Dovio	Valle Del Cauca	157.24
Carepa	Antioquia	156.43
Tubará	Atlántico	145.64
Argelia	Valle Del Cauca	137.65
Piojó	Atlántico	137.55
Santa Rosa Del Sur	Bolívar	137.27
Buga	Valle Del Cauca	136.31
Simacota	Santander	133.79
Alcalá	Valle Del Cauca	131.66
Toro	Valle Del Cauca	123.63
Calamar	Guaviare	120.68
Cartago	Valle Del Cauca	119.9
Villanueva	Bolívar	117.01
Calarcá	Quindío	115.74
Puerto Berrio	Antioquia	114.55
Puerto Colombia	Atlántico	105.62
Ansermanuevo	Valle Del Cauca	105.03
El Retorno	Guaviare	102.74
Acandí	Chocó	100.73

Table 3. Total incidence of leptospirosis per 100,000 people in selected municipalities.

Municipalities with the highest number of leptospirosis cases		
Municipality	Department	Total number of cases
Cali	Valle Del Cauca	682
Barranquilla	Atlántico	612
San José Del Guaviare	Guaviare	448
Cartagena	Bolívar	429
Turbo	Antioquia	392
Apartadó	Antioquia	285
Medellín	Antioquia	264
Santa Marta	Magdalena	261
Pereira	Risaralda	237
Bogotá	Cundinamarca	227
Soledad	Atlántico	213
Pueblo Rico	Risaralda	203
Tuluá	Valle Del Cauca	163
Buga	Valle Del Cauca	158
Cartago	Valle Del Cauca	155
Buenaventura	Valle Del Cauca	153
Sabanas de San Ángel	Magdalena	142
Ibagué	Tolima	115
Palmira	Valle Del Cauca	92
Calarcá	Quindío	88
Dosquebradas	Risaralda	82
Guapi	Cauca	80
Valledupar	Cesar	80
Carepa	Antioquia	79

The distribution of total cases of leptospirosis in each of the municipalities of Colombia is shown in Figure 1, left. White indicates that the municipalities did not report cases to the system during the study period. For the municipalities that reported cases to the system in the study period, the total cases vary from 1 (shown in green) to 680 (shown in red). Some municipalities on the Caribbean and Pacific coasts and in the Colombian coffee region, and one municipality in the Amazon, presented a high number of cases.
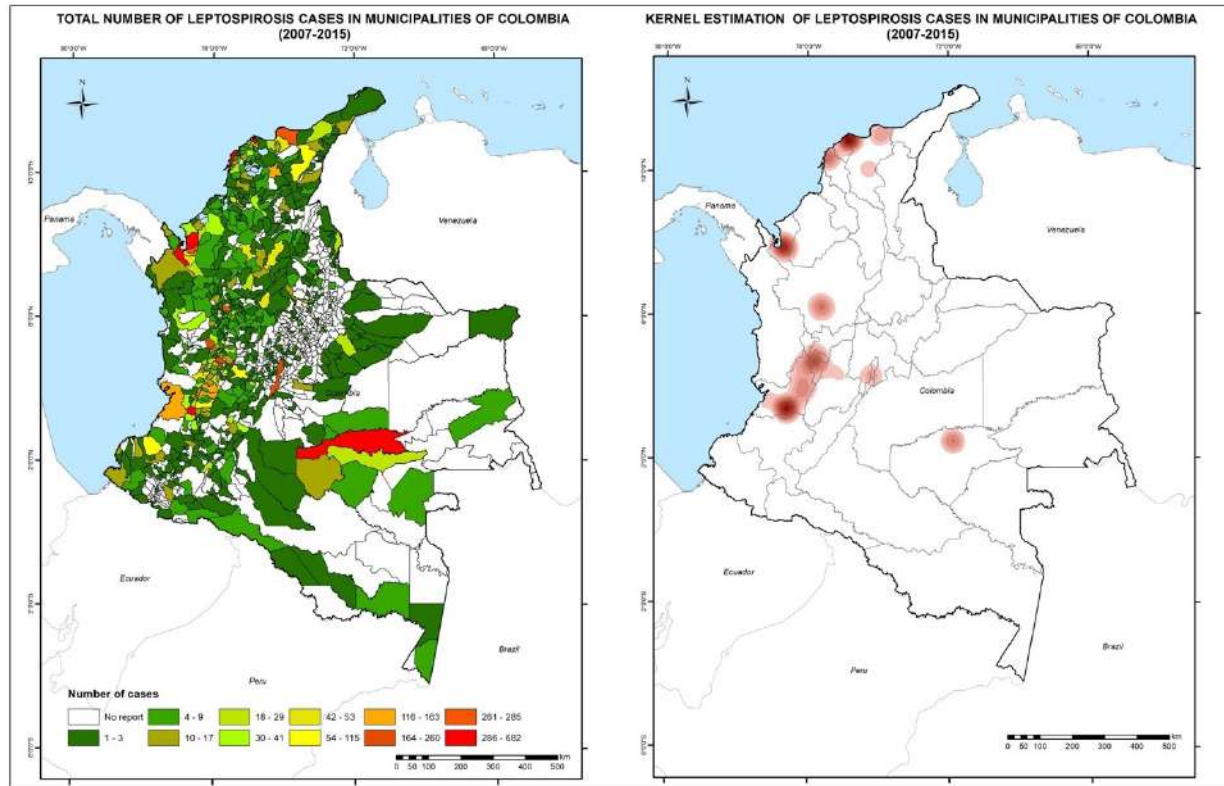
Figure 1. Left: Map of total number of cases in municipalities of Colombia for the period 2007 to 2015. Right: Hotspots of concentration of cases identified by Kernel density analysis.

Discussion

In Colombia, there were 9,449 confirmed cases of leptospirosis between 2007 and 2015, with annual incidence peaks in 2010, 2011 and 2012. Cases were distributed heterogeneously in all of the country's departments. At the municipal level, there was a large variation in the annual incidence, ranging from zero to 1,599 per 100,000 inhabitants.

In the period studied, Colombia had an average annual incidence rate of 2.3 per 100,000 inhabitants, with a minimum of 1.62 in 2015 and a maximum of 2.94 and 3.06 in 2010 and 2011 respectively. The annual incidence rates found in Colombia are within what the World Health Organization's Leptospirosis Burden Epidemiology Reference Group (LERG) estimates to be an endemic level for a humid tropical equatorial country. The years with the highest incidences coincide with the La Niña event that strongly affected the country in late 2010 and during 2011, causing increased rain and historical floods [14]. In recent years, the La Niña event has been indicated by several authors to be an important factor that influences leptospirosis in Colombia [15,16].

The reported incidences for countries in the region vary. In Brazil, the annual incidence for the period from 2010 to 2014 was 2.1 per 100,000 inhabitants; in Mexico, it fluctuated from 0.04 to 0.4 per 100,000 inhabitants between 2000 and 2010; in Peru, the incidence has increased in recent years with reports of one per 100,000 inhabitants in 2011, 6.3 in 2012 and 8.6 in 2013; in Ecuador, leptospirosis is reported to be a growing problem, with an average annual incidence of 0.5 cases per 100,000 inhabitants between 1996 and 2005; in Venezuela, there is only a report for the years 2004 and 2005 that indicates an incidence of 0.4 per 100,000 inhabitants [17–21].

Although countries in the region do not have consistent yearly data for the incidence of leptospirosis, the numbers reported in Venezuela, Ecuador and Mexico are still lower than those in Colombia, and are similar to those found in Brazil.

Our results show that the majority of cases of leptospirosis in Colombia come from urban areas, representing 82% of the total. Leptospirosis is a disease that can occur both in the countryside and in urban environments, but is more prevalent in the latter [22,23]. The most frequent presentation of this disease in urban areas is due to the most common forms of human infection,

including synanthropic rodents, overcrowding and precarious sanitation circumstances, which are typically found in cities [24]. At present, the majority of the population of Colombia lives in urban areas, which also contributes to the fact that the majority of cases come from these environments. Urbanization is a triggering factor for the increase in cases worldwide, affecting both developed and developing countries, with the significant difference that the latter have less resilience capacity to face healthcare problems of populations settled in places with poor infrastructure and with poor hygienic sanitary conditions [23]. In Colombia, we found that the population is mainly distributed in cities where favorable conditions exist for increased leptospirosis transmission.

Regarding distribution by sex, our results indicate that, in Colombia, the proportion of cases of leptospirosis in men is significantly higher than in women. Similar results have been reported in several European countries such as Germany, Italy, Bulgaria and Slovakia, and in Brazil [25,26]. In Colombia, a study was conducted in Turbo, a municipality in the department of Antioquia, which showed that 67.6% of cases there were male [27]. Our study's national results complement information on the increased presentation of leptospirosis in males in all age groups. Physiological factors have been ruled out as the cause of an increased number of cases among men [28]. We understand that the increased presentation of leptospirosis in males is attributed to behavioral and occupational factors.

Leptospirosis is associated with some agricultural occupations such as rice, yam, sugar cane and banana growers [3,29]. These activities have been traditionally performed by men and are also part of the rural Colombian economy. In this study we did not perform an analysis of occupational activities since the information for this variable was incomplete in the SIVIGILA databases. However, we assume that economic activity has an impact on the occurrence of leptospirosis, in particular in the Urabá region (Antioquia), where the present study found a hotspot for the disease in Colombia, since there is extensive banana and plantain farming in the region.

Some pleasure and recreational activities are gaining significance in relation to the presentation of leptospirosis worldwide [30–32]. In Colombia, bathing in rivers is part of the culture in warm areas. A study conducted in the Urabá area found that bathing in rivers is a risk factor for leptospirosis [27]. We infer that this practice may be associated with some of the hotspots of Urabá and Valle del Cauca.

The leptospirosis lethality found in this study was 2% per year at the national level. This lethality contrasts with countries like Brazil where the lethality is around 9% [17]. High fatality rates of leptospirosis suggest that the cases being confirmed are the severe cases and milder clinical forms are not being reported. Even though cases may not be reported in certain countries, the burden of the disease still affects those countries' public health. This low lethality in Colombia is a sign that the surveillance system is efficient at notifying based on diagnosis, detecting milder cases that usually represent the majority of cases.

We found six hotspots of leptospirosis in Colombia, located on the Caribbean coast, in the north-west and the center of the department of Antioquia, Valle del Cauca, the coffee region and the department of Guaviare. Previous studies identified incidence hotspots for Colombia, two of which coincide with the hotspots found in our study: north-west Antioquia (Urabá region) and Guaviare department [10]. It is important to note that the capital of the department of Guaviare, San José del Guaviare, has had an active epidemiological surveillance program since 2004, which tracks and diagnoses febrile cases that present within the health system. Moreover, in the Urabá region located in the north-west of the department of Antioquia, there is also an active surveillance program as the result of a commitment by the local authorities and institutions located in the area [33,34]. These programs are unique in Colombia and, therefore, the number of reports for these municipalities and regions are greater than those of its neighbors. Hotspots are places where there is a greater density of cases when comparing the number of cases with the municipality's area. Higher rates of incidence of cases do not always coincide with a higher density of cases, although it should also be considered that a higher density of cases could correspond to regions of greater clinical suspicion and better notification of the disease.

At the departmental level, 85% of Colombia's total cases for the period between 2007 and 2015 are concentrated in 10 of the country's 32 departments. The 10 departments are: Valle del Cauca, Antioquia, Atlántico, Bolívar, Risaralda, Magdalena, Guaviare, Cundinamarca, Tolima and Cauca. In turn, these departments also have the highest incidences in the country. This finding is an important tool in the efforts to optimize the resources of epidemiological surveillance programs since these could be used as sentinel or early-warning departments to establish the morbidity situation of leptospirosis in Colombia.

In terms of annual rates, there is a large variation in incidence rate, both when comparing different departments in the same year and when comparing a single department in different years, although a clear trend is not observed (see Supplemental material 2, Table 2).

In some departments there is a low number of cases, or even no cases. This low number of cases could be due to the fact that surveillance programs still do not report all cases that occur in their territory and do not necessarily reflect the risk of leptospirosis infection.

When comparing the annual departmental incidences of Colombia with those of the different states of Brazil (between 2010 and 2014) and Mexico (between 2000 and 2010) we find that, in general, Colombia's figures are higher than those presented in these two countries, even when considering the same years. This comparison at the departmental level contrasts with the results obtained at the national level, in which Colombia has similar incidences to these countries. This finding reaffirms the importance of the scale factor in analyzing a disease's epidemiological data.

At the municipal level, we found that the 30 municipalities with the highest number of cases were located within the focal points identified as hotspots and were concentrated in Valle del Cauca and Antioquia. The incidence of the majority of the country's municipalities was between 10 and 50 per 100,000 inhabitants. With the exception of San José del Guaviare, whose surveillance system is active, the municipalities with the highest number of cases in Colombia belong to large cities with large populations. In contrast, the highest incidences occur in small municipalities on the Caribbean coast, and in the center, west and south of the country, indicating that the risk of leptospirosis is distributed throughout the Colombian territory (see Supplemental material 3 for annual incidence and annual number of cases in selected municipalities).

Implications for epidemiological surveillance

Leptospirosis is a disease that is difficult to diagnose via both methods of diagnosis: laboratory confirmation and differential diagnoses. Laboratory confirmation requires two paired samples with an interval of 10 days. Frequently, patients do not return to their healthcare provider to get the second sample taken for confirmation. It is estimated that, for the region of Urabá, the number of patients who return for the second sample is close to 30% [33]. In addition, co-infection of dengue and leptospirosis has been documented in patients and in several regions of Colombia, and even in other countries [8,35,36]. Leptospirosis occurs in areas with a high incidence of dengue, making it difficult to detect other diseases as some clinical forms of leptospirosis can be confused with dengue. In this way, dengue acts as an umbrella disease under which many febrile cases are diagnosed and are not confirmed, thus masking other diseases such as leptospirosis. Based on a study conducted in Fortaleza, Brazil, the authors consider the possibility that, in endemic areas for dengue and leptospirosis, approximately 20% of suspected dengue cases may be leptospirosis [37]. All this leads to an underdiagnosis of leptospirosis, contributing further to ignorance of the disease's real extent in Colombia.

Limitations of the study

In this ecological study, the incidence rates were analyzed at different geographical scales corresponding to political divisions and over time. The socioeconomic and demographic heterogeneity of the spatial clusters (departments and municipalities) can contribute to inaccuracies in the disease's risk assessment.

The present study has used secondary data obtained from official databases that may undergo revision, which may affect consistency. Also, since the notification system is relatively new (since 2007), there are expected limitations in monitoring and difficulties such as the standardization of information flows, the omission of data in some of the variables of the notification form, and the absence of notification by some territorial entities. Although there are improvements in the system, there are still municipalities that fail to notify. These municipalities are concentrated in the departments of Vichada, Guainía, Vaupés, Arauca and Meta. There is uncertainty as to whether these municipalities did not actually register cases of leptospirosis during the study period because they belong to departments that historically have been neglected by the central government and face budgetary difficulties.

Conclusions

The notification of leptospirosis in Colombia is distributed progressively, that is to say, it has increased over the years throughout the national territory between 2007 and 2015. Some departments have higher incidences, such as Guaviare, Risaralda and San Andrés, while others have higher numbers of cases, such as Valle del Cauca, Antioquia and Atlántico. At the regional level, there are areas of concentration of cases in different regions on the Caribbean coast and in the north-west and center of Antioquia department, Valle del Cauca, the coffee region and the department of Guaviare. Despite improvements in the reporting system, there are still departments with few or no case records, especially in the Eastern Plains and the Amazon. In the country's municipalities, incidence rates of leptospirosis range from zero to 1,597.6 cases per 100,000 inhabitants, indicating that there are areas at high risk for the disease. The low lethality found in Colombia suggests that the surveillance system has detected mild cases of the disease.

It is suggested that more detailed research on factors associated with the occurrence of cases and the circulation of the bacteria is carried out. This epidemiological analysis of the leptospirosis situation in Colombia responds to a worldwide need for more accurate and real information on this significant zoonotic disease.

Conflict of interest

The authors declare that there are no conflicts of interest. The manuscript presents personal opinions as a result of data analysis and does not represent the institution's point of view.

Authorship declaration

Clara S Arias-Monsalve: conception of the article, data analysis and interpretation of the results.
Maria Rita Donalisio: conception of the article, data analysis and interpretation of the results.
Daniela Salas: data acquisition, data analysis and interpretation of results

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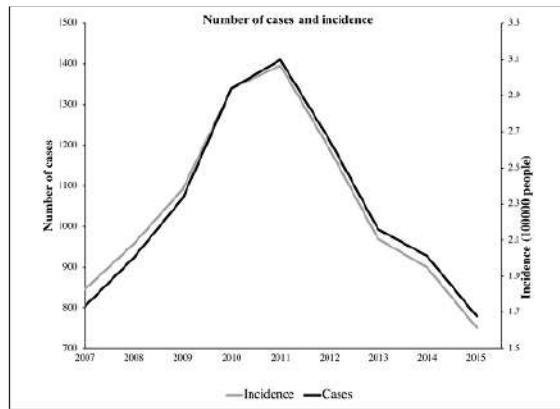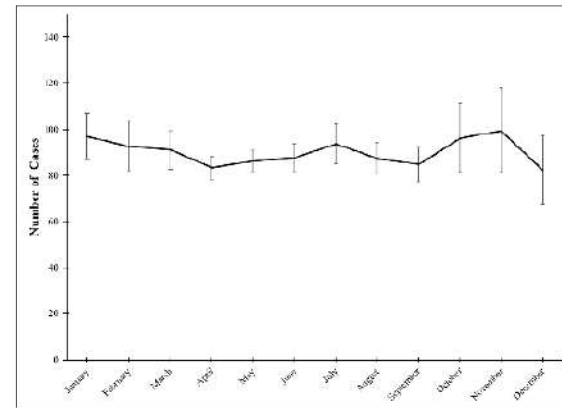
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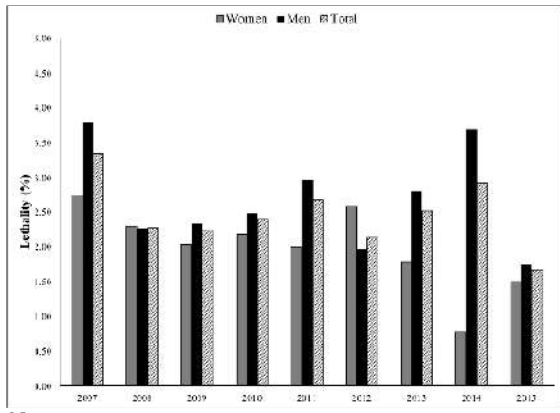
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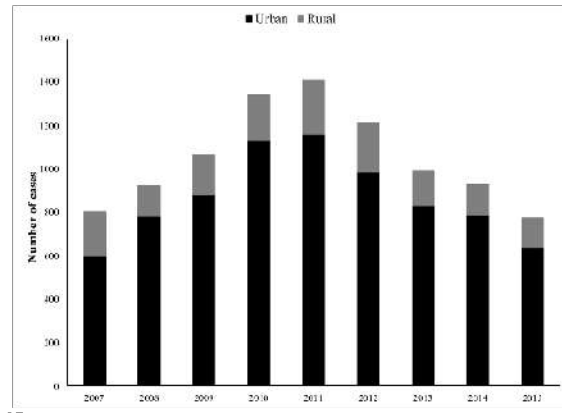
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Supplemental material 2

Number of cases of leptospirosis at the departmental level								
Department	2007	2008	2009	2010	2011	2012	2013	2014	2015
Amazonas	(…)	0	1	3	1	3	2	1	7
Antioquia	4	89	111	168	336	289	331	218	201
Arauca	(…)	0	0	0	0	1	1	0	3
Atlántico	212	204	114	223	110	71	82	80	63
Bolívar	63	42	37	122	141	87	72	78	41
Boyacá	(…)	2	1	2	0	9	6	7	5
Caldas	23	12	5	9	7	10	5	6	7
Caquetá	(…)	0	3	1	5	4	3	2	3
Casanare	5	4	3	1	8	12	3	2	1
Cauca	2	37	34	23	37	31	14	12	10
Cesar	3	20	4	36	15	31	17	6	2
Chocó	1	3	4	6	16	16	15	21	16
Córdoba	17	5	8	3	26	29	11	7	14
Cundinamarca	2	7	24	54	41	43	35	69	39
Guainía	(…)	0	1	5	0	0	1	0	0
Guaviare	72	94	55	83	29	12	20	38	85

Number of cases of leptospirosis at the departmental level								
Department	2007	2008	2009	2010	2011	2012	2013	2014	2015
Huila	2	0	24	11	10	18	8	17	20
La Guajira	6	6	3	6	16	19	12	2	10
Magdalena	18	18	188	103	69	63	54	24	14
Meta	1	0	6	2	2	3	2	5	9
Nariño	12	2	1	6	9	9	5	2	25
Norte de Santander	3	0	3	6	4	4	6	4	8
Putumayo	(…)	2	2	0	12	4	1	2	3
Quindío	14	6	18	19	5	5	9	76	6
Risaralda	273	66	48	55	51	61	38	53	35
San Andrés	5	2	8	9	10	5	3	1	1
Santander	(…)	2	7	10	31	11	8	10	20
Sucre	1	7	4	49	23	22	11	5	9
Tolima	5	7	18	15	29	53	38	43	33
Valle del Cauca	58	276	333	307	366	288	179	136	89
Vaupés	(…)	9	0	0	0	0	0	0	0
Vichada	(…)	0	0	0	0	0	1	1	0

Supplemental material 2 Table A: Annual number of leptospirosis cases at the departmental level. (…) corresponds to information not reported.

Incidence of leptospirosis per 100,000 people at the departmental level								
Department	2007	2008	2009	2010	2011	2012	2013	2014	2015
Amazonas	(…)	0	1.4	4.17	1.37	4.07	2.68	1.33	9.18
Antioquia	0.07	1.51	1.85	2.77	5.47	4.64	5.25	3.42	3.11
Arauca	(…)	0	0	0	0	0.39	0.39	0	1.14
Atlántico	9.53	9.05	4.99	9.64	4.69	2.99	3.41	3.29	2.56
Bolívar	3.29	2.17	1.89	6.16	7.04	4.3	3.51	3.76	1.96
Boyacá	(…)	0.16	0.08	0.16	0	0.71	0.47	0.55	0.39
Caldas	2.36	1.23	0.51	0.92	0.71	1.02	0.51	0.61	0.71
Caquetá	(…)	0	0.68	0.22	1.1	0.87	0.64	0.42	0.63
Casanare	1.63	1.28	0.94	0.31	2.41	3.55	0.87	0.57	0.28
Cauca	0.16	2.85	2.6	1.74	2.78	2.31	1.03	0.88	0.73
Cesar	0.32	2.12	0.42	3.72	1.53	3.13	1.69	0.59	0.19
Chocó	0.22	0.64	0.85	1.26	3.33	3.3	3.06	4.24	3.2
Córdoba	1.12	0.33	0.51	0.19	1.62	1.78	0.66	0.42	0.82
Cundinamarca	0.08	0.29	0.98	2.18	1.63	1.68	1.35	2.61	1.46
Guainía	NA	0	2.65	13.05	0	0	2.49	0	0
Guaviare	72.95	93.8	54.05	80.34	27.66	11.28	18.53	34.71	76.53
Huila	0.19	0	2.25	1.02	0.91	1.62	0.71	1.49	1.73
La Guajira	0.82	0.79	0.38	0.73	1.89	2.17	1.33	0.22	1.04
Magdalena	1.54	1.53	15.79	8.57	5.69	5.15	4.37	1.92	1.11
Meta	0.12	0	0.7	0.23	0.23	0.33	0.22	0.53	0.94
Nariño	0.76	0.13	0.06	0.37	0.54	0.54	0.29	0.12	1.43
Norte Santander	0.24	0	0.23	0.46	0.31	0.3	0.45	0.3	0.59
Putumayo	(…)	0.63	0.62	0	3.64	1.2	0.3	0.59	0.87

Incidence of leptospirosis per 100,000 people at the departmental level									
Department	2007	2008	2009	2010	2011	2012	2013	2014	2015
Quindío	2.59	1.1	3.29	3.46	0.9	0.9	1.61	13.52	1.06
Risaralda	30.04	7.22	5.22	5.95	5.48	6.52	4.04	5.6	3.68
San Andrés	6.98	2.77	11	12.27	13.53	6.71	3.99	1.32	1.31
Santander	(…)	0.1	0.35	0.5	1.53	0.54	0.39	0.49	0.97
Sucre	0.13	0.88	0.5	6.04	2.81	2.66	1.32	0.59	1.06
Tolima	0.36	0.51	1.3	1.08	2.08	3.8	2.71	3.06	2.34
Valle Del Cauca	1.36	6.43	7.68	7	8.26	6.44	3.96	2.98	1.93
Vaupés	(…)	22.14	0	0	0	0	0	0	0
Vichada	(…)	0	0	0	0	0	1.46	1.42	0

Supplemental material 2 Table B: Annual incidence per 100,000 people at the departmental level. (…) corresponds to information not reported.

Supplemental material 3

Municipalities with the highest number of cases.										
Municipality	Department	2007	2008	2009	2010	2011	2012	2013	2014	2015
Cali	Valle Del Cauca	11	101	78	101	145	132	60	33	21
Barranquilla	Atlántico	90	115	60	115	60	34	39	49	50
San José Del Guaviare	Guaviare	69	91	53	80	28	11	20	30	66
Cartagena	Bolívar	50	35	33	101	85	25	40	43	17
Turbo	Antioquia	(…)	24	19	50	64	64	51	59	61
Apartadó	Antioquia	(…)	16	13	27	63	44	66	34	22
Medellín	Antioquia	(…)	4	15	34	57	54	46	30	24
Santa Marta	Magdalena	10	11	15	88	49	43	23	13	9
Pereira	Risaralda	15	45	25	30	20	23	21	35	23
Bogotá	Cundinamarca	2	3	16	38	24	33	28	57	26
Soledad	Atlántico	43	44	28	40	13	17	12	9	7
Pueblo Rico	Risaralda	195	0	1	1	2	1	0	1	2
Tuluá	Valle Del Cauca	3	11	17	8	26	32	31	25	10
Buga	Valle Del Cauca	7	25	14	22	53	15	6	5	11
Cartago	Valle Del Cauca	(…)	5	49	29	41	11	16	2	2
Buenaventura	Valle Del Cauca	7	26	10	33	10	9	15	28	15
Sabanas de San Ángel	Magdalena	(…)	0	142	0	0	0	0	0	0
Ibagué	Tolima	4	5	13	6	16	26	17	15	13
Palmira	Valle Del Cauca	3	27	6	10	10	16	10	5	5
Calarcá	Quindío	10	0	3	3	2	1	0	69	0
Dosquebradas	Risaralda	21	11	5	8	6	9	6	9	7
Guapi	Cauca	(…)	23	7	9	19	15	3	1	3
Valledupar	Cesar	1	11	0	19	8	24	15	1	1
Carepa	Antioquia	(…)	1	3	5	28	14	16	4	8

Supplemental material 3 Table A: Annual number of leptospirosis cases in selected municipalities. (…) corresponds to information not reported.

Municipalities with the highest total incidence per 100,000 people										
Municipality	Department	2007	2008	2009	2010	2011	2012	2013	2014	2015
Pueblo Rico	Risaralda	159.97	0.00	0.81	0.80	1.58	0.78	0.00	0.76	1.50
Sabanas De San Ángel	Cesar	(…)	0.00	90.48	0.00	0.00	0.00	0.00	0.00	0.00
San José Del Guaviare	Guaviare	12.29	15.92	9.10	13.49	4.64	1.79	3.20	4.72	10.22
Puerto Arica (Cd)	Amazonas	(…)	0.00	0.00	0.00	0.00	0.00	0.00	0.00	44.44
El Cairo	Valle Del Cauca	(…)	0.00	23.98	3.11	1.03	6.14	0.00	1.01	0.00
Bolivar	Valle Del Cauca	2.01	2.71	17.84	5.56	2.11	0.00	0.72	0.00	0.74
Turbo	Antioquia	(…)	1.81	1.40	3.58	4.46	4.35	3.37	3.80	3.83
Guapi	Cauca	(…)	7.92	2.40	3.08	6.47	5.09	1.02	0.34	1.01
Roldanillo	Valle Del Cauca	0.58	2.93	12.39	5.04	1.79	0.30	0.00	0.00	0.00
Coloso (Ricaurte)	Sucre	(…)	0.00	0.00	21.58	0.00	0.00	0.00	0.00	0.00
Mistrato	Risaralda	1.96	1.95	1.93	0.00	6.36	6.32	1.88	0.62	0.00
Riofrio	Valle Del Cauca	2.39	10.33	1.23	0.63	3.19	0.00	1.32	0.67	0.00
Versalles	Valle Del Cauca	11.18	6.30	0.00	1.29	0.00	0.00	0.00	0.00	0.00
Apartado	Antioquia	(…)	1.11	0.87	1.76	3.99	2.70	3.93	1.97	1.23
La Celia	Risaralda	12.60	0.00	0.00	1.15	2.31	0.00	0.00	0.00	0.00
El Dovio	Valle Del Cauca	(…)	0.00	10.99	4.44	0.00	0.00	0.00	0.00	0.00
Carepa	Antioquia	(…)	0.21	0.63	1.02	5.55	2.71	3.02	0.74	1.43
Tubara	Atlántico	(…)	1.83	2.74	8.20	0.91	0.00	0.00	0.91	0.00
Argelia	Valle Del Cauca	3.01	3.03	0.00	6.09	1.53	0.00	0.00	0.00	0.00
Piojo	Atlántico	(…)	0.00	0.00	7.88	0.00	3.92	0.00	1.95	0.00
Santa Rosa Del Sur	Bolívar	0.56	0.00	0.27	0.00	2.34	8.39	1.49	0.49	0.00
Buga	Valle Del Cauca	0.60	2.15	1.20	1.89	4.57	1.30	0.52	0.43	0.95
Simacota	Santander	(…)	0.00	0.00	0.00	13.39	0.00	0.00	0.00	0.00
Alcala	Valle Del Cauca	(…)	0.54	1.58	2.59	1.01	1.49	1.95	3.34	0.47
Toro	Valle Del Cauca	(…)	0.00	3.11	2.48	0.00	6.78	0.00	0.00	0.00
Calamar	Guaviare	0.93	0.00	0.00	0.00	0.00	1.03	0.00	1.07	9.90
Cartago	Valle Del Cauca	(…)	0.39	3.84	2.26	3.17	0.85	1.22	0.15	0.15

Supplemental material 3 Table B: Annual incidence per 100,000 people in selected municipalities. (…) corresponds to information not reported.