JIDC | THE JOURNAL OF INFECTION IN DEVELOPING COUNTRIES

Original Article

Impact of El Niño-Southern oscillation on human leptospirosis in Colombia at different spatial scales

Clara S Arias-Monsalve[1], Alejandro Builes-Jaramillo[2]

[1] *Departamento de Ciencias Forestales, Universidad Nacional de Colombia Sede Medellín, Medellín, Colombia*
[2] *Institución Universitaria Colegio Mayor de Antioquia, Facultad de Arquitectura e Ingeniería, Medellín, Colombia*

Abstract

Introduction: Leptospirosis is a zoonotic disease caused by a bacteria of the genus *Leptospira*. Climate is key in order to understand leptospirosis dynamics. El Niño Southern Oscillation is the main modulator of climate in Colombia. Our goal was to analyze the changes that occurred in number of cases and incidence rate of leptospirosis during La Niña and El Niño episodes in Colombia at three spatial scales in the period between 2007 and 2015.
Methodology: A cross-sectional retrospective study was performed. Data analysis: correlation and lagged cross correlation between time series of Oscillation Niño Index and time series of standardized number of leptospirosis cases; construction of annual cycle of leptospirosis; comparison of changes of number of cases between Neutral, periods with El Niño and Neutral periods with La Niña.
Results: At the national level, monthly number of cases raised a 25% during La Niña and decreased of 17% during El Niño. At departmental level, increase of cases in both phases of ENSO, depending on the location in the country, was found. At the municipal level, 17 have a rise in the number of cases during La Niña months. Of those, seven presented also an increase of cases during El Niño months and eight have a significant negative correlation with ONI.
Conclusions: In Colombia, there exists a relationship between leptospirosis and the excess and lack of rainfall related with ENSO. The contrasting results from each spatial scale, reinforce that leptospirosis is a multidimensional disease with high complex interactions among its determinants.

Key words: Leptospirosis; El Niño -Southern Oscillation; water-borne disease; zoonotic disease.

J Infect Dev Ctries 2019; 13(12):1108-1116. doi:10.3855/jidc.11702

(Received 28 May 2019 – Accepted 16 October 2019)

Introduction

Leptospirosis is a zoonotic disease caused by a bacteria of the genus *Leptospira*. It is estimated that annually 1.03 million cases occur with 58,900 fatalities worldwide [1]. Due to a growing population, lack of sanitary infrastructure and climatic conditions, the tropics and subtropics are especially prone to the disease [2]. In the region of the Americas the incidence of leptospirosis varies between 0.1 and 306.2 per 100,000 people [3]. In Colombia, leptospirosis is of mandatory report since 2007. Between the period of 2007 and 2015, the average annual incidence was 2.3 per 100,000 people, with the lowest being 1.62 in 2015 and the highest being 3.06 in 2011. Leptospirosis incidence in Colombia is high compared to other Latin American countries such as Brazil where the incidence rate for the period between 2010 and 2014 was 2.1 per 100,000 people; Mexico where it varied from 0.04 to 0.4 between 2000 and 2010; Ecuador where it was reported to be 0.5 between 1996 and 2005; and Venezuela where there is data available only for 2004 and 2005 with 0.4 cases per 100,000 people [4–7]. In Colombia, during the period between 2007 and 2015 there was a total of 9,460 confirmed cases of leptospirosis distributed in all its territory.

Leptospirosis, as many other infectious diseases, is the result of multiple factors interacting [8]. Of particular importance is the long survival periods of the bacteria outside their hosts, which can sometimes be months [9,10]. As a result, environmental factors greatly affect the number of leptospirosis cases and even outbreaks in different parts of the world [11–13]. Temperature, water and humidity are determinants in the maintenance of the bacteria; thus, rainfall and flood are crucial factors to understand the ecology of the disease [14,15]. At interannual timescales, El Niño-Southern Oscillation (ENSO) is the main modulator of Colombia's hydro-climatology [16]. In its cold phase (La Niña), ENSO is associated with increased rainfall and flooding, while in its warm phase (El Niño), it is related to decreased rainfall, higher temperatures, and droughts [17,18]. Some studies have examined the relationship between ENSO and infectious diseases like malaria and dengue, but there is no research to link ENSO and leptospirosis in the country at different spatial scales [19,20].

Our hypothesis is that ENSO influences human leptospirosis dynamics in Colombia; thus, our goal was to analyze the changes that occurred in number of cases and incidence rate of leptospirosis during La Niña and El Niño episodes in Colombia at three different spatial scales in the period between 2007 and 2015.

This paper presents results of the first analysis of the relationship between ENSO and leptospirosis in Colombia and moreover in South America at three spatial scales: national, departmental, and municipal.

Methodology

A cross-sectional retrospective study was performed. The free software R version 3.5.0 from the R foundation was used to perform preliminary data analysis on leptospirosis cases and climatic factors and to calculate incidences and annual cycles. For spatial representation, ArcGis was used. The analysis performed at the national, departmental and municipal level, were:

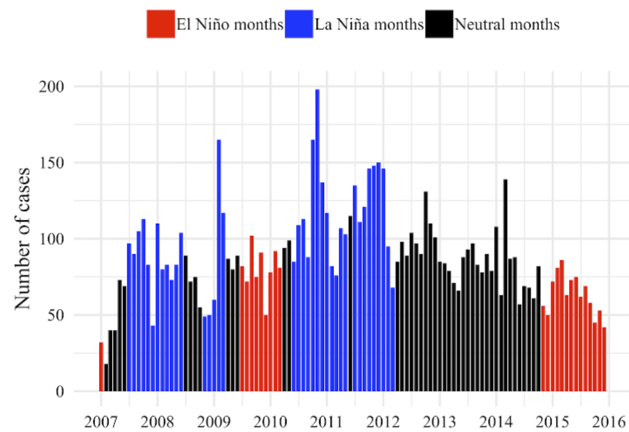
i) Calculation of total, annual, and monthly leptospirosis incidence rates.
ii) Construction of annual cycle of leptospirosis.
iii) Correlation between time series of ONI and time series of standardized number of leptospirosis cases.
iv) Lagged cross correlation among standardized monthly cases and ONI (lags from 1 to 12).
v) Comparison of changes (in percentage) of number of cases between Neutral periods with El Niño and Neutral periods with La Niña.

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 total incidence rate for nine years, the average population of the nine years was used; to calculate the annual incidence rate, population data for individual years was used. For monthly incidence, population in June 30 was used for all months [21]. Annual cycle of leptospirosis was constructed using the monthly average of cases for the nine years of the study period.

For the correlations between the different time series, coefficients of Pearson correlation were calculated simultaneously. Further, coefficients of Pearson correlation were calculated for monthly lags running from 1 to 12 months.

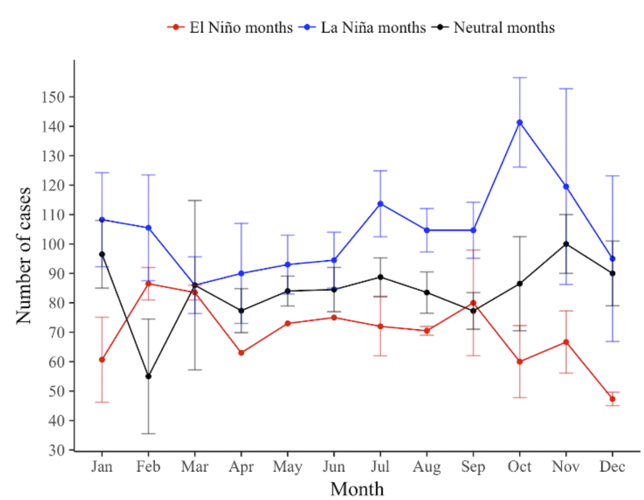
For comparisons of changes between Neutral periods with El Niño and La Niña periods, the average number of cases of each of the twelve months of the year in its different ENSO phases was calculated. After obtaining El Niño, La Niña, and Neutral average number of cases for each month, the results of the three different ENSO phases were compared. At the national level, the number of monthly cases in each of the different ENSO phases is depicted in Figure 1. Comparison of changes between neutral periods with El Niño and La Niña periods are shown in Figure 2. In

Figure 1. Monthly number of leptospirosis cases for Colombia in the period 2007 to 2015.



Color corresponds to El Niño (red), La Niña (blue), normal or Neutral (black).

Figure 2. Leptospirosis cases in Colombia, aggregated for months classified as El Niño, La Niña, and Neutral.



Average number of cases of each of the twelve months of the year in its different ENSO phases.

departmental and municipal levels, the percentage of changes between El Niño and Neutral periods and between La Niña and Neutral periods were calculated. The result of the analysis at the departmental level is illustrated in maps in Figure 3. This figure has two maps, one showing the increase in the number of cases during El Niño and another showing the increase in the number of cases during La Niña when compared to the Neutral periods for the nine years of study. When Pearson correlation coefficient between time series of ONI and time series of standardized number of cases was significant (at no lag), the department was highlighted with a weave. At the municipal level results are presented in a table indicating changes in percentage of number of cases during El Niño and/or La Niña compared to Neutral periods. Analysis similar to those presented in this study, can be performed in any country with high influence of ENSO whereas leptospirosis cases datasets can be accessed.

The study area is Colombia, a country located in the northern part of South America with latitude no higher than 12 degrees north and 4 degrees south. The country is crossed from south to north by the Andes mountain range. A large part of its territory has vegetation typical of areas with high humidity, about 50% is covered by forests [22]. The hydrometeorology of the country is characterized by two wet seasons during the year, one from March to May and the other from September to November [16]. Colombia is politically divided in departments and the departments are divided further into municipalities. In geographic terms, Colombia is divided into five main regions corresponding to homogeneous areas in terms of topography, climate, geology, geomorphology, soils, and culture. The continental regions are: Caribbean region, Pacific region, Andean region, Orinoco region and Amazon region [23].

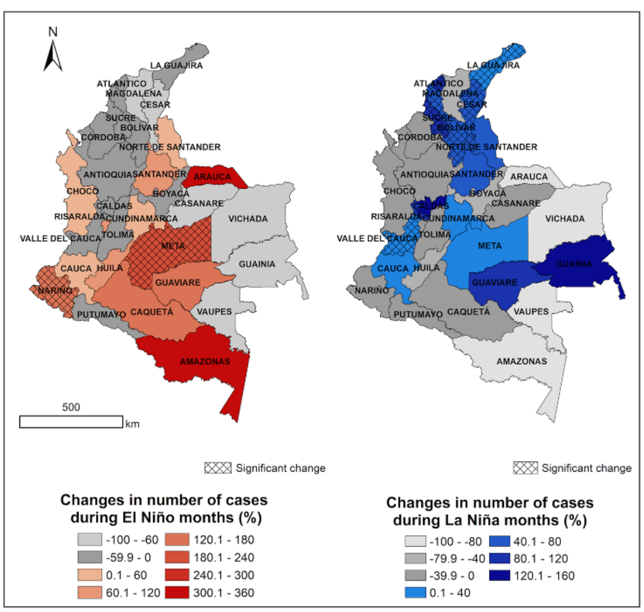


Figure 3. Changes in percentage of number of cases during El Niño (left) and La Niña (right) periods compared to neutral months at departmental level.

Data of leptospirosis cases was obtained from the National Public Health Surveillance System (SIVIGILA by its acronym in Spanish - http://portalsivigila.ins.gov.co), which is part of the National Institute of Health (INS by its acronym in Spanish - https://www.ins.gov.co/). In the analysis, all cases confirmed either by laboratory results or by epidemiological link were considered for the period between 2007 and 2015 [24]. Projected population for the country, departments, and municipalities for each year was taken from the National Department of Statistics (DANE by its acronym in Spanish - www.dane.gov.co). As an interannual climate variability indicator of ENSO we used the Oscillation Niño Index - ONI [25], obtained from the National Oceanographic and Atmospheric Administration (NOAA). Classification of each month as El Niño, La Niña or Neutral month was based on the NOAA criteria for ONI as follows: when five consecutive overlapping 3-month running mean periods have sea surface temperature anomalies above 0.5°C it is El Niño, below -0.5°C it is La Niña, and otherwise Neutral [26]. Climate data from hydro-meteorological stations at the municipal level was obtained from the Institute of Hydrology, Meteorology and Environmental Studies of Colombia (IDEAM by its acronym in Spanish - www.ideam.gov.co).

A more detailed analysis, comparing the annual cycle of leptospirosis cases and annual cycle of rainfall was performed for 25 municipalities (out of 1,122) of the country, focusing on those with higher incidences and higher number of cases during the study period (see Supplementary Figure 1, map for location of the selected municipalities). Annual cycle of rainfall was constructed using the average of accumulated daily rain for each month of the year for the nine years in the study period. Datasets for daily rainfall from each hydrometeorological station were obtained. Monthly rainfall time series were constructed by aggregating the daily rainfall datasets. For each municipality, data from several stations were used in order to avoid gaps or missing information. Monthly average among them was calculated to construct a complete time series of rainfall. Coefficients of Pearson correlation were calculated among the time series of monthly cases and rainfall series.

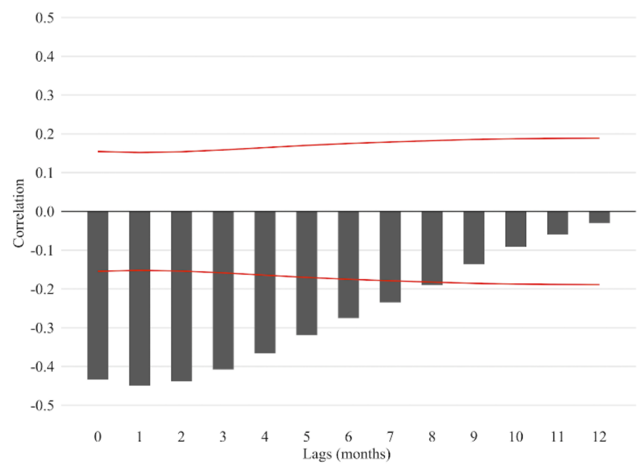
Results

National level

During the study time (2007-2015) NOAA reported three La Niña periods (July 2007 to June 2008, November 2008 to March 2009, June 2010 to March 2012) and two El Niño periods (July 2009 to April 2010, November 2014 to December 2015). During the interval from October to November 2010, Colombia experienced an enhanced wet season due to La Niña's influence. In the same period, Colombia experienced the maximum values of monthly leptospirosis cases (blue bars in Figure 1). While the lowest monthly leptospirosis cases occurred during El Niño periods (red bars in Figure 1). In the study time, during La Niña months, the average number of cases was 105, while during El Niño it was 70, and in Neutral months it was 84 (See Figure 2).

Cases of leptospirosis in Colombia are correlated with the ENSO index ONI (Figure 4). The *x* axis of the graph is lags in months, starting at zero (meaning no lags) and ending at 12 (meaning a relation lasting 12 months between the variables); the *y* axis is the Pearson coefficient correlation. Correlation between ONI index and leptospirosis cases for the study time is negative in Colombia. Increase in one variable (e.g higher precipitation due to negative ONI) is related with the decrease in the other variable (e.g decrease in number of cases). The correlation between the time series of ONI and leptospirosis is significant concomitant and from lag one to lag seven, see Figure 3 for detailed information.

Figure 4. Lagged cross correlogram between ONI and leptospirosis at national level.



p-values of significant lags ($p \leq 0.05$) (lag, p-value): 0, 0; 1, 0; 2, 0; 3, 0; 4, 0; 5, 0; 6, 0.01; 7, 0.02. Red lines represent the confidence interval.

Departmental level

A map indicating changes in percentage during La Niña and El Niño months compared to neutral months in all departments of Colombia are displayed in Figure 3. Number of cases and incidence in departments of Colombia is presented in supplementary material (see Supplementary Table 1).

During La Niña months, a rise in number of cases is observed in certain departments located in each of the five regions. In the Caribbean region, La Guajira, Cesar, Atlántico, Magdalena, Bolívar, Sucre; in the Pacific region Valle del Cauca and Cauca; in the Andean region Caldas, Risaralda, Cundinamarca, Santander and Norte de Santander; in the Orinoco region Meta; and in the Amazon region Guainía and Guaviare (Figure 3 right). Rises in number of cases comparing Neutral periods to El Niño months are observed in the departments of Chocó, Cauca and Nariño in the Pacific region; Santander, Norte de Santander, Cundinamarca, Quindío and Huila in the Andean region; Arauca and Meta in the Orinoco region; and in the departments of Guaviare, Caquetá and Amazonas in the Amazon region (Figure 3 left). Statistical significance is depicted with a weave.

Municipal level

Results at the municipal level showing rise in cases during El Niño and La Niña months are summarized in Table 1. Additionally, significance at the concomitant correlation between time series of ONI and time series of standardized leptospirosis cases is presented.

From the 25 municipalities analyzed, 17 have a rise in the number of cases during La Niña periods and from those, eight show a significant and negative correlation with ONI. There are eight municipalities that do not show increases during ENSO periods neither have a significant correlation with ONI. There are no municipalities with a rise in number of cases only during El Niño months.

In municipalities analyzed in the Caribbean region, Barranquilla, Cartagena, Santa Marta and Soledad, there is a rise in the number of cases during La Niña months, and there is also a negative significant correlation with ONI concomitantly. In Barranquilla, the intensification of cases occurs during El Niño months too. Located in the same region, Sabanas de San Ángel show rise in the number of cases during La Niña months but no significant correlation with ONI. Municipalities of Turbo, Apartadó and Carepa, in the department of Antioquia, do not show a rise in the number of cases during the different phases of ENSO compared to neutral months.

Municipalities analyzed in Valle del Cauca (in the Andean region) could be classified in three groups. The first group corresponds to those that respond with a rise in number of cases only during La Niña phase and includes: Cali, Riofrío and Versalles with a negative significant correlation between ONI and cases at no lags. The second group corresponds to municipalities that respond with a rise in number of cases in both ENSO phases and is compound by: Buga with a negative significant correlation between ONI and cases at no lags; Cartago, Roldanillo, and Bolívar with no significant concomitant correlation between ONI and cases. A third group includes the municipalities that do not respond to any of ENSO phases and includes Tuluá and El Cairo.

Municipalities of Pereira, in the Andean region, and San Jose del Guaviare, in the Amazon region bordering with the Orinoco region, have a rise in the number of cases in both ENSO phases. In the Pacific region, Buenaventura and Guapi show an increase in number of cases during La Niña periods with no significant concomitant correlation with ONI. From all the municipalities analyzed there are no results showing increases in number of leptospirosis cases only during El Niño periods.

Cross correlograms between time series of ONI and time series of standardized leptospirosis cases are presented as supplementary material (see Supplementary Figure 2). Total number of leptospirosis cases and total incidences at the municipal level are presented in supplementary material (see Supplementary Table 2).

Discussion

The main purpose of this research was to analyze the changes that occurred in the number of cases and incidence rate of leptospirosis during La Niña and El Niño episodes in Colombia at the national, departmental, and municipal levels in the period between 2007 and 2015. Our hypothesis is that ENSO influences human leptospirosis dynamics in Colombia.

At the national level, results indicate that there was a 25% rise in the monthly number of cases during La

Table 1. Percentage of changes in number of leptospirosis cases during La Niña and El Niño months compared to Neutral months and correlation between ONI and standardized leptospirosis cases at municipal level.

Id	Municipality	Department	Rise in number of cases during La Niña (%)	Rise in number of cases during El Niño (%)	Significant correlation with ONI at no lag	Region
1	Barranquilla	Atlántico	116.19	4.70	yes (-)	Caribbean region
2	Cartagena	Bolívar	78.55		yes (-)	
3	Santa Marta	Magdalena	67.11		yes (-)	
4	Soledad	Atlántico	35.71		yes (-)	
5	Sabanas de San Ángel	Magdalena	29300		no	
6	Turbo	Antioquia			no	
7	Apartadó	Antioquia			no	
8	Carepa	Antioquia			no	
9	Cali	Valle Del Cauca	59.46		yes (-)	Andean region
10	Buga	Valle Del Cauca	211.11	50	yes (-)	
11	Tuluá	Valle Del Cauca			no	
12	Riofrío	Valle Del Cauca	640		yes (-)	
13	Versalles	Valle Del Cauca	966.67		yes (-)	
14	Cartago	Valle Del Cauca	92.31	108.79	no	
15	Roldanillo	Valle Del Cauca	121.05	86.84	no	
16	Bolívar	Valle Del Cauca	566.67	1516.67	no	
17	El Cairo	Valle Del Cauca			no	
18	Pereira	Risaralda	9.09	5.74	no	
19	Pueblo Rico	Risaralda	741.82		no	
20	Mistrató	Risaralda			no	
21	Medellín	Antioquia			no	
22	Bogotá	Cundinamarca			no	
23	Buenaventura	Valle Del Cauca	26.47		no	Pacific region
24	Guapi	Cauca	100		no	
25	San José Del Guaviare	Guaviare	56.14	110.53	no	Amazon region

Niña periods, and a decrease of 17% during El Niño periods through the time frame studied. A significant negative correlation between ONI and cases at no lags and at lags one to seven was found. The significant negative correlation substantiates our claim that changes in leptospirosis dynamics are associated with La Niña.

It is especially important to mention that the La Niña episode of 2010-2011 was classified as strong [27–29]. It produced heavy flooding throughout Colombia, affecting approximately four million people, causing massive damages to infrastructure, and flooding agricultural lands [30]. During the peak of the 2010-2011 La Niña episode, in the months of November, December, and January, the total number of leptospirosis cases in Colombia also concurrently peaked.

Batchelor *et al.* (2012) proposed a conceptual model to illustrate the influence of rainfall on transmission of leptospirosis cases. The authors summarized the routes of human and animal transmission, based on time, in three groups: short lag, of 2 to 20 days; medium lag, of about 21 days, several times per year; extended lag, of weeks to months [31]. Considering these different delays, results of our study are consistent with the lags proposed by the authors. Notably, the results of our study strengthen the association that was made for the first time between leptospirosis and La Niña in the tropics by Weinberger *et al.* (2014) in New Caledonia, a Pacific island [32].

At the departmental level, results show that in departments located in the Caribbean coast of Colombia, there is a rise in monthly average number of cases during La Niña months. Besides this rise, the correlation between ONI and cases is significant concomitantly and at different lags (see supplementary table 3 with correlation coefficients and p-values). In general, the weather in the Caribbean coast is dry. Based on our results, the influence of La Niña with its accompanied rise in precipitation affects leptospirosis in this dry region. Considering that the country experiences intense precipitations during La Niña, the increased number of cases found during La Niña episodes in our study is consistent with our hypothesis. Rainfall, along with floods, are the most important factors associated with an increase in leptospirosis risk [14,33].

In Colombia, during El Niño months, the hydro-climatology is affected and there is seen a decline in precipitation, in the river discharge, and in the vegetation activity, along with a rise in average air temperature [16]. Some studies support the idea that rises in temperature have a positive effect on population growth of some rodent species [34–36], including the synanthropic ones (*Rattus rattus*, *Rattus norvegicus*, *Mus musculus*) which are one of the main sources of leptospirosis infection for humans. The rise in leptospirosis cases during El Niño periods seen in some departments of Colombia, may be attributed to a positive effect on the rodent population as they did in Guadeloupe island where they found a rise by four fold in the number of cases during El Niño events compared to other periods [37]. Another possible reasoning is that there are places in those departments that reached optimal temperatures for the bacteria during El Niño months, which in vitro are between 28-30ºC and sometimes up to 37ºC [11]. This could be the case of the department of Nariño where the average maximum multiannual temperature in some locations during Neutral months (years 1981 to 2010) is below the optimal for leptospirosis and during El Niño rises between 0.2 to 0.5 ºC [38] reaching optimal temperatures for bacterial survival and transmission. On the other hand, high temperatures could be a limiting factor for the survival of rodents and the bacteria itself. Pathogenic leptospiras can grow under laboratory conditions until 41-42ºC but could be killed by febrile animals at the same temperatures [39]. Previous hypothesis about rodents and optimal temperature for bacteria needs further research, because our study did not collect data on rodent abundance neither did it collect samples in the environment to test for the bacteria.

When looking a more detailed analysis in the 25 selected municipalities some contrasting results were found in terms of the relationship between leptospirosis and ENSO. In the north-east part of the department of Antioquia within the Caribbean region, near the border with Panamá, there is an important area, in epidemiological and economical aspects, called Urabá. We analyzed three of the municipalities that compound the region: Turbo, Carepa and Apartadó. In these municipalities, there is no rise in the number of cases when comparing El Niño or La Niña months with neutral months. Precipitation in the region of Urabá is high and does not have peaks, meaning that it is present throughout the year (see supplementary figure 3 for rainfall annual cycles). In this region, there are municipalities with areas that lack minimal sanitary conditions, like proper garbage disposal, limited access to potable water, etc; which can promote larger rodent populations. These factors potentially play a larger role in the upsurge of leptospirosis incidence than hydroclimatic fluctuations alone. Our results indicate that precipitation induced by ENSO is just one determining factor but is not the only one responsible for leptospirosis risk in this region.

The municipalities of Barranquilla, Cartagena, and Santa Marta, located in the north part of the Caribbean region, have a unimodal pattern of rainfall, with months that are very dry (see supplementary figure 3 for rainfall annual cycle). We found negative correlation between cases and ENSO leading us to think that in those municipalities leptospirosis incidence is highly affected by an excess of rainfall influenced by La Niña. Based on our results for the Caribbean coast, it can be inferred that some excess in precipitation where there is dry weather, could lead to a rise in the number of cases or even to outbreaks.

Cali is the capital and biggest city in Valle del Cauca. The influence of ENSO on this city is important in terms of leptospirosis cases, which rise during La Niña and at lags throughout 11 months. Cali, in its west side is bordered by the Cauca river, which has the second largest annual discharge and longitude in the country. Along the river, there is a 17 km dike. During the La Niña episode of 2010 – 2011, Cali suffered three main floods which covered most of the informal settlements located in the dike with water for weeks [40]. Based on our results relating wet periods to leptospirosis, it can be inferred that occurrence of La Niña puts this area in danger of Leptospirosis outbreaks. We conjecture that La Niña 2010-2011 affected municipalities located along the Cauca river with flood and a consequently rise in leptospirosis cases.

Some municipalities in Valle del Cauca saw a rise in the number of leptospirosis cases during El Niño as well. In addition to the positive effect that high temperatures have on rodent species carrying leptospirosis, the climatic conditions that El Niño brings motivates people to bathe in rivers and ponds more often, increasing the risk of exposition to the bacteria that could be contained in water where they survive for long periods [39].

Our contrasting results analyzing the relationship between leptospirosis and ENSO, are consistent with research conducted in India by Dhiman and Sarkar (2017) where varying results depending on spatial scales where found [41].

Conclusions

In Colombia, there exists a relationship between leptospirosis and the excess and lack of rainfall brought on by ENSO episodes. However, this relationship cannot be generalized across all spatial scales analyzed, as different regions respond differently to ENSO episodes. The results account for the immense diversity of Colombia in terms of geography, culture, socioeconomic status, and biodiversity which together makes a heterogeneous territory where health determinants interplay in different ways. Our results are further evidence that the changes induced by ENSO in the hydro meteorological regimes have impacts not only on environmental variables, but also on health and provision of healthcare. In a context of global climate change, the intensity and frequency of ENSO events is likely to increase [42], therefore healthcare systems should be prepared for the increase of cases of Leptospirosis. This is the first time a report is made about the association between ENSO and leptospirosis in South America at different spatial scales.

The different and contrasting results from each spatial scale, reinforce that leptospirosis is a multidimensional disease with high complex interactions among its determinants [33]. In order to develop accurate mathematical and statistical models to simulate infectious disease, particularly leptospirosis, researchers must consider its multiple causative factors beyond the hydroclimatic ones. Examining the multiple determinants of leptospirosis in an integrated way, may give a better understanding of its dynamics and thus give some insights for its control and prevention. A one health approach is needed for understanding leptospirosis dynamics.

Acknowledgements

The authors of this work thank the INS, in particular to the SIVIGILA, for providing the data of cases of leptospirosis; the IDEAM for providing the meteorological stations data at municipal level; Shornima KC for proof reading of the manuscript. C.A.M thanks the Departmento Administrativo de Ciencia, Tecnología e Innovación – Colciencias (http://www.colciencias.gov.co/) for the support in the 567 call for doctoral studies in Colombia. The funder had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript.

References

1. Costa F, Hagan JE, Calcagno J, Kane M, Torgerson P, Martinez-Silveira MS, Stein C, Abela-Ridder B, Ko AI (2015) Global morbidity and mortality of leptospirosis: A systematic review. PLoS Negl Trop Dis 9: 1–19.
2. Victoriano AFB, Smythe LD, Gloriani-Barzaga N, Cavinta LL, Kasai T, Limpakarnjanarat K, Ong BL, Gongal G, Hall J, Coulombe CA, Yanagihara Y, Yoshida SI, Adler B (2009) Leptospirosis in the Asia Pacific region. BMC Infect Dis 9: 147.

3. World Health Organization Leptospirosis Epidemiology Reference Group (LERG) (2011) Report of the Second Meeting of the Leptospirosis Burden Epidemiology Reference Group. Available: https://apps.who.int/iris/handle/10665/44588 Accessed: 10 October 2019
4. Costa F, Martinez-Silveira MS, Hagan JE, Hartskeerl RA, Reis MG dos, Ko AI (2012) Surveillance for leptospirosis in the Americas, 1996-2005: a review of data from ministries of health. Rev Panam Salud Pública 32: 169–177.
5. Gestal MC, Holban AM, Escalante S, Cevallos M (2015) Epidemiology of tropical neglected diseases in Ecuador in the last 20 years. PLoS One 10: 1–12.
6. Ministério da Saúde Brasil (2015) Epidemiological report for Leptospirosis Available: http://saude.gov.br/saude-de-a-z/leptospirose. Accessed: 10 October 2019. [Report in Portuguese].
7. Sánchez-Montes S, Espinosa-Martínez D V., Ríos-Muñoz CA, Berzunza-Cruz M, Becker I (2015) Leptospirosis in Mexico: Epidemiology and potential distribution of human cases. PLoS One 10: 1–16.
8. Laza Vásquez C (2006) Causality in epidemiology. Investig Andin 8: 12. [Article in Spanish].
9. Thibeaux R, Geroult S, Benezech C, Chabaud S, Soupé-Gilbert ME, Girault D, Bierque E, Goarant C (2017) Seeking the environmental source of Leptospirosis reveals durable bacterial viability in river soils. PLoS Negl Trop Dis 11: e0005414.
10. Saito M, Miyahara S, Villanueva SYAM, Aramaki N, Ikejiri M, Kobayashi Y, Guevarra JP, Masuzawa T, Gloriani NG, Yanagihar Y, Yoshida SI (2014) PCR and culture identification of pathogenic Leptospira spp. from coastal soil in leyte, Philippines, after a storm surge during super Typhoon Haiyan (Yolanda). Appl Environ Microbiol 80: 6926–6932.
11. Adler B (2015) Leptospira and leptospirosis. Adler B, editor Berlin: Springer. 293 p.
12. Lau CL, Smythe LD, Craig SB, Weinstein P (2010) Climate change, flooding, urbanisation and leptospirosis: fuelling the fire? Trans R Soc Trop Med Hyg 104:631–638.
13. Reis RB, Ribeiro GS, Felzemburgh RDM, Santana FS, Mohr S, Melendez AXT., Queiroz A, Santos AC, Ravines RR, Tassinari WS, Carvalho MS, Reis MG, Ko AI (2008) Impact of environment and social gradient on leptospira infection in urban slums. PLoS Negl Trop Dis 2: 11–18.
14. Cann KF, Thomas DR, Salmon RL, Wyn-Jones AP, Kay D (2013) Extreme water-related weather events and waterborne disease. Epidemiol Infect 141: 671–686.
15. Lau C, Smythe L, Weinstein P (2010) Leptospirosis: An emerging disease in travellers. Travel Med Infect Dis 8: 33–39.
16. Poveda G (2004) The hydroclimatology of Colombia: a synthesis from the inter-decadal scale to the diurnal scale. Rev la Acad Colomb Ciencias XXVIII: 201-222. [Article in Spanish].
17. Barreiro M, Díaz N (2011) Land-atmosphere coupling in El Niño influence over South America. Atmos Sci Lett 12: 351–355.
18. Poveda G, Álvarez DM, Rueda OA. (2011) Hydro-climatic variability over the Andes of Colombia associated with ENSO: a review of climatic processes and their impact on one of the Earth's most important biodiversity hotspots. Clim Dyn 36: 2233–2249.
19. Mantilla G, Oliveros H, Barnston AG (2009) The role of ENSO in understanding changes in Colombia's annual malaria burden by region, 1960-2006. Malar J 8: 6.
20. Poveda G, Rojas W, Quiñones ML, Vélez ID, Mantilla RI, Ruiz D, Zuluaga JS, Rua GL (2001) Coupling between annual and ENSO timescales in the malaria-climate association in Colombia. Environ Health Perspect 109: 489–493.
21. Departamento Administrativo Nacional de Estadísticas DANE (2009). National and Departmental Population Projections 2005 – 2020. 300 p. https://www.dane.gov.co/index.php/estadisticas-por-tema/demografia-y-poblacion/proyecciones-de-poblacion. Accessed: 10 October 2019. [Available in Spanish].
22. Sánchez-Cuervo AM, Aide TM, Clark ML, Etter A (2012) Land cover change in Colombia: Surprising forest recovery trends between 2001 and 2010. PLoS One 7: e43943.
23. Departamento Administrativo Nacional de Estadísticas DANE (2012) Volume I: Demography. In Statistical Atlas of Colombia. Available: http://sige.dane.gov.co/atlasestadistico/. Accesed: 10 October 2019. [Text in Spanish].
24. Instituto Nacional de Salud (2017) Public health surveillance protocol: leptospirosis. Available: https://www.ins.gov.co › Lineamientos › PRO Leptospirosis. Accessed: 10 October 2019. [Text in Spanish].
25. National Oceanic and Atmospheric Administration (2017) Historical El Niño / La Niña episodes (1950-present). Available: http://origin.cpc.ncep.noaa.gov/products/analysis_monitoring/ensostuff/ONI_v5.php. Accessed: 10 October 2019.
26. National Oceanic and Atmospheric Administration (2017) Equatorial Pacific Sea surface temperatures | teleconnections | national centers for environmental information (NCEI). Available: https://www.ncdc.noaa.gov/teleconnections/enso/indicators/sst.php. Accessed: 10 October 2019.
27. National Oceanic and Atmospheric Administration (2005) El Niño and La Niña ocean temperature patterns. Available: http://www.cpc.ncep.noaa.gov/products/analysis_monitoring/ensocycle/ensocycle.shtml. Accessed: 10 October 2019.
28. Trenberth KE (1997) The definition of El Niño. Bull Am Meteorol Soc 78: 2771–2777.
29. Zhang RH, Zheng F, Zhu J, Wang Z (2013) A successful real-time forecast of the 2010-11 la Niña event. Sci Rep 3: 1–7.
30. Hoyos N, Escobar J, Restrepo JC, Arango AM, Ortiz JC (2013) Impact of the 2010-2011 La Niña phenomenon in Colombia, South America: The human toll of an extreme weather event. Appl Geogr 39: 16–25.
31. Batchelor T, Stephenson T, Brown P, Amarakoon D, Taylor M (2012) Influence of climate variability on human leptospirosis cases in Jamaica. Clim Res 55: 79–90.
32. Weinberger D, Baroux N, Grangeon J-P, Ko AI, Goarant C (2014) El Niño Southern oscillation and leptospirosis outbreaks in New Caledonia. PLoS Negl Trop Dis 8: e2798.
33. Mwachui MA, Crump L, Hartskeerl R, Zinsstag J, Hattendorf J (2015) Environmental and behavioural determinants of leptospirosis transmission: A systematic review. PLoS Negl Trop Dis 9: e0003843.
34. Jiang G, Zhao T, Liu J, Xu L, Yu G, He H, Krebs CJ, Zhang Z (2011) Effects of ENSO-linked climate and vegetation on population dynamics of sympatric rodent species in semiarid grasslands of Inner Mongolia, China. Can J Zool 89: 678–691.
35. Meehan A (1984) Rats and mice : their biology and control. Felcourt East Grinstead: Rentokil Library 383 p.

36. Vadell M V., Gómez Villafañe IE, Cavia R (2014) Are life-history strategies of Norway rats (*Rattus norvegicus*) and house mice (*Mus musculus*) dependent on environmental characteristics? Wildl Res 41: 172.
37. Storck CH, Postic D, Lamaury I, Perez JM (2008) Changes in epidemiology of leptospirosis in 2003--2004, a two El Niño Southern Oscillation period, Guadeloupe archipelago, French West Indies. Epidemiol Infect 136: 1407–1415.
38. IDEAM: Institute of Hydrology, Meteorology and Environmental Studies of Colombia (2015) Scenarios of climate change for precipitation and temperature for Colombia 2011 - 2100. Scientific tools for decision making - complete technical study: Third communication on climate change. 279 p. [Report in Spanish].
39. Faine S, Adler B, Bolin C, Perolat P (1999) Leptospira and leptospirosis, 2nd edition. Melbourne: MedSci 293 p.
40. Fondo de Adaptación (2014) Macroprojects-Jarillón Cali. Available: http://sitio.fondoadaptacion.gov.co/index.php/programas-y-proyectos/macroproyectos/jarillon/antecedentes. Accessed: 10 October 2019. [Text in Spanish].
41. Dhiman RC, Sarkar S (2017) El Niño Southern Oscillation as an early warning tool for malaria outbreaks in India. Malar J 16: 122.
42. IPCC: Intergovernmental Panel On Climate Change (2014) Climate change 2014: Synthesis report. Contrib Work Groups I, II III to Fifth Assess Rep Intergov Panel Clim Chang Core Writ Team, Pachauri RK, Meyer LA IPCC, Geneva, Switzerland, 151 p: 1–112. Available: https://archive.ipcc.ch/report/ar5/syr/. Accessed: 10 October 2019.

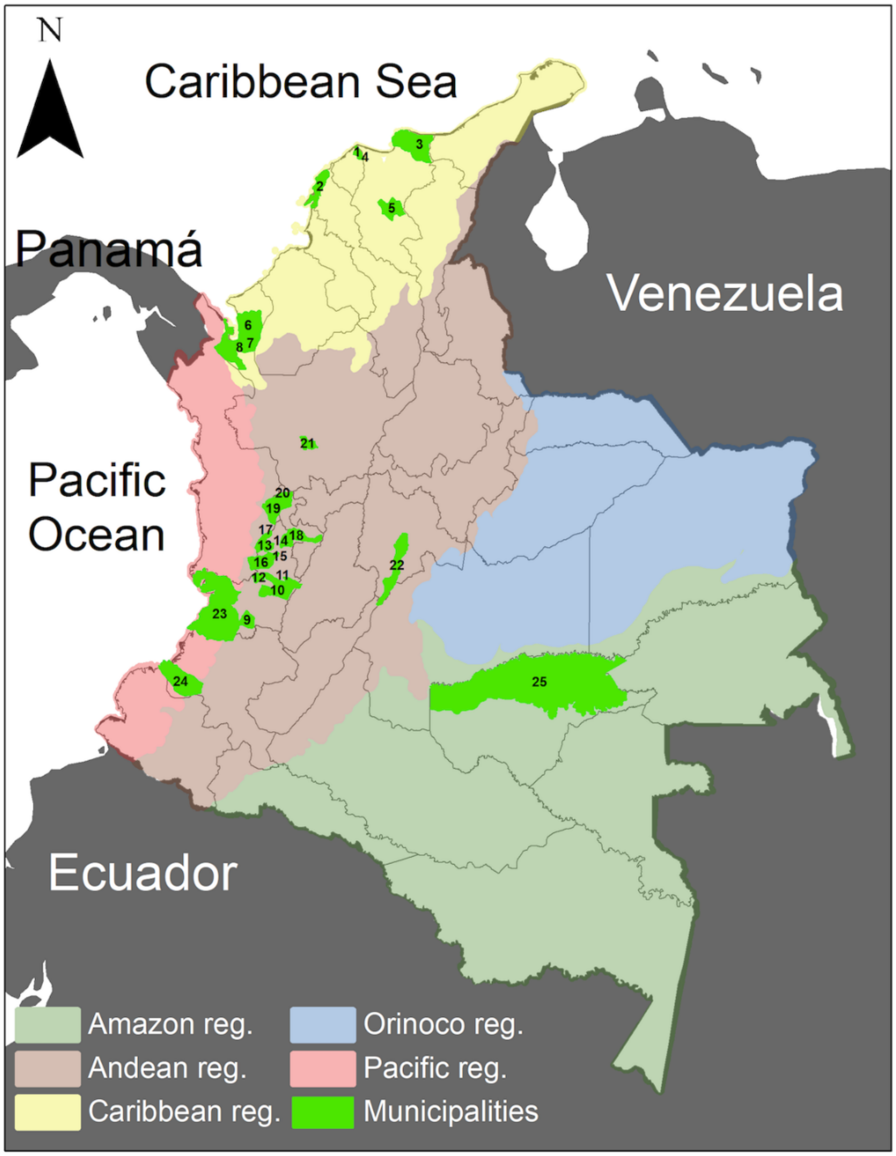
Corresponding author

Clara S Arias-Monsalve, DVM, MSc, PhD.
Universidad Nacional de Colombia, sede Medellín
Carrera 65 Nro. 59A-110 Bloque 20, oficina 204, Medellín, Colombia
Tel: (57) 313 645 40 77, (574) 430 91 34
Email: csariasm@unal.edu.co

Conflict of interests: No conflict of interests is declared.

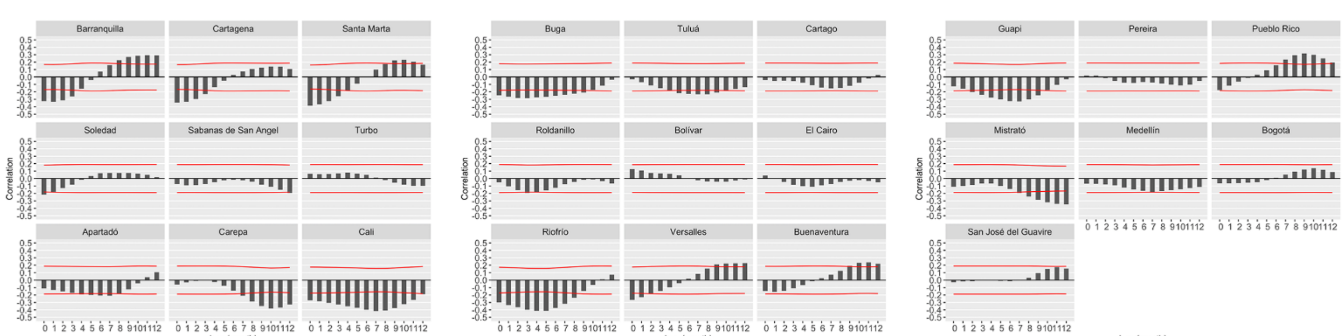
Annex – Supplementary Items

Supplementary Figure 1. Map with location of the 25 municipalities under further study.

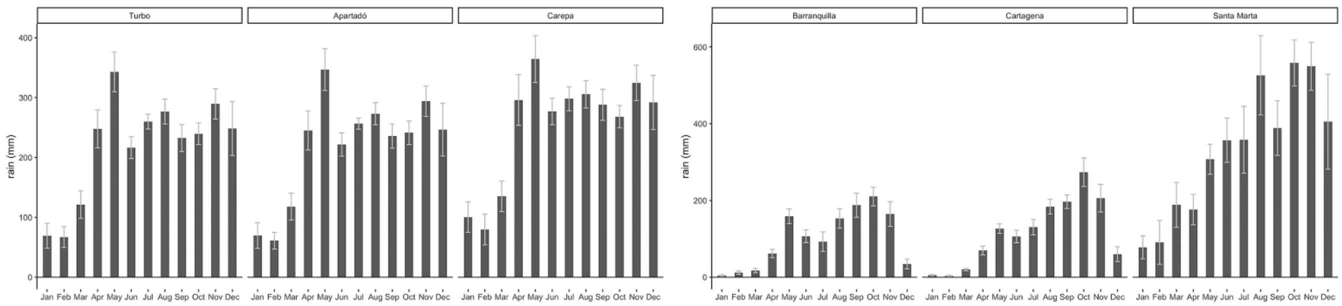


Municipality	ID
Barranquilla	1
Cartagena	2
Santa Marta	3
Soledad	4
Sabanas de San Ángel	5
Turbo	6
Apartadó	7
Carepa	8
Cali	9
Buga	10
Tuluá	11
Riofrío	12
Versalles	13
Cartago	14
Roldanillo	15
Bolívar	16
El Cairo	17
Pereira	18
Pueblo Rico	19
Mistrató	20
Medellín	21
Bogotá	22
Buenaventura	23
Guapi	24
San José Del Guaviare	25

Supplementary Figure 2. Correlograms of leptospirosis cases (standardized) and ONI at municipal level of the 25 selected.



Supplementary Figure 3. Rainfall annual cycle of some municipalities.



Supplementary Table 1. Total number of leptospirosis cases and total incidences at the departmental level.

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

Supplementary Table 2. Total number of leptospirosis cases and total incidences at the municipal level.

Id	Municipality	Department	Total number of cases	Total incidence (100,000 people)	Region
1	Barranquilla	Atlántico	612	50.65	Caribbean region
2	Cartagena	Bolívar	429	44.86	
3	Santa Marta	Magdalena	261	57.32	
4	Soledad	Atlántico	213	38.59	
5	Sabanas de San Ángel	Magdalena	142	883.41	
6	Turbo	Antioquia	392	272.83	
7	Apartadó	Antioquia	285	179.82	
8	Carepa	Antioquia	79	156.43	
9	Cali	Valle Del Cauca	682	30.05	Andean region
10	Buga	Valle Del Cauca	158	136.31	
11	Tuluá	Valle Del Cauca	163	80.79	
12	Riofrío	Valle Del Cauca	32	203.74	
13	Versalles	Valle Del Cauca	15	196.70	
14	Cartago	Valle Del Cauca	155	119.90	
15	Roldanillo	Valle Del Cauca	78	232.60	
16	Bolívar	Valle Del Cauca	46	323.92	
17	El Cairo	Valle Del Cauca	34	349.75	
18	Pereira	Risaralda	237	51.57	
19	Pueblo Rico	Risaralda	203	1597.60	
20	Mistrató	Risaralda	33	209.82	
21	Medellín	Antioquia	264	11.15	
22	Bogotá	Cundinamarca	227	3.04	
23	Buenaventura	Valle Del Cauca	153	41.31	Pacific region
24	Guapi	Cauca	80	272.60	
25	San José Del Guaviare	Guaviare	448	742.51	Amazon region

Supplementary Table 3. Correlation between leptospirosis and ONI at departmental level.

Department	Rise in number of cases during La Niña months (%)	Rise in number of cases during El Niño months (%)	Correlation between ONI and standardized leptospirosis cases		
			Lag (months)	correlation	p-value
Amazonas	No	346.15		Not significant	
Antioquia	No	No		Not significant	
Arauca	No	325		Not significant	
Atlántico	76.62	No	0	-0.40	0.00
			1	-0.35	0.00
			2	-0.28	0.00
			7	0.26	0.01
			8	0.31	0.00
			9	0.32	0.00
			10	0.29	0.00
			11	0.25	0.01
			12	0.22	0.02
Bolívar	26.66	No	0	-0.34	0.00
			1	-0.33	0.00
			2	-0.29	0.00
			3	-0.23	0.02
Boyacá	No	No	12	-0.22	0.03
Caldas	75.86	No	0	-0.21	0.03
			9	0.22	0.02
			10	0.26	0.01
			11	0.27	0.00
			12	0.28	0.00
Caquetá	No	125		Not significant	

Casanare	11.11	No	0	-0.24	0.01
			1	-0.23	0.01
			2	-0.22	0.02
			3	-0.21	0.03
			4	-0.20	0.04
			5	-0.19	0.05
Cauca	34.29	No	3	-0.19	0.05
			4	-0.24	0.01
			5	-0.31	0.00
			6	-0.35	0.00
			7	-0.38	0.00
			8	-0.36	0.00
			9	-0.32	0.00
			10	-0.26	0.01
Cesar	38.93	No	0	-0.30	0.00
			1	-0.31	0.00
			2	-0.30	0.00
			3	-0.29	0.00
			4	-0.27	0.01
			5	-0.22	0.02
Chocó	No	No		Not significant	
Córdoba	25.25	No	9	-0.23	0.01
			10	-0.28	0.00
			11	-0.32	0.00
			12	-0.32	0.00
Cundinamarca	No	No		No	
Guainía	1200	No		No	
Guaviare	48.85	129.9	9	0.19	0.05
			10	0.25	0.01
			11	0.26	0.01
			12	0.24	0.01
Huila	No	85.11		Not significant	
La Guajira	27.54	No	0	-0.20	0.04
			1	-0.25	0.01
			2	-0.28	0.00
			3	-0.29	0.00
			4	-0.27	0.00
			5	-0.25	0.01
			6	-0.22	0.02
Magdalena	94	No	0	-0.34	0.00
			1	-0.35	0.00
			2	-0.32	0.00
			3	-0.26	0.01
			4	-0.19	0.05
Meta	No	134.78	0	0.22	0.03
			1	0.19	0.06
Nariño	No	159.62	0	0.26	0.01
			1	0.28	0.00
			2	0.30	0.00
			3	0.32	0.00
			4	0.35	0.00
			5	0.36	0.00
			6	0.35	0.00
			7	0.31	0.00
			8	0.26	0.01
			9	0.19	0.05
Norte de Santander	16.67	40	5	0.20	0.04

			6	0.25	0.01
			7	0.28	0.00
			8	0.27	0.01
			9	0.22	0.03
Putumayo	84.21	No	0	-0.36	0.00
			1	-0.33	0.00
			2	-0.27	0.01
			5	0.20	0.04
			6	0.25	0.01
			7	0.28	0.00
			8	0.27	0.01
			9	0.22	0.03
Quindío	No	No	4	0.19	0.05
			5	0.19	0.05
Risaralda	105.23	No	0	-0.21	0.03
			7	0.21	0.03
			8	0.26	0.01
			9	0.28	0.00
			10	0.25	0.01
			11	0.20	0.04
Santander	116.67	96.67	Not significant		
Sucre	153.25	No	0	-0.19	0.04
			1	-0.22	0.02
			2	-0.26	0.01
			3	-0.26	0.01
			4	-0.25	0.01
			5	-0.24	0.01
			6	-0.20	0.04
Tolima	No	No	12	-0.19	0.04
Valle del Cauca	56.89	No	0	-0.33	0.00
			1	-0.38	0.00
			2	-0.43	0.00
			3	-0.45	0.00
			4	-0.46	0.00
			5	-0.46	0.00
			6	-0.44	0.00
			7	-0.41	0.00
			8	-0.36	0.00
			9	-0.30	0.00
			10	-0.22	0.02
Vaupés	750	No	0	-0.58	0.01
			1	-0.52	0.03
			12	0.53	0.02
Vichada	No	No	Not significant		

Correlation between ONI and leptospirosis cases (standardized) at department level (lag in months, coefficient correlation, *p*-value). Only significant lags are shown. Rise in number of cases comparing Neutral months with La Niña and El Niño months are also shown.