LEPTOSPIROSIS'S TREND AND SEASONALITY IN BRAZIL: STATISTICAL ANALYSIS OF NOTIFIED CASES BETWEEN 2008 AND 2012

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ABSTRACT: Leptospirosis is endemic in tropical countries such as Brazil. In order to quantify the cases stemming the trend of this disease in Brazil, free of seasonal variations, we conducted a statistical analysis of the time series of cases reported monthly between January 2008 and December 2012. We conducted periodicity analysis and seasonal decomposition using data reported in SINAN (Notifiable Diseases Information System). We create a graph with the original and the trend-cycle series, through which we make our analyzes and raise some hypotheses. Seasonal variables as the rain really can be associated with leptospirosis, but this disease may occurs independently of the rain and it is possible that the amount of cases could be greater if the search had been continued active throughout the dry season, as can be viewed in the comparative graph. This check is added to the results of previous studies, which warn of danger to be expected that cases of leptospirosis occur only during rainy periods and due to contact with rain or floods, which may decrease the active search for disease in dry periods and may neglect other possibilities of disease transmission.

KEY WORDS: Leptospirosis; Epidemiology, Descriptive; Neglected Diseases; Environmental Health.

TENDÊNCIA E SAZONALIDADE DA LEPTOSPIROSE NO BRASIL: ANÁLISE ESTATÍSTICA DOS CASOS NOTIFICADOS ENTRE 2008 E 2012

RESUMO: A leptospirose é endêmica em países tropicais como o Brasil. Para quantificar os casos decorrentes de sua tendência no Brasil, livre de variações sazonais, foi realizada uma análise estatística da série temporal de casos notificados entre janeiro de 2008 e dezembro de 2012. Realizou-se análise de periodicidade e decomposição sazonal usando dados notificados no SINAN (Sistema de Informação de Agravos de Notificação). Um gráfico comparativo contendo a série original e a série de tendência-ciclo foi criado para subsidiar as análises. Variáveis sazonais, como a precipitação, realmente podem estar associadas à leptospirose, mas esta doença pode ocorrer independentemente das chuvas e é possível que a quantidade de casos seja maior se a busca continuar ativa durante a estação seca, como pode ser visto no gráfico comparativo. Esta verificação se soma aos resultados de estudos anteriores que alertam para o perigo de se esperar que os casos de leptospirose ocorram apenas durante períodos de chuva e devido ao contato com chuva ou inundações, o que pode diminuir a busca ativa de doença em períodos de seca e pode negligenciar outras possibilidades de transmissão da doença.

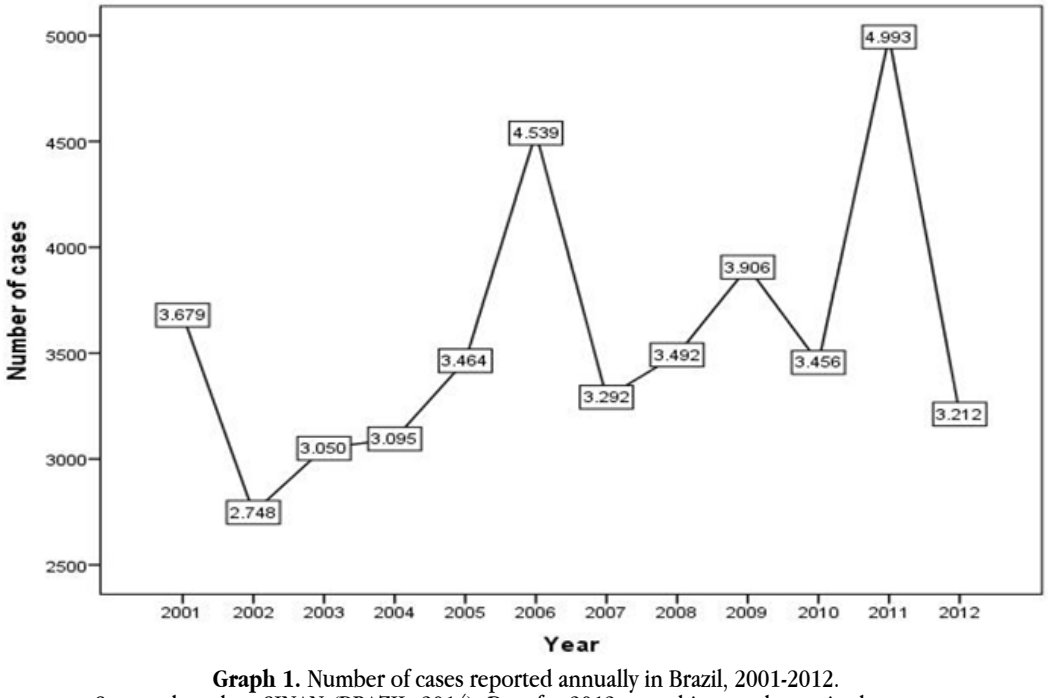
PALAVRAS-CHAVE: Doença Negligenciada; Epidemiologia Descritiva; Leptospirose; Saúde Ambiental.

INTRODUCTION

Leptospirosis is a febrile infectious disease that occurs worldwide (LEVETT, 2001; TASSINARI et al., 2004; SUPUTTAMONGKOL et al., 2010) and is endemic in tropical countries such as Brazil (BRAZIL, 2009). Its etiologic agent is the helical-shaped bacterium of the genus Leptospira (OLIVEIRA, D.; GUIMARÃES; MEDEIROS, 2009), which includes several pathogenic species (MARINHO, 2008). It is one of the diseases whose notification is compulsory, according to the provisions of Resolution GM/MS #1,271 of 2014 (BRAZIL, 2014), and is consolidated through SINAN - Notifiable Diseases Information System (BRAZIL, 2014). It is an extremely important zoonosis due to social and economic impacts related to high absenteeism rates and hospital costs; its incidence is high and its high lethality rate may even reach 50% on its more severe forms (BRAZIL, 2009). The Graph 1 present the number of cases reported annually in Brazil, since 2001.

make it easier the spread of rats and of their Leptospiras-contaminated urine (ÁVILA-PIRES, 2006). Souza et al. (2011) assert that the disease is endemic in all Brazilian states and epidemic in rainy seasons. However, there are documents (ÁVILA-PIRES, 2006; MELO et al., 2011; OLIVEIRA, T. et al., 2012) that warn about the dangers of misleading correlation of leptospirosis with the floods.

Ávila-Pires (2006) affirms that the practice of making a connection between flood or heavy rainfall and the occurrence of leptospirosis may lead to late diagnoses in dry seasons and to a misunderstanding of the disease's epidemiology, which can result in irregular inspection and control activities. Other researchers also reported not having found any connection between leptospirosis cases and meteorological events (MELO et al., 2011) or at least not in all analyzed years (OLIVEIRA, T. et al., 2012). Once one expects leptospirosis to occur in rain seasons, it is precisely in those periods that suspect cases will be better assessed and diagnostic tests will be required (ÁVILA-PIRES, 2006), and this is not due only



Graph 1. Number of cases reported annually in Brazil, 2001-2012.
Source: based on SINAN (BRAZIL, 2014). Data for 2012 are subject to change in the system.

The occurrence of leptospirosis is often associated with the flood events (TASSINARI et al., 2004; MACIEL et al., 2008; REIS, B. et al., 2008; BRAZIL, 2009; BRAZIL, 2010; ALBUQUERQUE FILHO et al., 2011; PELISSARI et al., 2011; REIS, M., 2011), since such events

to the disease's epidemiology but also by the effect of the searching for. Thus, one question arises: Disregarding the effect of the floods and heavy rains, that are seasonal variables, what would the behavior and the occurrence of the leptospirosis?

Whereas the disease can occur in any time of the year, the analysis of the leptospirosis behavior throughout year, free of seasonal and random variations, can be useful for knowing how many cases could be expected, even that no rain falls, i.e., how many cases one can expect stemming from the natural course of the disease. This information would be important to better understand the behavior of this disease and to help health professionals in organizing their activities in an active search for cases. In order to quantify the cases stemming the trend of this disease in Brazil, free of seasonal variations, we conducted a statistical analysis of the time series of cases reported monthly between January 2008 and December 2012, under the hypothesis that in dry season the amount of cases could be greater.

2 METHODOLOGY

2.1 STUDY DESIGN

This is a descriptive study of monthly leptospirosis cases reported in Brazil between 2008 and 2012. We conducted a time series analysis based in the seasonal decomposition, for remove the series cases that may be related to seasonal variables such as rain, and analyze how this series would be without these seasonal cases. We used the secondary data obtained from a computer system to record cases of diseases whose notification is compulsory in Brazil, the Notifiable Diseases Information System (SINAN). Access to this system is open to the public.

We analyzed the period from January 2008 to December 2012. Data were collected in January 2014. The SINAN have data since 2001, but we can't use the 2001-2007 data because, unfortunately, the system did not provide any information about 2007's monthly cases, only annual total. Therefore we lost one year of data in the middle of the series. Thus, we chose to perform the analysis with the data from 2008 to 2012, only. In the SINAN, cases of 2012 are subject to change and other cases that occurred in this year can still be included in the system.

2.2 OPERATIONALIZATION

For the purposes of this study, we defined as leptospirosis cases those that were notified in SINAN, due this system exhibits only confirmed cases. The confirmation can be either be by clinical/laboratory criteria or by clinical/epidemiological criteria. The parameter analyzed was the number of cases. We searched for the monthly cases in Brazil in the SINAN database (BRAZIL, 2014) for the entire period of study, that is, cases were tabulated by selection of the variable 'Month 1st symptom(s)'. Then, SINAN tables were exported to the software IBM SPSS Statistics 20, where a database was set up and where statistical analyses were conducted.

2.3 STATISTICAL ANALYSIS

Previously, the existence of periodicity was determined through the following steps: 1) we produced a sequence graph with the number of cases (Y) and time in months (X) in order to perform analysis of the behavior of data according to the presence of a periodic component and in order to make a decision as to which model would be used in analyses (additive or multiplicative); 2) we performed analysis of the presence of periodicity, through autocorrelation function (ACF) and partial autocorrelation function (partial ACF); and 3) we confirmed the existence of periodicity in the series, conducting a spectrum analysis (periodogram and spectral density).

Autocorrelation is a function that measures a variable's correlation with itself, at two or more points in time (LATORRE; CARDOSO, 2001). Partial autocorrelation has the same principle, but correlation is verified after the effect of correlations on intermediate lags is removed, and it is obtained by Yule-Walker equations (WERNER; RIBEIRO, 2003).

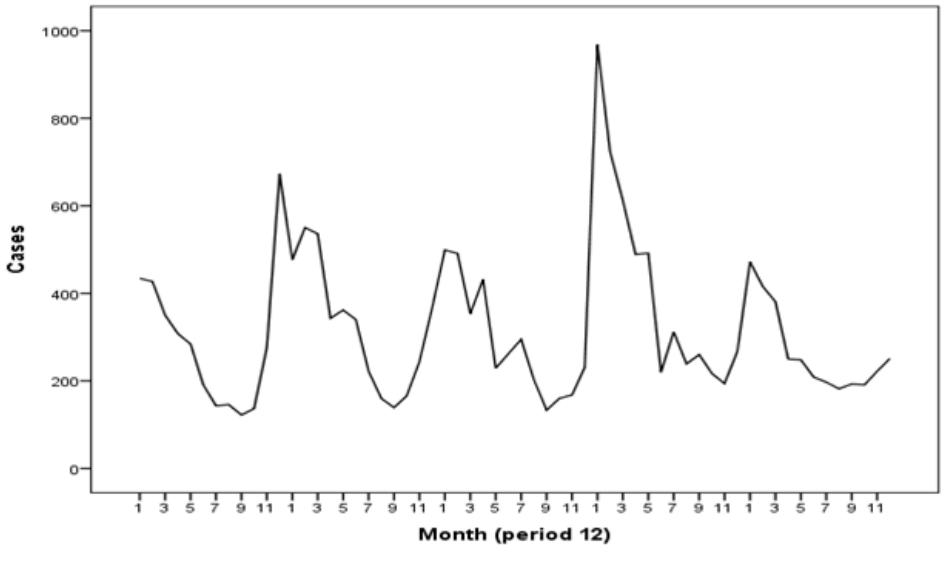
Once identified the existence of periodicity in the series, it was necessary to perform the seasonal decomposition in order to obtain a series free of seasonality. This method decomposes the series (Y) into three components, separating trend-cyclical variations (TC), from seasonal variation (S), and random (E), as the Equation. (DONOVAN, 2000)

$$Y_t = TC_t + S_t + E_t \quad for\, t = 0,1,2,3,...,n \quad (1)$$

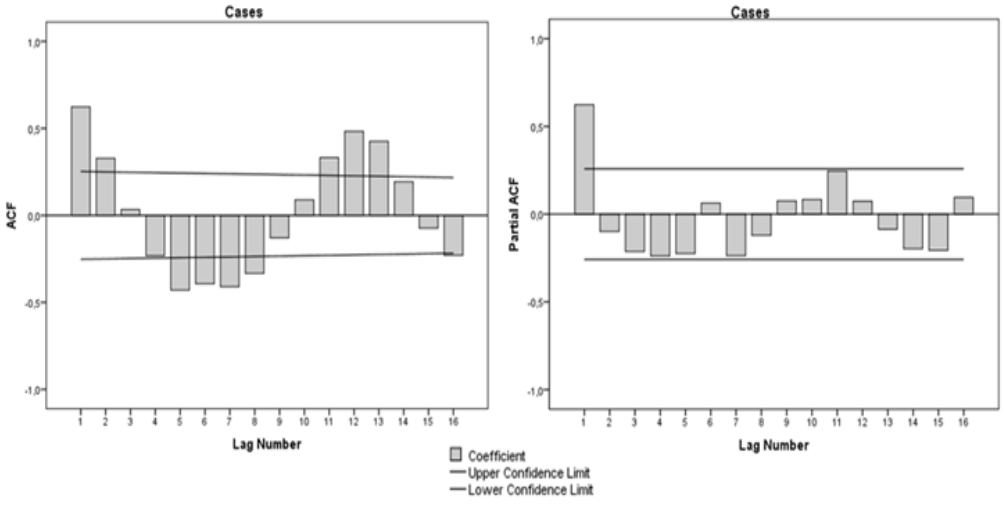
The data from the original series were corrected by decomposition, and the result was a series adjusted by seasonality, a smoothed trend-cycle series and a random variation series. Values in the series adjusted according to seasonality include random variations. As for the trend-cycle series, it did not integrate seasonal or random variations (FÁVERO; OLIVEIRA, M.; ÂNGELO, 2003). For this reason the trend-cycle series proved to be more appropriate for our analysis. We created a graph with both the original and the trend-cycle series; this graph has based our comparative analysis.

3 RESULTS

Based on the analysis of the sequence graph of the total cases notified monthly from January 2008 to December 2012, (Graph 2) we did not verify a periodic growth in variation throughout the series; that is, there was no evidence that the variation range increased according to sequence, which justifies the choose of an additive model for seasonal decomposition. The Autocorrelation Function (ACF), the Partial Autocorrelation Function (Partial ACF) (Graph 3) and the Spectrum Analysis (Graph 4) suggested the presence of a seasonal component in the time series. Therefore, the seasonal decomposition was performed.



Graph 2. Number of cases reported monthly in Brazil, 2008-2012.
Source: prepared by the authors based on SINAN data (BRAZIL, 2014).



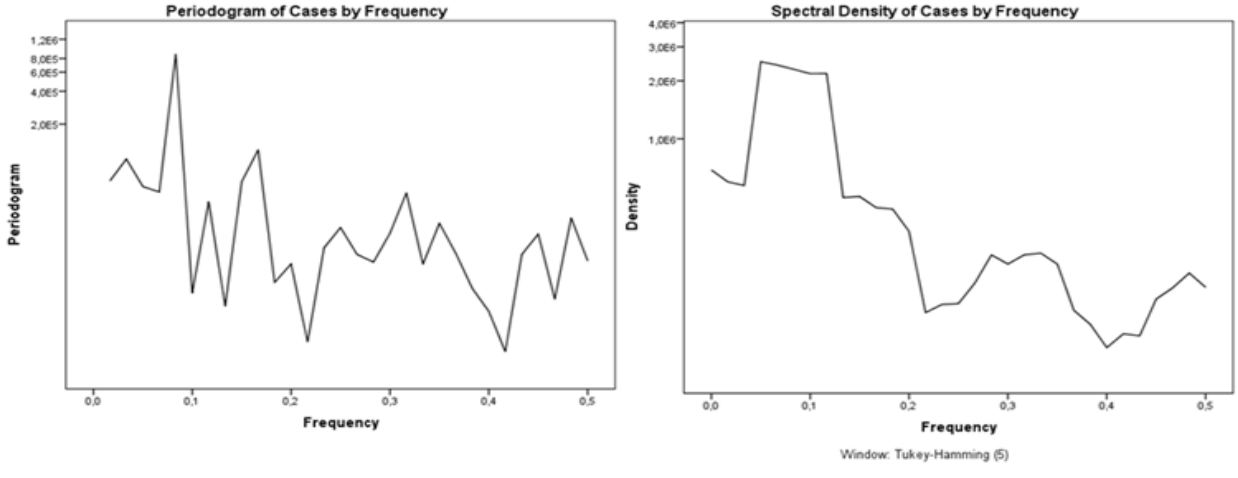
Graph 3. Autocorrelation (ACF) and Partial Autocorrelation (Partial ACF) Functions for Original Series.
Source: prepared by the authors based on SINAN data (BRAZIL, 2014).

By performing the seasonal decomposition, we obtained a corrected series, without the seasonal component. The Graph 5 illustrates the original series and the series of trend-cycle, smoothed. In this graph, the solid line represents the original series of cases and the dashed line represents the trend-cycle series created by seasonal decomposition.

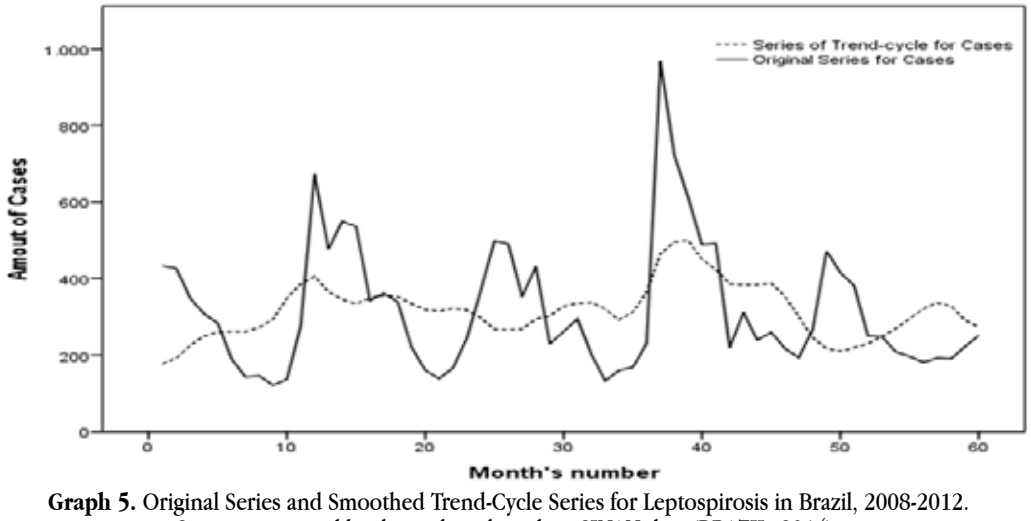
4 DISCUSSION

4.1 ON THE RESULTS

In this research we verified that notification of leptospirosis cases varies throughout the year. However, there are some notifications that occur regardless of



Graph 4. Spectrum Analysis for Original Series.
Source: prepared by the authors based on SINAN data (BRAZIL, 2014).



Graph 5. Original Series and Smoothed Trend-Cycle Series for Leptospirosis in Brazil, 2008-2012.
Source: prepared by the authors based on SINAN data (BRAZIL, 2014).

rainfall or floods. One can see in Graph 5 that the solid line peaks coincide with the rain period in the part of the Brazil, that occur normally between November and March, being more intense between December and January (MARENGO et al., [1995-2012]; RAO; SANTO; FRANCHITO, [1995-2012]), at least in the two regions wherein more notify leptospirosis cases according to data from SINAN (BRAZIL, 2014): South and Southeast Regions (data not show). Under the hypothesis that the search for disease is more active during periods of rain, therefore finding and notifying more cases, it can be said that the difference between the two lines in these peaks periods represents cases of the disease, which may occur due to rainy conditions.

On the other hand, when the amount of notifications (in the solid line) decreases, the amount plotted by the dashed line enhances. We suppose that, once finished the rainy period, the active search for the leptospirosis ends up and the amount of cases decreases, and do not reach, therefore, the amount that would be expected for the period (see dashed line). Thus, the diagnostics of this illness is hampered by the idea that, for the occurrence of the disease, the contact with rain is necessary, neglecting other forms of transmission, suspecting, thus, of other diseases. Therefore, we believe that the greatest amount fitted on the dashed line may represent cases of leptospirosis which could be notified if the active search continued during dry periods, i.e., can represent the cases that were not notified in dry seasons.

Through the Graph 5, we understand that the seasonal variables as the rain really can be associated with leptospirosis, but this disease may occur independently of the rain and it is possible that the amount of cases could be greater if the search had continued active throughout the dry season. Based in this interpretation, could be possible that leptospirosis really was being under diagnosed, and underreported, during dry seasons.

Maybe by the difficulty for performing the diagnosis due of the similarity of their symptoms with those of other febrile diseases is that one use the contact with flood as a differentiator for leptospirosis' diagnostic. For example, the Brazilian protocols for search of the disease (BRAZIL, 2009) include the screening of contact with flash floods and floods. However, this form of investigation can lead to underestimation of the number of cases and of the real social impact of the disease, especially in periods when heavy rains do not occur.

Despite floods, others forms of transmission can occur, not only during rain seasons, as by recreation or labor (OLIVEIRA, D.; GUIMARÃES; MEDEIROS, 2009), and by alimentation with contaminated foods (BRAZIL, 2009). About the rodents – the main reservoirs of Leptospiras – others species can participate of human transmission chain: dogs and cats (BRAZIL, 2009, 2010) – especially in rural zones (OLIVEIRA, D.; GUIMARÃES; MEDEIROS, 2009) –; animals for production such as cattle, swine and goats (BRAZIL, 2009) – mainly to livestock workers (OLIVEIRA, D.; GUIMARÃES; MEDEIROS, 2009). There are reports of *Leptospiras* even at sea mammals, as in Cameron's et al. study (CAMERON et al., 2008).

Knowing an estimated number of cases that may occur independently of the effects of rain, it is possible to improve the search for cases of the disease in times when rains or urban floods do not occur. What draws more attention is the amount of cases that could turn out to be diagnosed and reported during dry seasons, but are not, because, by that time, empirically, it is not expected that cases may occur.

The surveillance outside the rainy season is important because the active search, independent of the time of year, can have an effect on correct and early diagnosis of the disease, on reduction in the severity of cases, and on reduction of its lethality, which can reach 50%, among more severe forms. This could still cause economy to society – that would lose less in productivity and would suffer less from disease –, and to the health sector – because more severe cases tend to require long term care and more complex procedures, such as hospitalization. It is known that the hospital cost of leptospirosis is high and in some cases it is necessary an ICU (Intensive Care Unit) admission.

4.2 LIMITATIONS

It is worth noting that disease reporting conditions is variable into Brazilian States, and the notifications can be underestimated. Another factor that may lead to underestimating the number of reported leptospirosis cases is that, until 2012 there was no laboratory or clinical test used by the Brazilian Public Health System that was able to diagnose the disease safely in its initial stages. According to Albuquerque Filho et al. (2011), leptospirosis is often mistaken for other febrile diseases. It is estimated that in Brazil there are approximately 12 thousand leptospirosis cases annually, most of which are not confirmed or reported (REIS, M., 2011). We found reports that leptospirosis cases also being underreported in India (SETHI et al., 2010), Trinidad and Tobago (MOHAN; CHADEE, 2011) and Taiwan (YANG et al., 2012).

Furthermore, a case to be reported to the SINAN takes time. On average, it takes two years to consolidate

the data into the system. Cases for 2012 are subject to change and other cases occurred in this year can still be included in the system. Data for 2011 only consolidated in SINAN on January 30, 2014. However, we don't expect to be a major shift in the 2012 data, because we followed the consolidation of cases 2009, 2010 and 2011 and we found that there was little change in the number of cases entered into the system after one year term.

5 CONCLUSIONS

We pursue through this work alert the healthcare professionals about the situation of leptospirosis in Brazil, so they do not diminish the active search for disease during drought periods. To expect that cases of leptospirosis occur only during rainy periods and due to contact with rain or floods, may hinder access and adequate treatment of cases at these times in particular and contribute to the underreporting of leptospirosis.

We hope that our alert favors the surveillance actions, not only during periods of rain; and that active search may promote the access to the leptospirosis cases regardless of the time of the year. This should be done in all regions where this disease occurs.

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