Acta Tropica 125 (2013) 303–308

Contents lists available at SciVerse ScienceDirect

Acta Tropica

journal homepage: www.elsevier.com/locate/actatropica

Landscape determinants of Saint Louis encephalitis human infections in Córdoba city, Argentina during 2010

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A R T I C L E I N F O

Article history:
Received 8 October 2012
Received in revised form 3 December 2012
Accepted 7 December 2012
Available online xxx

Keywords:
Saint Louis encephalitis virus
Argentina
Geographical information systems
Human infections
Landscape elements

A B S T R A C T

Saint Louis encephalitis virus (SLEV) is endemic in Argentina. During 2005 an outbreak occurred in Córdoba. From January to April of 2010 a new outbreak occurred in Córdoba city with a lower magnitude than the one reported in 2005. Understanding the association of different landscape elements related to SLEV hosts and vectors in urban environments is important for identifying high risk areas for human infections, which was here evaluated. The current study uses a case–control approach at a household geographical location, considering symptomatic and asymptomatic human infections produced by SLEV during 2010 in Córdoba city. Geographical information systems and logistic regression analysis were used to study the distribution of infected human cases and their proximity to water bodies, vegetation abundance, agricultural fields and housing density classified as high/low density urban constructions. Population density at a neighborhood level was also analyzed as a demographic variable. Logistic regression analysis revealed vegetation abundance was significantly ($p < 0.01$) associated with the presence of human infections by SLEV. A map of probability of human infections in Córdoba city was derived from the logistic model. The model highlights areas that are more likely to experience SLEV infections. Landscape variables contributing to the outbreak were the proximity to places with vegetation abundance (parks, squares, riversides) and the presence of low density urban constructions, like residential areas. The population density analysis shows that SLEV infections are more likely to occur when population density by neighborhood is lower. These findings and the predictive map developed could be useful for public health surveillance and to improve prevention of vector–borne diseases.

1. Introduction

Saint Louis encephalitis virus (SLEV) is a mosquito-borne pathogen which belongs to family Flaviviridae, genus *Flavivirus*. SLEV has an extensive range in the Americas, and has been detected from isolations in mosquitoes, birds and mammals from Southern Canada to Argentina. SLEV is maintained by zoonotic transmission between birds and mosquitoes (Reisen, 2003); humans are considered dead-end hosts of the virus. Less than 1% of SLEV infections are clinically apparent (Tsai et al., 1987). Illness ranges in severity from transient fever and headache to severe meningoencephalitis and death.

In Argentina SLEV is endemic and extensively distributed. Serological evidence of SLEV infections fluctuates within different locations, affecting in some cases 50% of the population (Sabattini et al., 1998; Spinsanti et al., 2001, 2002). SLEV strains have been isolated from humans, *Culex* mosquitoes and wild rodents (Diaz et al., 2006; Sabattini et al., 1998) in Argentina. For this region, the principal vector is postulated to be *Culex quinquefasciatus* and the main avian hosts are Picui Ground Doves (*Columbina picui*) and Eared Doves (*Zenaida auriculata*) (Diaz, 2009; Diaz et al., 2006). However, Passerines bird species may also be involved in transmission (Diaz, 2009). In Córdoba province (central Argentina), where the population has a seroprevalence of 13.9% (Spinsanti et al., 2002), a human encephalitis outbreak caused by SLEV was reported in 2005 with 47 cases and 9 deaths (Spinsanti et al., 2008). In the following years only sporadic cases were registered, but during January to April of 2010 an outbreak occurred in Córdoba city with

Abbreviations: SLEV, Saint Louis encephalitis virus; WNV, West Nile virus; CSF, cerebrospinal fluid; NDVI, Normalized Difference Vegetation Index; LDC, low density urban constructions; HDC, high density urban constructions; GIS, geographic information systems.

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0001-706X/$ – see front matter © 2012 Elsevier B.V. All rights reserved.
http://dx.doi.org/10.1016/j.actatropica.2012.12.005

a lower magnitude than the one reported in 2005 (Vergara Cid et al., 2011).

Geographic information systems (GIS) have been extensively used for the surveillance of vector–borne diseases. Studies usually include spatial and temporal data in which environmental factors, landscape, climatic conditions and demography are analyzed in relation to *Flavivirus* dynamics among humans, mosquitoes, and zoonotic hosts (Bradley et al., 2008; Diuk-Wasser et al., 2006; Eisen and Lozano-Fuentes, 2009; Estallo et al., 2008, 2011; LaBeaud et al., 2008). Environmental conditions may regulate virus ecology due to their effect on the mosquito vectors and avian hosts necessary for virus transmission. Landscape attributes seem to have an important effect on West Nile virus (WNV, *Flavivirus*) disease dynamics and ecology by influencing host and vector presence. Therefore, factors such as vegetation abundance have been positively associated with human infections of WNV in urban and rural environments (Liu et al., 2008; Ruiz et al., 2004, 2007). Other environmental factors and land cover types like stream density, road density, slope, open water, agricultural and wetland areas were also classified as risk factors for WNV (Cooke et al., 2006; DeGroote et al., 2008; Liu et al., 2008). In addition, demographic patterns such as housing characteristics, population density, age and income have been associated to WNV human infections (Brownstein et al., 2002; DeGroote et al., 2008; Rochlin et al., 2011; Ruiz et al., 2004, 2007). Shaman et al. (2004) modeled land surface wetness and levels of SLEV transmission in humans, using a dynamic hydrology model in Florida. They found that drought followed by a wetting period is associated with SLEV human cases.

Even though there are numerous spatial and temporal studies related to WNV ecology and infection dynamics, there have been relatively few studies that have analyzed human SLEV infections. Therefore, understanding the patterns of SLEV hosts and vectors in urban environments will help us to identify high risk areas for human infections. The objective of our research is to identify landscape elements associated to the occurrence of SLEV human infections in Córdoba city throughout 2010.

2. Materials and methods

2.1. Study area

Córdoba city is located in the province of Córdoba, in the center of Argentina (31°24′S; 64°11′W), between 360 and 480 m above sea level (Fig. 1). It is an important urban settlement with a surface of 576 km^2 and with a population of 1,330,023 inhabitants as of the 2010 official census. Córdoba lies in a temperate semi-dry climate, with a mean annual precipitation level of 800 mm. The winter represents a markedly dry season, while in summer the most of precipitations occur. The Suquía River along with its creek La Cañada and other numerous water channels run through the city. The urban area is surrounded by agricultural fields which mainly produce vegetables, fruits and soy. The forest patches around the city have been drastically reduced in recent years.

2.2. Study subjects

The serological database used for the current study was obtained from different healthcare centers of Córdoba city that directly sent to our laboratory serum samples from symptomatic individuals who were suspected of *Flavivirus* infections during January to April of 2010. Besides of symptomatic infections, we included asymptomatic infections and study controls (non-infected individuals). The serum samples from these last two groups were also obtained from healthcare centers that had an agreement with our laboratory. People who went to the healthcare centers needed analysis of blood for different reasons and some of their serum was collected (August–September) and sent to our laboratory to detect antibodies against SLEV and other *Flavivirus*. The serological survey included 514 individuals from different areas of the city. To protect privacy, this study was designed as a non-associated anonymous survey, registering only date of sampling and address. Confirmed cases are defined by the presence of specific IgM antibody in cerebrospinal fluid (CSF) or serum plus ≥4-fold increase or decrease in neutralizing SLEV antibody titers in the serum (mainly IgG) between paired samples (obtained at least 1 week apart), while a probable case is defined by the demonstration of SLEV-IgM antibody in serum or CSF (Spinsanti et al., 2008). In this study 21 SLEV cases were classified as probable cases due to the absence of second serum samples.

2.3. Study design

In this study, a case–control design was selected at a household geographical location, considering a buffer area of 0.0225 km^2 (approximately 1.5 blocks) for each sample as the unit of analysis. The spatial scale of this model was based on the assumption that humans become infected by SLEV near their residence. The studied cases included 21 individuals infected with SLEV (with IgM and neutralizing antibodies). Study controls included 120 non-infected individuals (absence of antibodies against SLEV) randomly selected from the total of samples serologically analyzed for the year 2010. The explanatory variables for the analysis were chosen for being relevant to vector and host ecology for *Flavivirus* infections. Most of variables were Euclidean distances to important landscape elements like main vegetated areas, lotic and lentic bodies of water and agricultural fields, while the other two were absence/presence of high/low density urban constructions. We included agricultural fields as a variable because the production is under irrigation conditions, which generate moisture for mosquito breeding. Grech et al. (unpublished data) as well as Pires and Gleiser (2010) made mosquito and larvae samplings in agricultural fields around Córdoba city, and they found low to medium larvae density in irrigation canals.

Population density was included as an extra variable at a neighborhood level where presence and absence of cases were registered.

2.4. Data collection and processing

The satellite-derived variables were obtained from Landsat 5 (L5 TM) path/row 229/82. The satellite image, dated from February 2010 and it was obtained from the Argentine Space Agency (CONAE) catalog by academic cooperation. ENVI (Environment for Visualizing Images, Research Systems) 4.2 software (ENVI RS, 2004) was used for image processing. The images were georeferenced using a georeference image from the GLCF (Global Land Cover Facility). Subsequently, a subset area of 851 km^2 including Córdoba city and its surroundings was generated. From this image, five landscape elements were extracted using the software IDRISI Andes (Eastman, 2006). Supervised maximum likelihood classification was applied to produce agricultural fields and housing density classified as two categories: high/low density urban constructions. Lotic water bodies (Suquía River, La Cañada creek) and lentic water bodies (water channels and ponds) were obtained by a combination of maximum likelihood classification and georeferencing using Google Earth imagery and maps provided by the Municipality of Córdoba as reference. The Normalized Difference Vegetation Index (NDVI) was also calculated for the city and its surroundings. A threshold value of NDVI > 0.3 was selected according with literature where a marked positive correlation was observed between mosquitoes abundances of several species and places with NDVI > 0.3 (Lopes et al., 2005; Ozdenerol et al., 2008). Maps with Euclidean distance to the nearest source cell