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Spatio-temporal clustering of American Cutaneous Leishmaniasis in a rural municipality of Venezuela

Eva-Mary Rodríguez[a,*], Francisco Díaz[a], María-Virginia Pérez[b]

[a] Coordinación de Investigación, Centro de Investigación en Salud Pública "Jacinto Convit", Facultad de Medicina, Universidad Central de Venezuela, Venezuela
[b] Departamento de Parasitología, Escuela de Bioanálisis, Facultad de Medicina, Universidad Central de Venezuela, Venezuela

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ABSTRACT

Background: American Cutaneous Leishmaniasis (ACL) is an endemic disease in most Latin-American countries and a public health problem. The number of new cases in the world is thought to be about 1.5 million each year. A new epidemiologic pattern has been observed in the last years, in this sense, Geographic Information Systems (GIS) combined with methods of spatial analysis provide powerful new tools for understanding it.
Study objective: To investigate the spatial and temporal features of American Cutaneous Leishmaniasis, in an area known to be endemic.
Methods: We retrospectively conducted a space–time cluster analysis of incident cases of ACL using cross sectional data recorded from 1348 confirmed cases from 1992 to 2007 in a rural municipality in Venezuela, to test whether the cases were distributed randomly over space and time. We used the space–time permutation scan statistic and GIS. The identified clusters were analyzed for age, sex and job. These allowed us to investigate transmission patterns of ACL without an explicit entomological study.
Results: The analysis showed statistically significant space–time clusters of ACL (p-value < 0.01). The most likely cluster contained 35.47% of the total cases (n = 177) from 1995 to 1998. Four secondary clusters were identified for different periods. There was an indication of ACL cluster spread from the northeast to other points of the municipality. Three transmission patterns (domiciliary, peri-domiciliary and sylvatic environments) were identified along the study area.
Conclusion: The transmission of ACL has a spatial and temporal pattern in the studied area which is related to a complex cycle where the environment and other factors have a significant influence.

Introduction

Leishmaniasis constitutes a considerable public health problem. It is the second most important emerging and re-surging vector-borne protozoal disease, after malaria in terms of the number of people affected (Chaves and Pascual, 2006). Up to 350 million people are at risk in 88 countries around the world. It is considered that approximately 12 million people are currently infected, and 2 million new infections occur every year (WHO, 2009a). Leishmaniasis is a group of parasitic infectious diseases caused by several species of genus *Leishmania*, transmitted by the bite of infected *Phlebotomine* sandflies which primarily affect mammalian hosts. It includes four major eco-epidemiological entities: zoonotic and anthroponotic visceral leishmaniasis, zoonotic and anthroponotic tegumentary leishmaniasis. In anthroponotic forms, humans are considered to be the only source of infection for the sandfly vector; in zoonotic transmission cycles, animals are reservoirs which maintain and disseminate the *Leishmania* parasites (Desjeux, 2001).

There are two main clinical forms of leishmaniasis: the tegumentary and visceral forms, where the visceral disease is lethal if untreated (Fernando et al., 2001). Several clinical forms of tegumentary leishmaniasis are observed in America: cutaneous, mucocutaneous and disseminated forms. They are produced by at least fourteen different parasite species of the *Viannia* and *Leishmania* subgenus (Silveira et al., 2004). American Cutaneous Leishmaniasis (ACL) is the most frequent form of tegumentary leishmaniasis, and it is an endemic disease in most Latin-American countries, where nearly 200 million people in 24 countries, from the south of Texas to the north of Argentina, are at risk of infection, and 300,000 cases occur annually (WHO, 2009b).

Cutaneous forms of the disease normally produce skin ulcers on the exposed parts of the body, such as: the face, arms and legs. The disease can produce a large number of such ulcers – sometimes

* Corresponding author at: Calle Lara entre Calles Realidad y La Paz (ZIP 3028), Sanare, estado Lara, Venezuela. Tel.: +58 253 4490267; fax: +58 252 4490267.
E-mail address: evamary@gmail.com (E.-M. Rodríguez).

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up to 200 – causing a serious disability, and invariably, leaving the patient permanently scarred, a stigma that can cause serious social prejudice (WHO, 2009b). The pathological manifestations differ, both in their clinical expression and their severity, depending on the geographic area, the parasitic species, and the species of vector involved in transmission (OPS/OMS, 1994). Many *Leishmania* species seem to have a unique life cycle with different vectors (*Lutzomyia* genus) and/or an animal reservoir, and all of them have a particular geographic distribution (Cupolillo et al., 2003). Possibly, this is due to specificity factors of the *Leishmania* – vector and multiple interactions that happen within the vector's digestive system (Nieves and Rondón, 2007).

Cutaneous leishmaniasis has been considered an occupational disease because it has been associated mainly with males in productive age, agricultural activities, wood extraction, chestnut harvest, hunting, fishing, gold mining, research activities in tropical forests (Ampuero et al., 2005), establishment of new houses and communities adjacent to old-growth forest, road building, oil exploitation, deforestation and re-afforestation (Molineux, 1998), among others. The intrusion of man within the wild life cycle, frequently found in America, can result in a greater exposure to the vectors and, therefore, a greater risk of infection.

However, unprecedented widespread deforestation in recent decades has led to a gradual domiciliation of transmission throughout Latin America. As the old-growth forest close to the settlements is progressively disappearing, the number of cases related to professional activities is decreasing as well (Desjeux, 2001). The vegetation density and the deforestation pattern are related to ACL transmission in the vicinity of human dwellings, which have been suggested using remote sensing and geoprocessing techniques in Itapira, Brazil (Aparicio and Bitencourt, 2004). Hence, the transmission is not exclusively associated with the tropical humid forest. Given the appropriate conditions, the transmission may happen in intra or peri-domiciliary environments, in secondary forests and cultivated areas, as shown in the finding of American tegumentary leishmaniasis in coffee zones in Venezuela and Colombia (Palma, 2000). Since the beginning of the last decade, an increase of the total number of cases, a wider age groups distribution, similar frequency between men and women, and cases of whole families with the disease showing an intra and peri-domiciliary transmission pattern have been observed in Latin America (Ampuero et al., 2005).

For instance, in Venezuela the drastic increase in the number of zoonotic cutaneous leishmaniasis cases in recent decades, from 600 in 1995 to 2000 in 1998, is believed to be partly due to the spread of *L. braziliensis* from sylvan to peri-domiciliary and intra-domiciliary environments and even peri-urban foci (Feliciangeli, 1997). In this country, the number of registered annual cases has been maintained over 2400 cases since 1999, and the incidence rate is variable in each state. The highest incidence rates are present in: Cojedes, Lara, Yaracuy and Mérida states. In 2007, around half of the cases (41.77%) was observed in Lara state, which had the second highest incidence rate, and from that state, Andrés Eloy Blanco Municipality had the highest incidence rate (72.3 cases per 100,000 inhabitants); more than the incidence rate for Lara state (33.3 cases per 100,000 inhabitants) in the same year.

In spite of this situation, the spatial and temporal dynamics of the transmission patterns in the zone have not been characterized. For this, it is necessary to characterize the ACL presentation patterns at municipal level, including time and place variables simultaneously. The identification of significant clustering serves as the starting point for further investigation and the creation of hypothesized relations between the environment and the health outcome (Glass, 2000). A temporal and spatial picture of these dynamics can be generated to help identify possible areas of intervention, and applying control strategies that can have greater impact on the transmission, and consequently, in the incidence of this disease in the risk groups.

The purpose of this study was to investigate the spatial and temporal features of American Cutaneous Leishmaniasis in an area known to be endemic by answering the following specific questions: (1) Were there space–time clusters in Andrés Eloy Blanco Municipality (Lara, Venezuela) from 1992 to 2007? (2) Is there any evidence of ACL incidence spread from one place to another in this municipality? and (3) What was the transmission pattern in this area?

Methods

Study design

We retrospectively conducted a space–time cluster analysis of incident cases of ACL using cross-sectional data recorded from 1348 confirmed cases from 1992 to 2007 in a rural municipality in Venezuela, to test whether the cases were distributed randomly over space and time.

Study area

Andrés Eloy Blanco Municipality is located in the west central region of Venezuela, in Lara state. It has a total area of 708 km^2 with a regional area of 7.3% from the national area, and it has approximately 14.98% of the population from the state. Its geographical coordinates are: 8°6′ and 12°12′ northern latitude and 68°13′ and 71°17′ western longitude. It is a region of transition located between the mountainous systems of the Caribbean and the Venezuelan Andes. This municipality displays a medium topography with altitudes between 500 and 1700 m above sea level, with valleys moderately sloped to the northwest and delimited by the savannahs of Lara state.

The municipality is eminently rural, except for its capital which is urbanized. It has a population of approximately 42,067 inhabitants according to the 2001 census. It is a municipality with few migratory movements, and its growth rate has been maintained in the last two census periods between 2.6% and 2.4% (1981–1990, 1991–2001 respectively) (FUDECO, 2004). Most rural villages are difficult to access because of the unpaved roads.

Subjects

In the study, 1348 cases with confirmed diagnosis of ACL were included. The cases were patients assisted in the service of Leishmaniasis of the Jacinto Convit Research Center in Public Health (Central University of Venezuela) located in Sanare. They had positive diagnosis of cutaneous leishmaniasis by *Leishmania* identification through smear, culture, histopathology or polymerase chain reaction (PCR), and whose date of symptoms started between January 1st, 1992 and December 31st, 2007. When the probable place of infection was not found within the Andrés Eloy Blanco Municipality the cases were excluded from the study.

Population data

From each included case, the demographic data of patients such as: age, sex, education, activity, probable place of infection and clinic diagnosis were obtained from the patients' clinical history. We visited the probable place of infection, to take measures of its geographic location with a GPS 62 csx Garmin™ (Global Positioning System). These data were stored in an electronic questionnaire made in the Epi Info software version 6.04b and later exported to dBase and ASCII format, for further analysis.