Transmission of cutaneous leishmaniasis associated with cacao (*Theobroma cacao*) plantations in Tabasco

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Abstract

Introduction: *Tabasco is the Mexican state that reported the highest number of patients with leishmaniasis (37.4%) during the 1990-2011 period. About 90% of these cases occurred in La Chontalpa, with the Cunduacán municipality at first place. This region is characterized by housings located within cacao plantations.* **Objective:** *To determine if cacao crops constitute a risk factor for the transmission of leishmaniasis in that zone.* **Materials and methods:** *An analytical, retrospective study was conducted in 115 locations of Cunduacán; areas with or without leishmaniasis cases recorded between the years 2000 and 2011 and whether they had cacao crops were analyzed using a map where different crops were geo-referenced. The association magnitude was measured (odds ratio [OR]; 95% confidence interval [CI]).* **Results:** *In 2000-2011, leishmaniasis cases were reported in 77 (67.0%) Cunduacán locations, out of which 55 (71.4%) had cacao, 5 (6.5%) banana and 5 (6.5%) sugar cane plantations and 12 (15.6%) had no geo-referenced crops. We found cacao crops to be a risk factor for the transmission of leishmaniasis (OR: 3.438; 95% CI: 1.526-7.742).* **Conclusions:** *The probability of leishmaniasis transmission is higher in areas with cacao crops than in those without this type of crops.* (Gac Med Mex. 2014;150:494-502)

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KEY WORDS: *Leishmaniasis. Cutaneous leishmaniasis. Leishmania. Cacao.*

Introduction

Leishmaniasis is endemic in 88 countries and there are 12 million persons estimated to be infected in the world, with more than 350 million in at-risk situation. Annual incidence is estimated to be two million cases: 500,000 of visceral leishmaniasis (VL) and 1.5 million cutaneous leishmaniasis (CL)[1]. In America, cases have been reported from the south of the U.S.A. to the north of Argentina[2]. The disease is produced by a parasite of the *Leishmania* genus, transmitted by the bite of small diptera that in America belong to the *Lutzomya* genus. Transmission occurs when the vector feeds on blood of an infected individual or reservoir, and it can be anthroponotic (human-to-human) or zoonotic (animal-to-human)[3]. Leishmaniasis is divided in four clinical forms: localized cutaneous leishmaniasis (LCL), characterized by skin ulcers that heal in a few months (Fig. 1); disseminated cutaneous leishmaniasis (DCL), chronic, difficult to treat and characterized by nodules throughout the skin (Fig. 2); mucocutaneous leishmaniasis (MCL), with partial or total destruction of nose, mouth and throat mucosal membranes, and VL, the most serious form, which affects the spleen, the liver and the bone marrow. Elevated fever, weight loss, wasting, spleen and liver enlargement and anemia can occur, and it is mortal in two years if left untreated[4]. The distribution of leishmaniasis depends on the *Leishmania* species, on the ecology of the place of transmission, on exposure to the parasite and on human behavior. In the Old World, transmission is favored by sleeping outdoors or on the floor, without mosquito nets or by living in houses built with grass-based materials.

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Modified version reception: 27-10-2013
Date of acceptance: 04-02-2014

In the New World, epidemiology is complex, with variations in transmission cycles, reservoirs, vectors, clinical manifestations and response to treatment. The risk of leishmaniasis is increased by poverty, nutritional deprivation, housing deficiencies, peridomestic sanitation conditions and over-crowding. Transmission can vary due to temperature changes, precipitations and humidity, since these alter the distribution and amount of vectors and reservoirs. Additionally, man-made changes (urbanization, agricultural exploitation and settlements in tropical rainforest zones) can modify their distribution. Some years ago, it was described as an occupational disease, associated with the collection of chicle gum, military operations, road construction and new agricultural developments; however, deforestation has favored peridomestic, periurban and even urban transmission[3]. Sometimes, the *Lutzomya* species found in the woods are also abundant in agricultural crops (especially coffee and cacao), which represents a risk for people living and working in those places[5]. This indicates an adaptation capability of the vector, which, nevertheless, prefers shaded crops resembling primary rainforests[6]. Transmission has been demonstrated in crops such as coffee, cacao, sugar cane and banana[7]; bamboo canes fencing the houses have also been reported as a risk factor[8]. In Mexico, transmission has been found to be associated with the growth of coffee and the time dedicated to this kind of crop[9]. In Peru, a strong association has been demonstrated between transmission and peridomiciliary coffee (odds ratio [OR]: 7.83; 95% CI: 1.94-8.14), sugar cane (OR: 4.99; 95% CI: 2.42-10.27) and fruit trees plantations (OR: 3.62; 95% CI: 1.72-7.61)[10], and in Brazil, with the proximity to banana plantations (OR: 5.98; 95% CI: 1.49-39.84)[11]. Over the past few years, Tabasco has occupied the first place, with 37.4% of all cases reported in the country (Table 1)[12]. The highest incidence has been recorded in La Chontalpa, particularly in Cunduacán (Fig. 3). Currently, Tabasco is the leading producer of cacao *(Theobroma cacao)* in Mexico, especially the municipalities of La Chontalpa[13]. In this region, Chontal Mayans achieved Mesoamerica's highest cacao production during the pre-Columbian era[14]. It is possible for endemic zones to exist and to have persisted for many years; for example, in Venezuela, the existence of ulcers among cacao and coffee native pickers was known since the colonial period[15]. It is also possible for leishmaniasis to have existed since the flourishing of the Olmec culture and to have been associated with the growth of coffee, since a pre-Classic period urn (1200 BC-100 AD) has been described as showing "skin lesions" very similar to DCL[16]. Figure 4 shows the resemblance between this and a patient with DCL. Current cacao plantations produce a damp, less warm, poorly illuminated micro-environment and abundant detritus, which favor the proliferation of the vector, where *Lutzolya olmeca* adult specimens and larvae have been found. Although the reservoirs are not known, the *Didelphis* sp and bats are suspected to be involved. Due to the high number of cases, to the existence of the vector and possible reservoirs, as well as to the abundance of cacao crops surrounding the houses in Cunduacán, we decided to analyze if these plantations represent a risk factor for the transmission

Figure 1. *Patient with LCL in a rural community of the Cunduacán municipality, in Tabasco (Mexico); it is an ulcer with an evolution of 3 months.*

Figure 2. *Patient with DCL in a rural community of the Cunduacán municipality, in Tabasco (Mexico); these are lesions with 4 years evolution.*

of cutaneous leishmaniasis in this endemic area, which is the most important in the state of Tabasco and probably in Mexico.

Material and methods

Type of study

An epidemiological, analytical, retrospective study was conducted analyzing Cunduacán locations with or without cacao plantations and with cutaneous leishmaniasis cases recorded during the 2000-2011 period.

Site of study

The state of Tabasco is located in the south-eastern region of Mexico. From the Gulf of Mexico coastal flatlands to the mountains of northern Chiapas, it can be geographically demarcated between the 17° 15' and 18° 39' North latitude and 91° 00' and 94° 07' West longitude. It is divided in two large regions: the Grijalva and the Usumacinta regions. The Grijalva region comprises the following three sub-regions: Chontalpa, Centro and Sierra. Territorially speaking, the Chontalpa sub-region is the second most important of the state, since it covers 31.34% of Tabasco's territory; it has 593,668 inhabitants, out of which 241,168 belong to urban and 352,500 to rural areas. It is comprised by five municipalities: Cunduacán, Cárdenas, Comacalco, Huimanguillo and Paraíso. The land in this subregion is flat, with slight 40-m elevations, and abundant wetlands and mangrove swamps.

The Cunduacán municipality represents 2.4% of the state's surface and occupies the 12th place in the municipality extension scale; it borders with the Comacalco and Jalpa de Méndez municipalities to the North, and with Cárdenas and Comacalco to the East. The word *Cunduacán* comes from the Mayan expression *cum-ua-can,* which means "place of pots of corn and snakes". The climate is warm-humid, with abundant rainfall in summer and a mean annual temperature of 26.2 °C. The altitude of the municipality seat is 10 m above sea level. Thirty-five percent of the land is agricultural, 57% for live stock farming, 1% are forests and 7% are urban areas, bodies of water and improductive areas[17]. This municipality has 126,416 inhabitants, which account for 5.6% of the state population, and it comprises 115 active settlements[18]. The municipality has a flat topography, with the highest elevation being 40 m above sea level. Cunduacán is the third municipality with more hectares dedicated to cacao plantations, after Cárdenas

Table 1. Cases of leishmaniasis in Mexico by state

State	1990-2011
Aguascalientes	0
Baja California	0
Baja California Sur	1
Campeche	2,104
Coahuila	1
Colima	0
Chiapas	1,862
Chihuahua	3
Distrito Federal	5
Durango	3
Guanajuato	0
Guerrero	3
Hidalgo	0
Jalisco	37
México	0
Michoacán	1
Morelos	0
Nayarit	1,649
Nuevo León	2
Oaxaca	391
Puebla	3
Querétaro	0
Quintana Roo	5,022
San Luís Potosí	0
Sinaloa	117
Sonora	2
Tabasco	6,944
Tamaulipas	1
Tlaxcala	8
Veracruz	370
Yucatán	18
Zacatecas	0
Total	18,547

Adapted from: Sistema Único de Información para la Vigilancia Epidemiológica, CENAVECE, Mexico.

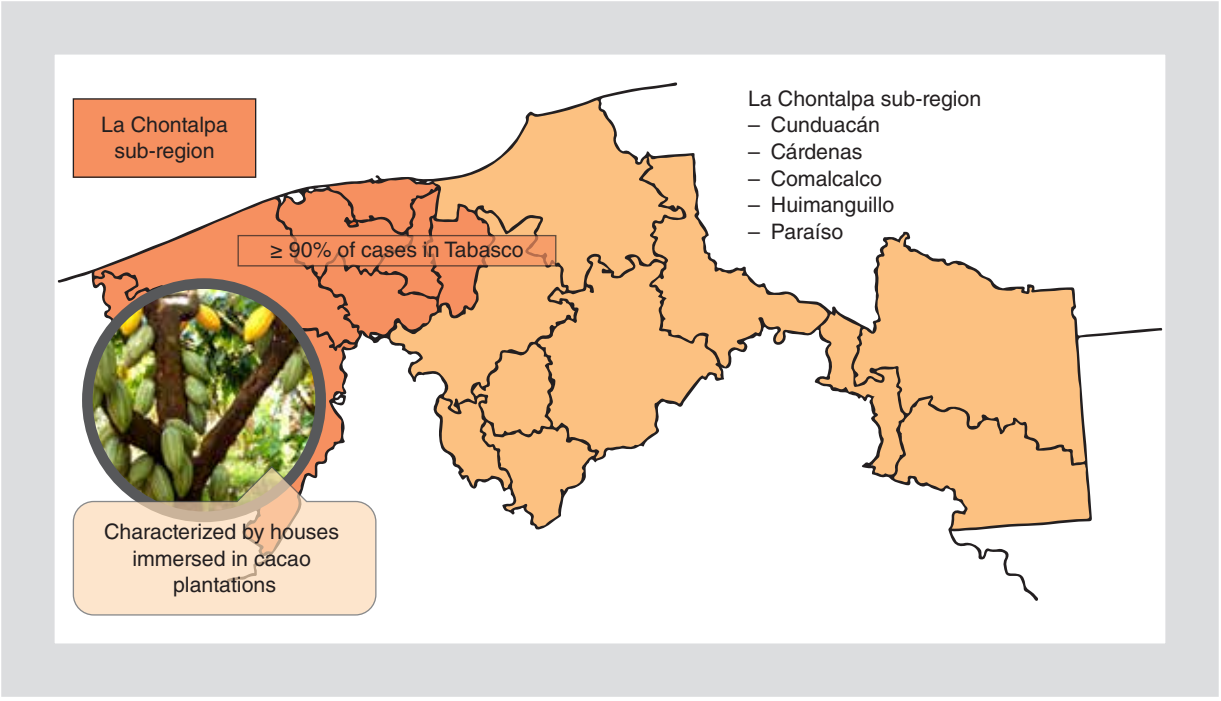

Figure 3. *La Chontalpa sub-region, in Tabasco. Leishmaniasis cases reported in Tabasco from 1990 to 2011.*

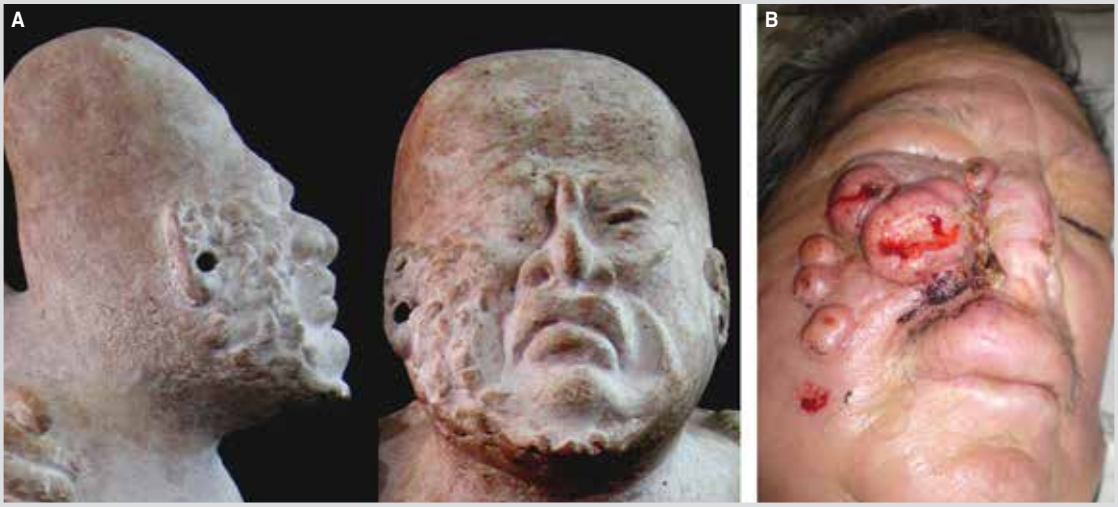

Figure 4. ***A:*** *Pre-Classic period (1200 BC-100 BC) Olmec urn found in La Venta (Tabasco).* ***B:*** *patient with DCL from the Chicozapote village at Comacalco, in Tabasco, with an evolution of 18 years.*

in first place and Comalcalco. In this municipality there are about 6,797 cultivated plots, with 5,501 producers[13].

In Cunduacán, cacao farming has a huge economical importance, both with regard to its commercialization and to local consumption. Cacao plantations are small plots with cacao grown at regular heights (5-8 m), which are covered by tall trees that provide them with shadow, thereby generating a damp microenvironment, which is less warm than the environment, with scarce light and abundant organic detritus in the soil. These conditions favor the survival and proliferation of the vector. In several settlements of this municipality, houses are practically immersed in the cacao plantations, favoring transmission to children and women, which is why leishmaniasis should no longer be considered exclusively an occupational disease.

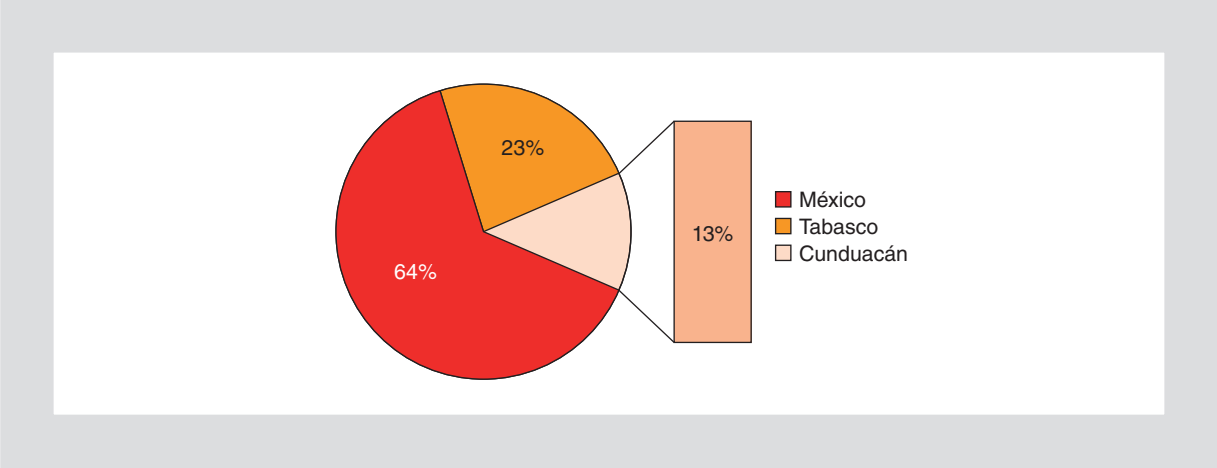

Figure 5. *Leishmaniasis cases in México, Tabasco and Cunduacán (2000-2011).*

The number of cases per location from 2000 to 2011 was taken from the Cunduacán Healthcare Jurisdiction Leishmaniasis Control Program Record of Cases, after application and registration of the project with the Tabasco State Ministry of Health. All cases recorded by the jurisdiction were clinically diagnosed as LCL and one as disseminated cutaneous leishmaniasis (DCL), using the imprint technique in all cases and applying Montenegro's intradermal reaction test to the patient with DCL. The cases were grouped by year and location according to the settlements catalogue of the Social Development Ministry *(Secretaría de Desarrollo Social,* SEDESOL)[18]. Subsequently, each location was identified as "with cacao" and "without cacao", following a map of the Cunduacán municipality where cacao, sugar cane, coconut and banana plantations were geo-referenced *(Mosaico de Cultivos Geo-referenciados del Municipio de Cunduacán,* of the State Information Office for Rural Sustainable Development *[Oficina Estatal de Información para el Desarrollo Rural Sustentable,* OEIDRUS]/State Committee of Statistical and Geographical Information for Rural Sustainable Development *[Comité Estatal de Información Estadística y Geográfica para el Desarrollo Rural Sustentable,* CEIEGDRUS]/National Information System for Rural Sustainable Development *[Sistema Nacional de Información para el Desarrollo Rural Sustentable,* SNIDRUS])[19]. Additionally, the zone was explored in order to visually verify the existence of cacao plantations. Following these criteria, four groups were obtained: locations with cases and cacao, locations with cases and without cacao, locations without cases and with cacao, and locations without cases and without cacao. To establish if cacao plantations are a risk factor for the occurrence of leishmaniasis cases, the odds ratio (OR) with a 95% CI was calculated. Locations with cases of leishmaniasis were marked with dots on the Cunduacán map where different crops, including cacao plantations, were geo-referenced.

Results

During the studied period (2000-2011), 9,605 leishmaniasis cases were recorded in the entire country, out of which 3,486 (36.0%) corresponded to the state of Tabasco. Of these, Cunduacán reported 1,225, which accounted for 13.0% of all cases in the country (Fig. 5).

Annualy-occurring cutaneous leishmaniasis cases from 2000 to 2011 in the Cunduacán municipality were observed to be reported predominantly in communities with cacao. Overall, 1,031 (84.0%) occurred in locations with cacao and only 194 (16.0%) in places where other types of crops were predominant (Table 2).

When the communities with cases presenting in the same period were analyzed, out of the 115 active locations, 77 (67%) were observed to record cases, while 38 (33%) did not. Of the communities with cases, 55 were located in areas with cacao plantations and 22 in areas without cacao plantations. In five locations of the 22 with cases but without cacao crops, there were predominantly banana plantations; in other five, there were sugar cane plantations and 12 did not have geo-referenced crops (Table 3).

As for the number of locations with cacao and without cacao that record cases on a yearly basis, cases were found to be recorded during this period in up to 48 places in one year (2002), at a 3:1 ratio; *i.e.*, the communities with cacao that recorded cases tripled

Table 2. Number of cutaneous leishmaniasis cases per year in locations with cacao and without cacao of the Cunduacán municipality, in Tabasco (Mexico)

	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	Total n (%)
Cases in locations with cacao	41	78	134	82	140	146	68	73	71	72	82	44	1,031 (84.0%)
Cases in locations without cacao	4	11	27	13	36	25	16	14	16	14	10	8	194 (16.0%)
Total	45	89	161	95	176	171	84	87	87	86	92	52	1,225 (100.0%)

Table 3. Locations with and without cacao that recorded, or not, cutaneous leishmaniasis cases in Cunduacán (Tabasco), during the 2000-2011 period

Locations	With cacao (n)	Without cacao (n)	Total (%)
With cases	55	22	77 (67.0%)
Without cases	16	22	38 (33.0%)
Total	71	44	115 (100.0%)

those that reported cases but did not have this type of crops. There were years when the ratio could rise up to 6:1 (Table 4).

When the main locations with more recorded cases during the 2000-2011 period were categorized, Huimango 2nd Section occupied the first place with 104, and the 10th place was for Libertad 1st Section, with 35 cases (Table 5). These 10 communities accounted for 45.0% of all cases reported in the entire municipality over the studied period.

In the Cunduacán municipality map (Fig. 6), where different crops were geo-referenced (OEIDRUS/CEIEG-DRUS/SNIDRUS)[19], such as cacao (brown color), sugar cane (green color), banana (purple color), citrus fruits (orange color) and coconut (pale green color), the geographic distribution of the 10 settlements with the highest number of cases (red numbered circles) and their location with regard to zones where cacao plantations are abundant can be observed. The map shows that all the marked places are located in areas where cacao plantations are abundant; however, the location occupying the 10th place is closer to the sugar cane crops.

Figure 7 shows the total number of locations with cacao and without cacao that reported cases or did not. These data were used to create the contingency table to obtain an odds ratio (OR: 3.438; 95% CI: 1.526-7.742) indicating that an association exists between locations with cacao plantations and leishmaniasis cases: locations with cacao plantations are 3.4-fold more likely to have cutáneous leishmaniasis cases than those without this type of crops.

Discussion

In some countries of Latin America, *Leishmania*-infected cases and vectors have been reported in areas with sugar cane, cacao, banana or coffee plantations;

Table 4. Locations of Cunduacán (Tabasco) with cacao and without cacao that recorded leishmaniasis cases, per year

Locations	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011
With cacao	20	24	36	33	32	35	27	27	31	25	26	24
Without cacao	3	7	12	5	12	6	10	6	9	6	5	4
Total	23	31	48	38	44	41	37	33	40	31	31	28

Table 5. Locations with the highest number of cutaneous leishmaniasis cases in the Cunduacán municipality, in Tabasco (Mexico) during the 2000-2011 period

N.°	Code	Crop	Locations	Number of cases
1	0028	Cacao	Huimango, 2nd Section	104
2	0049	Cacao	La Piedra, 2nd Section	80
3	0051	Cacao	La Piedra, 4th Section	55
4	0067	Cacao	Yoloxochitl, 2nd Section	51
5	0013	Cacao	Cúlico, 1st Section	49
6	0030	Cacao	José Ma. Pino Suárez	47
7	0007	Cacao	Carlos Rovirosa	46
8	0026	Cacao	Huimango, 1st Section	46
9	0034	Cacao	Mantilla	38
10	0032	Cacao	Libertad, 1st Section	35
			Total	551

even the presence of vegetation in the proximity of houses has been shown to favor leishmaniasis transmission[7]; however, few published studies have measured the association with crops such as coffee, sugar cane and banana[10,11]. In this zone, tropical rainforest vectors adaptation to secondary plantations has been proposed to have occurred as a result of deforestation; thus, the species of vectors found in primary forests

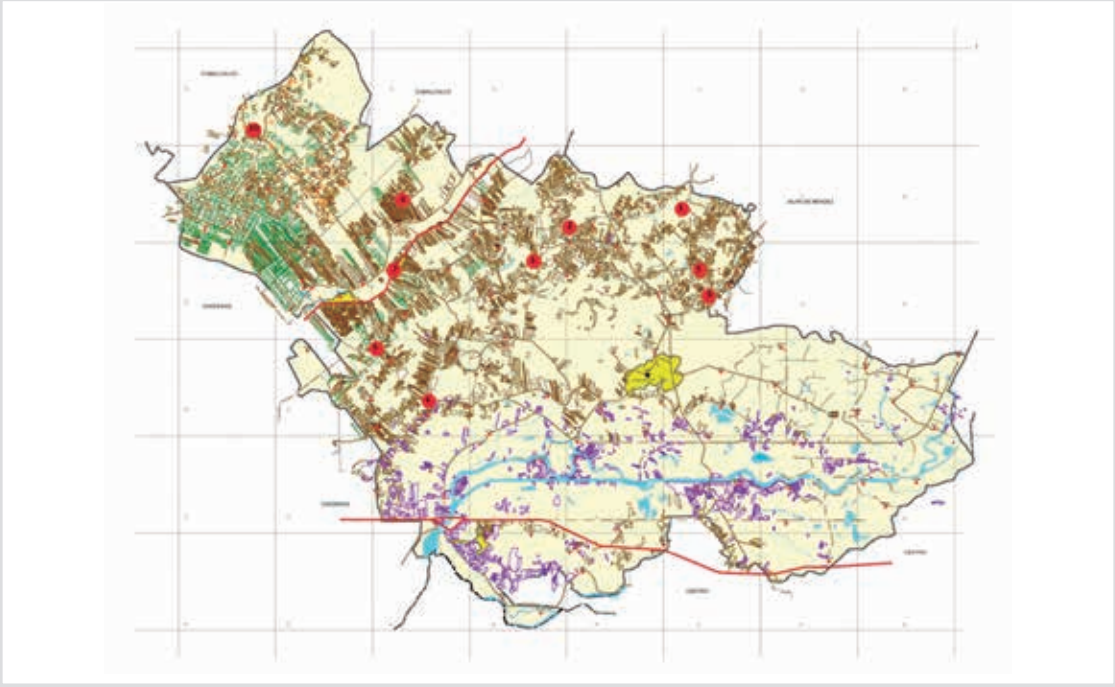

Figure 6. *Map of the Cunduacán municipality, showing the 10 settlements with the highest number of leishmaniasis cases in 2000-2011. (Adapted from the OEIDRUS/CEIEGDRUS/SNIDRUS Mosaico de Cultivos referenciados).*

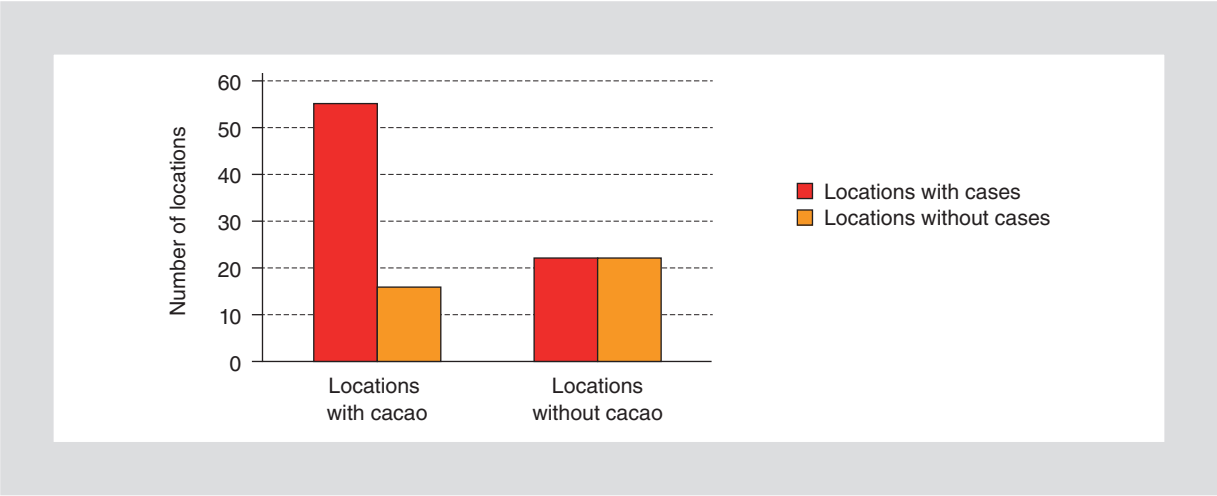

Figure 7. *Number of locations with cacao and without cacao where cases of cutaneous leishmaniasis were recorded. Cunduacán municipality, Tabasco, Mexico.*

can also be abundant in agricultural crops, such as coffee and cacao, suggesting that they have adapted to changes in the use of land due to human colonization, and that this has allowed for very close associations with human beings, favoring for them to be abundant in small settlements[5]. Leishmaniasis transmission in agricultural crops occurs due to the preference of the vector for places with less light and more humidity. This has been demonstrated by studying vector populations and some *Lutzomya* species have been found to prefer traditional coffe cultivation systems with shadow over intensive cultivation, where there is more sunlight[6]. In Mexico, there are no publications on risk factors incriminating agricultural crops; there is only one study, conducted in the state of Nayarit, where coffee harvesting and cultivation, as well as the time dedicated to this activity, have been associated with the transmission of the disease in this endemic zone[9].

In other countries of the world, trees and plantations that produce dark and damp places in the surroundings of houses have also been shown to favor leishmaniasis transmission; for example, in India, bamboo plantations (OR: 2.3; p = 0.001) are able to create this type of microenvironment and are also considered a source of fructose for phlebotomine fauna[8]. It is also possible for endemic zones to exist, and to have persisted for many rears. For example, there are records that, in Venezuela, the presence of ulcers among native cacao and coffee pickers was known since the colonial period, and this was attributed to "fallen leaves on the ground, good shadow and high humidity", and they also knew that it was caused by very tiny mosquitoes (gnats) that bit them when they removed the fallen leaves[15]. It is possibble for leishmaniasis to have been present in Tabasco since more remote ages, as there are archeological evidences suggesting its presence since the flourishing of the Olmec culture. According to a study conducted in the decade of the 80's by Dr. Martínez Marañón on an Olmec urn (1200 BC-100 AD) discovered in Tabasco, a symbolic depiction is found of an individual with skin lesions suggestive of the diffuse form of leishmaniasis (Fig. 4)[16]. Cacao crops were present in the zone since the development of the Olmec culture (1900-900 BC); Olmecs were the first to domesticate cacao and use it as a beverage and its growth persisted until the Spanish conquest, time at which La Chontalpa was the zone with the highest production of cacao in all Mesoamerica[13]. When the coexistence of cacao plantations and the disease during that period is considered, it can be assumed that leishmaniasis transmission has been occurring since that era and that la Chontalpa might even be an ancestral ecological niche.

The Cunduacán municipality, which is the most important endemic zone of the state of Tabasco and possibly of Mexico, is found in this zone, and cacao plantations constitute a risk factor for the transmission of cutaneous leishmaniasis; most cases (1031) (84.0%) occurred in communities with cacao plantations. The magnitude of the association of cacao plantations with the transmission of leishmaniasis found in this zone (OR: 3.438; 95% CI: 1.526-7.742) indicates that in communities with cacao plantations there is a 3.4-fold higher probability of leishmaniasis cases being reported that in those without this type of crops. These data are similar to those reported in Peru for fruit trees (OR: 3.62; 95% CI: 1.72-7.61), coffee (OR: 7.83; 95% CI: 3.57-17.17) and

sugar cane plantations (OR: 4.99; 95% CI: 2.42-10.27)[10]. The existence of areas with banana and sugar cane plantations reporting cases in Cunduacán allows for the assumption that the vector can survive in these types of crops; however, these crops were found not to be associated with transmission. These results differ from the association with banana plantations (OR: 5.98; 95% CI: 1.49-39.84) found in Brazil[11].

The possibility of more than one transmission pattern in the same region has been described in some countries. For example, there are Andean regions where intra- and peri-domiciliary, as well as rural transmission coexist. It is possible that, in Cunduacán, two types of transmission, intra- and peri-domiciliary, could be occurring; even the houses, practically immersed in cacao plantations, could be allowing for the vector to enter the housings. It is also possible for peri-domiciliary transmission to occur, since inhabitants cook and rest in hammocks outdoors, besides of collecting water and going to the bathroom outside their houses.

Other factor that might be driving the persistence of these transmission patterns is the difficulty to control the vector. The pesticides used affect beneficial insects as well, such as the cacao pollinators or those that control other types of plagues. Since cacao is the main source of income for some local residents, they refuse to have their plots fumigated.

Currently, local population is not the only one exposed to the risk of suffering leishmaniasis. An increasing number of eco-tourism visitors to the "chocolate route" are highly exposed to leishmaniasis, since the in the tours, they are offered to visit cacao *haciendas* in several municipalities of the La Chontalpa region, such as Nacajuca, Cunduacán, Jalpa de Méndez, Comacalco and Paraíso, where more than 90% of Tabasco's cutaneous leishmaniasis cases occur.

The continuous risk local residents live in, as well as the increasing number of persons at risk of suffering leishmaniasis in cacao plantations-associated regions of Tabasco, make the search for new control strategies a prioritary issue, which will require larger studies that include ecological characteristics of the zone and intra- and peri-domiciliary risk factors, as well as human behavior.

Acknowledgements

To the archeologist Rebeca Perales Vela, director of the Carlos Pellicer Cámara Regional Museum of Tabasco, for the Olmec urn photographs. To the OEIDRUS/CEIEGDRUS/SNIDRUS, for the Cunduacán geo-referenced crops map. To Dr. Luis Felipe Graham Zapata, secretary of heath of the state of Tabasco from 2006 to 2012, for all the logistic support provided.

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