

Short Report: Clinical Cutaneous Leishmaniasis Rates Are Associated with Household *Lutzomyia gomezi*, *Lu. Panamensis*, and *Lu. trapidoi* Abundance in Trinidad de Las Minas, Western Panama

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Abstract. American cutaneous leishmaniasis (ACL) transmission patterns have been increasingly associated with domestic and peridomestic environments. Here, we present results from an epidemiological survey of 94 people from 24 households in Trinidad de Las Minas, western Panama. We studied the role of sand fly abundance, housing quality, peridomicile landscape matrix, and vegetation structure on shaping household clinical ACL rate patterns at Trinidad de Las Minas. We found that sand fly abundance was significantly associated with household clinical ACL rates, with a 6% rate increase for each additional *Lutzomyia gomezi* sand fly found inside a domicile.

American cutaneous leishmaniasis (ACL) is an increasing public health concern in the New World.¹ Disease burden is primarily concentrated in the most socially excluded populations of Panama, a pattern common in Central America.^{2,3} In Panama ACL control is focused on the clinical treatment of human patients with skin lesions, without considering active surveillance and sand fly control.² Nevertheless, the increased evidence for domiciliary and peridomiciliary transmission calls for improving current vector control strategies.^{2,4,5}

Here, we present results from a baseline epidemiological survey, conducted before a sand fly control insecticide thermal fogging intervention. We surveyed 24 households (with 94 residents in total) at Trinidad de Las Minas (8°46'32"N; 79°59'45"W), western Panama province. Climate has a dry (December to March) and a rainy (April to November) season, the mean temperature is 26°C year-round and rainfall can vary between 28 and 570 mm³ per month. The survey was conducted during May 2010 in 24 houses (out of 128 houses in the village). Households were selected based on sand fly presence and presence of wild animal reservoirs (both confirmed by residents). The number of selected houses was limited by existing resources for the study, especially the availability of light traps (we only had 48 traps). On average (\pm SE) households had 3.91 \pm 0.09 individuals. Clinical ACL was considered when the next conditions were met: 1) *closed lesions*: presence of characteristic ACL scars assessed by experienced clinicians and parasitologists of the research team, and self-reported parasitologic positive diagnosis at a health center (confirmed by the attendance record to the local government health facility); 2) *active lesions* were parasitologically diagnosed at the Parasitology Department and Clinical Tropical Medicine unit of the Gorgas Institute in Panama and were clinically treated at the local government health facility.

From April to June 2010, sand flies were collected monthly using modified HP light-traps with an additional LED light.⁶ Monthly sand fly collections included one trap

placed 2 m above the ground for one night in the main bedroom of every household (domicile) and a second trap was placed at the same height, above vegetation, within 50 m of the house (i.e., peridomicile). Traps were set to sample sand flies from 6:00 PM to 6:00 AM. We also collected data on different aspects of the housing quality (materials, floor, electricity, ceiling and whether walls and doors had gaps or holes that allowed the entrance of insects), the peridomiciliary landscape matrix (presence of rubbish, water bodies, wood logs, cultivation of vegetables, kind of tree: palms, fruits, or ornamental) and vegetation structure (percentage of: canopy cover, canopy height, vegetation ground cover, bush cover, and shade, all measured following standard ecological protocols⁷) for each household. This study was approved by the National Review Board, Comité Nacional de Bioética de la Investigación, Instituto Conmemorativo Gorgas de Estudios de la Salud, Panamá City, Panamá (561 /CNBI/ICGES/06).

In the 94 people surveyed we found a total of 32 closed lesions and 6 active lesions. Combining closed and active lesions each household had an average (\pm SE) of 1.58 \pm 0.09 ACL cases. The most common sites of lesions were the legs and arms (58%), followed by lesions in the face (29%). Single lesions were observed in 75% of cases (range 1–3), and no apparent mucosal involvement was observed in this sample. Most of the active lesions were in children \leq 12 years of age (5 of 6; 83%).

To assess the role of sand fly abundance, housing quality, peridomicile landscape matrix, and vegetation structure on clinical ACL rates at surveyed households, we used Poisson rate generalized linear models (PRGLM).⁸ The PRGLMs have the advantage of accounting for household size (i.e., number of individuals living in a household)⁸ and residuals can be further inspected for unaccounted spatial autocorrelation.⁸ Given that we had 24 observations (households), i.e., at most 23 parameters could be estimated, we reduced the number of predictors by estimating the first principal component (pc) of a variance–covariance matrix,⁸ respectively, for the group of variables related to housing quality (DI), peridomicile landscape matrix (PI) and vegetation structure (EI). In all three sets of variables the first pc accounted for slightly over 40% of the variability, and in all cases the first pc could be interpreted as weighted averages

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TABLE 1

Model selection for the best entomological variable associated with household clinical American cutaneous leishmaniasis rates at Trinidad de Las Minas, Panama*

Entomological variable	AIC
Domiciliary sand fly abundance, DSFA (all species)	69.96
DSFA <i>Lutzomyia panamensis</i>	72.49
DSFA <i>Lu. Gomezi</i>	69.76
DSFA <i>Lu. Trapidoi</i>	70.97
Peridomiciliary sand fly abundance, PSFA (all species)	70.98
PSFA <i>Lu. panamensis</i>	73.46
PSFA <i>Lu. gomezi</i>	73.73
PSFA <i>Lu. trapidoi</i>	73.78

*AIC indicates the Akaike information criterion of each model. Minimum AIC is bolded.

for the presence of the different variables. We then fitted PRGLMs for different parameter combinations (including interactions and independent effects) of the first pc for DI, PI and EI with either: total (i.e., domiciliary + peridomiciliary, SFA), domiciliary (DSFA), and peridomiciliary (PSFA) sand fly abundance (which was defined as the average of the three trap nights during which sand flies were collected). After a process of model selection we found that infections were primarily associated with domiciliary sand fly abundance (Supplementary online information, Table S1). Further model selection (Table 1), considering the abundance of the three most dominant vector species in this sample: *Lutzomyia panamensis*, *Lutzomyia gomezi*, and *Lutzomyia trapidoi* (together these species accounted for over 60% of the 2,613 sand flies we caught in the total 144 trap-nights), showed that *Lu. gomezi* had the best association with household clinical ACL rates, where each additional sand fly found inside a house increased by 6% the rate of people with clinical ACL symptoms (Table 2). This model also met all the assumptions of the PRGLM⁸ and the residuals were not spatially autocorrelated (Moran's I = -0.051, $P > 0.511$), thus warranting statistically valid inferences.

Our observations emphasize patterns already described in Panama,² and expected in light of the fundamental role vectors play on the transmission of *Leishmania* spp. parasites,⁵ where the abundance of sand flies is closely associated with clinical *Leishmania* infections, even considering the potential bias introduced by the clinical diagnoses. Similar patterns have reported elsewhere in Latin America.^{9,10} *Lutzomyia gomezi*, the vector presenting the best association with household clinical ACL rates, has previously been reported as major vector in Panama^{2,5,11} and Latin America.¹⁰

In recent years an average of 2,188 clinical ACL cases have been reported in Panama,¹ although a 50% underestimation in this number is highly likely.² Interestingly, during the first

TABLE 2

Parameter estimates for the best Poisson rate generalized linear model explaining the household clinical cutaneous leishmaniasis infection rates at Trinidad de Las Minas, Panama*

Variable	Rate change (95% CI)	Estimate	SE	z-value	Pr(> z)
Intercept	–	-1.45	0.33	-4.43	9.21E-06†
<i>Lu. gomezi</i> / Trap night	1.063 (1.004 – 1.125)	0.0613	0.0288	2.12	0.0336†

*The model successfully fitted the data ($\chi^2 = 21.61$, d.f. = 22, $P > 0.048$) and all assumption of the Poisson generalized linear model were met.

†Statistically significant ($P < 0.05$).

6 months of 2012 a significant increase in ACL cases was reported in the western region of the province of Panama, where Trinidad de Las Minas is located. During this period more than 500 new cases (50% of them in children < 5 years of age) were officially reported, approximately twice the annually expected number in this region. The possible causes of these “hot spots” are unclear, and may be related to emerging ecological and environmental changes.^{2,3}

We are currently analyzing our vector samples to determine parasite infection rates and to evaluate insecticide thermal fogging impacts on sand fly abundance at Trinidad de Las Minas, in studies subsequent to this one. Nevertheless, the association of sand fly abundance with clinical ACL household rates highlights the need to better understand the ecology of sand flies, for example, which factors underpin the domiciliary abundance, and also for the development of new strategies for phlebotomine sand fly control.⁴

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