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Spatiotemporal trends of cutaneous leishmaniasis in Costa Rica.

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Title: Spatiotemporal Trends of Cutaneous Leishmaniasis in Costa Rica

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Abstract:

Background:

Cutaneous leishmaniasis (CL) remains an important neglected tropical disease in Costa Rica, which has one of the largest burdens of this disease in Latin America.

Methods:

We identified district-level hotspots of CL from 2006 to 2017 and conducted temporal analysis to identify where hotspots were increasing across the country.

Results:

Clear patterns of CL risk were detected, with persistent hotspots located in the Caribbean region, where risk was also found to be increasing over time in some areas.

Conclusions:

We identify spatiotemporal hotspots, which may be used in support of the leishmaniasis plan of action for the Americas.

Keywords: Costa Rica, spatial analysis, leishmaniasis

INTRODUCTION

Leishmaniasis, a zoonotic disease caused by the Leishmania parasites and transmitted to humans via phlebotomine sandflies, remains a significant neglected tropical disease (NTD) with an estimated 350 million people at risk for infection, yielding two million new cases each year[1]. Costa Rica shoulders the third largest burden of cutaneous leishmaniasis (CL) in Central America, where the disease is increasing at a greater rate than other parts of the Central American subregion[2].

Reducing leishmaniasis cases in vulnerable populations, including children who represent 30.8% of CL cases, is one of the primary goals of the leishmaniasis plan of action for 2017-2022 for the Americas[1]. Quantifying the spatiotemporal dynamics of CL is crucial for targeted disease control. Such assessments are available at broader scales, but are less common in the countries of Latin America at a more actionable level of granularity (i.e. district level)[2,3].

To support the goals of the Plan of Action 2017-2022, the aim of this study was to: 1) map CL incidence rates for years 2006-2017, and 2) quantify spatiotemporal trends to increase efficacy and local relevance of leishmaniasis interventions.

MATERIALS and METHODS

Disease Data

Georeferenced data on all laboratory-confirmed cases of CL during 2006-2017 was obtained from the Costa Rica Ministry of Health (see Supplemental Table 1 for case definition). District-level incidence rates per 100,000 persons were calculated using annual census estimates obtained from Costa Rica's National Institute of Statistics and Census (INEC).

Spatiotemporal Analysis

Optimized hotspot analysis with the Getis-Ord Gi* statistic was used to assess whether the annual spatial pattern of CL was significantly different than would be expected if the underlying spatial dynamics were randomly distributed. Districts were classified as “CL hot spots” (the magnitude of CL incidence, compared to other parts of the country, was higher than would be expected by chance) or “CL cold spots" (the magnitude of CL incidence is lower than would be expected by chance). Hotspots were considered statistically significant with z-scores and corresponding confidence intervals >95%. Correspondingly, cold spots (areas where fewer than expected cases were identified compared to random distribution) were considered statistically significant. With z-scores and confidence intervals >95%. Spatial analysis was conducted using ArcGIS v10.5 (ESRI Corporation, https://www.esri.com).

Temporal trends were quantified using the Mann-Kendall test to identify districts with statistically significant increases or decreases in CL incidence over time. The magnitude, direction, and statistical significance of the Mann-Kendall Tau statistic were used to categorize the temporal trend of CL risk as either: 1) increasing significantly ($p<0.05$), 2) increasing non-significantly ($p\geq0.05$), 3) decreasing non-significantly ($p\geq0.05$), or 4) decreasing significantly ($p<0.05$). Statistical analysis was conducted using R version 3.3.1 (https://www.r-project.org/).

Ethical Considerations

Analysis was conducted on de-identified, aggregated secondary data and did not require approval of an ethics committee.

RESULTS and DISCUSSION

A total of 12,853 cases of CL were reported in Costa Rica between 2006-2017 and the average annual incidence rate was 20.3 per 100,000 (Supplemental Table 2). Disease varied throughout the country (Supplemental Figure 1); however, statistically significant hotspots of elevated CL risk were detected during each year of the study period (Supplemental Figure 2). Persistent hotspots were found along the Caribbean coast in districts around the city of Limón and in the southeastern region of Costa Rica nearest the Panamanian border (Figure 1, panel A). These areas have some of the lowest development indices in the country, with the highest concentration of households living in poverty, the highest unemployment rates, and highest proportion of households with unmet basic needs[4].

Over 20 districts were classified as hotspots for at least five years during the study period. Five districts (Bratsi, Cahuiti, Sixaola, Matina, and Valle de la Estrella) were classified as hotspots for 11 years, all of which are found in the Limón province along the Caribbean coast. This region was also highlighted in the United Nations Economic Commission for Latin America and the Caribbean (Comisión Económica para América Latina e Caribe) report on the social panorama of Latin America[5] as an area in which 25% of children under the age of 18 are experiencing housing deprivation, a proxy measure for child poverty and a specific risk factor for CL.

Vector habitat suitability, and resulting vector-human contact, is a necessary cause of CL, affected by environmental parameters such as elevation, precipitation, and land cover change[6]. Costa Rica maintains large areas of protected forest; however, as a biodiversity hotspot, the country is also experiencing significant changes to its ecosystems. Human-modified environments, driven in large part by agricultural intensification (sugar cane, palm oil, pineapple, and coffee), and coupled with conservation and reforestation efforts, have created new or altered focal points of potential disease risk. This may explain, in part, the sporadic and emerging dynamics of hotspot risk seen in districts outside regions of persistent risk that are more spatially aligned with protected forest area.

Average annual incidence rates ranged from 1.5 per 100,000 persons in 2006 to 32.4 per 100,000 persons in 2014. Incidence rates in 22 districts throughout the country increased at a significant rate during the study period (Figure 1, panel B). Two districts (Cariari in Limon province and Corralillo in Cartago province) had incidence rates that decreased at a statistically significant rate. The remaining districts did not show evidence of consistent change over time, suggesting non-changing or oscillating risk over time. Space-time hotspots of CL, where risk was geographically elevated and increasing over time, were also identified in the Caribbean and Southern Pacific regions (Figure 1, panel C).

Identifying hotspots of geographic and temporal risk may be used to better direct public health interventions. CL is likely more prevalent in Costa Rica and other parts of Latin America than previously suspected due, in part, to underreporting of cases in endemic countries. A subset of these cases may also be travel-associated. This can obscure causal linkages, although the use of spatial statistics can mitigate this uncertainty.

CONCLUSIONS

The spatial distribution of leishmaniasis risk was non-random across the 12-year study period, with distinct patterns of concentrated risk. While it is likely that social and ecological factors work in tandem to create an environment of increased disease risk, more research is needed in this area to determine the mechanisms of interaction. Our findings may be used to support the 2017-2022 Action Plan endeavors to target this disease with enhanced surveillance, prevention, and control efforts.

Authors' contributions: BB conceived and designed the study, acquired and analyzed the data and contributed to the writing of the manuscript. AR, CG, MAP, and SM contributed to the writing of the manuscript. BC, KD, TH, and KK contributed to data management and analysis. All authors approved the final manuscript.

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Figure 1. Spatial and temporal distribution of district-level cutaneous leishmaniasis (CL) risk across Costa Rica between 2006 and 2017; A) the cumulative number of years each district was classified as a CL hotspot during the study period; B) temporal trends in CL risk across the study period (*denotes statistically significant increases or decreases over time, $p<0.05$); and C) districts classified as space-time hotspots if they were both a CL spatial hotspot at least once during the study period and where CL was increasing at a statistically significant rate.