The Urban Spread of Visceral Leishmaniasis: Clues from Spatial Analysis

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Background. The pattern of spread of visceral leishmaniasis in Brazilian cities is poorly understood.
Methods. We used geographic information systems and spatial statistics to evaluate the distribution of 1061 cases of visceral leishmaniasis in Teresina, Brazil, in 1993 through 1996.
Results. A locally weighted (LOESS) regression model, which was fit as a smoothed function of spatial coordinates, demonstrated large-scale variation, with high incidence rates in peripheral neighborhoods that bordered forest land and pastures. Moran's *I* indicated small-scale variation and clustering up to 300 m, roughly the flight range of the sand fly vector.
Conclusions. Spatial analytical techniques can identify high-risk areas for targeting control interventions.
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Key words: visceral leishmaniasis, spatial analysis, smoothing, clustering, geographic information systems, infectious disease, Brazil.

Worldwide, 400,000 cases of visceral leishmaniasis (VL) with 50,000 fatalities occur annually.[1] Over 90% of cases in the Americas arise in Brazil, where the protozoan *Leishmania chagasi* is the responsible agent.[2,3] Recently, several Brazilian cities of over 500,000 inhabitants experienced epidemics of this typically rural disease as a result of massive population movements and rapid, uncontrolled urbanization.[4,6,7] Efforts to control the canine reservoir host and the phlebotomine vector, *Lutzomyia longipalpis*, failed to interrupt transmission and prevent new epidemics.[4,5,8] The broad geographic dimensions of Brazilian cities make control interventions logistically and economically difficult to sustain.

Although foci of high incidence are readily identified in rural areas,[9] little is known about the distribution of cases in densely populated urban areas, where social networks and interactions between human settlements and the natural environment are more varied and complex. We therefore sought to determine spatial patterns of disease in an urban site and to identify high-risk areas for efficient targeting of control measures.

We used geographic information systems (GIS) and spatial statistical techniques to identify patterns of the occurrence of VL during an urban epidemic. To accurately define these patterns it was necessary to examine both large-scale and small-scale variation in incidence rates.[10,11] Large-scale variation, or spatial gradient, refers to the trend in the mean value of a process (*eg*, incidence) in space and can be represented as a function of geographical coordinates.[12] Small-scale variation, or second order effect, results from clustering of high or low values across the region and from spatial autocorrelation, the property by which nearby areas tend to have similar values of a variable.[11,13] To measure small-scale variation, it is helpful first to remove the effects of large-scale variation.[11]

Methods

Study Area

Teresina, the capital of Piauí State, lies at 05°05' South latitude at the convergence of the Parnaíba and Potí rivers (Figure 1). Shrubs and sparse mango and palm trees are the predominant vegetation in the city, which is surrounded by tropical forest and pastureland.

Teresina was the site of Brazil's first urban epidemic of VL[4] in 1980–1985, when approximately 1000 cases oc-

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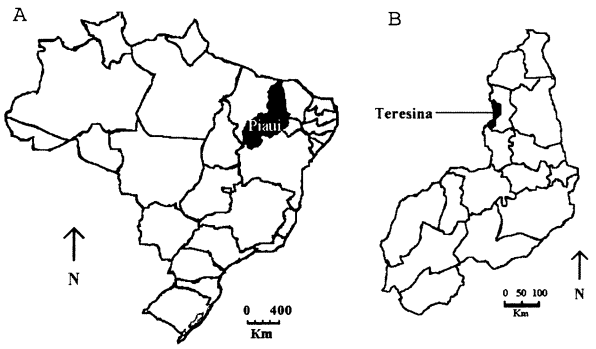

FIGURE 1. Piauí State, Brazil, and the city of Teresina. Brazil (*A*), Piauí State (*B*).

curred. During a second epidemic in 1993–1996, 1140 cases were detected among the population of 650,000 persons (Figure 2). Nearly all cases required hospitalization and 5% of patients died despite appropriate treatment.

Data Collection

The age, date of diagnosis, and location of the residence of 1061 persons with VL in Teresina in 1993–1996 were determined. This figure, which was confirmed by clinical and laboratory records from all hospitals in Teresina, accounts for 93% of all cases reported to the National Health Foundation (Fundação Nacional de Saúde or FNS) during this period. We believe that few cases were missed, because, by law, all suspect and confirmed cases are reported to FNS, which controls distribution of antileishmanial drugs. There is no alternative center for treating VL close to Teresina.

Incidence rates were calculated for each of the city's 430 census tracts using data from the 1991 and 1996 censuses. These rates were then linked to each census tract on a digital map by GIS (CartaLinx® and IDRISI®, The Clark Labs, Worcester, MA).

Statistical Analysis

The standard procedure for exploring large-scale variation is to derive a trend surface in which the outcome variable is expressed as a polynomial function of spatial coordinates.[12] We fitted a locally weighted regression model[14] to the entire trend surface as a single smoothed function of spatial coordinates, where:

$$\log(\text{rate}) = \text{LOESS}(\text{longitude}, \text{latitude})$$

LOESS stands for locally weighted regression smoothing; in this analysis, window span was set to 0.5. The LOESS smoother first identifies the 50% of observations that are nearest geographically to the target observation. The smoothed value at the target point is the fitted value from a locally weighted quadratic fit. Weights are supplied by a tri-cube kernel that is centered at the target observation and declines to zero at the furthest neighbor.[14]

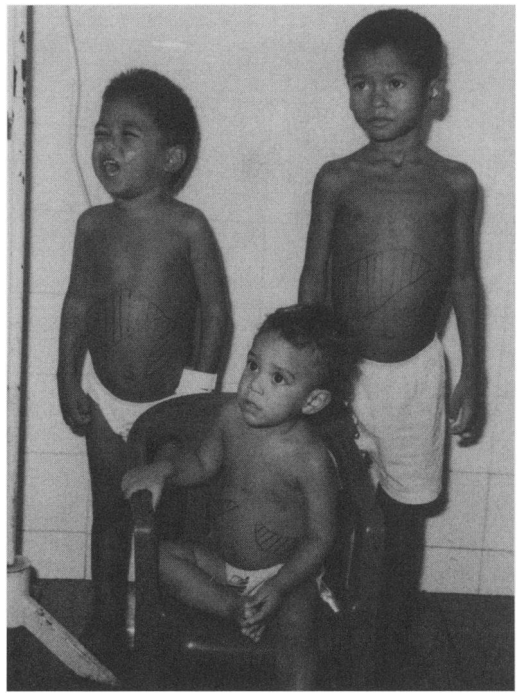

FIGURE 2. Three children with visceral leishmaniasis in the hospital in Teresina, Brazil. The marks indicate their enlarged livers and spleens, with large numbers of parasites. Treatment resulted in cure of this disease, which otherwise would have been fatal. (Parents gave permission for publication of photo.)

We then used the residuals of this model to explore the second-order component of variation. We used Moran's *I* as a measure of spatial autocorrelation to identify spatial clustering of rates of VL and the geographical scale at which spatial correlation occurs.[15]

Moran's *I* statistic is defined as:[15]

$$I = \frac{n\sum_{i}^{n}\sum_{j}^{n} W_{ij}(X_i - \bar{X})(X_j - \bar{X})}{\sum_{i}^{n}\sum_{j}^{n} W_{ij} \sum_{i}^{n}(X_i - \bar{X})^2}$$

where n is the number of regions; X_i and X_j are the values of the variable of interest at regions i and j; and W_{ij} is a measure of connectivity between all pairs of regions (i,j) based on the distance between the centroid of each census tract. In this study, we used a distance decaying function[10] where

$$W_{ij} = \begin{cases} (\min[d_{ij}: i = 1,\ldots,n]/d_{ij}) & (\textit{person-years}_j/\textit{person-years}_i)^{1/2}, \\ & j \in N_i, \text{ if } d_{ij} \text{ is closer than } d' \\ 0 \text{ otherwise.} \end{cases}$$

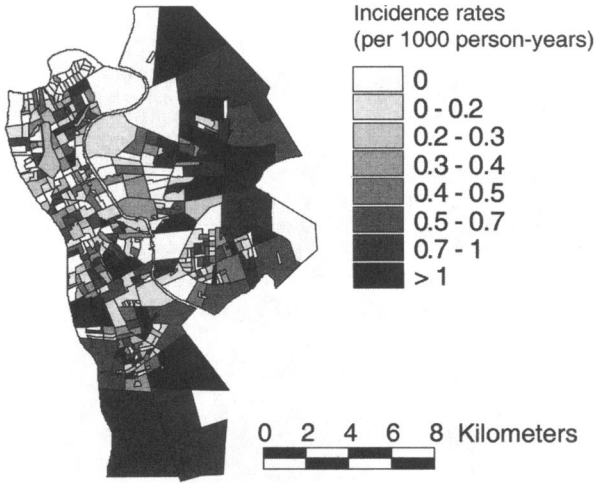

FIGURE 3. Incidence rates of visceral leishmaniasis (per 1000 person-years) by census tracts in Teresina, 1993–1996.

and N_i is the set of neighbors of region i, and d_{ij} is the distance between two neighbors. The summation is taken over all neighbors falling within a range of distances d'' to d'. Six distance ranges (d'' to d') were specified: up to 300 m, 301 m to 500 m, 501 m to 1000 m, 1001 m to 1500 m, 1501 m to 2000 m, and 2001 m to 2500 m.

Moran's I is similar to the Pearson correlation coefficient with values ranging from -1 to $+1$, although these limits can be exceeded depending on the connectivity matrix chosen. I is zero when there is no spatial autocorrelation, negative when there is negative autocorrelation, and positive when there is clustering.

Under the assumptions of normally distributed variables and constant variances, the distribution of Moran's I under H_0 (no spatial autocorrelation) is normal with a known mean and variance.[15] The residuals of our smoothed trend surface were approximately normally distributed; in any case, the autocorrelation statistic is robust to departures from normality when the sample size is greater than 20 observations.[16] S+SpatialStats (Insightful Corporation, Seattle, WA) was used for statistical analysis.

Results

Figure 3 shows the incidence rates of VL in the census tracts of Teresina in 1993–1996. Areas with high incidence rates appear to cluster in the northeastern and southern sectors, and regions with low rates cluster in the west.

Figure 4 shows a LOESS model fitted to the whole trend surface. There are increasing trends running from the northwest to southeast and from southwest to northeast. There are also two circumscribed areas of low incidence and one of moderately high incidence in the middle regions of the city.

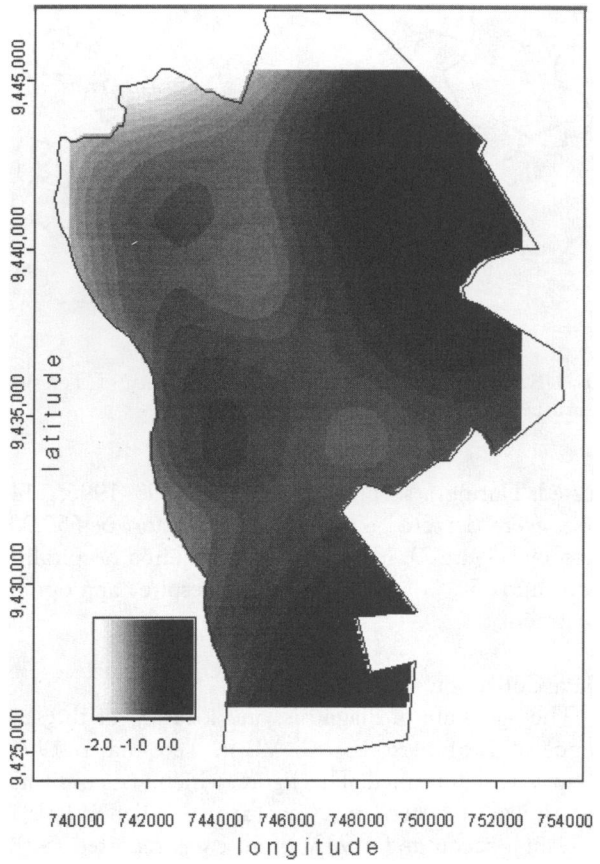

FIGURE 4. Trend surface showing smoothed incidence rates of visceral leishmaniasis as a function of spatial coordinates. Rates are expressed as the logarithm, and coordinates are in the Universal Transverse Mercator (UTM) reference system.

Table 1 shows the results obtained using tests of spatial autocorrelation applied to the residuals of the locally weighted regression model calculated for each distance. The results indicate spatial autocorrelation that decreases as the distance d' increases. The autocorrelation measured by Moran's I is positive up to 300 m. After 1000 m, a negative spatial correlation is observed.

TABLE 1. Spatial Autocorrelation Measured by Moran's *I* for the Residuals of Rates of Visceral Leishmaniasis at Increasing Distance Among Census Tracts in Teresina, Brazil

Distance	Moran's *I*	95% CL
0m–300 m	0.207	0.064, 0.350
301m–500 m	−0.005	−0.087, 0.077
501m–1000m	0.016	−0.027, 0.059
1001m–1500m	−0.103	−0.138, −0.068
1501m–2000m	−0.064	−0.097, −0.031
2001m–2500m	−0.007	−0.038, 0.024

Discussion

We found that the distribution of incidence rates of VL in Teresina was spatially aggregated, with high rates in the periphery of the northeastern and southern sectors, and low rates in the southeast and west. The west side of the city consists of densely settled residential and commercial neighborhoods, and is separated from a similar region (the city of Timor) by the Parnaíba River. In contrast, many of the regions with highest rates lie near forested areas and pastures, which suggests that transmission of infection to the human population may originate, at least in part, from a sylvatic cycle and not depend exclusively on the presence of infected domestic dogs. If so, control programs that rely heavily upon the identification and elimination of infected dogs may fail to prevent new cases of VL.

We also found that positive spatial correlation in incidence rates disappears when the distance between census tracts exceeds 300 m. Thus, transmission of VL appears to be limited to areas corresponding to the short flight range of sand flies[17–19] and the ranging behavior of domestic dogs. Accordingly, the efficiency of control measures may be improved by targeting interventions at high-risk areas and buffer zones around them based on these dimensions.

Our study demonstrates the importance of considering both large- and small-scale variation when investigating spatial patterns of vector-borne diseases. If a process that strongly influences vector occurrence (*eg*, temperature or altitude) varies at a large geographic scale, clustering of disease may reflect merely a spatial trend in this variable. Alternatively, if there is no such large-scale process, vector occurrence may depend entirely on more localized factors (*eg*, microhabitat, reservoir distribution). In large geographic areas both sources of variation are likely to occur, and if no attempt is made to separate them, the significance of clusters can be misconstrued. Analysis of residuals of a trend surface analysis or median polishing techniques for large-scale variation are indicated before examining second-order variation.[20]

In this report, we attribute the spatial heterogeneity in incidence rates to different exposures to vectors and reservoir hosts. However, malnutrition and other host factors may also be important determinants of the distribution of disease.[9]

Spatial analytical techniques were developed first for use in geology, ecology, and agriculture,[21] and only recently have been applied to epidemiologic research. In this study, we identified patterns of variation of incidence rates of VL in an urban setting to detect sources of infection that can be targeted to improve the efficiency of control measures. This work represents an initial approach, and more powerful designs are necessary to confirm our findings.

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