Factors associated with the incidence of urban visceral leishmaniasis: an ecological study in Teresina, Piauí State, Brazil

Fatores associados à incidência da leishmaniose visceral em área urbana: um estudo ecológico em Teresina, Piauí, Brasil

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Abstract

The objective of this study was to identify socioeconomic and environmental factors associated with the incidence of visceral leishmaniasis in the city of Teresina, Piauí State, Brazil. This was an ecological study based on 1,744 cases reported from 1991 to 2000, and the city's neighborhoods served as the unit of analysis. Mean annual incidence rates were related to socioeconomic and demographic indicators and a vegetation index derived from remote sensing images by means of spatial multiple linear regression models. The neighborhoods with the highest incidence rates were mostly located in the city's peripheral areas. Multivariate analysis identified an interaction between population growth and the vegetation index, so that areas with high population growth and abundant vegetation showed the highest incidence rates. The percentage of households with piped water was inversely associated with visceral leishmaniasis incidence. Spatial distribution of visceral leishmaniasis in Teresina during the 1990s was heterogeneous, and incidence of the disease was associated with the peripheral neighborhoods with the heaviest vegetation cover, subject to rapid occupation and lack of adequate sanitation infrastructure.

Visceral Leishmaniasis; Geographic Information Systems; Spatial Analysis

Introduction

Visceral leishmaniasis is a serious international public health problem, affecting some 65 countries, with an estimated annual incidence of 500 thousand new cases, 90% of which occur in India, Nepal, Sudan, Bangladesh, and Brazil [1]. Case-fatality is high, and an estimated 59 thousand persons die of the disease every year [2]. In Brazil, visceral leishmaniasis is caused by the protozoan *Leishmania (Leishmania) chagasi* and is transmitted by sandflies of the genus *Lutzomyia*, with dogs considered the principal source of infection in the urban setting [3].

Viewed historically as a rural endemic, visceral leishmaniasis has undergone changes in its transmission pattern in various areas of the world, usually associated with alterations in the socially built space. Since the early 1980s, Brazil has undergone a gradual process of urbanization of the disease. Teresina, capital of the State of Piauí, was stage to the first major urban epidemic in the country, with more than a thousand cases reported from 1981 to 1986 [4]. Epidemics were later described in other State capitals in the Northeast Region, like Natal (Rio Grande do Norte) and São Luis (Maranhão), and more recently the disease has also been found in other urban areas like Araçatuba and Baurú (São Paulo), Belo Horizonte (Minas Gerais), Fortaleza (Ceará), Campo Grande (Mato Grosso do Sul), Palmas (Tocantins), and Timon (Maranhão) [3].

Although some studies have examined the impact of deforestation, migration, and urban land occupation on the incidence of visceral leishmaniasis [4,5,6], few empirical studies have taken an ecological and spatial approach to measure the strength of association between these variables. The aim of the current study was thus to identify socioeconomic and environmental factors associated with visceral leishmaniasis incidence in the urban area of Teresina from 1991 to 2000, using spatial analysis tools.

Methods

Study area

Founded in 1852 as the capital of the State of Piauí [7], Teresina is located where the Parnaíba and Potí Rivers join, neighbors on the municipality of Timon in the State of Maranhão, and is located at 05º05' South and 42º48' West. The climate is tropical, with a dry winter and rainy summer, with a mean annual temperature of 26.8ºC. Vegetation consists of medium-sized brush cover, with two forms of savannah, the *cerrado* and *cerradão*, as the most common plant cover, and including babassu and carnauba palm groves as part of the landscape [7], with areas of pasture and tropical forest coexisting on the outskirts of the city. The current population of Teresina is more than 700 thousand, with a territory of 1,673km². The urban area of the municipality covers some 10% of its total territory and has 95% of the total population [7,8].

Study design

This was a multiple-group analytical ecological study, focusing on spatial analysis and environmental and socioeconomic factors potentially associated with the average annual incidence of visceral leishmaniasis in 101 neighborhoods in the city of Teresina from 1991 to 2000.

Data sources and variables

From 1991 to 2000, 1,818 cases of visceral leishmaniasis were reported to the Municipal Health Secretariat and National Health Foundation office in Teresina. Of the 1,818 cases, 45 (2.5%) were excluded because they resided outside the city limits and 29 (1.6%) because their addresses were not confirmed, leaving 1,744 (95.9%) patient records included in the analysis.

Based on the patient addresses obtained from the notification forms and confirmed with the Teresina street map and documents from the Teresina Municipal government [7,9], the cases were assigned manually to the city's neighborhoods.

The number of new cases of visceral leishmaniasis and the mid-year population for each year from 1991 to 2000 and in each neighborhood were used to calculate the average annual incidence rates for visceral leishmaniasis during the study period. The annual population estimates for each neighborhood were obtained by interpolation, using a geometric growth equation with annual compounding, based on population data from the 1991 and 2000 censuses and the population count for 1996 [8,10,11]. Thus, for each neighborhood, an average incidence rate for the 10 years included in the study can be obtained by dividing the total number of visceral leishmaniasis cases in the decade by the sum of the mid-year population estimates. We chose to perform a Freeman-Tukey transformation [12] of the incidence rates to achieve an approximately normal distribution and stabilization of variance:

$$y = \sqrt{1000}\left[\sqrt{S/n} + \sqrt{(S+1)/n}\right]$$

where y = transformed incidence rate, S = number of cases in each neighborhood during the 1990s and n = sum of mid-year population estimates for each year in each neighborhood.

The socioeconomic indicators used here correspond to the means for the study period in each neighborhood, and were constructed from population census data for 1991 and 2000 [8,10].

Three indicators were used to reflect the urban infrastructure: the mean percentage of households with piped water from the city water supply in at least one room; the mean percentage of households with regular garbage collection; and the mean percentage of households with at least one indoor bathroom connected to the sewage system.

Population characteristics, specifically for heads of households, comprised the socioeconomic indicators: mean percentage of heads of household with less than one year of schooling, including those with no schooling; and mean income of heads of household, expressed as times the prevailing monthly minimum wage.

The population growth rate for each neighborhood from 1991 to 2000 was calculated with a geometric growth equation with annual compounding and used as a measure of urban land occupation rate. The variable was dichotomized as greater than versus less than 10% per year.

A remote sensing image was used (a Landsat 5 TM type scene for Teresina, for October 1995) to extract a vegetation index, the Normalized Difference Vegetation Index (NDVI) [13]. The NDVI varies from (-1.0) to (+1.0), with positive values indicating the presence of green vegetation and negative values its absence. The NDVI correlates with precipitation and humidity, factors associated in turn with sandfly density [13]. The mean NDVI for each neighborhood was extracted using a geographic information system (IDRISI, The Clark Labs, Clark University, Worcester, USA), and for analytical purposes the variable was dichotomized using a cutoff point derived from classification tree models (≥ 0.2 and > 0.2) [14].

A digital map of the neighborhoods in Teresina was produced with CartaLinx (The Clark Labs, Clark University, Worcester, USA). The incidence rates and socioeconomic and environmental variables were related to the digital map using the IDRISI application.

Data analysis

Initially, a correlation matrix was constructed (Pearson correlation coefficient) between the transformed incidence rate, socioeconomic indicators, and vegetation index. Next, we examined the relationship between the transformed incidence rate and the continuous variables, using simple linear regression models. The regression diagnosis used graphic analysis of residues against the predicted values, and to verify whether some observation exerted an exaggerated influence on the results, Cook's distance analysis was used [15]. Using the Cook & Weisberg criterion [16], where distances greater then 1 can exert an exaggerated influence, all the observations were considered adequate. Residual analysis revealed the need to conduct a log transformation of the variable "mean income of heads of households" to produce an approximately linear relationship with the transformed incidence rate.

Evaluation of the spatial distribution of visceral leishmaniasis incidence used a thematic map and the Moran global spatial autocorrelation statistic. The Moran index (*I*) is a weighted autocorrelation coefficient whose values tend to be situated between -1 and +1. Values close to +1 indicate that the data possess positive spatial autocorrelation, i.e., neighboring areas tend to display similar incidence rates. Values close to -1 indicate that dissimilar values tend to aggregate in space, constituting a negative autocorrelation pattern. Values close to zero indicate absence of spatial correlation, i.e., a random process in space. The Moran index *I* is defined as follows [17]:

$$I = \frac{N\sum_{i=1}^{N}\sum_{j=1}^{N} w_{ij} z_i z_j}{S_0 \sum_{i=1}^{N} z_i^2}$$

where N is the number of areas, z_i and z_j are the differences between the incidence rates in areas i and j, respectively, and the overall mean incidence, w_{ij} is a neighborhood matrix between areas i and j, and S_0 is the sum of the weights assigned to the degree of neighborhood between the geographic units. To calculate the global Moran index, a neighborhood matrix was constructed, considering the contiguity of neighborhoods, attributing weights of 1 to contiguous neighborhoods and 0 to other situations.

To contemplate the spatial heterogeneity in the distribution of potential risk factors, a spatial linear regression model was used [18,19]. This regression technique allows a more accurate estimate of the regression coefficients and their confidence intervals, taking into account the existence of spatial autocorrelation. A spatial linear regression technique was used in which the errors are considered correlated according to a spatial dependency model of the conditional autoregressive type, implemented in the spatial statistics module of the S-PLUS application (Mathsoft, Seattle, USA). All the variables associated with the outcome in the analysis through simple spatial regression, considering 10% level of significance, were included in a multivariate model. A stepwise backward elimination procedure was used with the variables, leaving in the final model only the variables and interaction terms associated with the outcome, considering a 5% level of significance.

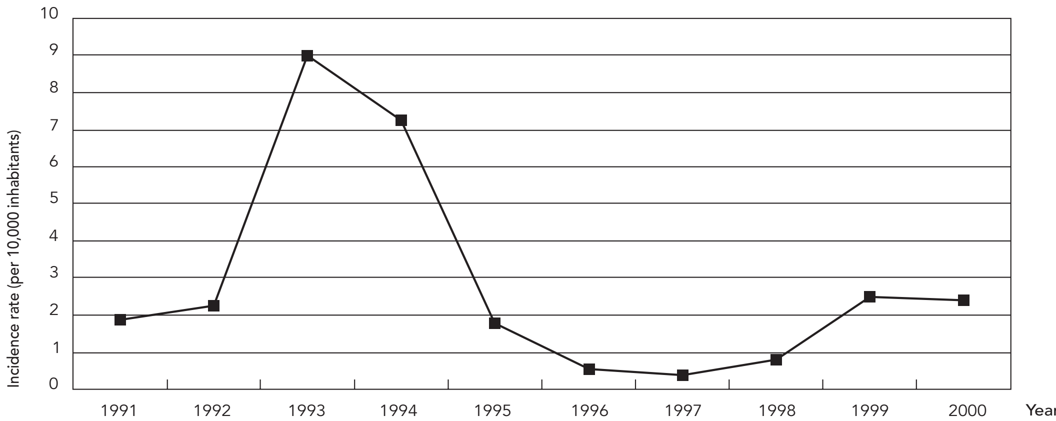
Results

Analysis of visceral leishmaniasis incidence in Teresina during the period showed an epidemic from 1992 to 1995, with the highest incidence in 1993 (Figure 1). The epidemic period was followed by lower incidences rates until 1998, when there was a new upward trend. The incidence map for visceral leishmaniasis by neighborhood in the 1990s shows a heterogeneous distribution in the occurrence of this disease in Teresina (Figure 2), particularly the presence of higher rates in the peripheral neighborhoods, which represent the city's most recent expansion area. The Moran index *I* showed the existence of significant spatial autocorrelation in the average annual incidence rate ($I = 0.292$; p value < 0.001).

Analysis of the correlation matrix between the socioeconomic indicators, environmental indicator, and transformed average annual incidence rate for visceral leishmaniasis (Table 1), first showed that all the socioeconomic indicators are heavily and significantly inter-correlated. The households' characteristics are directly associated with each other, showing that the three indicators representing the urban infrastructure

Figure 1

Annual incidence rate of visceral leishmaniasis. Teresina, Piauí State, Brazil, 1991-2000.



and sanitation conditions vary jointly across the neighborhoods. As for the population's characteristics, the higher a neighborhood's mean income, the lower the illiteracy rate and population growth rate and the better the infrastructure. The vegetation index, in turn, correlates with all the other indicators and shows that the neighborhoods with the heaviest vegetation cover have the worst socioeconomic indicators. The population growth rate is directly related to the vegetation index and inversely related to the presence of urban sanitation infrastructure and mean income. Visceral leishmaniasis incidence correlated with all the variables, and the strongest correlation was with the presence of green areas, absence of water supply and garbage collection, and higher population growth rates.

The spatial multiple regression analysis, with transformed average annual incidence as the response variable, evaluated not only the effects of each variable but also the presence of interactions between them. First-order interaction was identified between population growth rate and NDVI, indicating that the effect of population growth rate on the visceral leishmaniasis incidence rate varied according to the level of vegetation cover in the neighborhoods. Neighborhoods with heavy vegetation cover that experienced a high population growth rate showed higher incidence than expected based only on the independent influence of these variables. In the final model, the percentage of households with running water also remained, and was inversely and significantly associated with the visceral leishmaniasis incidence rate (Table 2).

Discussion

Until the 1970s, visceral leishmaniasis in Brazil was limited to rural areas, but starting in the 1980s the disease began to occur endemically and epidemically in large Brazilian cities. This urbanization of visceral leishmaniasis occurred first in the State capitals of the Northeast [4,20,21], and has since extended to cities in other regions of the country, including the Southeast [3,22,23,24], and to other Latin American countries [25].

What factors led to the change in the epidemiological pattern for the occurrence of this disease? Importantly, the conditions for the introduction, establishment, and spread of a disease frequently result from the process of occupation and social organization of the geographic space at a given moment in history. Such conditions may go overlooked if the analysis is limited merely to natural determinants [26]. In relation to the urbanization of visceral leishmaniasis, studies have suggested that the form of occupation of space, in particular the environmental, social, and economic transformations associated with migratory movements and population growth and increased population density in large cities are involved in the genesis of the phenomenon [4,5,27]. The present study aimed to contribute to this debate by empirically evaluating the role of demographic and environmental aspects and those related to the occupation of urban space as potential determinants of the spread of visceral leishmaniasis in Teresina.

Observation of the thematic map showed that the neighborhoods with the highest incidence rates were situated in the northeastern and southern areas of the city, while the lowest rates were found in the neighborhoods in the central and northwestern areas (Figure 2). The northeastern and southern neighborhoods correspond to the city's areas of expansion, with a rural/urban transition occupied by low-income population contingents lacking adequate infrastructure [7,14]. These are the same areas that had the highest incidence during the first epidemic in the city, from 1980 to 1986 [4]. Meanwhile, dense commercial and residential neighborhoods characterize the city's central area, and the northwestern neighborhoods are mostly older, including the area called Poti Velho, considered Teresina's original city center. It was also possible to detect areas at increased risk for visceral leishmaniasis in São Luís, Maranhão State [5,21], and more recently in Belo Horizonte, Minas Gerais [22,24]. In these capitals, the areas with the highest incidence were described as peripheral, lacking adequate sanitation, and with recent population growth due largely to migratory waves.

The results of the multivariate analysis indicate that the neighborhoods with heavy vegetation cover, at the rural-urban interface, that have undergone rapid increases in population density and disordered land occupation (without adequate urban sanitation infrastructure), have suffered the highest visceral leishmaniasis incidence rates. Specifically, the percentage of households with piped water, the population growth rate, and the neighborhood's mean vegetation index, particularly the interaction between these last two variables, were significantly associated with visceral leishmaniasis incidence. The percentage of households with piped water reflects the neighborhood's sanitation conditions and can be considered a measure of the quality of urbanization in the area. Besides serving as a marker for housing conditions, inadequate sanitation can favor both the proliferation of vectors and the presence of animal reservoirs in the peridomicile. In light of this finding, one can draw a parallel with the epidemiological situation of visceral leishmaniasis in Mediterranean countries of Europe, with better urban infrastructure. In Europe, despite the existence of endemic areas close to large cities [28], there have been no urban epidemics on the scale seen in Brazil, and the increase in the number of cases observed recently appears to be associated with the behavior of visceral leishmaniasis as an opportunistic infection related to AIDS [29]. Meanwhile, the interaction between population growth and the vegetation index demonstrates the impact of recent, rapid occupation of the city's peripheral areas on the risk of visceral leishmaniasis. Interaction between these two variables indicates that population growth in an area that is already urbanized has a much smaller impact on visceral leishmaniasis incidence than the same level of growth in an area with heavy vegetation cover. In the latter scenario, the incidence rates were higher than expected according to the sum of influence of the two factors. This finding should be interpreted considering the time factor, expressed as the velocity of occupation, and the space factor, represented by the area's characteristics and the way it was

Figure 2

Spatial distribution of average annual incidence rate of visceral leishmaniasis. Teresina, Piauí State, 1991-2000.

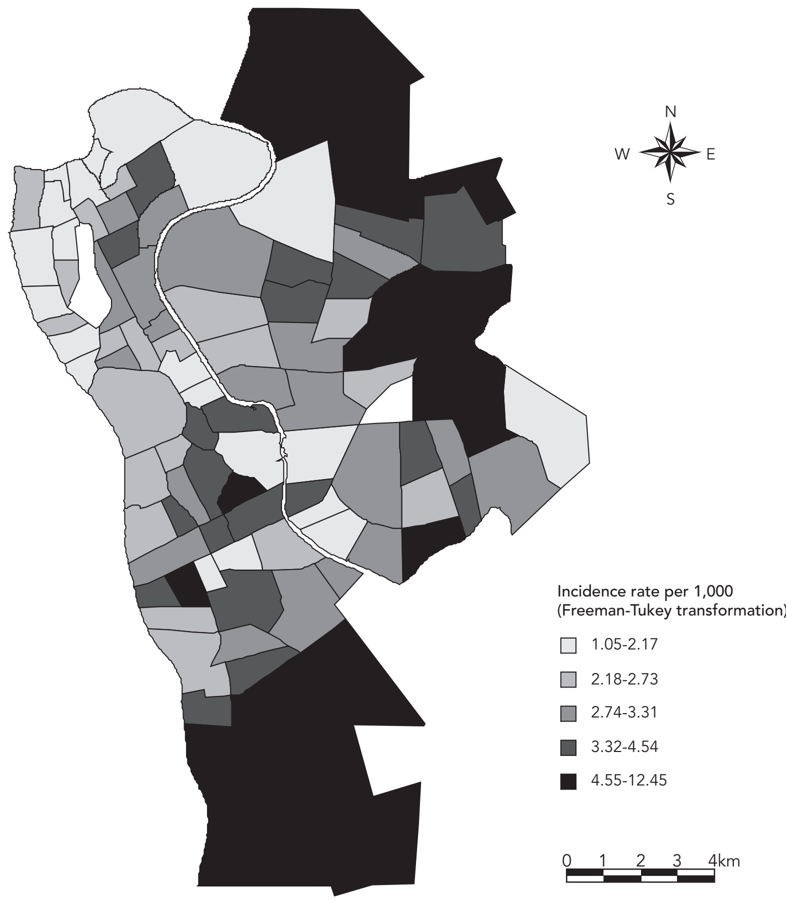


Table 1

Correlation matrix between visceral leishmaniasis incidence rate and environmental and socioeconomic indicators. Teresina, Piauí State, Brazil, 1991-2000.

	Transformed incidence rate	Piped water	Sewage connection	Garbage collection	Illiteracy rate	Mean income	Vegetation index	Population growth rate
Transformed incidence rate	1.00							
Piped water	-0.42 *	1.00						
Sewage connection	-0.25 **	0.76 *	1.00					
Garbage collection	-0.29 *	0.88 *	0.72 *	1.00				
Iliteracy rate	0.21 **	-0.80 *	-0.78 *	-0.77 *	1.00			
Mean income	-0.23 *	0.54 *	0.52 *	0.42 *	-0.61	1.00		
Vegetation index	0.45 *	-0.67 *	-0.48 *	-0.64 *	0.46 *	-0.22 **	1.00	
Population growth rate	0.34 *	-0.22 **	-0.03	-0.05	-0.04	-0.30*	0.32 *	1.00

* p < 0.01;
** p < 0.05.

Table 2

Results of spatial multiple linear regression between transformed average annual incidence of visceral leishmaniasis and socio-economic and environmental indicators. Teresina, Piauí State, Brazil, 1991-2000.

Variables	Coefficient	95%CI	p value
Constant	4.57	3.40; 5.74	< 0.001
Mean percentage of households with piped water	-2.16	-3.67; -0.67	0.006
Vegetation index	-1.09	-2.45; 0.27	0.120
Population growth rate	1.33	0.28; 2.38	0.015
Interaction between vegetation and population growth rate	3.76	1.83; 5.70	< 0.001

transformed. The introduction of a large population contingent in a short period of time favors the formation of a pocket of susceptible individuals exposed to ideal ecological conditions for the development of the infection cycle, which might not occur in the case of gradual occupation without such an abrupt environmental impact. In fact, we observed that neighborhoods with heavy vegetation cover, but which did not undergo substantial population growth, were not associated with high visceral leishmaniasis incidence rates. This finding is consistent with previous observations, like those of Deane & Deane [30] who, in their classic study on the distribution of visceral leishmaniasis in an endemic rural area, comment on the temporal association between the encroachment of "items of progress", like highways, and the establishment of visceral leishmaniasis foci. Further, the report by Mendes et al. [5] describes the juxtaposition of areas with increased visceral leishmaniasis incidence in the urban epidemic in São Luís and population settlements along recently built highways.

The current study's results should also be interpreted in light of its potential limitations and possible biases. First, the visceral leishmaniasis incidence rates are based on secondary data, which can lead to underestimation due to possible underreporting of cases. Conceivably, this problem may not have been that important, since visceral leishmaniasis is a serious disease whose treatment requires specific medication controlled by the Municipal Health Secretariat, the dispensing of which is conditioned on notification of the case. A second potential problem relates to the construction of socioeconomic indicators, since we only used data from the first and last years of the period analyzed, given the lack of annual census data. The mean value for a very long time period does not contemplate potential variations in the neighborhoods' characteristic over the course of a decade. In addition, the creation of the environmental indicator (NDVI) used an image obtained by remote sensing in the mid-period, thus impeding the evaluation of the impact of possible changes in the vegetation cover over time on the annual visceral leishmaniasis incidence rates. An additional problem results from the assumption that the place of infection was the peridomicile. This assumption is based on previous evidence that the existence of a case in the same household is one of the strongest risk factors for visceral leishmaniasis, with a threefold increase in the odds of developing the disease [20,28]. In addition, development of the disease after infection is known to be directly related to the volume of the parasite inoculum [31], and it is thus believed that prolonged contact with the vector is necessary for the disease to develop [28], reinforcing the idea of predominantly peridomiciliary transmission of the infection, in addition to the fact that the majority of cases occur in children up to four years of age, who rarely leave the peridomicile [3]. Despite this evidence of the association between the household's location and the occurrence of visceral leishmaniasis, the susceptibility conferred by genetic [32] and nutritional factors [33] could partially explain the clusters of cases in families, even if the place of infection were not the peridomicile. Another limitation was the fact that we did not direct evaluate the canine infection rates and vector distribution in the neighborhoods, both essential elements for transmission. Use of the NDVI may have helped minimize this problem, since its association with these variables has been demonstrated [14,34]. It is also possible that unknown or unmeasured determinants are influencing the distribution of visceral leishmaniasis in the city, as suggested by the presence of spatial autocorrelation in the residues from the multiple linear regression. The control measures conducted during the 1990s, although unsuccessful in interrupting the urbanization of the disease [3,35], have already proven effective in other contexts [36] and may have had a heterogeneous impact on the transmission of visceral leishmaniasis in terms of time and space. Nevertheless, there are no data to allow quantifying these measures in the city of Teresina, much less aggregate them in temporal units (years) or spatial units (neighborhoods). Finally, there are limitations typical of spatial analysis itself. The scale of the spatial unit of aggregation can influence the results [37], and the incidence rates in small populations can be highly unstable, although the rate transformation used here may have partially minimized this problem [12].

An essential closing comment relates to the potential contribution of these findings for purposes of visceral leishmaniasis control in Brazil, especially in light of the relative failure of current control measures [3,38]. One the one hand, strategies focused on ordering the urban territory and providing public services, targeting peripheral areas of large cities, could have a direct impact on visceral leishmaniasis incidence, both by limiting favorable conditions for vector proliferation and reducing the rates of contact between the vector, reservoir, and humans. On the other, the identification of situations that favor the spread of the disease, based on environmental and socioeconomic indicators, could eventually be used to set priorities for implementing disease control measures, thus decreasing costs and potentially increasing their effectiveness.

Resumo

O objetivo deste estudo é identificar fatores sócio-ambientais associados à incidência de leishmaniose visceral na área urbana de Teresina, Piauí, Brasil. Este estudo ecológico é baseado em 1.744 casos ocorridos entre 1991 e 2000 e tem como unidade de análise os bairros da cidade. As taxas de incidências anuais médias foram relacionadas a indicadores sócio-econômicos e demográficos e a um índice de vegetação derivado de imagem de sensoriamento remoto por meio de modelos de regressão linear múltipla espacial. Os bairros que apresentaram maiores incidências estavam majoritariamente localizados nas regiões periféricas da cidade. Na análise multivariada identificou-se uma interação entre crescimento populacional e índice de vegetação, de forma que áreas com alto crescimento populacional e com vegetação abundante apresentaram as maiores taxas de incidência da doença. O percentual de domicílios com água canalizada esteve inversamente associado à incidência da leishmaniose visceral. A distribuição espacial da leishmaniose visceral na área urbana de Teresina durante a década de 1990 foi heterogênea, estando sua incidência associada aos bairros periféricos com maior cobertura vegetal, submetidos à ocupação rápida e sem infra-estrutura sanitária adequada.

Leishmaniose Visceral; Sistemas de Informação Geográfica; Análise Espacial

Contributors

J. Cerbino Neto and G. L. Werneck designed the project, collected, processed, and analyzed the data, and participated in writing the article. C. H. N. Costa participated actively in the discussion of the results and collaborated in writing the article.

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