

An analysis of the spatiotemporal distribution of American cutaneous leishmaniasis in counties located along road and railway corridors in the State of Maranhão, Brazil

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ABSTRACT

Introduction: The incidence of American cutaneous leishmaniasis (ACL) is increasing in Latin America, especially in Brazil, where 256,587 cases were confirmed in the last decade. **Methods:** This study used a Bayesian model to examine the spatial and temporal distribution of ACL cases between 2000 and 2009 in 61 counties of State of Maranhão located along the three main road and railway corridors. **Results:** During the study period, 13,818 cases of ACL were recorded. There was a significant decrease in the incidence of ACL in the ten study years. The recorded incidence rate ranged from 7.36 to 241.45 per 100,000 inhabitants. The relative risk increased in 77% of the counties, decreased in 18% and was maintained in only five counties. **Conclusions:** Although there was a decreased incidence of the disease, ACL was present in all of the examined municipalities, thus maintaining the risk of contracting this illness.

Keywords: American cutaneous leishmaniasis. Bayesian model. Spatio temporal distribution. Relative risk.

INTRODUCTION

American cutaneous leishmaniasis (ACL) is an infectious disease affecting the skin and mucosa. It is caused by protozoa of the genus *Leishmania* and is transmitted by different species of phlebotomine sandflies¹.

The incidence of ACL is increasing in Latin America, especially in Brazil, where 256,587 cases were recorded from 2000 to 2009. In this period, 82,510 (32.2%) cases were reported in the northeastern region of the country, of which 32,548 (39.4%) came from the State of Maranhão².

The State of Maranhão is located among three biomes that display variations in physiographic, climatic and ecosystem diversity. These regions are of critical importance in the

epidemiology of ACL, as they are highly endemic for the disease. The Cerrados of central Brazil are situated in the eastern portion of this region, while Caatinga ecosystems are found to the northeast and the Amazonian forest to the west³.

Several researchers have conducted spatial analyses of the dynamics of infectious diseases^{4,5}. The analysis of relative risk (RR) over space and time has received a great deal of attention in epidemiological studies over the last few decades. Many studies assume that RR is composed of several random components, and these components explain different variations related to risk, such as temporal and spatial effects^{4,6,7}.

In this study, data on ACL from 2000-2009 were analyzed. The ACL data were expected to be correlated in space due to exposure to common environmental characteristics that influence transmission similarly in neighboring areas. The standard statistical methods assume independent observations. To take spatial correlations into account, Bayesian spatiotemporal models^{8,9} were developed to evaluate the spatiotemporal autocorrelation of the disease. Due to the large number of model parameters, a Markov Chain Monte Carlo (MCMC) simulation was used for model fitting.

This study aimed to assess the spatiotemporal distribution of ACL in counties located along road and railway corridors in the State of Maranhão, Brazil.

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METHODS

We conducted a retrospective ecological study describing the spatiotemporal distribution of ACL cases in 61 counties in the State of Maranhão, Brazil, from 2000 to 2009. Sixty-one counties located along the main road and railway corridors were selected as the study sites: I - São Luis-Timon (construction started in 1895): 27 counties along roads 135 and 316 and the line of the Northeastern Railway Company; II - São Luis-Açailândia (beginning of the 1980s): 20 counties along roads 135 and 222 and the line of the Carajás Railroad; and III - Açailândia-Carolina (beginning of the 1980s): 14 counties along road 010 and the North-South Railroad (**Figure 1**).

The ACL data were obtained from the Ministry of Health of Brazil and the demographic data from the Brazilian Institute of Geography and Statistics (IBGE).

An initial descriptive analysis of ACL incidence was conducted. Bayesian spatiotemporal Poisson regression models were constructed using WinBUGS software¹⁰. The response variable, y_{it} , was the number of ACL cases reported in county i in year t (for $i = 1, 2, \dots, 61$ and $t = 1, 2, \dots, 10$). We assumed that y_{it} followed a Poisson distribution with a mean of $e_{it}\theta_{it}$, where e_{it} is the number of cases expected in county i at time t , and θ_{it} is the area-specific risk rate in county i at time t .

The number of expected cases, e_{it} , between 2000 and 2009 for each county was calculated with the equation $e_{it} = p_{it}P_t / P_i$, where p_{it} is the population in county i at time t .

In the disease-mapping literature, estimates of RR are obtained through a maximum likelihood estimator, which, in this case, is given by $\theta_{it} = y_{it}/e_{it}$. Estimates of θ_{it} based on maximum likelihood estimators are biased, especially when the disease is rare, or the region of interest has a small population⁸.

In the present study, the spatiotemporal model considers $\log(\theta_{it}) = \beta_t + b_{it}$, where the temporal effect is given by $\beta_t = \beta_{t-1} + w_t$, and w_t is a normally distributed random error with a mean of zero and an unknown variance. This model assumes that the RR is related to both the temporal effect β_t and spatiotemporal effect b_{it} .

Prior distributions must be specified for the model parameters. We modeled the random effects terms, b_{it} , as a conditional auto-regressive (CAR) model with variance of σ_b^2 . For w_t , we assumed an a priori non-informative Gaussian distribution with a mean of zero and an unknown variance of σ_w^2 . Additional references using CAR prior distributions for disease mapping are provided by Bernardinelli et al.^{6,11,12}. Inverse-gamma prior distributions were specified for all of the variance parameters, with a shape of $a=1$ and a scale of $b=1$.

We estimated the parameters through an MCMC simulation. Three parallel chains were run with different initial values for the parameter estimates. A burn-in of 5,000 interactions, followed by 10,000 interactions was allowed, and the values of the main

parameters were stored. Terra View software, version 3.5, was used for mapping the resulting posterior distribution of the estimated RR parameters.

Ethical considerations

This study was approved by the Ethics Committee of the University Hospital of Maranhão Federal University (243/2008).

RESULTS

From 2000 to 2009, there were 13,818 cases of ACL recorded, including 4,571 cases along Line I (169 cases/county), 7,137 cases (357 cases/county) along Line II and 2,110 cases (151 cases/county) along Line III.

The annual incidence of ACL is shown in **Figure 2**. Since 2000, a gradual decrease in ACL incidence has been reported in the studied areas. This pattern of occurrence was common to the three lines.

The RRs for each of the 61 counties during 2000-2009 are provided in **Figure 3** and **Table 1**. The counties along Line II always presented a high risk. However, the eastern region (Line I) of the state showed a significant decrease in risk over the study years. Along Line III, different risks were observed in the counties.

Throughout the study period, the RR increased in 77% of counties, decreased in 18% and was maintained in only five counties.

DISCUSSION

Recent advances in techniques and computer-based programming have helped scientists and researchers monitor environmental and ecological factors affecting the spatial and temporal distribution of several vector-borne diseases, including malaria, leishmaniasis and schistosomiasis, among other diseases^{7-9,13}.

The Bayesian model employed here provided an estimate of the RR of ACL in the examined counties during the study period. The epidemiologic data indicated a significant decrease in the incidence of ACL over the ten years addressed in this study. The examined counties were situated in an historical area for ACL transmission and displayed incidences ranging from 7.36 to 241.45/100,000 inhabitants^{14,15}.

The area with the highest incidence of ACL was located in the western region of the state (Line II), which is under the influence of the Amazon rainforest and is known as an endemic disease area in Brazil^{14,15}. The climate and vegetation of this forest favor a high diversity of vector species, reservoirs and etiological agents¹⁶⁻¹⁸. The phlebotomine fauna found in this area are quite diverse, with an abundance of *L. whitmani*, *L. migonei*, *L. umbratilis* and *L. complexa* being observed^{14,19,20}.

The eastern region of the state (Line I) is also under the influence of the Amazon forest, combined with the transitional palm forest and *Cerrado* moving from west to east. These

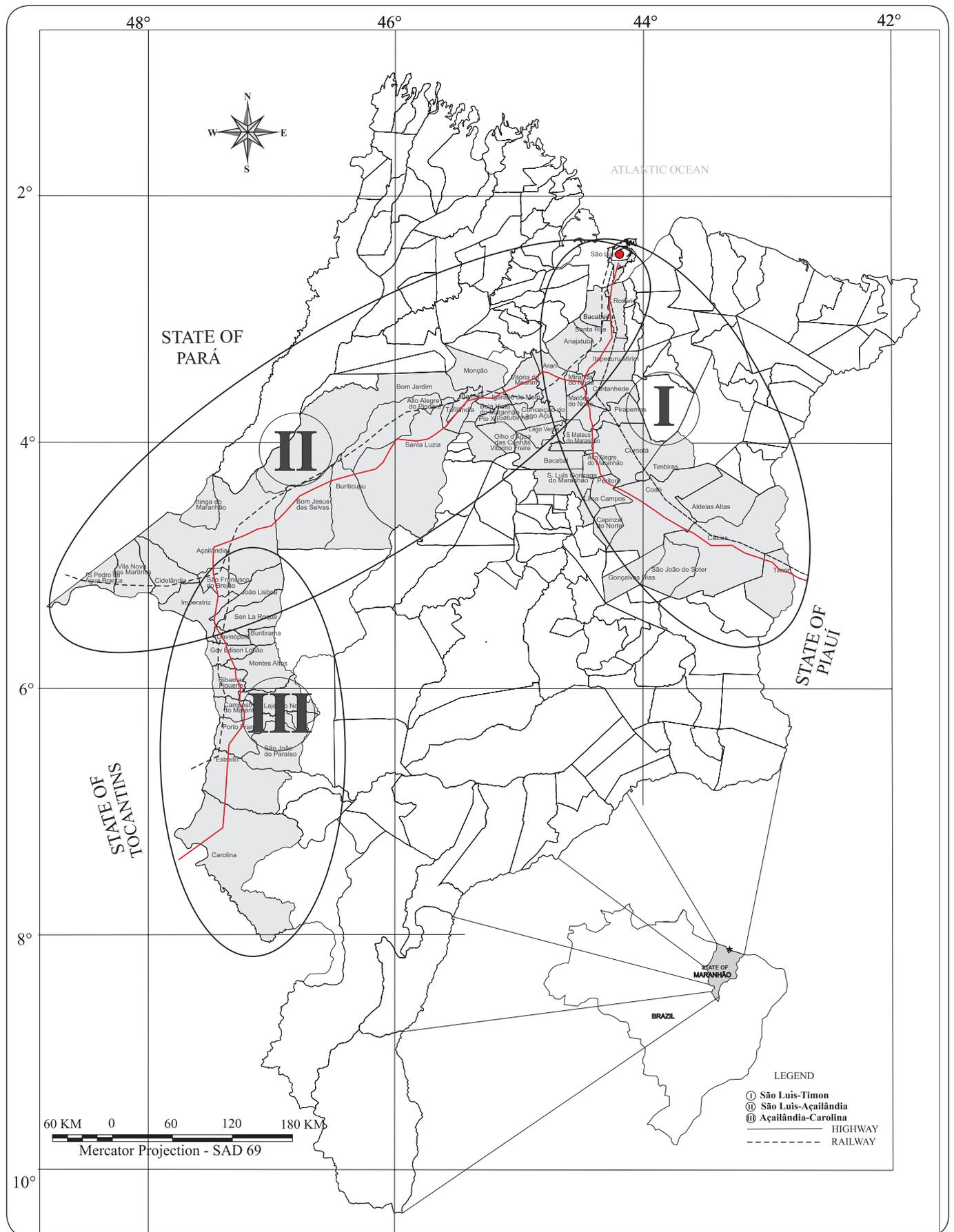


FIGURE 1 - Map of the State of Maranhão, Brazil, showing the studied counties located along the road and railway corridors, 2000-2009.

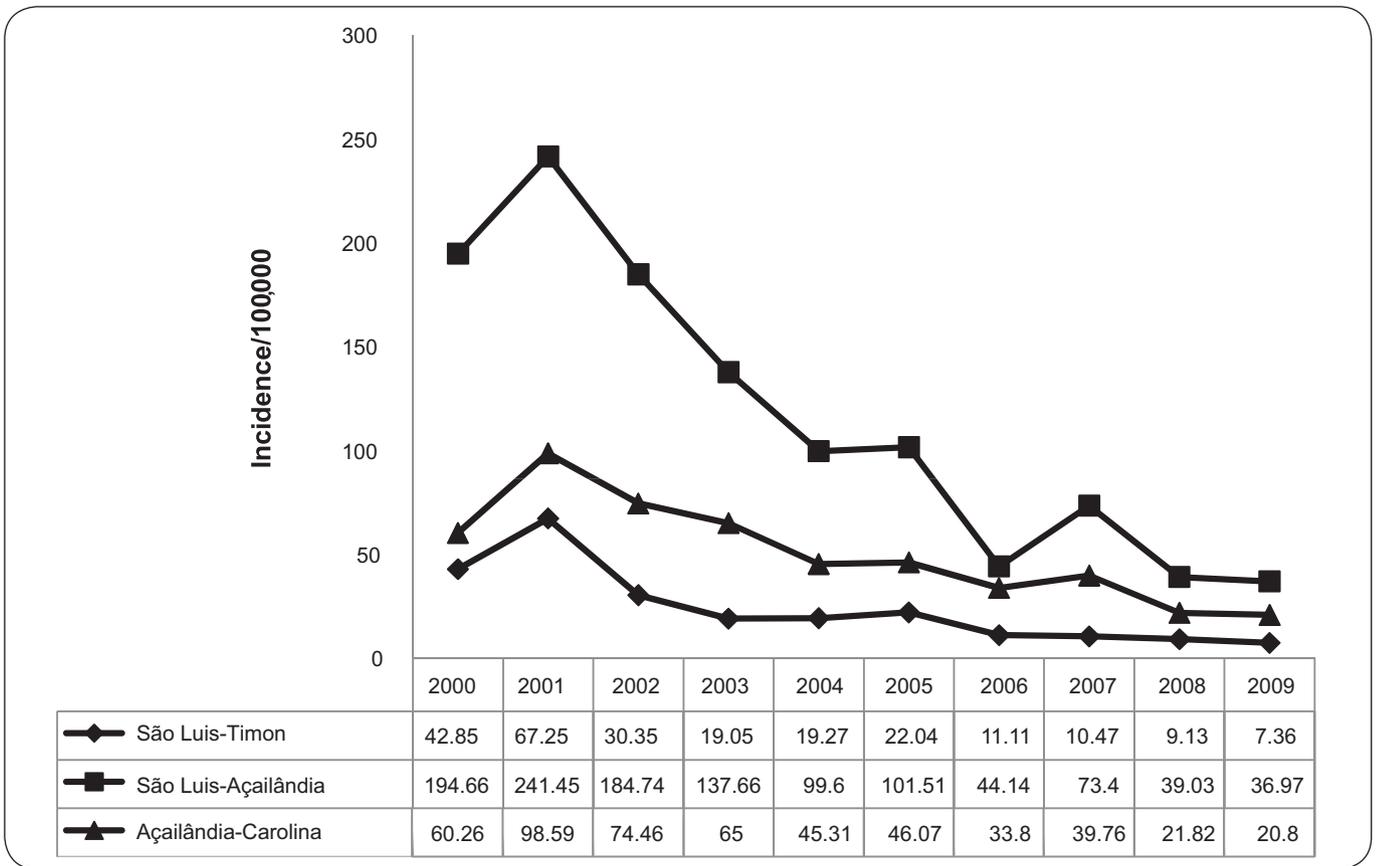


FIGURE 2 - Incidence of American cutaneous leishmaniasis cases along road and railway corridors in the State of Maranhão, Brazil, 2000-2009.

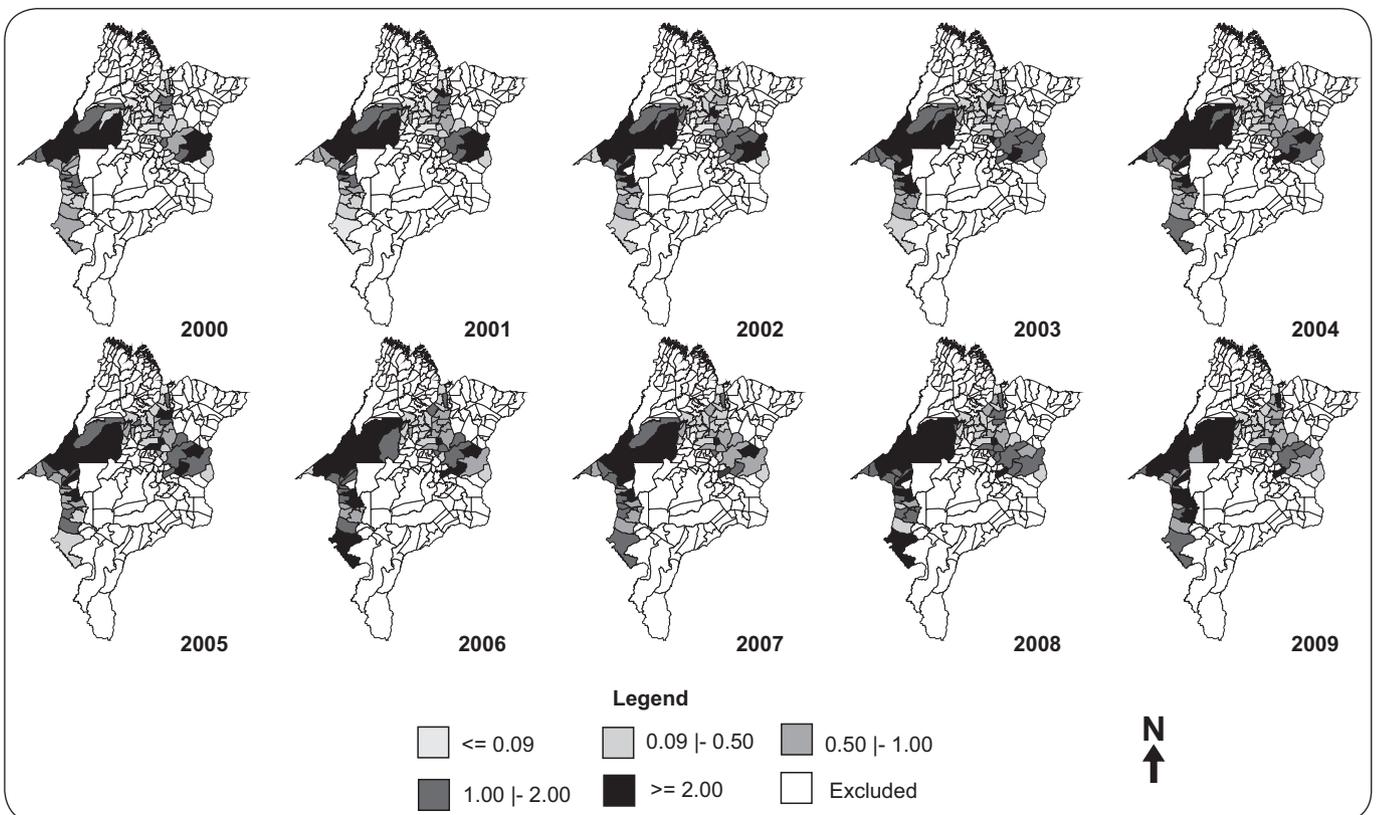


FIGURE 3 - The relative risk of American cutaneous leishmaniasis in the counties located along road and railway corridors in the State of Maranhão, Brazil, 2000-2009.

TABLE 1 - Relative risk of American cutaneous leishmaniasis in the cities located along the road and railway corridors, State of Maranhão, Brazil, 2000-2009.

County	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009
Line I										
Rosário	0.598	0.071	0.245	0.128	0.485	1.407	1.792	1.260	1.933	3.069
Alto Alegre do Maranhão	0.069	0.261	0.615	0.415	0.741	2.297	6.733	4.998	3.903	4.094
Cantanhede	1.089	1.312	0.456	0.662	0.595	1.251	0.585	0.427	1.659	1.957
Codó	0.713	1.116	1.093	1.100	1.192	1.139	1.035	0.783	1.063	1.159
Gonçalves Dias	0.357	0.485	0.953	1.428	3.316	1.395	4.193	3.176	3.203	4.196
São Luís Gonzaga do Maranhão	0.381	0.192	0.574	0.824	0.527	2.208	0.953	0.722	1.203	1.144
São Mateus do Maranhão	0.063	0.170	0.143	0.114	0.133	0.195	0.364	0.222	0.247	0.201
Timbiras	0.209	0.491	0.606	0.527	0.970	1.170	1.244	0.833	0.304	0.948
Timon	0.121	0.180	0.317	0.222	0.243	0.190	0.144	0.108	0.287	0.268
Santa Rita	0.141	9.080	0.464	0.185	0.734	0.441	0.261	0.188	0.402	0.508
São Luis	0.001	0.033	0.047	0.032	0.084	0.058	0.093	0.063	0.120	0.082
Miranda do Norte	0.377	0.185	0.381	2.434	1.425	0.647	0.872	0.647	0.478	0.412
Peritoró	0.217	0.438	1.190	0.555	0.581	0.427	1.164	0.865	1.739	0.802
Lago Verde	0.036	0.118	0.123	0.206	0.131	0.128	0.403	0.344	0.214	0.144
Conceição do Lago-Açu	0.033	0.099	0.132	0.189	0.214	0.215	0.257	0.288	0.242	0.162
Coroatá	0.140	0.743	0.663	0.769	0.815	0.419	0.748	0.550	0.815	0.714
Bacabal	0.040	0.086	0.073	0.084	0.102	0.104	0.193	0.103	0.470	0.200
Bacabeira	0.043	0.099	0.099	0.229	0.175	0.279	0.239	0.174	0.666	0.730
Anajatuba	0.149	0.097	0.264	0.139	0.190	0.356	1.146	0.850	0.633	0.226
Aldeias Altas	2.938	2.740	1.996	1.654	2.886	3.496	3.098	2.365	0.626	1.608
Capinzal do Norte	1.020	0.633	0.643	1.776	0.539	0.241	0.463	0.349	1.167	0.451
Caxias	4.867	3.098	2.084	1.012	1.652	1.781	0.781	0.569	1.154	0.661
São João do Soter	1.208	1.930	1.660	4.004	2.615	2.352	2.378	1.795	1.399	0.689
Itapecuru Mirim	1.068	1.378	0.808	0.636	1.362	2.207	0.627	0.415	1.427	0.933
Pirapemas	0.442	0.700	0.357	0.316	0.576	0.736	0.829	0.457	0.486	0.323
Lima Campos	0.673	1.103	1.634	2.886	0.495	0.637	1.452	1.103	1.111	0.652
Matões do Norte	0.297	0.882	2.516	0.454	0.258	0.528	0.563	0.399	0.334	0.295
Line II										
Açailândia	2.002	3.869	2.703	2.707	3.938	2.723	3.026	3.025	2.225	3.390
Alto Alegre do Pindaré	0.139	1.319	1.579	1.102	1.058	2.281	2.947	2.736	5.620	7.780
Arari	0.055	0.081	0.098	0.123	0.129	0.125	0.237	0.176	0.221	0.154
Bela Vista do Maranhão	0.035	0.097	0.371	0.436	1.435	0.679	0.495	0.683	1.005	0.338
Bom Jardim	1.077	1.509	1.497	1.449	2.200	1.611	2.311	1.686	2.947	2.551
Cidelândia	2.285	0.830	2.537	1.468	1.149	1.615	2.221	1.036	5.947	3.629
Igarapé do Meio	0.039	0.120	0.282	0.712	0.232	1.013	0.276	0.393	0.329	0.243
Monção	0.042	0.087	0.174	0.239	0.299	0.232	0.317	0.286	0.296	0.227
Pindaré-Mirim	0.067	0.487	0.700	0.348	0.488	0.851	0.852	0.839	0.847	0.765
Pio XII	0.038	0.159	0.440	0.174	0.238	0.378	0.320	0.728	0.201	0.143
Santa Inês	0.037	0.311	1.110	0.532	0.470	0.632	0.371	0.769	0.437	0.410
São Pedro da Água Branca	1.080	0.128	0.876	1.087	2.880	1.223	0.298	1.190	1.926	1.296
Satubinha	0.035	0.087	0.197	0.176	0.554	0.357	0.256	0.315	0.327	0.239
Tufilândia	0.189	0.755	1.156	0.883	1.261	0.851	2.043	3.763	1.562	8.660
Vila Nova dos Martírios	1.369	0.609	0.395	1.639	1.768	0.770	2.059	0.648	1.132	3.330

TABLE 1 - Continue.

County	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009
Line II										
Vitória do Mearim	0.031	0.060	0.081	0.287	0.392	0.146	0.210	0.209	0.310	0.131
Bom Jesus das Selvas	4.472	1.867	5.459	5.301	4.644	6.323	5.631	5.960	3.463	0.952
Buriticupu	12.910	7.875	11.98	10.13	6.431	7.162	4.172	4.636	2.504	2.609
Itinga do Maranhão	7.582	5.025	3.944	5.035	8.994	4.460	6.334	8.221	6.615	7.347
Santa Luzia	4.196	3.119	2.986	5.171	2.376	3.358	1.677	4.797	4.282	3.582
Line III										
Campestre do Maranhão	0.487	0.531	0.414	0.886	0.407	0.605	0.878	1.067	0.456	0.622
Carolina	0.539	0.060	0.203	0.428	1.035	0.435	3.500	1.636	3.275	1.200
Davinópolis	0.949	2.847	2.079	3.875	0.407	1.720	1.558	1.250	1.423	1.527
Governador Edson Lobão	1.557	1.675	1.386	0.860	0.588	0.987	1.322	0.778	2.188	2.777
Imperatriz	0.659	0.948	0.930	0.749	0.995	0.861	1.034	1.160	1.001	0.769
João Lisboa	0.694	0.463	1.591	2.282	1.694	1.992	1.890	2.532	1.057	0.932
Lajeado Novo	1.229	0.581	0.581	3.144	1.641	0.779	2.329	1.140	1.056	3.198
Montes Altos	1.007	1.025	3.237	4.434	3.446	2.744	10.570	3.725	2.280	3.450
Porto Franco	0.460	0.420	0.628	0.838	0.824	1.076	0.852	1.245	1.033	1.169
Ribamar Fiquene	0.556	0.412	0.741	1.517	1.095	0.794	1.609	1.127	1.432	2.425
São João do Paraíso	0.173	0.228	0.342	0.944	0.577	0.283	0.690	0.527	1.601	10.41
Senador La Rocque	0.641	1.645	3.173	5.899	3.006	2.904	1.541	2.937	2.898	2.239
São Francisco do Brejão	7.120	2.991	2.608	1.573	1.376	0.844	2.602	3.381	1.574	1.599
Estreito	0.538	0.292	0.520	0.732	0.810	1.487	1.426	0.958	0.343	0.563

Source: Secretary of Health Surveillance/Ministry of Health of Brazil.

characteristics may explain why the incidence found in this region is higher than that recorded in the southwest of the state, which is dominated by *Cerrado* formations, as the climate is drier in the south^{21,22}.

Studies have shown that many species of phlebotomine ACL vectors previously found in wild environments^{19,20} are encroaching on rural and peri-urban areas, where they are becoming infected by *Leishmania* spp.^{17,23}.

The first records of ACL in Maranhão come from the late 1970s from an outbreak detected in Buriticupu¹⁵ on the Amazon side of the state. A number of outbreaks recorded in Maranhão, São Paulo and Bahia were associated with the introduction of roads and railway lines in forest areas^{24,25}, and we believe the same phenomenon may have occurred along road and railway Line I. However, this line is much older and has existed for more than a century with no record of an infection. Thus, it is possible that the lack of cases reported in association with this line resulted from the absence of disease specialists at the time.

This hypothesis finds support in current records of autochthonous cases of ACL in urban areas of Caxias²⁶, which suggest a long-term adaptation process among phlebotomine sandflies (*L. cortelezii*, *L. evandroi*, *L. goiana*, *L. intermedia*, *L. lenti*, *L. longipalpis*, *L. longipennis*, *L. squamiventris*, *L. termitophila*, and *L. whitmani*) in these environments. This

phenomenon was previously observed in an entomological survey conducted in several counties along this road and railway line²⁷. However, such adaptation has not yet been detected on the Amazonian (west) side, where ACL remains rural or peri-urban^{27,28}.

Given the above findings, it is presumed that the studied road and railway lines have increasingly been drawing populations from Maranhão and other states from different regions in the country. The northwest road and railway line receives migrants from Pará, Tocantins and other Amazon states, whereas the northeast road and railway line mainly receives migrants from the States of Piauí and Ceará but also from other northeastern States and Minas Gerais. Thus, these lines facilitate the transmission of ACL in the oldest settled areas, such as the area along road and railway Line I receiving a large population flow from the northeastern states, as well as areas settled more recently, including along access routes to the Amazon states and the central region of Brazil.

In Brazil, health records are critical sources of data for studies. However, the availability and quality of the data are matters of great concern. For example, the lack of coverage of the entire population and diagnostic errors can affect the quality of the data and lead to underreporting. Reliability and validity are essential in large database studies to accurately assess the possibility of bias in spatial research based on secondary data²⁹.

Nevertheless, the results of this study can be interpreted despite their limitations and potential biases. First, the incidence rates of ACL are based on secondary data, which may underestimate the true incidence due to underreporting. A second potential problem was the failure to consider socioeconomic and environmental indicators given the difficulty of obtaining such data²⁹.

To better understand the influence of roads on the epidemiological profile of this disease, further research will be required to identify variables that can contribute resolving the complex factors contributing to disease transmission.

Road and railway corridors may play an important role in the spread of LTA by facilitating the movement of populations with varying risks of contracting the disease, thus influencing its epidemiology.

The data presented and discussed in this report allow us to conclude that although there was a decrease in the incidence of ACL over the study period, the risk of contracting the disease remains in all of the studied municipalities. Therefore, preventive measures implemented by the Unified Health System should be directed towards the control of disease expansion.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

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