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Ecoepidemiology of American Visceral Leishmaniasis in Tocantins State, Brazil: Factors Associated with the Occurrence and Spreading of the Vector *Lutzomyia (Lutzomyia) longipalpis* (Lutz & Neiva, 1912) (Diptera: Psychodidae: Phlebotominae)

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Additional information is available at the end of the chapter

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Abstract

Leishmaniasis are considered serious public health problems, and their geographical expansion has enabled their establishment in urban areas of medium and large cities in Brazil. Continuous processes of deforestation, construction of dams, and hydroelectric plants, among others, cause environmental impact and may favor the increase in the number of human cases of leishmaniasis, as well as the establishment of epidemic outbreaks. This scenario reflects the reality of some regions of Brazil, such as Tocantins State, which in recent years has recorded high levels of American visceral leishmaniasis (AVL). This study is aimed to analyze environmental and epidemiological factors related with the spatial and temporal distribution of AVL and with the occurrence of *Lutzomyia (Lutzomyia) longipalpis*, the main vector of AVL, in the state of Tocantins. The results indicate that the vector is adapted to all environments, especially the ones under human influence, and that anthropogenic environmental impacts can support the development and adaptation of AVL in Brazil. Such information could be applied in control strategies aimed at decreasing AVL incidence.

Keywords: *Lutzomyia (L.) longipalpis*, American visceral leishmaniasis, urbanization and expansion, deforestation, land use, Tocantins

1. Introduction

Leishmaniasis is a zoonosis caused by heteroxenous flagellate protozoa of genus *Leishmania* (Ross, 1903), order Kinetoplastida and family Trypanosomatidae. The infection is transmitted by the bite of infected female sand flies, dipteran insects of family Psychodidae, and subfamily Phlebotominae, genus *Lutzomyia* (New World) and *Phlebotomus* (Old World) [1]. These diseases are major public health problems, affecting indiscriminately men, women, and children, and are the ninth leading cause of infectious diseases in the world, despite remaining within the framework of neglected diseases [2–4]. Leishmaniasis manifests in different clinical forms, mainly due to the variety of parasites that affect the human population [5]. They are endemic in 98 countries, reaching America, Europe, Asia, Africa, and Australia, with about 350 million people living in risk areas [2, 6, 7].

American visceral leishmaniasis (AVL) has become one of the most important tropical diseases, due to its high incidence, high mortality rates in untreated individuals, and malnourished children, and it can also progress to death [3]. In Latin America, AVL has been recorded in 12 countries, with 90% of cases occurring in Brazil. The geographical expansion of AVL in Brazil has enabled its establishment in urban areas of medium and large cities [3]. Autochthonous human cases are recorded in most Brazilian states, except Acre, Amapá, Amazonas, Paraná, Rondônia, and Santa Catarina [3, 8].

The etiologic agent of AVL in the Americas is *Leishmania (Leishmania) infantum chagasi* (Cunha and Chagas, 1937), whose main vector is *Lutzomyia (Lutzomyia) longipalpis* (Lutz and Neiva, 1912), a species with strong evidence of vector competence, and closely linked to the expansion process of the disease, as revealed by its wide geographical distribution in the Americas [9]. In Brazil, it is currently considered the main vector of AVL in all regions; however, its presence was not yet detected in the states of Acre, Amazonas, Rondônia, and Santa Catarina. The ability of *L. (L.) longipalpis* to often feed on domestic and synanthropic animals, as well as its remarkable anthropophily favored its adaptation to changing environments, favoring the maintenance of the transmission cycle in the rural environment and, at the same time, the spread of the disease into urban areas [9–12].

A variant epidemiological situation is observed in the central region of Brazil, in Corumbá and Ladário (Mato Grosso do Sul State), and Jaciara (Mato Grosso State), where *L. (L.) longipalpis* is absent and *Lutzomyia (Lutzomyia) cruzi* (Mangabeira, 1938) has been incriminated as a vector because of its high abundance, anthropophily, and natural infection with *L. (L.) infantum chagasi* [13–15].

Leishmaniasis produces major impacts on human health as a consequence of environmental change, mainly through the possible expansion of transmission areas. Continuous environmental change processes, such as deforestation, fires, agriculture, mining, construction of dams and hydroelectric power plants, migration, unplanned urbanization, and lack of urban infrastructure are examples of situations that have led to an increase in people at risk of infection, and fostered the emergence of outbreaks of leishmaniasis in a new ecoepidemiological pattern [10, 16].

Geographic information systems (GIS) have generated valuable contributions to the control and prediction of vector-borne diseases [17–19], and to evaluate the influence of environmental factors on the habitats of vectors and hosts, and the risk of transmission to humans [20]. Such studies aim to characterize and analyze the spatial and temporal dynamics of the diseases and consequently identify epidemiological patterns, generating information that can be valuable tools when planning control actions.

The AVL shows a persistent scenario in Brazil, with most of the factors contributing for its endemicity residing in processes that are external to the health sector. This makes the strengthening of new strategies necessary. Thus, this study is aimed to analyze the spatial and temporal distribution of AVL in Tocantins State, through evaluation of epidemiological and environmental factors that are potentially related to its expansion: disease incidence, presence of the vector *L. (L.) longipalpis*, type of land use, and deforestation. In the current scenario, where environmental changes impact public health, it is essential to intensify research in diseases related to the environment, especially vector-borne diseases such as AVL.

2. American visceral leishmaniasis and *Lutzomyia (Lutzomyia) longipalpis* in Tocantins

Tocantins is the newest of the 26 Brazilian states, its territory has 277,720.567 square kilometers, and it is located in the geographical center of the country, in the North Region (**Figure 1**). Most of the state is made up of plains and plateaus, and it has the largest river basin in the entire country, the Tocantins-Araguaia basin. Tocantins is one of nine states that form the Amazon region, its vegetation consists of 88% of the Cerrado biome and 12% of the Amazon biome (**Figure 1**). It has a semihumid tropical climate with two seasons: wet and dry. Its annual average temperature varies between 25°C and 29°C and average rainfall is around 1200–2100 mm [21, 22]. Among the phytoecological regions found in the state, the savannah (52%) and pasture (27%) are the majority [21, 23].

In the last decade, the state of Tocantins has suffered environmental changes from agricultural activities and construction of hydroelectric plants. In such scenarios, high numbers of human cases of leishmaniasis were recorded [24]. To quantify and describe the spatial and temporal distribution of AVL in Tocantins, the number of human cases recorded from 2000 to 2015 was provided by the Health Department of Tocantins State [personal communication]. All maps and spatial analysis were performed in ArcGIS (version 10.4).

In the analyzed period, Tocantins State had records of 4476 human cases of AVL in 124 of its 139 municipalities. From 2001 to 2013, 212 deaths were reported, and the municipalities Araguaína and Palmas (the state capital) reported 37% of the human cases of the state [24]. The spatiotemporal map (**Figure 2**) shows that human cases of AVL in the state are concentrated in the cities of Araguaína, Palmas, Porto Nacional, Paraíso do Tocantins, Araguatins, and Tocantinópolis, comprising 66% of the state's human cases. The municipality

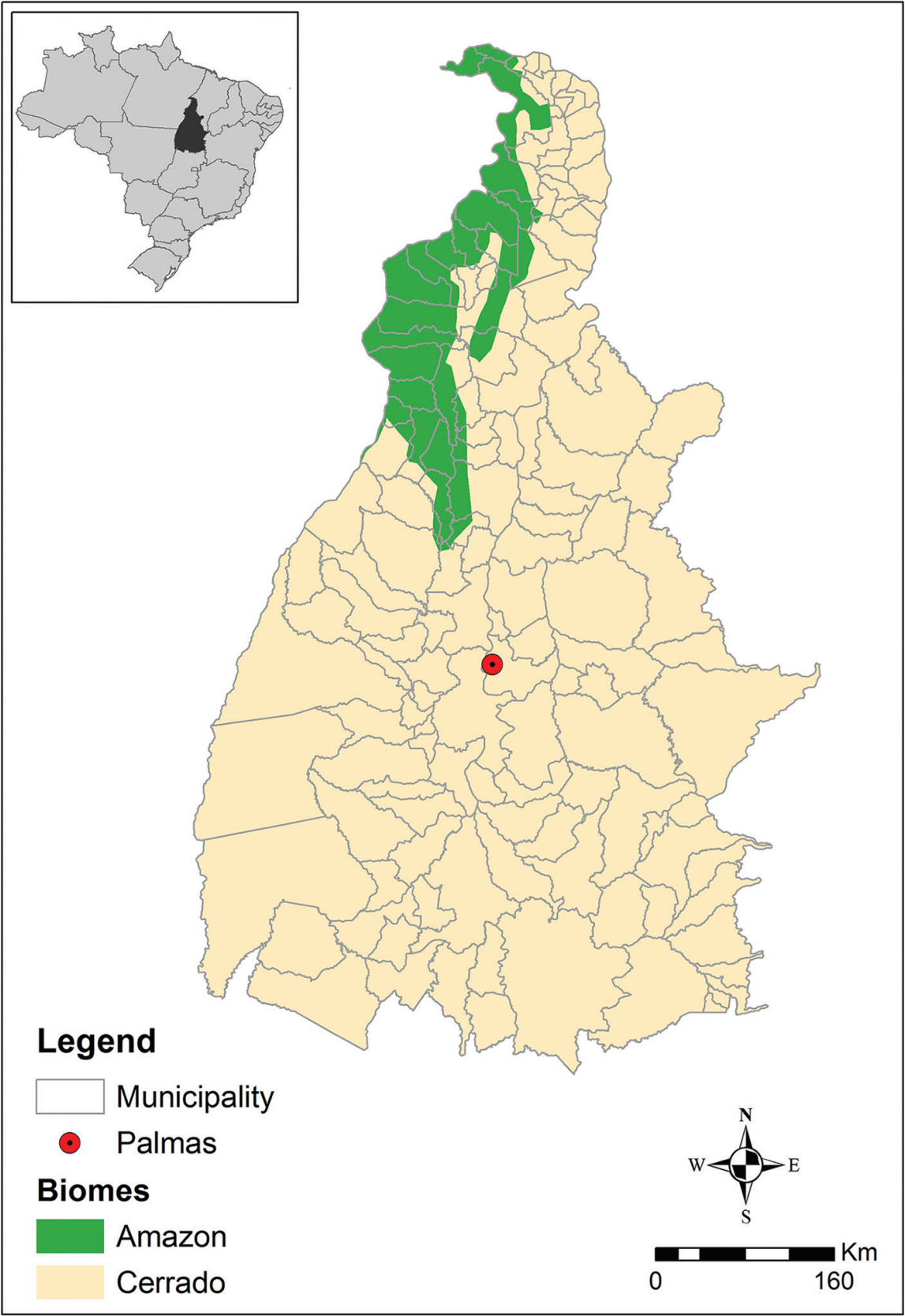


Figure 1. Biomes of Tocantins State, Brazil. Source: IBGE. Map design: Laboratório Interdisciplinar de Vigilância Entomológica em Díptera e Hemiptera LIVEDIH/IOC/FIOCRUZ.

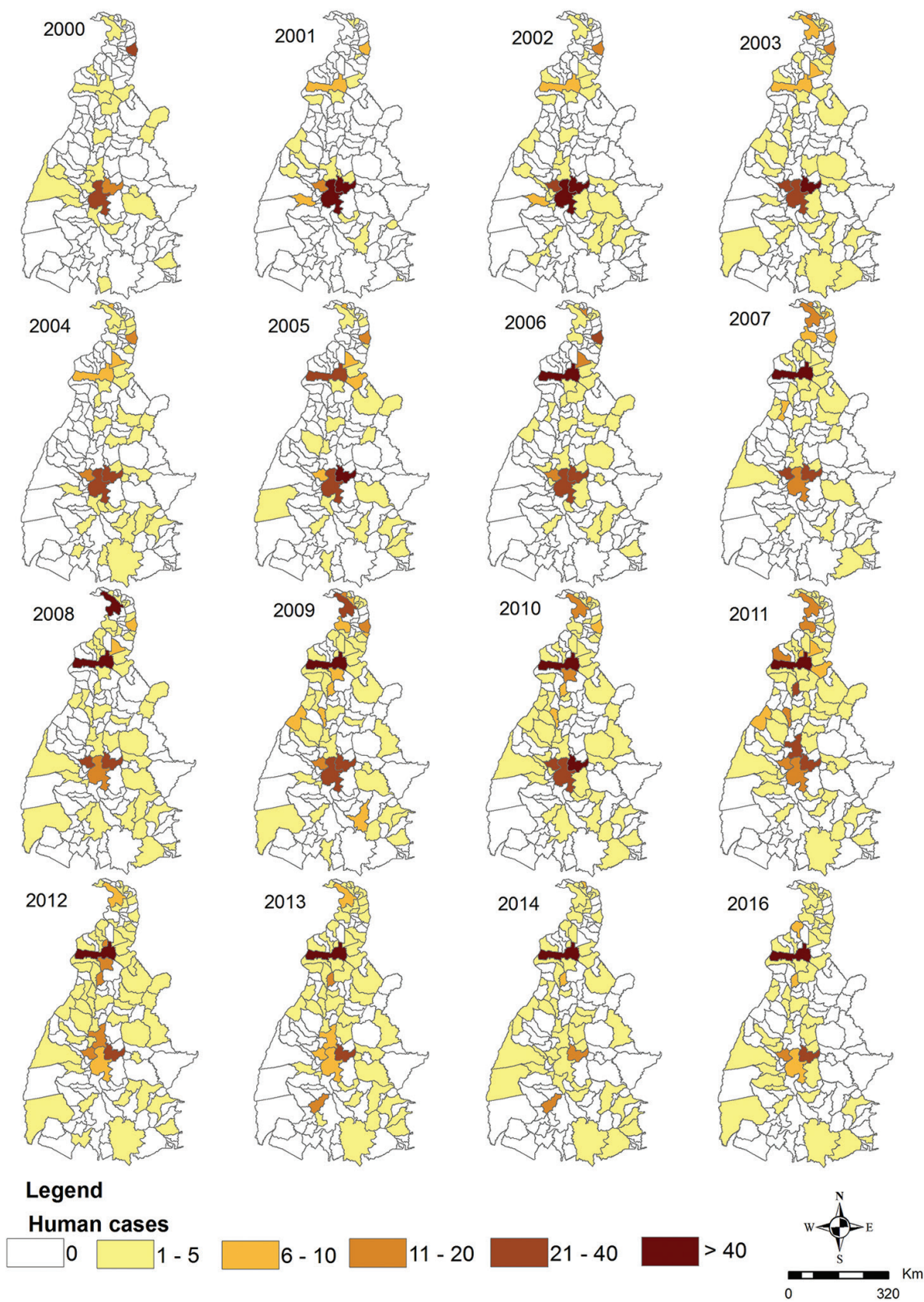


Figure 2. Spatiotemporal profile of American visceral leishmaniasis human cases in the State of Tocantins, 2000–2015. Source: Health Department of Tocantins State. Map design: Núcleo de Geoprocessamento LIS/ICICT/FIOCRUZ.

of Araguaína is mainly responsible for the increased production of human cases in the state, with the temporal pattern of human cases matching the state's pattern (**Figure 3**).

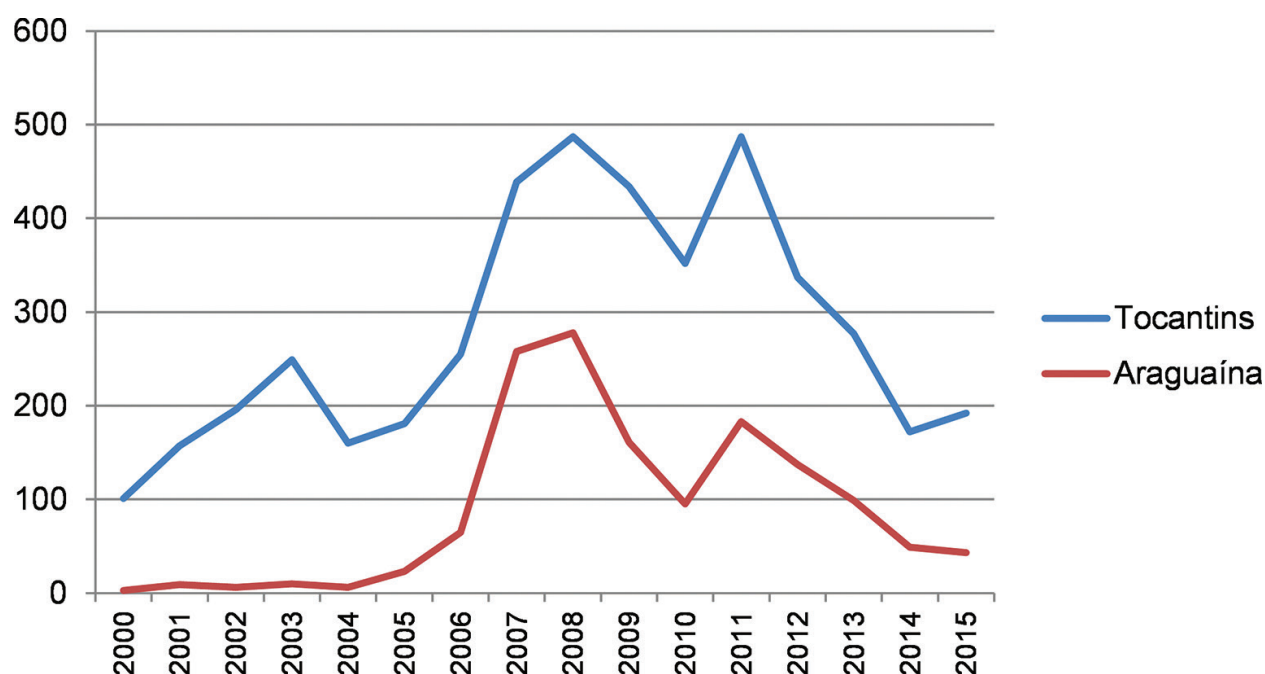


Figure 3. Number of American visceral leishmaniasis human cases recorded in Araguaína municipality and in Tocantins State, 2000–2015. Source: Health Department of Tocantins State.

Epidemiological surveillance is a major component of the Brazilian Control Program of Visceral Leishmaniasis (CPVL). The program has guidelines for stratifying municipalities under different categories, as areas with or without transmission of AVL. Through epidemiological analysis, health professionals and managers can thus classify the municipalities then adopt the adequate actions for monitoring, surveillance, and control of AVL [3].

According to the methodology proposed by the CPVL, municipalities with transmission are stratified according to the average of human cases reported in the last 3 years and then are categorized as sporadic, moderate, or intense transmission [3]. In Tocantins State, from 2004 to 2015, some municipalities remained classified as intense transmission, especially in the northern and central region, showing that the number of human cases remained high and constant throughout the years, especially in areas where there is high environmental impact (**Figure 4**).

From 2004 to 2015, intense transmission remained in the municipalities of Araguaína, Paraíso do Tocantins, Porto Nacional, and Palmas. However, municipalities such as Gurupi, Miracema do Tocantins, Nova Olinda, Araguatins, Carmolândia, Colinas do Tocantins, and Sampaio, in recent years, have moved from the sporadic or moderate category to the intense category, possibly due to environmental impacts. Other 57 municipalities were now classified as of sporadic transmission, originally being municipalities without transmission, comprising 50% of the municipalities with expansion of transmission. Only 15 municipalities, equivalent to 11% of the state, do not have transmission, and 34% of the municipalities have decreased the number of cases during the study period.

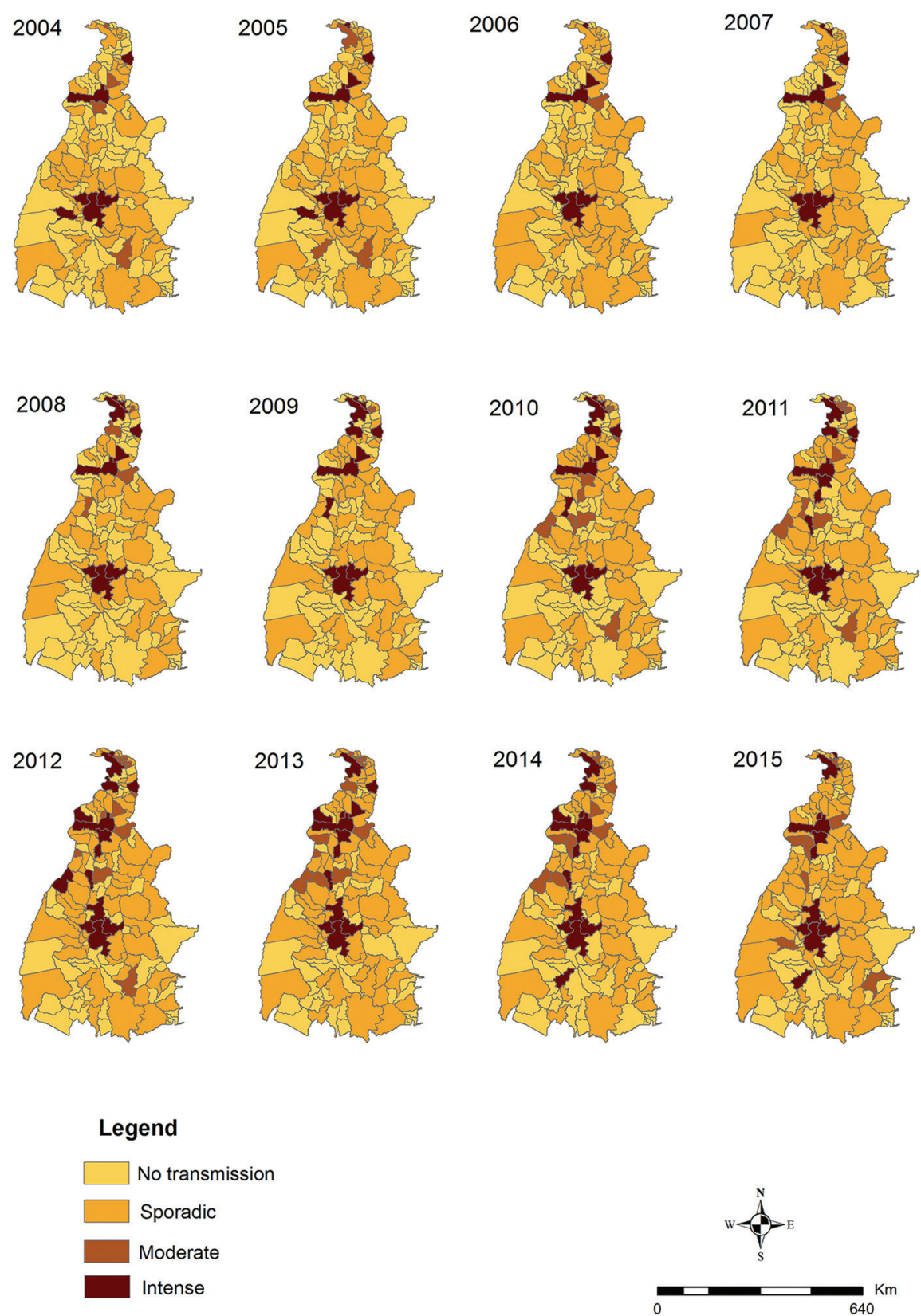


Figure 4. Spatiotemporal profile of the stratification of municipalities for American visceral leishmaniasis in Tocantins State, 2004–2015. Source: Health Department of Tocantins State. Map design: Núcleo de Geoprocessamento LIS/ICICT/FIOCRUZ.

To characterize the municipalities with the presence of the vector *L. (L.) longipalpis*, a literature search was held in the following databases: LILACS [25], MEDLINE [26], and SciELO [27]; using the keywords [28]: *Lutzomyia*, American visceral leishmaniasis, *L. (L.) longipalpis*, and Tocantins. Searches were also performed for conference abstracts, theses, dissertations, and monographs, and unpublished information was provided by the Health Department of Tocantins State [personal communication].

For the municipalities without information on the vector, it was assumed that *L. (L.) longipalpis* occurs where there are human cases of AVL, because so far *L. (L.) longipalpis* is the only vector species associated with the disease in the state of Tocantins and there is no record of *L. (L.) cruzi* in the state [personal communication Health Department of Tocantins State]. While this assumption does introduce a minor uncertainty in the analyses, not considering the presence of the vector in areas where AVL transmission is well-known would compromise the results.

From the scarce bibliographic records that were found (9), the vector was recorded in only 22 municipalities of Tocantins [29–37]. In contrast, there are records of human cases in 124 municipalities, which demonstrate the lack of entomological studies in the state (**Figure 5**).

3. Environmental factors

In order to evaluate the association between AVL, *L. (L.) longipalpis*, and different environmental factors (land use and deforestation), nonparametric Spearman correlation tests were applied to the data. Analyses were performed in the software SPSS (version 22) and correlations were considered significant at levels 0.95–0.99.

3.1. Land use

Data on land use for the Cerrado biome was provided by the Federal University of Goiás [23]; the data for the Amazon biome was obtained at the Web site of the Brazilian Institute of Geography and Statistics [21]. The land use maps and municipal boundaries were integrated in ArcGIS, which enabled the calculation of the percentage of land use class in each municipality (**Figure 5**).

Significant positive correlation was identified between the cumulative incidence of human cases (2000–2015) and area with urban influence, ombrophilous forest, and ecological tension areas (**Table 1**). The land use classes that had positive correlation with the yearly incidence were secondary vegetation, urban area, ombrophilous forest, ecological tension areas, pioneer vegetation areas, and agriculture. Savannah had negative correlation with the yearly AVL incidence (**Table 1**).

The presence of *L. (L.) longipalpis* was significantly correlated with secondary vegetation and with ombrophilous forest (**Table 1**). Considering the occurrence of *L. (L.) longipalpis* in all municipalities where there are records of autochthonous human cases of AVL, in addition to the information from the literature [29–37], it is suggested that the vector is present in all classes of land use (**Figure 5, Table 1**).

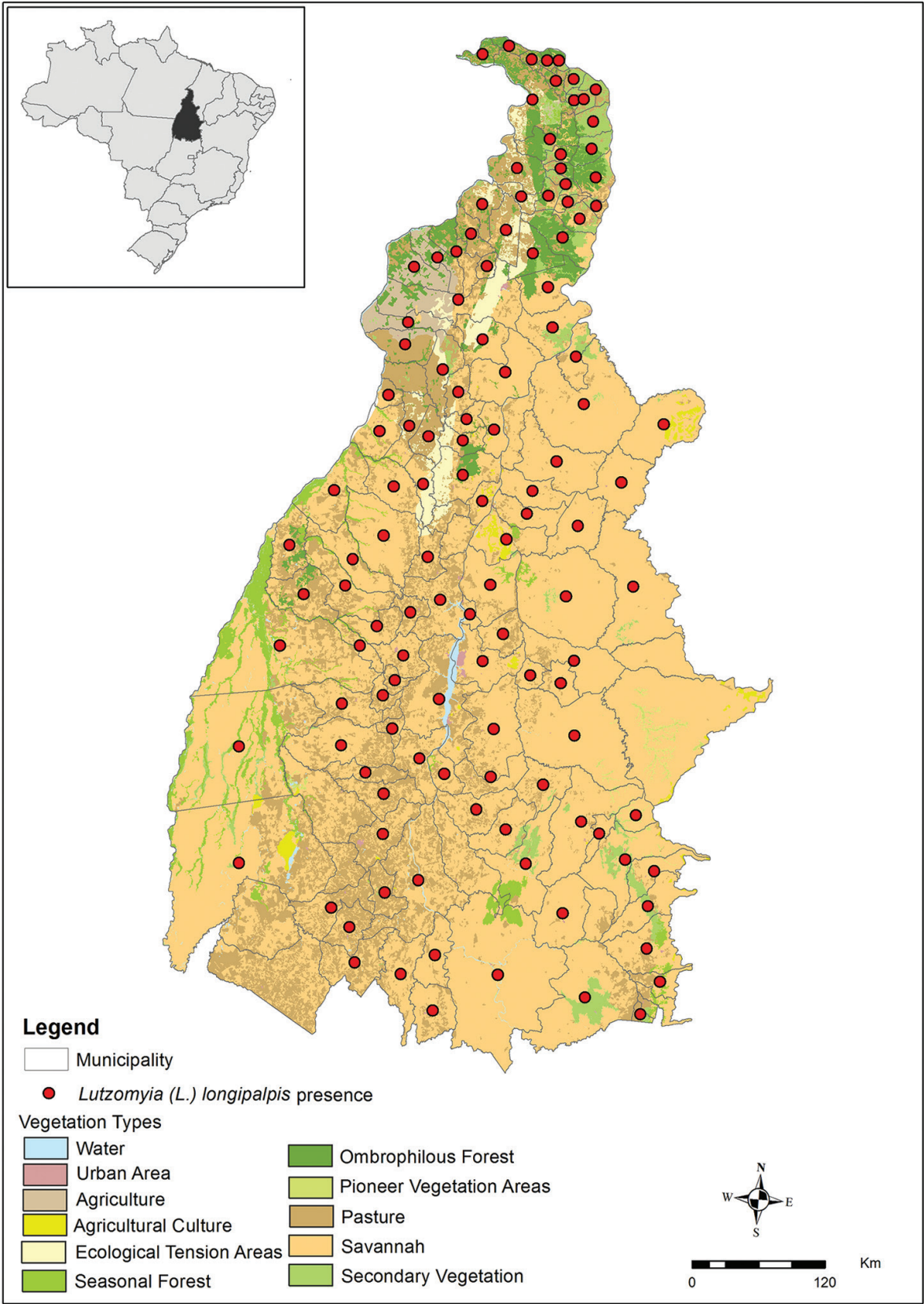


Figure 5. Map of Tocantins State with land use classes in association with the presence of *Lutzomyia (Lutzomyia) longipalpis*. Source: UFG, IBGE. Map design: Núcleo de Geoprocessamento LIS/ICICT/FIOCRUZ.

AVL incidence	Pasture	Secondary vegetarian	Urban area	Ombrophilous forest	Savannah	Pioneer vegetation areas	Agriculture culture	Ecological tension areas	Agriculture	Seasonal forest
	r	r	r	r	r	r	r	r	r	r
2000	-0.072	-0.010	0.067	0.129	0.027	-0.049	-0.002	-0.088	-0.052	-0.032
	0.399	0.910	0.431	0.132	0.749	0.570	0.977	0.304	0.544	0.707
2001	-0.022	-0.033	0.144	-0.080	0.068	0.254**	-0.024	-0.060	-0.039	0.019
	0.800	0.698	0.090	0.348	0.423	0.003	0.775	0.480	0.646	0.824
2002	0.000	-0.053	0.163	-0.038	0.068	-0.048	-0.055	-0.094	-0.020	-0.001
	0.999	0.538	0.055	0.655	0.426	0.574	0.520	0.269	0.813	0.986
2003	0.042	0.026	0.247**	0.209*	-0.144	-0.063	-0.049	0.084	-0.034	-0.080
	0.624	0.758	0.003	0.014	0.092	0.461	0.563	0.324	0.690	0.352
2004	-0.136	0.044	0.062	0.202*	0.011	-0.062	-0.040	-0.003	-0.081	-0.105
	0.112	0.610	0.466	0.017	0.899	0.467	0.642	0.968	0.345	0.219
2005	-0.045	0.025	0.130	0.155	-0.051	-0.042	0.006	0.030	-0.038	-0.081
	0.595	0.768	0.126	0.068	0.553	0.625	0.944	0.726	0.655	0.344
2006	-0.018	-0.007	0.085	0.134	-0.047	-0.075	-0.055	0.073	-0.033	-0.054
	0.835	0.937	0.320	0.115	0.582	0.379	0.524	0.394	0.703	0.529
2007	0.117	-0.006	0.094	0.152	-0.263**	-0.062	-0.080	0.232**	0.232**	-0.034
	0.169	0.942	0.269	0.074	0.002	0.469	0.352	0.006	0.006	0.690
2008	0.061	0.050	0.141	0.156	-0.220**	-0.067	-0.064	0.251**	0.117	-0.042
	0.478	0.557	0.099	0.067	0.009	0.437	0.455	0.003	0.172	0.622
2009	0.099	0.039	0.046	0.110	-0.231**	-0.055	-0.091	0.282**	0.071	0.048
	0.244	0.647	0.588	0.197	0.006	0.523	0.286	0.001	0.407	0.574

Table 1. Correlation between classes of land use and incidence of American visceral leishmaniasis; correlation between classes of land use and the vector, *Lutzomyia (Lutzomyia) longipalpis*, from 2000 to 2015, in Tocantins State.

AVL incidence	Pasture	Secondary vegetarian	Urban area	Ombrophilous forest	Savannah	Pioneer vegetation areas	Agriculture culture	Ecological tension areas	Agriculture	Seasonal forest
	r	r	r	r	r	r	r	r	r	r
2010	0.020	0.169*	0.084	0.044	-0.165	-0.097	-0.114	0.280**	-0.014	-0.050
	0.813	0.047	0.326	0.604	0.052	0.254	0.182	0.001	0.866	0.558
2011	0.104	-0.044	0.046	0.151	-0.246**	-0.078	-0.084	0.290**	0.212*	-0.087
	0.225	0.608	0.588	0.076	0.004	0.361	0.324	0.001	0.012	0.310
2012	0.103	-0.031	0.039	0.038	-0.139	-0.059	-0.055	0.247**	0.061	-0.063
	0.226	0.717	0.649	0.654	0.102	0.493	0.524	0.003	0.473	0.459
2013	-0.006	0.120	-0.023	0.231**	-0.198*	-0.086	-0.022	0.153	0.116	-0.142
	0.944	0.160	0.792	0.006	0.020	0.314	0.793	0.073	0.174	0.095
2014	0.005	-0.014	0.080	0.170*	-0.148	-0.050	-0.069	0.066	0.205*	-0.043
	0.952	0.869	0.349	0.046	0.082	0.556	0.423	0.441	0.016	0.617
2015	-0.082	-0.003	0.051	0.140	0.027	-0.047	-0.008	-0.083	-0.050	-0.043
	0.335	0.968	0.552	0.101	0.754	0.585	0.925	0.331	0.557	0.618
2000–2015	0.104	0.029	0.171*	0.216*	-0.270**	-0.100	-0.091**	0.273**	0.104	-0.090
	0.222	0.737	0.044	0.011	0.001	0.243	0.027	0.001	0.222	0.292
Presence of the vector	-0.116	0.203*	0.104	0.213*	-0.044	-0.011	-0.077	0.070	0.091	-0.080
	0.173	0.017	0.222	0.012	0.605	0.896	0.370	0.412	0.284	0.352

*Significant correlation at level 0.05.

**Significant correlation at level 0.01.

Table 1. Correlation between classes of land use and incidence of American visceral leishmaniasis; correlation between classes of land use and the vector, *Lutzomyia (Lutzomyia) longipalpis*, from 2000 to 2015, in Tocantins State (Continued).

3.2. Deforestation

To assess deforestation in each municipality, the rates of the yearly increase of deforestation for the period 2001–2014 were produced through digital classification of satellite imagery and provided by the PRODES project [38].

In the state of Tocantins, the increase of deforested areas remained constant throughout the years in some municipalities, mainly in the north and west of the state (**Figure 6**).

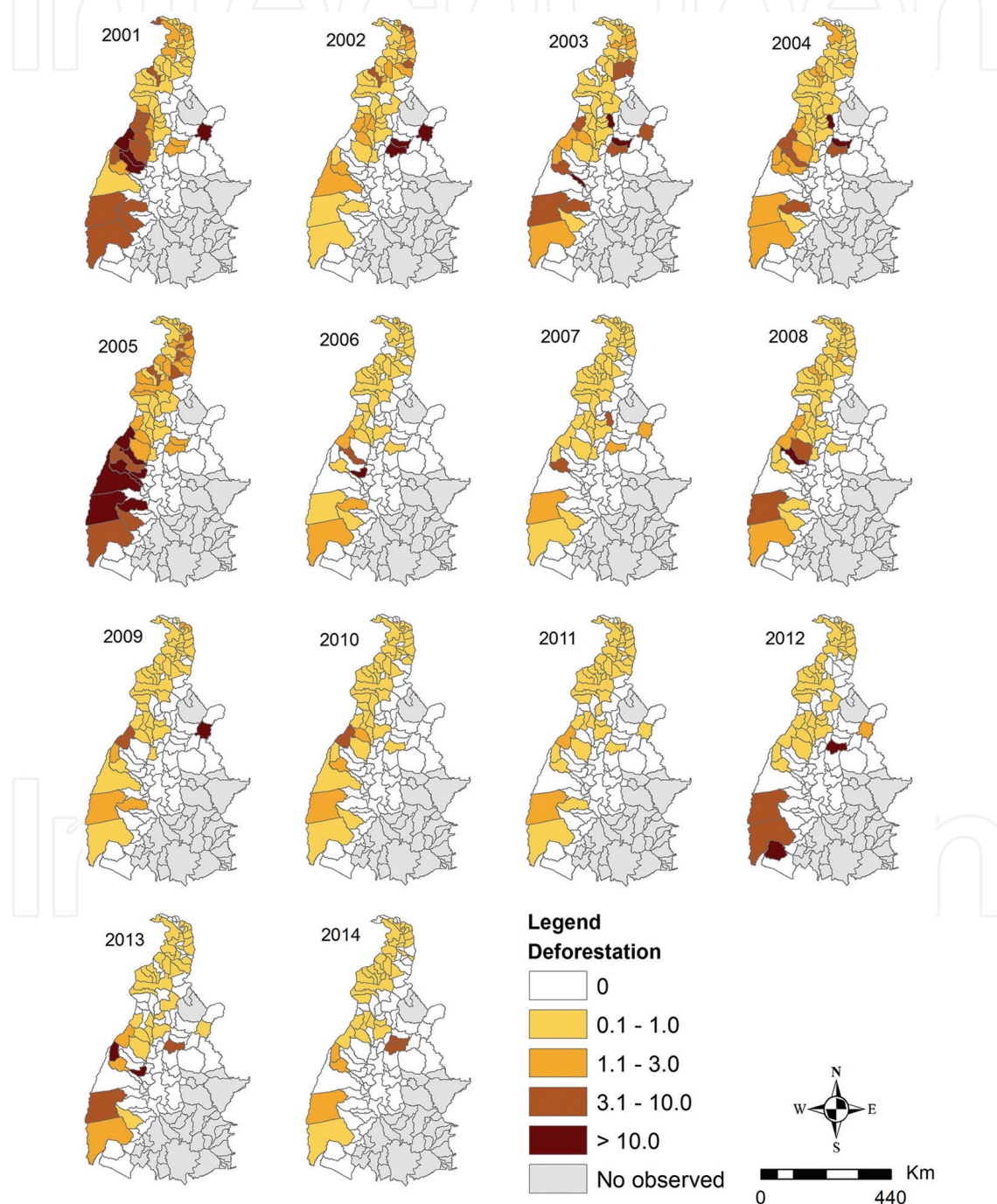


Figure 6. Spatiotemporal profile of the increase of deforestation in Tocantins State, 2001–2014. Source: PRODES. Map design: Núcleo de Geoprocessamento LIS/ICICT/FIOCRUZ.

Deforested area	<i>r</i>	<i>p</i> -value	Deforested area	<i>r</i>	<i>p</i> -value
AVL cases 2000	-0.017	0.845	AVL incidence 2000	-0.070	0.475
AVL cases 2001	-0.103	0.294	AVL incidence 2001	-0.107	0.279
AVL cases 2002	-0.067	0.496	AVL incidence 2002	-0.130	0.187
AVL cases 2003	0.098	0.322	AVL incidence 2003	-0.004	0.969
AVL cases 2004	-0.067	0.498	AVL incidence 2004	-0.132	0.178
AVL cases 2005	0.054	0.582	AVL incidence 2005	-0.030	0.763
AVL cases 2006	0.005	0.957	AVL incidence 2006	0.021	0.835
AVL cases 2007	0.247*	0.011	AVL incidence 2007	0.506**	0.000
AVL cases 2008	0.220*	0.024	AVL incidence 2008	0.512**	0.000
AVL cases 2009	0.337**	0.000	AVL incidence 2009	0.358**	0.000
AVL cases 2010	0.207*	0.034	AVL incidence 2010	0.195*	0.047
AVL cases 2011	0.266**	0.006	AVL incidence 2011	0.322**	0.001
AVL cases 2012	0.286**	0.003	AVL incidence 2012	0.203*	0.038
AVL cases 2013	0.246*	0.012	AVL incidence 2013	0.262**	0.007
Casos de LVA ano 2014	0.111	0.260	AVL incidence 2014	0.085	0.391

*Significant correlation at level 0.05.

**Significant correlation at level 0.01.

Table 2. Correlation between deforested areas and human cases of American visceral leishmaniasis; correlation between deforested area and incidence of American visceral leishmaniasis from 2000 to 2014, in Tocantins State.

Deforested area	<i>r</i>	<i>p</i> -value
Stratification 2004	-0.033	0.742
Stratification 2005	-0.022	0.824
Stratification 2006	0.035	0.721
Stratification 2007	-0.011	0.914
Stratification 2008	0.149	0.129
Stratification 2009	0.192*	0.050
Stratification 2010	0.337**	0.000
Stratification 2011	0.299**	0.002
Stratification 2012	0.307**	0.001
Stratification 2013	0.337**	0.000
Stratification 2014	0.327**	0.001

*Significant correlation at level 0.05.

**Significant correlation at level 0.01.

Table 3. Correlation between deforested area and stratification for American visceral leishmaniasis; correlation between the increase of deforestation and stratification of AVL, from 2004 to 2014, in Tocantins State.

The municipalities that had higher increase of deforestation were Aragominas, Araguaatins, Lagoa da Confusão, Araguaína, Ceará, Xambioá, Santa Fé do Araguaia, Pequizeiro, and Piraquê. Araguaína was the municipality that showed the most deforested area in the state.

As it was with the incidence of AVL and land use, deforested areas were positively correlated with human cases of AVL from 2007 to 2014 (Table 2).

Deforested areas and stratification of AVL were positively correlated in the last years, from 2009 to 2014 (Table 3).

4. Discussion

American visceral leishmaniasis is a disease that has been showing significant geographic expansion in Brazil. Decades ago, it was mainly present in the states of the Northeast and North regions. Currently, it has gained importance spreading into the Southeast and Midwest regions, and recently in the South region [3, 39].

Lutzomyia (L.) longipalpis is present in most of the states of Brazil, except in Santa Catarina, Acre, and Amazonas, demonstrating the high adaptability to different types of vegetation, climate, habitats, and feeding sources [3, 9, 11, 40]. The state of Tocantins lacks entomological studies with records of *L. (L.) longipalpis* in 16% of its municipalities [29–37], while there are reported human cases in 89% of the municipalities [24]. These facts show the need for further entomological studies, given the wide distribution of the disease in the state. The assumption of the presence of *L. (L.) longipalpis* in municipalities with AVL records does introduce some minor uncertainty in the analyses. The vector could be absent from an AVL focus if another sand fly species acts locally as a competent vector. So far, the only species that gathers enough evidence in the literature that plays an important role in the transmission of *L. (L.) infantum chagasi* is *L. cruzi* [13–15], and its distribution is restricted to Mid-West Brazil, in municipalities as far as 600 km from Tocantins State. Its presence in Tocantins is unlikely, then. The presence of *L. (L.) longipalpis* was assumed only in municipalities where the information was missing, so given the wide distribution of *L. longipalpis* in Brazil [12] and, more specifically, in Tocantins State [29–37], the chances of its capture in a new sand fly survey are high.

It is noteworthy that the 13 municipalities that have no record of human cases can be classified as vulnerable areas to AVL, because they border other municipalities that have records of human cases. Such municipalities deserve special attention, because according to the guidelines of the Manual of Surveillance and Control of AVL, conducting entomological survey is recommended in order to verify the presence or absence of the vector, and to check its spread in the city, in order to classify the vulnerable municipality as receptive (with the presence of vector) or unreceptive [3].

The application of remote sensing products and techniques in epidemiological studies began in the 1970s [41], and in conjunction with the use of GIS, it has facilitated the integration of environmental parameters and health data to develop models that can be used

for understanding the AVL epidemiology [42]. The analysis of the stratification of the municipalities showed that Araguaína, Paraíso do Tocantins, Porto Nacional, and Palmas retained the intense transmission through the years, while 50% of the municipalities had expansion of the transmission of AVL, demonstrating its importance as a public health issue in the state.

Some studies used GIS as an important analysis tool of the distribution of leishmaniasis vectors. In Belo Horizonte, an area that has one of the highest rates of human and canine AVL of Brazil, it was possible to correlate peridomestic environmental features and the vectors. *Lutzomyia (L.) longipalpis* showed higher abundance in areas of animal sheds with poor hygiene conditions, which favor the development of sand flies. In contrast, the proximity of areas with vegetation exerted little influence on the incidence of AVL, corroborating its urban profile [43].

In studies in Maranhão State, *L. (L.) longipalpis* was the most abundant sand fly species found in the Cerrado biome; in Bahia State, specimens were captured in areas of Caatinga and Atlantic Forest, demonstrating its adaptation to different environments [44–46].

Considering the assumption of *L. (L.) longipalpis* being present in municipalities where there are autochthonous records of human cases of AVL in Tocantins, the vector occurs in all classes of land use, being adapted to all environments including disturbed areas, corroborating studies that discuss its adaptation to changing environments [9, 34, 40, 47, 48]. A positive correlation was observed between the presence of *L. (L.) longipalpis* and areas of secondary vegetation [49] and ombrophilous forest in Tocantins, indicating that the vector is adapted to different environments, especially in areas recovering from human interventions or from natural causes.

In the analysis of the cumulative incidence of AVL and classes of land use, there was a negative correlation with agricultural areas, which can be explained by the increasing use of chemicals in plantations that reduce the number of insects [50–53], including sand flies [54, 55], and consequently reduce the number of human cases.

In the state of Mato Grosso, *L. (L.) longipalpis* occurs in the Cerrado biome, in forests and transition zones, which were suggested by some authors as potential breeding sites for this sand fly [56]. *Lutzomyia (L.) longipalpis* is also present in areas of different climatic conditions, such as semiarid areas (in the Caatinga biome), and wetter areas, with high adaptability to different habitats and environmental conditions [57–59]. Considering that the state of Tocantins covers two distinct biomes, Cerrado and Amazon, the occurrence of *L. (L.) longipalpis* in both biomes confirms its generalist behavior, being associated with diverse habitats [14].

Environmental changes, such as deforestation, impact the distribution of tropical diseases [60–63], potentially affecting the spatial distribution of the vectors of leishmaniasis [64]. The state of Tocantins presented constant increase of deforestation, especially in northern and western regions, areas with occurrence of human cases of AVL. In this scenario, Araguaína (municipality with the highest deforested area from 2001 to 2014) has become a priority for the Ministry of Health, for surveillance and control of AVL. In recent years, Araguaína has been producing high records of AVL. From 2007 to 2014, it was the second Brazilian municipality

with the highest production of AVL, while in the years 2007 and 2008 it had the highest number of human cases in Brazil [24].

It is known that AVL transmission remains active in areas with environmental changes, such as deforestation [65]. Thus, it is argued that continuous deforestation processes increase the number of people exposed to infection, creating conditions for the emergence of epidemic outbreaks [10, 16, 48], because it alters the natural conditions and habitats of some species of mammals, hosts of *leishmania*, that become closer to areas inhabited by the human population. This fact enables sand fly vectors with feeding plasticity, such as *L. (L.) longipalpis*, to transmit the parasite to humans [9, 10, 66, 67].

Studies conducted in Mato Grosso do Sul (area that has experienced a loss of native vegetation), demonstrated the presence of *L. (L.) longipalpis* in regions with little vegetation and low humidity, suggesting that the species would be adapted to different environmental conditions, and that it has been associated with human dwellings (captured inside houses) [68]. This study showed positive correlation between deforested areas and human cases, as well as with the incidence of AVL, from 2007, showing that deforested areas have higher incidence rates for AVL, and that deforestation would maintain transmission.

In the state of Tocantins, *L. (L.) longipalpis* was present in all classes of land use, and its dispersion into new areas clearly demonstrates that it is a species adapted to impacted environments, such as large areas of deforestation. In recent years, 57 municipalities, equivalent to 47% of the total, were originally classified as municipalities without transmission of AVL, and they are currently classified as sporadic transmission. According to the Manual of Surveillance and Control of Visceral Leishmaniasis [3], in municipalities with sporadic transmission, the actions related to the vector are limited to the knowledge of the species and dispersion of the sand fly population, besides the canine survey. Such evidence suggests that the actions of surveillance and control, in Tocantins, are not planned in a satisfactory manner, i.e., without considering the loss of large areas of vegetation and as a result people live in risk areas, becoming exposed to the infection of AVL.

The current aims of the CPVL [3] highlight silent municipalities (those with no human or canine cases), suggesting that they must be incorporated into surveillance and control actions of AVL, in order to avoid or minimize the spread of the disease into new areas. For example, in Tocantins, the analysis of stratification in the state has shown that nearly half of the municipalities have gained transmission of AVL through the years. The results presented here show that in the last 12 years, the cities of Araguaína, Paraíso do Tocantins, Porto Nacional, and Palmas remained as intense transmission areas, which demonstrates the continued production of new human cases. The positive correlation between deforested areas and stratification since 2009 clearly shows the influence of growing deforestation on the disease in the state. These observations, coupled with the fact that there was an increase in transmission in 50% of municipalities, possibly due to changes in the environment, demonstrates the real need for an evaluation of the control and surveillance actions being carried

out, and that in the future the AVL can surprise health managers with a high number of human cases.

In a recent study conducted in the city of Porto Nacional (TO), *L. (L.) longipalpis* was more abundant in urban areas compared to rural areas, confirming its adaptation to these environments. In addition, its anthropophilic behavior and feeding plasticity might have contributed to the installation of the AVL transmission cycle in urban areas and to its maintenance in rural areas [34].

The correlation analysis of the incidence of AVL with the classes of land use showed distinct correlations over the years, demonstrating again that the vector of AVL, *L. (L.) longipalpis* is adapted to different types of vegetation. The positive correlation with urban areas shows that human cases are present in the urbanized environment, and that *L. (L.) longipalpis* was near the urban areas of the state of Tocantins municipalities, corroborating studies that indicate its adaptation to this modified environment [3, 9, 69, 70].

In the urban area of Campo Grande (MS), correlation was found between the abundance of *L. (L.) longipalpis*, percentage of vegetation cover, and the average vegetation index. However, there was no significant association between the diversity of habitats and abundance of the vector; the authors suggest that large trees can offer better microenvironmental conditions favoring the reproduction of the sand fly [71].

Urbanization changes the microclimate in cities and nearby locations, creating heat islands that result in warmer average temperatures when compared to less disturbed areas [72, 73]. Temperature changes might increase vectorial capacity and reshape epidemic curves that determine the receptivity of areas for the pathogen [73].

A study conducted in northeast Brazil showed no significant correlation of *L. (L.) longipalpis* with the average monthly temperature, relative humidity, or precipitation, demonstrating its adaptation to different climatic conditions [74]. In Barra do Garças (MT), a priority municipality to the Ministry of Health, it was found that *L. (L.) longipalpis* was the most abundant sand fly species with abundance peaks occurring during the rainy season, and correlation with relative humidity in urban areas [75].

The diversity of environments where AVL should be considered as determinant factors in the maintenance of the disease added to the biological, geographical, and social factors [12, 48]. This evidence is related with epidemiological data from last decades, which reveals the suburbanization and urbanization of the disease, with outbreaks in major cities and capitals [3].

Most of Tocantins State (88% of its area) is covered by the Cerrado biome, which had 49% of its forest cover cleared due to anthropogenic environmental interventions in the period 2002–2011. The state of Tocantins lost 0.45% of the biome between 2010 and 2011. It is noteworthy that the Cerrado is the second Brazilian biome that suffered the most changes with human occupation, following the Atlantic Forest [49].

5. Concluding remarks

In the current scenario, where environmental changes enhance implications on public health, it is critical that the studies of environmental-related diseases are intensified, especially for vector-borne diseases, such as AVL. *Lutzomyia (L.) longipalpis* is the most important link in the transmission chain of AVL and it is undoubtedly a major biological risk factor, essential for the transition between different epidemiological profiles and for the increasing urbanization of the disease. Clearly, the urbanization of the vector has been the main challenge for the surveillance and control of the disease.

The results presented here demonstrate a correlation between deforestation and the possible emergence of outbreaks, since AVL persists in areas with environmental changes. The increase of deforested areas remained constant in the state of Tocantins, and also showed expansion in the record of human cases, especially in the municipality of Araguaína.

The vector *L. (L.) longipalpis* was present in all land use classes, being adapted to all environments, including impacted areas. This information coupled with the correlation between the incidence of the disease and urban areas demonstrate once again the vector's adaptation to anthropic environments.

Brazil faces geographic expansion and urbanization of AVL and the Manual of Control and Surveillance of AVL from the Ministry of Health has as one of its goals to decrease the vector population and/or the minimization of vector contact with man (reducing the risk of transmission); the manual also has as a challenge to evaluate the vector behavior in the urban area and the factors of its adaptation to new habitats and environmental changes in a way to better understand the spatial dynamics of the disease. It is also hypothesized that vector populations are already resistant to insecticides applied against adult sand flies. As a result, recommended control actions for AVL are focused on early diagnosis and treatment of human cases, reduction of the sand fly vector population, elimination of domestic reservoirs, and additionally, health and education activities aimed in particular at patients and populations at risk of contracting the disease. However, despite well-defined guidelines, the actions are not always successful in controlling the vector.

In this context, despite the efforts made by the local Health Department, the state of Tocantins has a persistent scenario of AVL transmission. It is also important to note that the state has suffered over the last few years through major environmental impacts, especially through large enterprises. Such evidence points to a disturbing scenario regarding the transmission of AVL, one of expansion and urbanization; therefore, the determinants of such impacts must be constantly evaluated.

In conclusion, planning and implementation of public policies are necessary to minimize the impacts of anthropogenic environmental change. The results demonstrate the need to incorporate integrated actions, since AVL is expanding as a result of environmental impacts and the adaptation of the vector *L. (L.) longipalpis* to various habitats.

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