Magnitude and trend of American Tegumentary Leishmaniasis in the State of São Paulo, Brazil, 1975 to 2008

Magnitude e tendência da Leishmaniose Tegumentar Americana no Estado de São Paulo, Brasil, 1975 a 2008

Abstract

The aim of this study was to analyze the magnitude and trend of American Tegumentary Leishmaniasis (ATL) in the State of São Paulo from 1975 to 2008. An ecological study that classified municipalities according to the magnitude of transmission was performed. From 1975 to 1985, 1,281 cases of ATL were registered in 45 municipalities, rising to 258 municipalities and 4,093 cases from 1986 to 1995; and reaching 385 municipalities and 7,604 cases from 1996 to 2008. *Lutzomyia intermedia s.l.* was collected in most of the entomological surveys. In the classification of municipalities according to magnitude, 67.5% were observed to have a "small magnitude," 19.2% "moderate magnitude" and 13.3% "high magnitude." The highest incidences of ATL have been restricted to underserved areas close to the Atlantic forest. There was an increase in the number of municipalities with small occurrence of cases and expansion in the area of risk.

Keywords: American Tegumentary Leishmaniasis. Entomological Surveillance. Control. Epidemiology. State of Sao Paulo. Brazil.

Rubens Antonio da Silva
Vanessa Taís Cruz Mercado
Lúcia de Fátima Henriques
Ricardo Mário de Carvalho Ciaravolo
Dalva Marli Valério Wanderley

Departamento de Combate a Vetores - Superintendência de Controle de Endemias - Secretaria de Estado da Saúde de São Paulo

Correspondência: Rubens Antonio da Silva. Departamento de Combate a Vetores, Superintendência de Controle de Endemias, Secretaria de Estado da Saúde de São Paulo. Rua Paula Sousa 166, 1º andar, Luz, CEP 01027-000 São Paulo, SP. E-mail: rubensantoniosilva@gmail.com

Resumo

O objetivo deste estudo foi analisar a magnitude e tendência da Leishmaniose Tegumentar Americana (LTA) no Estado de São Paulo entre 1975 e 2008. Foi conduzido um estudo ecológico que categorizou os municípios segundo a magnitude da transmissão. No período de 1975 a 1985, 45 municípios foram responsáveis pelo registro de 1.281 casos de LTA, passando a 258 municípios e 4.093 casos entre 1986 e 1995, e a 385 municípios e 7.604 casos entre 1996 a 2008. O vetor *Lutzomyia intermedia s.l.* foi coletado na maioria das pesquisas entomológicas. Na classificação dos municípios segundo a magnitude pode-se verificar que 67,5% possuíam "pequena magnitude", 19,2% "média magnitude" e 13,3% "grande magnitude". As maiores incidências de LTA permanecem restritas a algumas áreas carentes e próximas à Mata Atlântica. Houve aumento no número de municípios com pequena ocorrência de casos e ampliação da área de risco.

Palavras-chave: Leishmaniose Tegumentar Americana. Vigilância entomológica. Controle. Epidemiologia. Estado de São Paulo. Brasil.

Introduction

The American Tegumentary Leishmaniasis (ATL) is a zoonosis widely spread around the American continent, extending from the Southern United States to northern Argentina. It is considered to be one of the most relevant infectious diseases in this continent[1]. In the last 20 years, in Brazil, the number of ATL cases and its geographic occurrence have increased. Currently, this disease is found in all Brazilian states, with different epidemiological profiles and transmission patterns[2].

In the state of São Paulo, ATL is an endemic disease transmitted by insects of the Order Diptera, Family Psychodidae, mostly belonging to the genus *Lutzomyia* and having two epidemiological patterns of transmission: the first one involves human beings coming into contact with the wild enzootic cycle; and the second one involves household transmission and human beings, synanthropic animals and Phlebotominae species that are adapting to rural and periurban environments[3], in areas where the natural environment has greatly changed. Currently, the ATL transmission in the state of São Paulo is considered to remain associated with the place where the case has been recorded and the woods; this disease has affected all age groups regardless of gender. In the past, ATL had a localized geographical aspect and high incidence in workers who performed forest-related activities[4]. This situation changed with the years and a new epidemiological profile appeared in the 1970s, in which the occurrence of sporadic and/or small outbreaks characterizes the current pattern of ATL transmission in the state of São Paulo[5 6 7].

The steady increase in the number of cases led to the formation of an inter-institutional group in 1993, under the coordination of the *Centro de Vigilância Epidemiológica da Secretaria de Estado da Saúde de São Paulo* (CVE/SES/SP – State of São Paulo Department of Health Epidemiological Surveillance Center) and participation of the *Superintendência de Controle de*

Endemias (SUCEN – Center for Endemic Disease Control) and *Instituto Adolfo Lutz* (IAL – Adolfo Lutz Institute) to reassess the Technical Norms of American Tegumentary Leishmaniasis Epidemiological Surveillance and Control. In this group, SUCEN was responsible for the assessment and development of an information system for entomological surveillance, case reporting and feedback of information to Health Services[9]. The Surveillance System is defined as a passive system, where reports derived from the public health network through primary health centers (PHC) are mandatory when a case is confirmed. Nonetheless, although efforts have been made for prompt reporting, the underreporting of an important number of cases is still observed[9].

With regard to entomological surveillance, *Lutzomyia intermedia s.l.* (Lutz & Neiva, 1912) has been pointed out as the most important taxon in the current epidemiological profile of ATL in the state of São Paulo, due to its predominance in altered environments and constant presence in the intra and peridomicile[7 10 11 12 13], although being considered as a well-defined species complex: *Lu. intermedia s.str.* and *Lutzomyia neivai*[14 15]. However, transmission cannot be only attributed to *Lu. intermedia s.str.* [10 16]. This taxon has a major role as a vector of *Leishmania (Viannia) braziliensis* in the home environment, whereas *Lutzomyia whitmani* (Antunes & Coutinho, 1939) and *Lutzomyia migonei* (France, 1920) have this role in the out-of-home environment[17].

The present study aimed to analyze the magnitude and trend of ATL in the cities of the state of São Paulo, between 1975 and 2008, with the purpose of supporting the control program developed by the state.

Methods

An ecological descriptive study was conducted to analyze secondary data on autochthonous ATL cases and their geographical distribution, obtained from the CVE/SES/SP between 1975 and 2008; and information about the entomological surveys conducted by SUCEN and originated from the confirmation of autochthonous cases between 1985 and 2008.

The entomological survey methodologies used were as follows: without luminous bait, in a resting place, in the intradomicile or on the walls of outbuildings, with a minimum duration of three hours, using Castro traps, a deadly chamber or manual aspirator on the inner walls of the home with the use of the sheet technique when these walls are not dark or plastered; with luminous bait, using CDC electric traps installed in different points of the possible place of transmission in the home, from dusk to dawn, with a duration of 12 hours; and Shannon trap for three hours after dusk, preferably situated in the peridomicile or by the edge of the woods when these are close to the home[8]. The objective of the entomological traps is to identify the vector species instead of quantifying it. Species were classified according to the classification developed by Young & Duncan, 1994[18].

In the present study, the *Lu. intermedia s.l.* classification was taken into consideration rather than *Lu. intermedia s.str*. or *Lu. neivai*, due to the data found in the databases referring to information previous to the distinction of this species complex.

Mean incidence rates were calculated from autochthonous cases reported to the CVE/SES/SP. The dates when clinical manifestations of each case reported between 1998 and 2008 began to occur were considered for these incidences.

Cities were classified based on the magnitude of occurrence of cases as "small magnitude" (occurrence of 1 to 5 cases), "average magnitude" (occurrence of 6 to 20 cases) and "great magnitude" (occurrence of 20 or more cases) and analyzed according to their environmental characteristics, their ATL incidence rates and magnitude.

The figures that show the occurrence of vectors were developed with data from Pessoa and Barretto[4] in the 1940s and from entomological surveys conducted by SUCEN between 1985 and 2008, having considered the studies by Marcondes

(1996)[14] and Andrade-Filho et al. (2003 and 2007)[19,20] on *Lutzomyia intermedia* and *Lutzomyia neivai*, represented in this study by *Lutzomyia intermedia s.l.*

This study was conducted with secondary data derived from the SUCEN and CVE/SES/SP and only grouped data were published. The research protocol was submitted to and approved by SUCEN.

Results

Between 1975 and 2008, the CVE/SES/SP recorded 12,978 autochthonous ATL cases distributed in 385 cities, with a predominance of those situated in the areas mostly covered by the Atlantic Forest. From 1975 to 1985, 45 cities were responsible for the recording of 1,281 ATL cases, increasing to 258 cities and 4,093 cases from 1986 to 1995 and to 32.9% of cities affected from 1996 to 2008, thus representing a linear trend of increase in number of cases (r^2=0.5243) (Figure 1). There was an increase in the number of cities in the state of São Paulo where 1 to 5 autochthonous cases of ATL were reported. Between 1986 and 1995, cities with 1 to 5 cases represented 58.9% and those with up to 20 cases represented 80.6%; between 1998 and 2008, these percentages were 67.5 and 86.7, respectively. A number higher than 20 cases was observed in 19.4% of the cities in the state from 1986 to 1995 and in 13.3% from 1998 to 2008.

The coefficients of accumulated mean incidence between 1998 and 2008 were calculated and they varied from 0.00 to 152.48 cases/ 100,000 inhabitants, when the highest indices were found in cities mainly situated in the eastern part of the state (Figure 2). The southeastern, northeastern and central-west regions of Brazil contributed with high percentages. In the classification of cities according to the magnitude of occurrence of cases, 67.5% had a "small magnitude", 19.2% had an "average magnitude" and 13.3% had a "great magnitude".

The *Lutzomyia intermedia s.l.* vector was associated with the majority of entomological surveys conducted by SUCEN. When compared to the distribution of *Lu. intermedia* made by Pessoa and Barretto (1948)[4], an increase in its distribution area can be observed (Figure 3). Between 1998 and 2008, 14,354 Phlebotominae specimens of 16 species of the genus *Lutzomyia* were collected, mainly represented by *Lu. intermedia s.l.* (81.25%), *Lu. whitmani* (7.28%) and *Lutzomyia pessoai* (3.28%) (Table 1). When the 645 cities of the state and the entomological collections performed between 1985 and 2008 were considered, *Lu. intermedia s.l.* was recorded in 148 of these cities (22.9%), *Lu. whitmani* in 111 (17.2%), *Lutzomyia fischeri* in 102 (15.8%), *Lu. migonei* in 87 (13.4%) and *Lu. pessoai* in 66 (10.2%). Lower percentages were obtained for species of minor epidemiological importance.

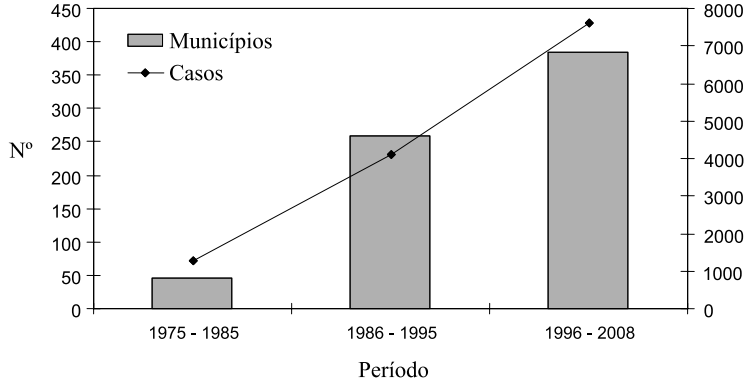

Figure 1 - Number of autochthonous cases of American Tegumentary Leishmaniasis and municipalities affected by period. State of São Paulo, 1975 to 2008.
Figura 1 *- Número de casos autóctones de Leishmaniose Tegumentar Americana e municípios acometidos segundo período. Estado de São Paulo, 1975 a 2008.*

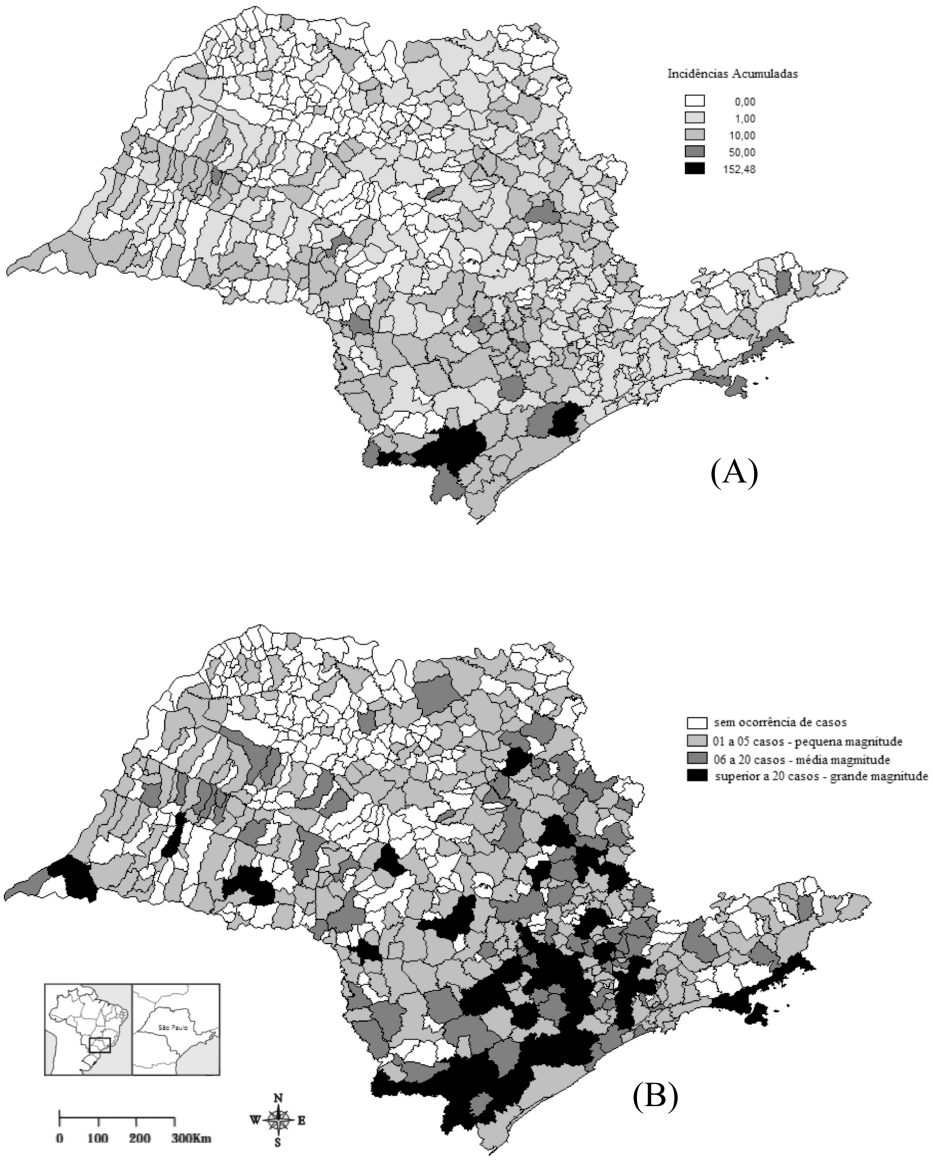

Figure 2 - American Tegumentary Leishmaniasis in the State of São Paulo: (A) Cumulative incidence, 1998 to 2008, (B) Distribution of autochthonous cases according to the magnitude, 1998 to 2008.

Figura 2 *– Leishmaniose Tegumentar Americana no Estado de São Paulo: (A) Incidência acumulada, 1998 a 2008; (B) Distribuição dos casos autóctones segundo magnitude, 1998 a 2008.*

In possible areas of infection, the presence of only one Phlebotominae species was observed in 41 (6.3%) cities of the state of São Paulo, two sub-species in 33 cities (5.1%), and a number higher than three species in 132 cities (20.5%).

The cross-over between ground cover and geomorphological[21] data and case distribution data, according to the magnitude between 1998 and 2008 and distribution of ATL vectors between 1985 and 2008, enabled researchers to observe an increase in high-risk areas.

Discussion

In the first decades of the 20th century, when the western part of the state of São Paulo was colonized, important endemic areas of ATL appeared, especially in the

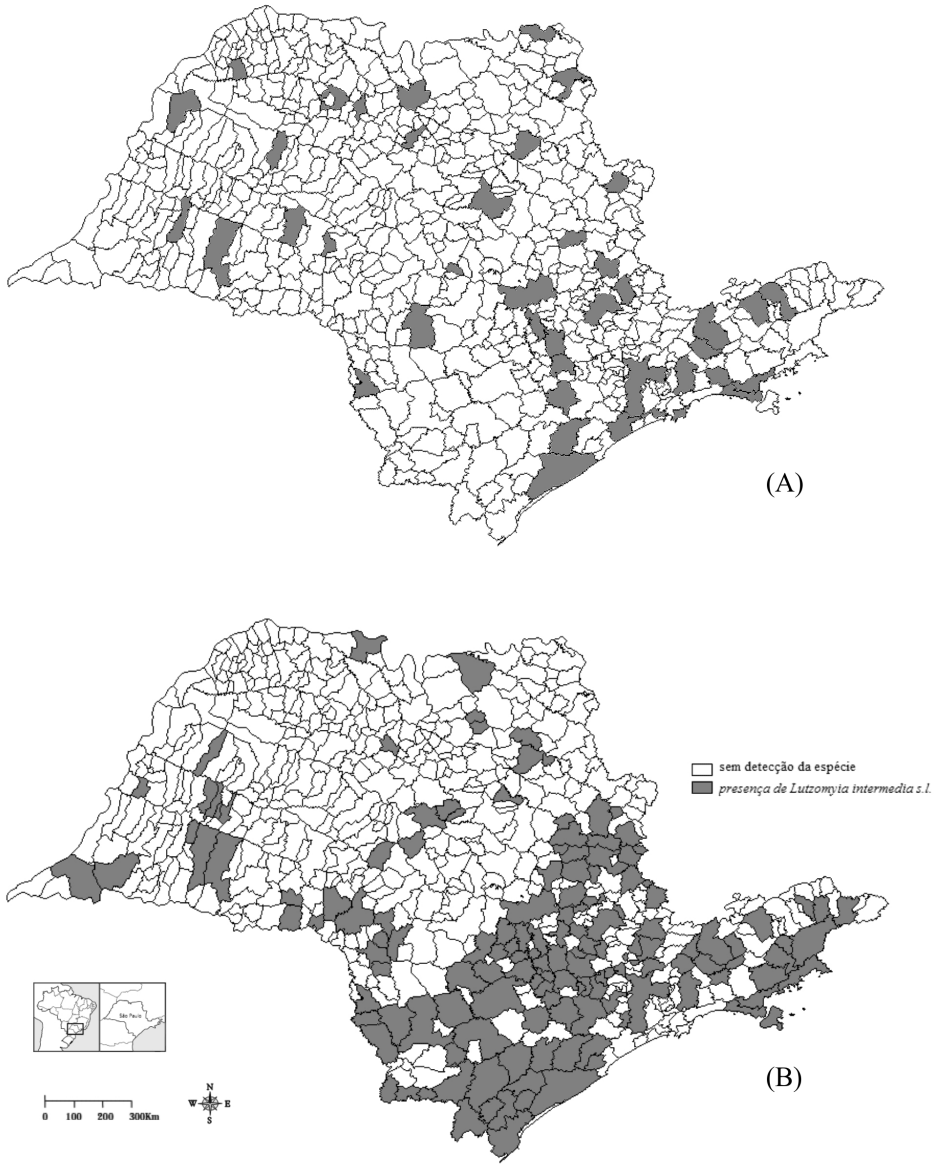

Figure 3 – *State of São Paulo: Distribution of Lutzomyia intermedia according to Pessoa and Barretto[4] (A) and Lu. intermedia s.l. from 1985 to 2008 (B).*
Figura 3 – *Estado de São Paulo: Distribuição de Lutzomyia intermedia segundo Pessoa e Barretto, 1948[4] (A) e de Lu. intermedia s.l. no período de 1985 a 2008 (B).*

Alta Sorocabana, Noroeste and Alta Paulista regions[22]. After this stage, the cases were concentrated in certain areas in a non-homogeneous way. Currently, the epidemiological status of ATL is characterized by the predominance of autochthonous cases with transmission occurring in the entire state and coinciding with the distribution of Phlebotominae vectors.

Higher incidence coefficients have been observed in the southern, eastern, western and southeastern regions of the state of São Paulo. Previously known incidence areas increased and a great number of cases were recorded in new rural areas. The highest incidences of ATL remain restricted to certain areas close to the Atlantic Forest in the state of São Paulo. There was an increase in the number of cities with a low occurrence of cases ("small magnitude"). Cases

Table 1 - Sand flies collected in entomological surveys at probable sites of transmission of leishmaniasis in the State of São Paulo, 1998 to 2008.

Tabela 1 *– Flebotomíneos coletados em pesquisas entomológicas realizadas em locais prováveis de transmissão de Leishmaniose Tegumentar Americana no Estado de São Paulo, 1998 a 2008.*

Species	Specimens	
	Number	%
Lutzomyia intermedia s.l.	11,661	81.25
Lutzomyia whitmani	1,044	7.28
Lutzomyia pessoai	470	3.28
Lutzomyia fischeri	404	2.81
Lutzomyia longipalpis	328	2.29
Lutzomyia migonei	206	1.43
Brumptomyia sp	78	0.55
Lutzomyia ayrozai	37	0.25
Lutzomyia firmatoi	35	0.24
Lutzomyia lenti	28	0.19
Lutzomyia cortellezzii	16	0.11
Lutzomyia shannoni	6	0.04
Lutzomyia lanei	3	0.02
Lutzomyia lloydi	3	0.02
Lutzomyia edwardsi	2	0.01
Lutzomyia pascalei	2	0.01
Lutzomyia monticola	1	0.01
Others	30	0.21
Total	14,354	100.0

Fonte/*Source*: SUCEN.

are concentrated in growing populations, in areas with precarious housing and a low per capita income[23] and which are exposed to the vector[24], where control strategies must emphasize measures directly associated with the human environment.

The presence of 17 Phlebotominae species indicates a high diversity, probably due to the diverse vegetation and terrain. The climate is a factor that affects the distribution of *Lutzomyia* species. The rise in global temperature has an impact on climatic variability, enabling an increase in the density of Diptera species with an effect on the increase in ATL cases, which was observed with the El Niño Southern Oscillation (ENSO) in certain places of Colombia[25].

When the species found per city of the state are observed, even if they are in the same landscape features, one species or another seems to have a major role in ATL transmission, thus agreeing with data from other authors[11,26,27]. In the past, during the 1930s and 1940s, ATL transmission was associated with *Lu. whitmani*, *Lu. pessoai* and *Lu. migonei*, species with wild behavior[28,29]. Currently, *L. (V.) braziliensis* is found to be associated with a variety of Phlebotominae species with different transmission cycles in many geographic areas, where the vector is present in and around homes and in domestic animal shelters[25].

Lu. intermedia s.l. has been pointed out as the most important taxon in the current epidemiological profile of ATL, due to its predominance in altered environments and constant presence in the intra- and peridomicile, corroborating the studies by Shimabukuro et al.[30]. At that time, Pessoa and Barretto (1948)[4] classified the coastal area of the state of São Paulo as an area without human cases or vectors and the Western Plateau as a high-endemicity area, where *Lu. whitmani* and *Lu. pessoai* predominate.

In the present assessment, *Lu. intermedia s.l.* was the main species involved in ATL transmission in coastal areas and plateaus. The overlapping of distribution of species in the majority of cities with autochthonous cases of ATL indicates the need to perform longitudinal studies in different places as a strategy to understand the transmission cycles of *Leishmania (V.) braziliensis*. According to Neves et al.[31], it could be assumed that the mere identification of one of the Phlebotominae species of greatest epidemiological importance already represents a risk factor for ATL. In addition, this risk is not increased by the identification of more than one species.

The spatial distribution analysis of species in the state of São Paulo showed wide dispersion, although with a strong concentration in certain areas, enabling areas with lower endemicity or the occurrence of isolated cases to be identified. Phlebotominae species seem to occur in a distribution pattern, according to the natural ground cover, geomorphological aspects, isotherms and precipitation. Although certain wilder species have shown a different distribution pattern in the past and are associated with areas where there used to be woods, species with an endophilic behavior showed slight changes in distribution, when compared to literature data. Areas characterized as of average endemicity by Neves (1999)[24] became areas with a great magnitude of cases, including an abundance and diversity of vectors and resulting in the expansion of the ATL transmission area. This increase was also observed in the Pontal do Paranapanema region, in the westernmost part of the state, an area considered to be of low endemicity. There is a considerable level of exposure in this region, associated with farming population settlements that were formed and promoted the adaptation of mammal hosts and vectors to a new environment, resulting in an impact on human health[31].

The fact is that the onset of this infection is primarily associated with the migratory process and semi-urbanized areas where the presence of domestic animals seems to play a key role as new hosts of parasites[24,31,32]. In this case, the infection only needs to enter the peridomestic cycle through synanthropic (or domestic) animals and the disease will occur and increase due to unhealthy and precarious living conditions.

ATL is increasing in the state of São Paulo and the highest incidence rates are found in the Vale do Ribeira region, situated in the southern part of this state[33]. Although this region includes a great environmental and cultural heritage, it lacks sanitation infrastructure and adequate economic alternatives for sustainable development to enable the rational use of resources. The extensive areas with remnants of Atlantic Forest in the Vale do Ribeira region and the fact that homes are located near the woods have promoted the presence of Phlebotominae species, increasing the probability of autochthonous ATL transmission[33].

Although knowledge about the epidemiology and behavior of vectors has been increased, there is much to be investigated in terms of their dispersion and survival mechanisms due to the ecological imbalance. The existence of vectors out of the wilderness represents a chance of dissemination of parasites away from the limits of the natural area of the disease and the occurrence of secondary cycles of *Leishmania*, which means that several factors translate into the occurrence of cases and dynamics of transmission. This should be investigated to guarantee more adequate and efficient control strategies and protection measures to prevent transmission in the areas emphasized in this study. The diversity of epidemiological and ecological profiles for different regions prevents the adoption of common disease control measures[34]. Program surveillance and control are based on specific measures for each area, according to the epidemiological situation. In addition, they focus on early diagnosis and adequate treatment of human cases, apart from the identification of the etiological agent present and the primary vector and reduction in the human-vector contact,

through the adoption of individual and collective protection measures[35].

Enabling the population to understand this is essential to control ATL. When children and teachers are informed, they can disseminate knowledge at home and in the community and perform relevant work to control endemic diseases[36].

The importance of reporting ATL cases should be emphasized, especially when considering the need to bring about and implement control measures. This is because the underreporting of cases hinders the understanding of the behavior of the disease in possible areas of transmission and its follow-up in areas already known, in addition to causing distortions in terms of incidence rates. With regard to the distribution of ATL vectors, knowledge about high-risk areas and the dissemination of such knowledge provide support to the surveillance of this disease.

Authors declared that there were no conflicts of interest.

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