



EPIDEMIOLOGICAL PROFILE OF AMERICAN TEGUMENTARY LEISHMANIASIS IN THE STATE OF MARANHÃO IN RECENT YEARS

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ABSTRACT

American Tegumentary Leishmaniasis (ATL) is a non-contagious disease, caused by a protozoan of the genus *Leishmania*, vector-borne by sandflies. Initially it is enzootic, but it can affect humans in a secondary way, characterizing itself as a zoonosis. It has great epidemiological importance due to the complexity of the treatment. The disease has been spreading on a large scale throughout Brazil, as well as in the State of Maranhão. This study is a descriptive approach with the use of confirmed cases of ATL by the Department of Informatics of the Unified Health System, for the years 2010 to 2019 for the State of Maranhão. The following variables were analyzed: annual notifications, gender, age group, clinical forms, case evolution and municipalities with the most notifications. During the study period, 19,043 cases were confirmed in the state. The year 2011 had the highest number of notifications, with 2,948 cases and an incidence of 44.83 cases per 100,000 inhabitants. The male gender was the most affected with 71.9%. The predominant age group was between 20 and 39 years old, with 42.7%. The cutaneous form was prevalent with 96.4%. The three municipalities with the highest number of records were Montes Altos (West Mesoregion), Buriticupu (West Mesoregion) and Arame (Centro Maranhense Mesoregion). The State of Maranhão is endemic for ATL, so it is considered essential to continuously adopt measures to combat the vector and to conduct educational campaigns that inform the population about minimizing the possibilities of disease transmission.

Keywords: American Cutaneous Leishmaniasis. Epidemiology. Prevalence. Maranhão.

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INTRODUCTION

Leishmaniasis have a broad epidemiological and clinical spectrum, but they are portrayed within the group of Neglected Tropical Diseases (NTDs)^{1,2,3}. American Tegumentary Leishmaniasis (ATL) is caused by protozoa of the genus *Leishmania* (Ross, 1903) and presents in amastigote forms in vertebrate hosts and promastigote in vectors⁴. Transmission occurs vectorial through the bite of female sandflies (Order Diptera: Family Psychodidae), commonly known as the "mosquito palha", "birigui", "tatuquira", among others. In Brazil, the main species involved in the transmission of ATL are *Lutzomyia whitmani*, *L. intermedia*, *L. umbratilis*, *L. wellcomei*, *L. flaviscutellata*, and *L. migonei*^{5,6}.

Initially, ATL is an enzootic disease, that is, it affects other animals, except humans, but it can affect it secondarily, characterizing it as a zoonosis⁷. ATL is a non-contagious infection, with a low mortality rate, with a chronic course that affects the skin and mucous membranes¹. In Brazil, seven species of these parasites that cause Leishmaniasis are reported: *Leishmania (Viannia) braziliensis*, *L. (V.) guyanensis*, *L. (V.) naiffi*, *L. (V.) shawi*, *L. (V.) lainsoni* and *L. (Leishmania) amazonensis*¹.

Among the clinical forms, ATL can present mucosa, diffuse and cutaneous⁸, the latter being responsible for more than 90% of the cases reported in Brazil¹. Studies reveal changes in the standard panorama of disease transmission, in which the occurrence of adaptation of host vectors is noted, mainly related to demographic changes that have been taking place over the years, leading them to become increasingly urbanized⁹. However, ATL behaves like an occupational disease, as it mainly affects professions that develop activities in the forest, such as farmers, geologists, loggers, hunters and miners¹⁰.

Currently, it is estimated that approximately 350 million people are exposed to ATL and 2 million are affected annually worldwide⁷. In 2019, the countries with the highest number of notified cases were Brazil, Colombia, Peru, Nicaragua and Bolivia (Plurinational State of), which summed together represent 77% of the cases in the Americas¹¹. In Brazil, in 2019, 15,484 new cases of ATL were confirmed, with a detection coefficient of 7.37 cases per 100,000 inhabitants¹². Currently, the disease is distributed

throughout the Brazilian territory, with the highest percentage of cases recorded in the North region (42.8%)¹². In addition, difficulties in both the diagnosis and the follow-up of cases are present in a way that justifies a geographically high distributive incidence of the disease, since the lack or abandonment of treatment leaves sequelae that psychologically affect the lives of those affected^{13,14}.

Additionally, there is a lack of more detailed studies on ATL throughout the country, as well as in the State of Maranhão, which demonstrates the importance of this compulsory disease and the need to carry out studies on it. As a result, the objective of this study was to trace the epidemiological profile of ATL cases reported in the State of Maranhão, in the period from 2010 to 2019, in order to contribute to the knowledge about the dynamics of transmission of the disease in that State.

METHODS

Study area

State of Maranhão is one of the 27 federative units in Brazil, located in the Northeast region of the country. It is limited to three Brazilian states: Piauí (East), Tocantins (South and Southwest) and Pará (West), in addition to the Atlantic Ocean (North). With an area of 329,642,182 km² and with 217 municipalities, it is the second largest state in the Northeast region and the eighth largest state in Brazil. With a population of 7,114,598 inhabitants, and a density of 19.81 inhabitants/km², it is the 11th most populous state in the country. The capital and most populous city is São Luís¹⁵.

Study design

This is an observational, descriptive and retrospective study, in which the data obtained were collected from the Department of Informatics of the Unified Health System (Departamento de Informática do Sistema Único de Saúde do Brasil - DATASUS) of the Ministry of Health (Ministério da Saúde - MS), available at the electronic address <<http://www2.datasus.gov.br/DATASUS/index.php?area=0203>>, comprising the period between the years 2010 to 2019, in relation to the State of Maranhão [epidemiological aspects of ATL - field Doenças e Agravos de Notificação - 2007 em diante (SINAN)], using as variables gender, age range, entry type, confirmation criterion, clinic forms and case evolution. Data were collected from December 28, 2020 to January 13, 2021.

Descriptive, statistical and spatial analysis

Exploratory (descriptive) analyzes of the data were carried out, based on the determination of absolute and relative frequencies for the categorical variables and organization of the results in tables and graphs. To calculate the incidence indicators in the years of study, per 100,000 inhabitants, the population count of the 2010 Census for the State of Maranhão (6,574,789 inhabitants) was used as a reference, carried out by IBGE and made available on its electronic platform¹⁶.

To examine whether there was a difference in the medians of confirmed cases by year of notification, age range, and case evolution, the Kruskal-Wallis (H) analysis was used. When the difference was found, Dunn's a posteriori test was used. To examine whether there was a difference in the medians of confirmed cases by gender, entry type, confirmation criteria, and clinic forms, the Mann-Whitney (U) test was used^{17,18}. The level of significance adopted in all analyzes was 5% ($p < 0.05$). The data were managed using Microsoft Excel 2013 (Washington, United States of America), GraphPad Prism 7 (San Diego, United States of America) and OpenEpi 3.01¹⁹.

The distribution maps to ATL confirmed notifications in the State of Maranhão were grouped in three-year periods from 2010 to 2012, and from 2013 to 2015, with the exception of the period between 2016 and 2019, with a four-year period. The Geoda 1.18.0.0 software (Chicago, United States of America) was used. The shapefiles of the State of Maranhão were taken from the platform of the Center for Regional and Urban Economics of the State of São Paulo²⁰.

Ethical aspects

The data described in this study were available on a platform of the Informatics Department of the Unified Health System of the Ministry of Health of Brazil. The data included had the characteristic the anonymity of the cases and did not include information that allows the identification of people or that could affect their confidentiality. Therefore, the present study only included secondary public data without any individual identifiers, and the approval of the Research Ethics Committee was unnecessary, in accordance to with the Resolution of the National Health Council (Conselho Nacional de Saúde - CNS) number 466/2012, of December 12, 2012 (CNS, 2012)²¹.

RESULTS

Between 2010 and 2019, 19,043 cases of ATL were reported in the State of Maranhão, with the majority recorded in 2011 (2,948 cases; 15.4%) (Figure 1A), which also had a higher incidence rate with 44.8 cases per 100,000 inhabitants (Figure 1B). It was found that the years 2010, 2011, 2012 and 2014 had medians of cases significantly higher than the years 2016, 2017 and 2019 ($H = 61.6$; $p < 0.0001$) (Figure 1C).

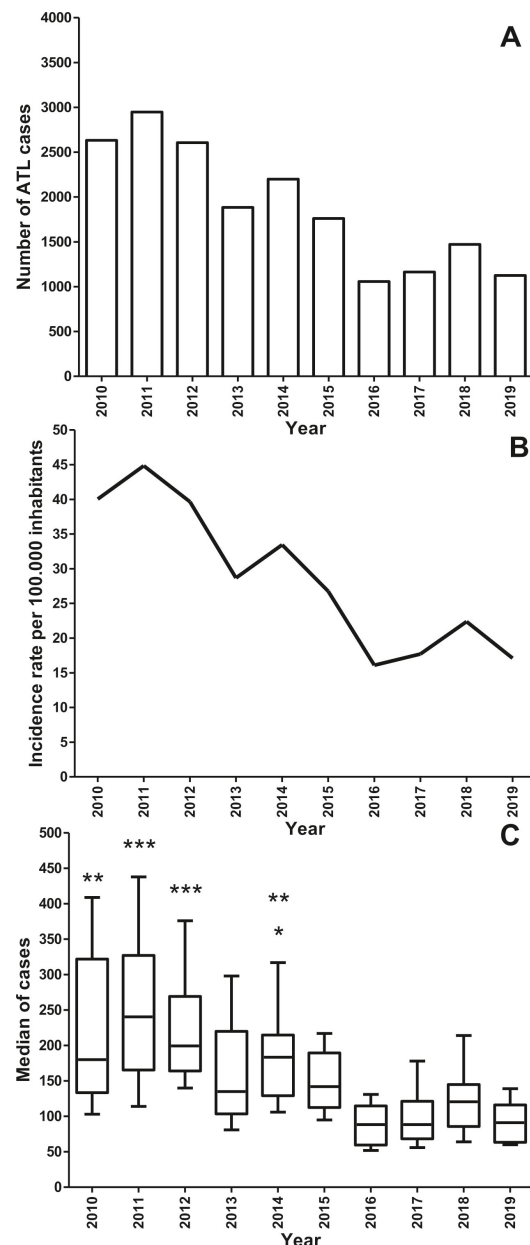


Figure 1. Historical series of American Tegumentary Leishmaniasis in the State of Maranhão between the years 2010 to 2019. (A) Number of confirmed cases of the disease. (B) Incidence rate per 100,000 inhabitants. (C) Comparison between the medians of confirmed cases of the disease. ATL = American Tegumentary Leishmaniasis; *Significant at the level of $p < 0.05$; **Significant at the level of $p < 0.01$; ***Significant at the level of $p < 0.0001$. Source: DATASUS from 2010 to 2019 (<http://www2.datasus.gov.br/DATASUS/index.php?area=0203>).

Most of the notifications was verified in males (13,564 cases; 71.9%; U = 14.0; p = 0.0052); in people aged 20 to 39 years (8,040 cases; 42.7%; H = 89.4; p < 0.0001); related to new cases (17,902 cases; 95.2%; U = 0.0; p < 0.0001); in people who are undergoing laboratory

tests (14,416 cases; 75.7%; U = 3.0; p < 0.0001); in cutaneous form (18,349 cases; 96.4%; U = 0.0; p < 0.0001); and in people whose outcome was the cure (12,298 cases; 95.6; H = 45.5; p < 0.0001) (Table 1).

Table 1. Absolute and relative frequencies, and statistical analysis, of confirmed American Tegumentary Leishmaniasis cases in the State of Maranhão, between the years 2010 to 2019, by gender, age range, entry type, confirmation criterion, clinic forms and evolution.

Variables	N	%	Statistical analyses
Gender¹ (Total = 18,851)			
Males	13,564	71.9	U = 14.0
Females	5,287	28.1	p = 0.0052
Age range (years)² (Total = 19,022)			
Under 1	327	1.7	
1 to 4	411	2.1	
5 to 9	737	3.8	
10 to 14*	1,260	6.6	
15 to 19** ***	1,936	10.1	
20 to 39* ** ***	8,040	42.7	H = 89.4
40 to 59* ** ***	4,115	21.6	p < 0.0001
60 to 64	652	3.4	
65 to 69	536	2.8	
70 to 79	704	3.7	
Older than 80	304	1.5	
Entry type³ (Total = 18,794)			
New cases***	17,902	95.2	U = 0.0
Relapses	892	4.8	p < 0.0001
Confirmation criteria (Total = 19,043)			
Clinic-epidemiological	4,627	24.3	U = 3.0
Laboratorial***	14,416	75.7	p < 0.0001
Clinic forms⁴ (Total = 19,039)			
Mucosal	690	3.6	U = 0.0
Cutaneous	18,349	96.4	p < 0.0001
Case evolution⁵ (Total = 12,892)			
Cure* ** ***	12,298	95.6	
Abandonment of treatment	146	1.1	
Death by ATL	7	0.05	H = 45.5
Death from another cause	84	0.6	p < 0.0001
Transfer to another state	167	1.2	
Diagnostic change	190	1.4	

N = number of American Tegumentary Leishmaniasis cases; % = percentage; ATL = American Tegumentary Leishmaniasis; H = value of the Kruskal-Wallis test; U = value of the Mann-Whitney test; p = p value; ¹Ignored or blank data = 192 cases; ²Ignored or blank data = 21 cases; ³Ignored or blank data = 249 cases; ⁴Ignored or blank data = 4 cases; ⁵Ignored or blank data = 6,151 cases. *Significant at the level of p < 0.05; **Significant at the level of p < 0.01; ***Significant at the level of p < 0.0001. Source: DATASUS from 2010 to 2019 (<http://www2.datasus.gov.br/DATASUS/index.php?area=0203>)

Between the years 2010 to 2012, the municipalities of Montes Altos (West Mesoregion), Buriticupu (West Mesoregion) and Arame (Centro Maranhense Mesoregion) obtained the majority of notifications with 345 (4.2%), 338 (4.1%), and 247 (3.0%), respectively. In relation to the years from 2013 to 2015, the municipalities of Açailândia (West Mesoregion), Turiaçu (West Mesoregion), and Barreirinhas (North Mesoregion), presented the majority of notifications with 194 (3.4%), 194 (3.4%), and 193 (3.3%), respectively. Considering

the years 2016 to 2019, the municipalities of Barreirinhas (North Mesoregion), Urbano Santos (East Mesoregion), and Açailândia (West Mesoregion), obtained the majority of notifications with 234 (4.8%), 207 (4.3%), and 174 (3.6%), respectively. Throughout the study period, Barreirinhas (North Mesoregion) was the municipality with the highest number of notifications, totaling 666 (4.3%) cases of ATL (Figure 2).

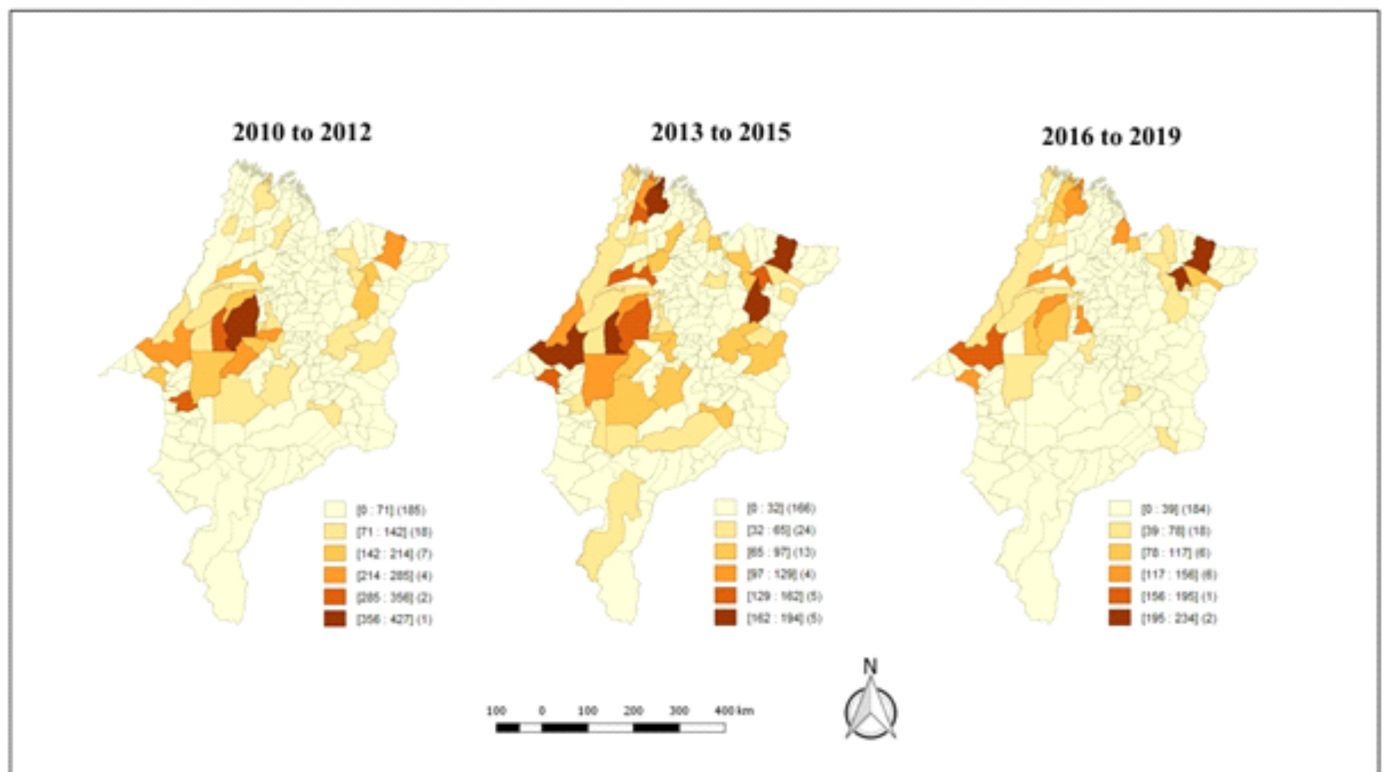


Figure 2. Distribution of confirmed cases of American Tegumentary Leishmaniasis in the State of Maranhão, between the years 2010 to 2019. Source: DATASUS from 2001 to 2019 (<http://www2.datasus.gov.br/DATASUS/index.php?area=0203>).

DISCUSSION

This study describes the epidemiological profile of ATL between 2010 and 2019 in the State of Maranhão, through the compilation of public consultation data from the Brazilian Ministry of Health, available by SINAN, in order to cooperate for a better understanding of the disease. A total of 19,043 cases were reported in the analyzed period. Most cases was reported in males, aged between 20 and 39 years and in individuals with low education. The municipalities most affected by the ATL, Montes Altos (West Mesoregion), Buriticupu (West Mesoregion) and Arame (Centro Maranhense Mesoregion) are located in Mesoregions with forest predominance, a fact that

reflects the presence of the vector and reservoirs, which favors the dissemination of the protozoan by residing in these conditions.

According to the Brazilian Ministry of Health¹, there was an increase in the number of ATL cases throughout the country from the 1980s onwards, ranging from 3,000 notifications in 1980 to 35,748 in 1995. From 1995 to 2014 an average of 26,000 new cases were registered annually. The North and Northeast regions have presented higher numbers of the disease in relation to other regions. In the Northeast, Maranhão is one of the states that has high rates of ATL, in addition to maintaining the expansion character of notifications over the years¹. Regarding the study period, the year

2011 had the highest number of people affected by the disease (2,948 cases; 15.48%), in addition to having presented the highest incidence of cases. The year 2011 was characterized in the State of Maranhão by high rainfall, with the record of floods and floods that affected more than 190,000 people directly or indirectly²². These natural events may have caused the destruction of areas where the vector predominates, leading them to search for a new environment, especially in the most peripheral regions of cities.

A total of 71.95% of the reported cases were in males. The pattern of infection in males takes into account the greater exposure to the vector that they have shown, mainly due to the occupational factor, such as in farmers, geologists, loggers, hunters and miners¹⁰ since, even without realizing it come into contact with the area of predominance of the vector and end up being affected by parasitosis²³. Other studies carried out in other states in the North and Northeast regions of the country also found a higher incidence of cases among males^{24,25,26}.

The age group between 20 and 39 years old is more active and productive in the work form. This was the most prevalent for ATL among the years of study, in the State of Maranhão. In search of life improvements for themselves and their families, young adults migrate to regions which end up involved in activities such as occupation of areas with agricultural projects, deforestation, among others^{27,28}. However, it is also observed that no age group is free from this infection. The data analyzed in this study point to the involvement of 327 children under 1 year of age.

Concerning to the forms of recording the disease, it could be observed that 95.2% of the affected patients were registered as new cases and 4.8% corresponded to recurrences. Other studies have shown similar results^{23,24}. From another perspective, evidencing the clinical variables, most new cases were notified through clinical-laboratory criteria (75.7%) as a finding. The diagnosis of ATL can be performed by means of parasitological tests (lesion smear, direct demonstration of the parasite or isolation in an aspirated lesion culture), immunological tests (Montenegro intradermal reaction), serological tests (indirect immunofluorescence

reaction, Enzyme Linked Immunosorbent Assay - ELISA), molecular tests (Polymerase Chain Reaction - PCR), histopathological tests and differential diagnosis⁸. In the State of Maranhão, the predominant performance is parasitological and immunological tests, not discarding the clinical-epidemiological, which consists of collecting information about the patient, their living environment and history of the disease: site of infection, time of onset, disease evolution, clinical characteristics, location and number of skin lesions⁹.

As for the clinical form, it was found that the cutaneous form represented the highest percentage of reported cases. The literature has pointed out that the mucosal form varies only from 3 to 5% of ATL involvement^{8,27}. The vast majority of cases of the mucosal form derive from the lack or abandonment of treatment for cutaneous leishmaniasis, since the mucosal form occurs secondary to the cutaneous form. In other words, mucosal involvement occurs due to a pre-existing cutaneous lesion (contiguous mucosal form) or still in an asymptomatic stage (late mucosal form) because of a rapid improvement with treatment followed by abandonment^{1,8}.

Taking into account the evolution of the cases, there was a cure in patients who sought the appropriate treatment, with 64.58% among the notified cases. However, other developments cannot be disregarded, such as cases of dropout (1.1%) and change in diagnosis (1.4%). The lack or abandonment of proper treatment can affect the lives of those affected in order to present future sequelae, since the disease can even lead to death in more extreme cases. Therefore, diagnosis and treatment must be carried out as soon as possible^{1,23}. To consider the patient's cure criteria, monthly follow-up is recommended in the first trimester and, when cured, bimonthly, until completing one year after the end of treatment¹.

American Tegumentary Leishmaniasis is endemic in the State of Maranhão, where it is considered a serious public health problem. It is noteworthy that in the state, there is still agricultural predominance and ATL is a disease linked to areas of recent occupation²⁹. Additionally, in Maranhão, there are traces of the Amazon biome in a large part of its territory⁹

and there are records of more than 60 species of sandflies distributed throughout the state, seven of which are incriminated in the transmission of protozoa of the genus *Leishmania*³⁰. Thus, the more human activities intensify in the areas where the vector encounters, the more the pattern of infection tends to change, so as to give a natural response to anthropogenic pressures^{25,26}. The increase in the number of migrants, without protective habits and, above all, without immunity to the parasites present in sandflies, opens up the possibility of continuous ATL outbreaks in the state²⁶. Additionally, the exploitation of ecological tourism causes a very large flow of people at certain times of the year to wild areas that have *Leishmania* vectors, as is the case in the municipality of Barreirinhas, which can also contribute to the spread of the disease³⁰.

Given the data exposed, it becomes evident that ATL is an infection that needs to be monitored, notified and prevented by health agencies, as well as constantly investigated due to the risk it represents. For an effective reduction in cases, it is extremely necessary to adopt prophylactic measures such as the use of protective screens on doors and windows, the constant use of mosquito nets and repellents, in addition to the role of health professionals in the active search for cases in considered areas endemic, in the community¹⁴.

The present study, despite focusing on some aspects of the epidemiology of ATL in the State of Maranhão, has limitations. By using SINAN databases, underreporting should be considered, as well as the inadequate completion of notification forms, facts verified by the considerable numbers of variables with ignored information, which limit the accuracy of the analyses, thus demonstrating the need for improvement in filling, mainly by health professionals.

The basic health network plays a crucial role with regard to the effective control of the disease, since its role is to directly monitor the evolution of patients with possible suspicion of ATL, as well as make the appropriate referrals if necessary. Therefore, continuous training of professionals who will work in the diagnosis and treatment is needed. Both in basic units and in the field, it is crucial that health services are able

and willing to confirm the diagnosis, institution of treatment and follow-up of patients infected with ATL, to reduce transmission and deaths from this important parasitosis.

CONFLICT OF INTERESTS

The authors declare that there is no conflict of interest.

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