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Article

Epidemiological Approach to Human Visceral Leishmaniasis in the Macroregions of Brazil Between 2011 and 2021

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ABSTRACT
Introduction: Visceral Leishmaniasis (VL) transcends the biology of the pathogen, constituting a complex socio-environmental and public health problem. In Brazil, the territorial expansion of the disease is closely linked to processes of environmental degradation, disorderly urbanization, and social vulnerability. Objectives: To analyze the epidemiological profile of VL in the Brazilian macroregions between 2011 and 2021, with emphasis on the spatial and socio-environmental determinants that drive its incidence and distribution. Methodology: This is an ecological and retrospective study, built on secondary data from the Notifiable Diseases Information System (SINAN/DATASUS). Demographic and spatial variables (sex, age group, area of residence, and type of entry) were analyzed. Results: A clear transition in the disease profile was evidenced. Noteworthy are the consolidation of the endemic in urban areas of the Southeast, South, and Central-West regions; the persistence of high vulnerability among children in the North and Northeast, reflecting socioeconomic inequalities; and the advance of new cases in the North region, driven by dynamics of territorial occupation and deforestation. Conclusion: The mitigation of VL requires intersectoral public policies that go beyond the strictly biomedical model. It is imperative to integrate health surveillance with urban planning, environmental management, and the improvement of sanitary conditions of marginalized populations.
Keywords**:** Visceral Leishmaniasis; Brazil; Social Determinants of Health; Environmental Health; Urbanization.

ABSTRACT
Introduction: Visceral leishmaniasis (VL) goes beyond the biology of the pathogen, presenting as a complex socio-environmental and public health problem. In Brazil, the disease's territorial spread is closely linked to processes of environmental degradation, unplanned urbanization, and social vulnerability. Objectives: To analyze the epidemiological profile of VL in Brazilian macroregions between 2011 and 2021, with an emphasis on the spatial and socio-environmental determinants that drive its incidence and distribution. Methodology: This is a retrospective ecological study based on secondary data from the Notifiable Diseases Information System (SINAN/DATASUS). Demographic and spatial variables (sex, age group, residential area, and type of admission) were analyzed. Results: A clear shift in the disease profile was evident. Notable findings include the consolidation of endemicity in urban areas of the Southeast, South, and Central-West regions; the continued high vulnerability of children in the North and Northeast, reflecting socioeconomic inequalities; and the rise in new cases in the North, driven by land-use dynamics and deforestation. Conclusion: Mitigating lung disease requires intersectoral public policies that go beyond the strictly biomedical model. It is imperative to integrate health surveillance with urban planning, environmental management, and the improvement of sanitary conditions for marginalized populations.
Keywords: Visceral Leishmaniasis; Brazil; Social Determinants of Health; Environmental Health; Urbanization.

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Introduction

Visceral Leishmaniasis (VL) is a severe systemic anthropozoonosis that has historically illustrated the profound intersection between health, society, and the environment. Caused by the protozoan ***Leishmania infantum*** and transmitted by sand flies (primarily ***Lutzomyia longipalpis)***, the disease is classified by the World Health Organization (WHO) as a Neglected Tropical Disease (NTD). The importance of VL is not limited to individual clinical severity. The occurrence of the disease and the possibility of severe outcomes involve biological, territorial, and social components. The World Health Organization characterizes the leishmaniases as diseases associated with poverty and with conditions such as precarious housing, gaps in environmental sanitation, population displacement, and difficulty in accessing diagnosis and treatment (Who, 2020). This relationship should be understood as a context of population vulnerability, and not as an attribution of responsibility to the affected individuals. The concept of neglected tropical disease draws attention to the unequal distribution of the disease burden, limited political visibility, and the persistence of structural barriers to prevention, care, and knowledge production.

VL is considered the most severe clinical form of the leishmaniases and, without diagnosis and treatment, may progress to death. Possible manifestations include prolonged fever, hepatosplenomegaly, weight loss, and hematological alterations. According to the WHO (World Health Organization), the presentation may be nonspecific and may be confused with other systemic diseases, a circumstance that reinforces the importance of clinical suspicion and diagnostic confirmation (Who, 2020 and Burza et al. 2018).

This categorization reflects not only the lack of investment in therapeutic innovation but, above all, the fact that the infection predominantly affects populations in situations of extreme socioeconomic vulnerability (Silva et al. 2021). Neglect is also reflected in the high burden imposed on the health system. VL is responsible for about 80% of hospitalizations and more than 90% of deaths caused by the leishmaniasis complex in Brazil, generating high public costs (Nascimento et al. 2023).

Brazil holds unparalleled epidemiological relevance in the continental and global context, recording approximately 90% of all human cases reported in the Americas (Reis 2017; Santos et al. 2019). Historically, the distribution of VL in the country exhibited a strictly rural and sylvatic profile, restricted to traditional endemic foci concentrated mostly in the Northeast region. However, over the last four decades, the country has witnessed a drastic spatial, ecological, and demographic transition, characterized by the expansion of the disease to all geographic macroregions and by an intense and accelerated process of urbanization (Alves and Fonseca 2016; Toledo et al. 2017). Alongside the apparent stabilization of crude incidence at certain national levels, the literature shows that VL case fatality in Brazil presents a worrying linear upward trend, of approximately 4% per year. This phenomenon reveals critical and persistent failures in the health care network, such as barriers to access to timely laboratory diagnosis, delays in instituting adequate clinical management, and weaknesses in the support of severely ill patients (Cota et al. 2021). VL remains a relevant problem for epidemiological surveillance. The country encompasses a great diversity of ecosystems, population densities, forms of territorial occupation, and local health service capacities. For this reason, notification patterns are not necessarily uniform across macroregions. Regional comparison is useful for describing where records are concentrated and how they are distributed according to selected characteristics

To critically understand the dynamics of VL, it is essential to master the terminology and epidemiological metrics used in health surveillance. The absolute number of cases indicates the crude magnitude of the disease in a territory, but it is insufficient for spatial or temporal comparisons without proper demographic weighting. Incidence expresses the risk of occurrence of new cases in a population exposed over a given period, commonly calculated per 100,000 inhabitants. Proportion, in turn, reflects the relative weight of a specific category (such as sex, age group, or area of residence) in relation to the total number of reported cases. Regarding care outcomes, hospitalizations represent the hospital demand generated by complex clinical forms or those with comorbidities, while death reflects the fatal outcome. Case fatality, in turn, expresses the percentage of diagnosed patients who die as a result of the disease, serving as a direct indicator of the quality of the medical care provided.

The epidemiological transition of VL cannot be explained solely by biological factors of the parasite or the vector, being vigorously driven by socio-environmental, ecological, and climatic determinants. The accelerated deforestation of biomes, the expansion of agricultural and livestock frontiers, and intense disorderly migratory flows cause profound disruptions in natural ecotopes. Such environmental disturbances forced the behavioral and ecological adaptation of the sand fly Lutzomyia longipalpis, which migrated from the sylvatic environment to the peridomicile and the domicile in the outskirts of cities. In these peripheral spaces, the chronic absence of basic sanitation, the accumulation of organic matter in the soil, precarious housing, and the ubiquitous presence of domestic animals, especially the dog (Canis lupus familiaris), recognized as the main urban reservoir

of the zoonosis, create the microclimate and the ideal trophic conditions for vector proliferation and the uninterrupted maintenance of the transmission cycle (Cruz 2021; Benedetti and Pezente 2021).

The discussion of climate change requires similar caution. Temperature, humidity, and precipitation may influence vector biology and ecological dynamics, while changes in land use and land cover may modify *habitats*. Recent studies demonstrate that VL incidence is positively associated with rising average temperatures and the presence of savanna and pasture areas. Furthermore, transition zones between biomes (ecotones) have proven to be true "hotspots" for the disease, demonstrating the high adaptive plasticity of vectors and reservoirs in the face of environmental changes (Kersul et al. 2025). It should be emphasized, however, that variables such as climate, deforestation, and structural sanitation were not directly measured as quantitative statistical parameters in the present ecological study, appearing in the literature as a conceptual framework and fundamental explanatory hypotheses for the interpretation of the observed results.

Despite the existence of the Visceral Leishmaniasis Surveillance and Control Program (PVCLV), which advocates early diagnosis, environmental management, and reservoir control, government actions often run up against structural limitations (Zuben and Donalísio 2016). Epidemiological surveillance plays a central role in identifying cases, monitoring territorial distribution, and producing information for public health actions. Notification systems allow comprehensive population-scale analyses and are particularly useful for retrospective studies. The ineffectiveness of VL control shows that strictly biomedical approaches are insufficient when dissociated from urban planning, housing, and environmental education policies. The choice of the 2011 to 2021 period makes it possible to examine a decade of records according to the availability reported in the data of this research.

Given the complexity of this scenario and the continental dimensions of Brazil, it becomes essential to understand how the different socio-environmental realities of each territory influence the dynamics of the disease. Therefore, the present study aims to describe the distribution of confirmed VL cases in the five Brazilian macroregions, in the reported period from 2011 to 2021, according to sex, age group, area of residence, and type of entry, as well as to present the mean coefficients by age group reported by the authors, in order to provide support for the improvement of public policies related to health and the environment.

Methodology

This is an ecological, descriptive, and retrospective epidemiological study, structured on public-domain secondary databases. Because it used aggregated information, with no possibility of nominal identification of individuals, the study was exempt from prior review by a Research Ethics Committee, in accordance with the guidelines and regulatory standards established by the National Health Council.

Data extraction was carried out through the Department of Informatics of the Unified Health System (DATASUS), consulting the official records of the Notifiable Diseases Information System (SINAN). Data collection took place between March and October 2023, through the official institutional portal (https://datasus.saude.gov.br/). All confirmed cases of Visceral Leishmaniasis reported in humans throughout the national territory between 2011 and 2021 were included in the scope of the investigation.

For the detailed characterization of the epidemiological profile, the database was stratified according to the five political-administrative macroregions of Brazil (North, Northeast, Southeast, South, and Central-West). The demographic and spatial variables analyzed included: sex, age group, area of residence (classified as urban or rural), and type of entry into the surveillance system (defined as new case or relapse).

The mean incidence coefficients by age group were calculated based on the official population projections and estimates for the study period, with results expressed per 100,000 inhabitants. The other categorical variables were processed by calculating relative frequencies (percentages).

Initial data tabulation was performed using Microsoft Excel software, while descriptive and inferential statistical analyses were conducted in GraphPad Prism 8.0. In order to compare proportions among the five Brazilian macroregions, the nonparametric Kruskal-Wallis statistical test was applied, complemented by Dunn's multiple comparisons post-test. For all inferential analyses, the level of statistical significance was set at 5% ($p<0.05$).

Results

The analysis of the distribution of confirmed cases according to the sex variable (Figure 1) showed that, in the overall Brazilian scenario, males remain the most affected by Visceral Leishmaniasis. However, regional stratification revealed a distinct and statistically significant dynamic in the North region, which presented a markedly lower proportion of cases in men compared with the other macroregions ($p<0.05$). Complementarily,

the North region recorded the highest proportion of infections affecting females relative to the rest of the country ($p<0.05$).

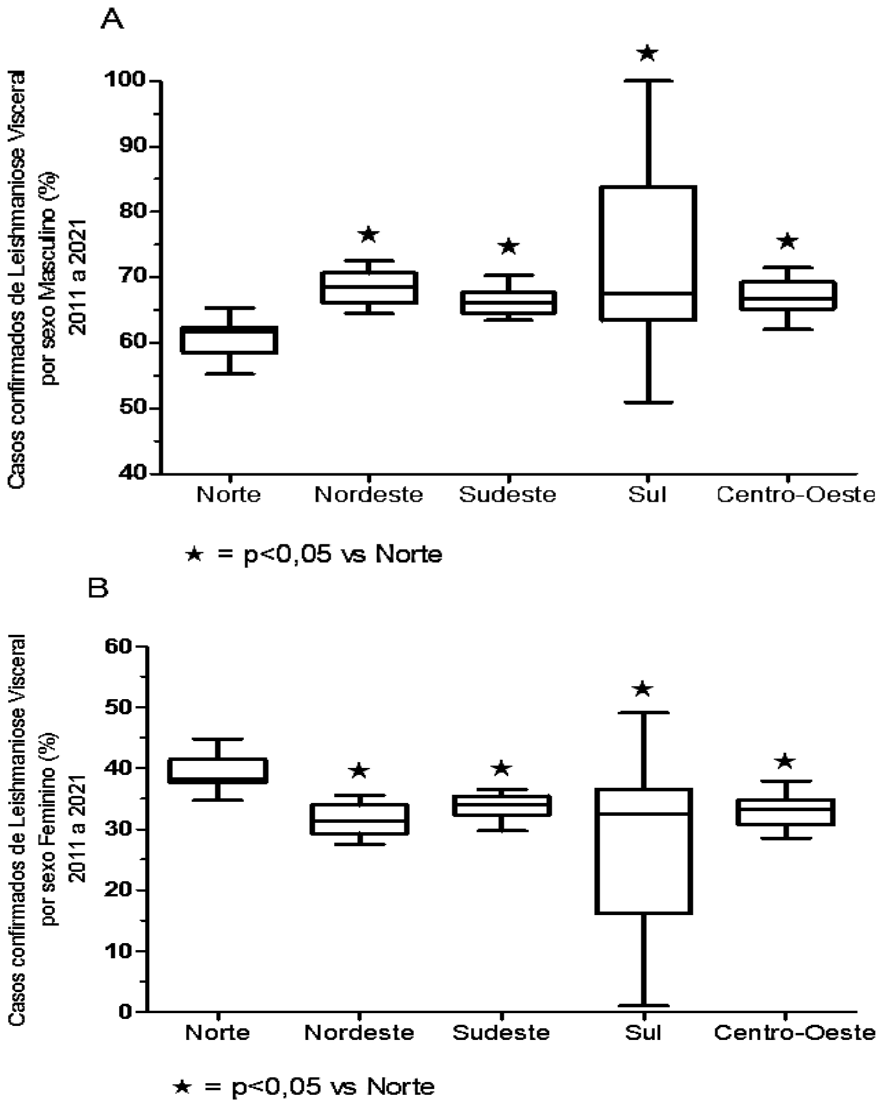


Figure 1. Confirmed cases of Visceral Leishmaniasis infection among the macroregions of Brazil from 2011 to 2021 between males and females. Legend: data analyzed according to the sex variable in %, where 1A shows the values for the number of cases referring to males and 1B to females. The "Kruskal-Wallis" test with the "Dunn's Multiple Comparison" post-test was used. Results were expressed as percentages and considered statistically significant when $p<0.05$. Source: DATASUS, 2023.

Regarding age group (Table 1), the evaluation of the mean incidence coefficients (expressed per 100,000 inhabitants) showed the persistence of a pattern of high vulnerability concentrated in child populations and young adults. The North and Northeast regions stood out with the highest incidence rates in these specific age groups, although the overall statistical analysis did not indicate globally significant differences in the comparison between the age strata of the different macroregions.

Table 1. Incidence of Visceral Leishmaniasis among the macroregions of Brazil from 2011 to 2021 by age group.

Regiões do Brasil	Faixa etária (anos)						
	0 a 9	10 a 19	20 a 39	40 a 59	60 a 69	70 a 79	> 80
Norte	291,2	58,3	124,0	81,3	17,8	11,9	4,5
Nordeste	684,8	171,7	413,0	319,4	75,3	36,2	17,0
Sudeste	176,4	44,5	141,2	150,9	48,6	26,4	13,4
Sul	2,4	1,3	3,4	2,4	0,8	0,5	0,2
Centro-Oeste	77,5	15,7	68,3	71,8	17,7	11,8	5,4
Mediana	176,5	44,5	124,0	81,3	17,8	11,9	5,4
Valor Máximo	684,8	171,7	413,0	319,4	75,3	36,2	17,0
Valor Mínimo	2,4	1,3	3,4	2,4	0,8	0,5	0,2

Legend: Mean of the corrected values per 100,000 inhabitants between 2011 and 2021. Source: DATASUS, 2023.

Regarding area of residence (Figure 2), the results confirmed the profound transition in the spatial profile of the disease in the national territory. The Southeast, South, and Central-West regions presented proportions of cases from urban areas significantly higher than those observed in the North and Northeast regions ($p<0.05$). In contrast, the North and Northeast regions maintained proportions of notifications from rural areas statistically higher than the other regions of the country ($p<0.05$).

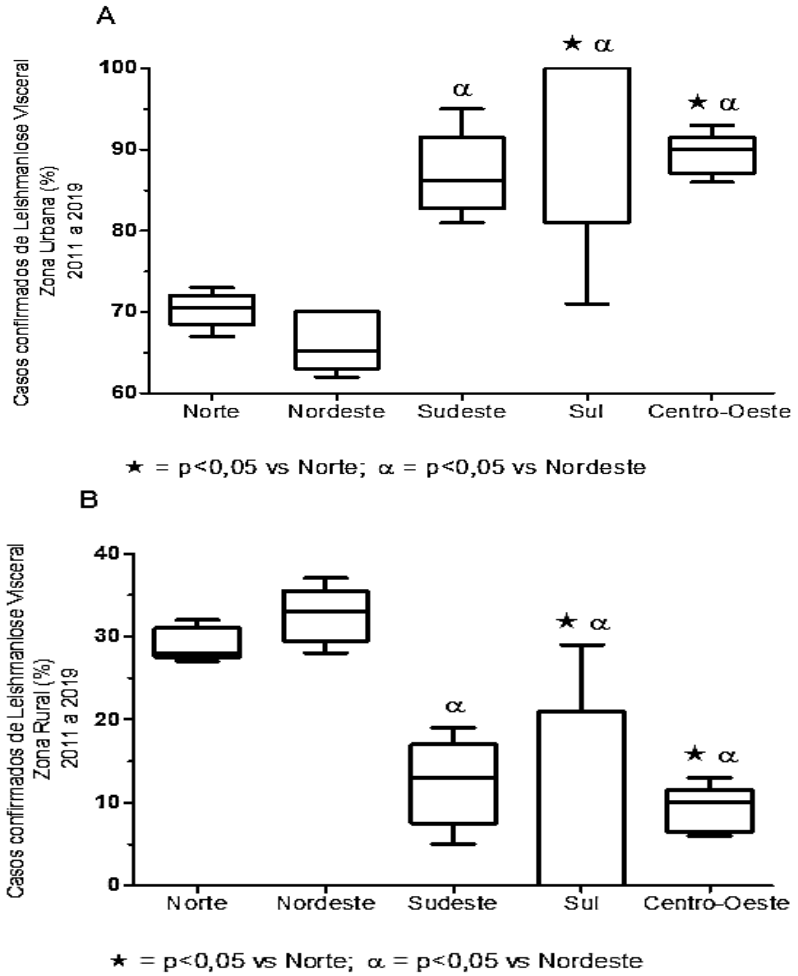


Figure 2. Confirmed cases of Visceral Leishmaniasis infection among the macroregions of Brazil from 2011 to 2021 between Urban and Rural Areas. Legend: data analyzed according to the Area of Residence variable in %, where 2A shows the values for the number of cases referring to residents of the Urban Area and 2B to the Rural Area. The "Kruskal-Wallis" test with the "Dunn's Multiple Comparison" post-test was used. Results were expressed as percentages and considered statistically significant when $p<0.05$. Source: DATASUS, 2023.

Finally, the analysis of the patients' type of entry (Figure 3) revealed that the North region concentrated a significantly higher proportion of new cases when compared with the Southeast and Central-West regions ($p<0.05$). Conversely, the Southeast and Central-West regions showed significantly higher proportions of disease relapse episodes compared with what was observed in the North region ($p<0.05$). The comparison among the five regions makes it possible to visualize broad contrasts and may indicate where sub-regional

analyses are needed. Municipal or state studies may verify whether the macroregional pattern is concentrated in a few locations or distributed more homogeneously.

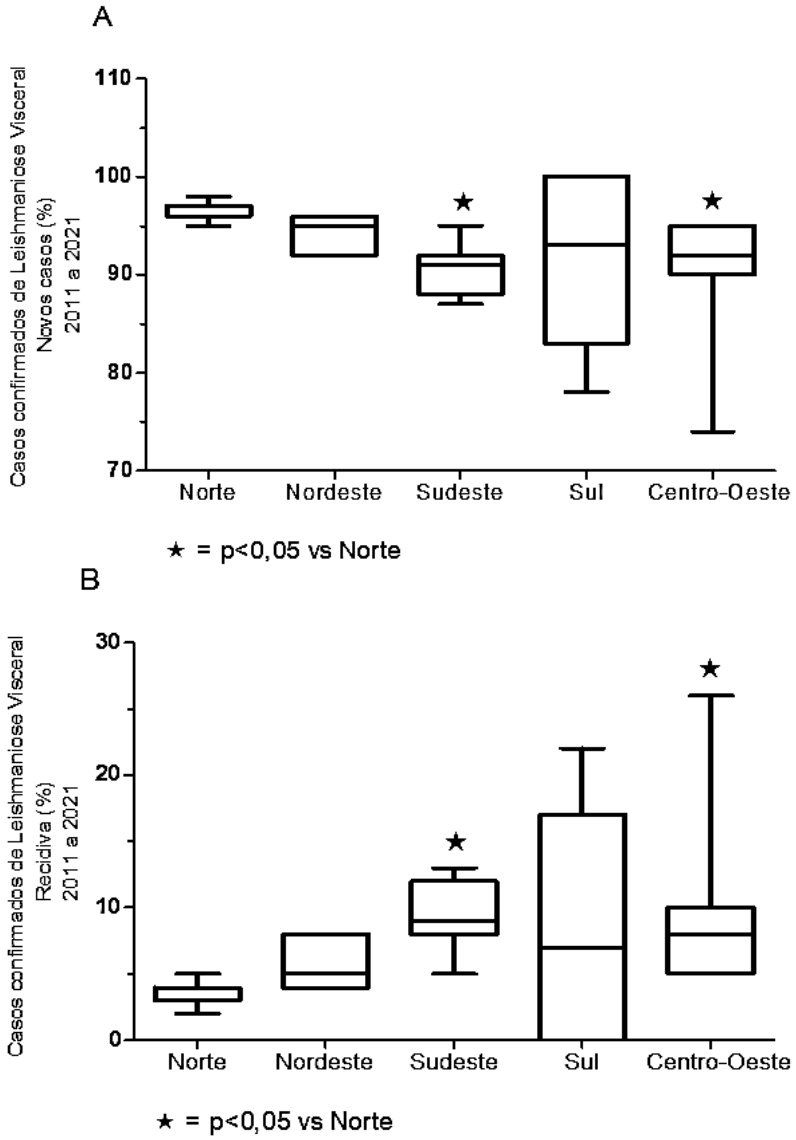


Figure 3. Confirmed cases of Visceral Leishmaniasis infection among the macroregions of Brazil from 2011 to 2021 regarding the number of new cases and relapses. Legend: data analyzed according to the Type of case entry variable in %, where 3A shows the values for the number of new cases and 3B for relapses. The "Kruskal-Wallis" test with the "Dunn's Multiple Comparison" post-test was used. Results were expressed as percentages and considered statistically significant when p<0.05. Source: DATASUS, 2023.

Discussion

This study describes the distribution of confirmed VL cases in the Brazilian macroregions according to sex, age group, area of residence, and type of entry, from 2011 to 2021, in addition to presenting mean coefficients by age group. The main interpretive aspect is the regional heterogeneity recorded in the notification database. This description offers an overview of the profile of reported cases, but does not identify the causes of the differences. Throughout this discussion, the results of the study are distinguished from the possible interpretations based on the literature, in accordance with the ecological design and the variables effectively described.

The epidemiological findings of the present study compellingly demonstrate the complexity of the transmission dynamics of Visceral Leishmaniasis in Brazil, showing that the disease does not follow a homogeneous spatial or demographic pattern, but rather strongly regionalized socio-environmental conditioning factors. Historically, the literature corroborates that males are the most affected in the national scenario, which is classically and frequently associated with greater occupational and environmental exposure in rural work fronts, deforestation, and extractive activities (Sousa et al. 2021; Benedetti and Pezente 2021).

However, the finding of a significant change in the North region, characterized by a proportional reduction of cases in men and a significant increase in females, suggests a profound change in the infection scenario. Human exposure ceases to be strictly sylvatic or occupational and begins to occur within the peridomicile and the domicile. Women's longer permanence in the domestic environment and its immediate surroundings, combined with contexts of precarious housing, inadequate sanitation, and lack of basic infrastructure in the urban peripheries and riverside communities of the North region, outlines a scenario of socio-environmental vulnerability that favors frequent contact with the vector (Benedetti and Pezente 2021; Cavalcante and Gonçalves 2019). It should be noted that environmental and housing factors act here as an explanatory context from the literature, since they were not directly quantified as independent variables in this study. The observation of a greater relative share of notifications in a region may justify a local evaluation of surveillance and services, but it is not sufficient to determine the allocation of resources or to establish priorities without considering population, incidence, severity, care capacity, and data timeliness. General recommendations for integration between surveillance, diagnosis, and care are pertinent as public health guidelines, but their application must be adjusted to the territorial reality and supported by complementary information.

The analysis by age group reinforces the social determination of the disease. The persistence of high infection rates in children in the North and Northeast regions is a direct reflection of the historical socioeconomic inequalities of these macroregions. Child vulnerability to VL is closely linked to malnutrition and the lack of adequate sanitary infrastructure, factors that compromise the immune response and perpetuate the cycle of poverty and illness (Sousa et al. 2019; Pacheco et al. 2021). In contrast, infection in young adults remains tied to exposure in precarious work fronts and agricultural expansion. The high burden of the disease in these regions is directly reflected in the hospital system. According to Nascimento et al. (2023), the Northeast accounts for more than 40% of VL hospitalizations in the country, highlighting the impact of social vulnerability and child malnutrition on the progression to clinical forms that require hospitalization. Moreover, the precariousness of sanitary infrastructure perpetuates the cycle of illness, imposing high costs on the public health system for the management of complications.

The most striking finding regarding the epidemiological transition of VL is its definitive consolidation as an endemic disease with an urban profile in the Southeast, South, and Central-West regions, in sharp contrast with the still predominantly rural profile observed in the North and Northeast (Alves and Fonseca 2018). This process of urbanization of the zoonosis results directly from anthropogenic environmental pressures and impacts. Disorderly and unplanned urban expansion over natural ecotopes, associated with intense population migratory flows, compelled the vector *Lutzomyia longipalpis* to successfully adapt to the urban environment. The peripheral areas of cities, commonly lacking regular solid waste collection and environmental sanitation services, accumulate organic matter and harbor domestic animals, constituting the ideal microclimate for vector proliferation (Alves and Fonseca 2018; Oliveira and Moreira 2021).

Furthermore, the establishment of VL as an urban endemic disease in the Central-West and South is catalyzed by border territorial dynamics, where the presence of integrated municipalities in international border strips facilitates the free movement of reservoir dogs and vectors, challenging conventional sanitary barriers (Oliveira and Moreira 2021). From a bioclimatic perspective, VL incidence is strongly associated with ecological transition zones (ecotones), such as the interfaces between the Cerrado, the Amazon, and the Atlantic Forest, where temperature fluctuations and changes in land use enhance vector dispersal (Kersul et al. 2025). It should be emphasized that climatic and ecological variations serve as supporting interpretive literature and do not constitute direct statistical measurements of the present ecological design.

The evaluation of the patients' type of entry reveals two distinct territorial realities. In the North region, the marked predominance of new cases reflects the active expansion of transmission fronts in areas of epidemiological frontier, driven by illegal mining activities, deforestation of the Amazon rainforest, and disorderly occupation of conservation areas that introduce immunologically naive populations into enzootic zones (Benedetti 2020). In contrast, the high proportion of relapses observed in the Southeast and Central-West regions unveils a complex clinical and social challenge: the syndemic between Visceral Leishmaniasis and the human immunodeficiency virus (HIV). These macroregions concentrate significant portions of the population living with HIV/AIDS in Brazil (Santos et al. 2021; Fenelon et al. 2021). Profound cellular immunosuppression hinders the success of the parasitological cure of VL, leading to high rates of therapeutic relapse (Farias 2023). This finding demonstrates that the urbanization of leishmaniasis has placed the disease on a collision course with other urban endemic diseases, requiring the articulation of integrated surveillance and care protocols.

Finally, the regional variations in type of entry raise an alert about the response capacity of health services. The high proportion of relapses in these regions, associated with Leishmania-HIV coinfection, showed that

VL case fatality in Brazil is associated with low educational attainment, unavailability of emergency beds, and, paradoxically, areas of lower disease incidence. This suggests that, in regions where VL is in recent expansion, medical unfamiliarity with the disease generates critical delays in diagnosis and initiation of treatment, increasing the risk of unfavorable outcomes (Cota et al. 2021).

Conclusion

Visceral Leishmaniasis remains a serious marker of socio-environmental and structural inequalities in Brazil. The present study showed that the disease expresses heterogeneous epidemiological profiles across the macroregions: while the North and Northeast face the expansion of new cases associated with child vulnerability and with rural and deforestation dynamics, the Central-Southeast of the country consolidates a profile of urbanization of the endemic, facing the care challenge of relapses strongly linked to coinfections in large urban centers.

It is evident that strictly biomedical and vertical approaches are insufficient for the sustainable control of the disease. The mitigation of VL requires the formulation and implementation of intersectoral public policies that integrate health surveillance with urban planning, rigorous environmental management, and the universal guarantee of basic sanitation, adapting preventive interventions to the ecological, climatic, and social reality of each Brazilian territory. Among the main limitations are the possibility of underreporting of mild or asymptomatic cases, possible inconsistencies in completing compulsory notification forms, and the inability to directly correlate environmental variables. Therefore, the strengthening of continuing medical training for early diagnosis and the improvement of monitoring in areas of ecological transition and borders are recommended.

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