

Spread of Human Visceral Leishmaniasis in Brazil

Expansão da Leishmaniose Visceral Humana no Brasil

Expansión de la Leishmaniasis Visceral Humana en Brasil

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Abstract

Visceral leishmaniasis is a neglected tropical disease and a public health issue. The present study analyzed the spatial-temporal behavior of human visceral leishmaniasis in Brazil. This ecological study used secondary data from DATASUS between 2010 and 2020. Male individuals, with brown skin color, and young adults with low education level were the most affected. The disease was reported in all Brazilian regions. The Annual Increase Rate was upwards in the South and downwards in the Midwest. The Northern and Northeastern regions had the worst rates of sanitary overload, illiteracy, and Gini Index. Social and health public policies must be established, aiming at improvements in the socio-economic and environmental conditions of vulnerable populations, which are at a higher risk of falling ill to human visceral leishmaniasis. Improving these conditions shall help with the goals of the 2030 Agenda, which shall result in quality healthcare and wellbeing for the population, regardless of Brazilian region.

Keywords: Visceral Leishmaniasis; Epidemiological Profile; Neglected Tropical Disease.

Resumo

A leishmaniose visceral é uma doença tropical negligenciada e um problema de saúde pública. Este estudo analisou o comportamento espaço-temporal da leishmaniose visceral humana, no Brasil. É um estudo ecológico que utilizou dados secundários do DATASUS, entre 2010 e 2020. Indivíduos do sexo masculino, pardos, crianças e jovens adultos e com baixo nível de escolaridade foram mais afetados. Em todas as regiões brasileiras houve o registro de casos da doença. A Taxa de

Incremento Anual apresentou-se crescente na região Sul e decrescente no Centro-Oeste. As regiões Norte e Nordeste apresentaram a pior condição de esgotamento sanitário, analfabetismo e Índice Gini. Há necessidade do estabelecimento de políticas públicas sociais e de saúde visando melhorias nas condições socioeconômicas e ambientais da população vulnerável e de maior risco de adoecimento pela leishmaniose visceral humana. A melhoria dessas condições irá contribuir com os objetivos da Agenda 2030, que resultará em saúde de qualidade e bem-estar da população, independente da região brasileira.

Palavras-chave: Leishmaniose Visceral; Perfil Epidemiológico; Doença Tropical Negligenciada.

Resumen

La leishmaniasis visceral es una enfermedad tropical desatendida y un problema de salud pública. Este estudio analizó el comportamiento espaciotemporal de la leishmaniasis visceral humana en Brasil. Es un estudio ecológico que utilizó datos secundarios de DATASUS entre 2010 y 2020. Los hombres, morenos, niños y adultos jóvenes con bajo nivel educativo fueron los más afectados. En todas las regiones brasileñas hubo registro de casos de la enfermedad. La tasa de incremento anual aumentaba en el sur y disminuía en el medio oeste. Las regiones Norte y Nordeste presentaban las peores condiciones de alcantarillado sanitario, analfabetismo e Índice Gini. Es necesario establecer políticas públicas sociales y de salud dirigidas a mejorar las condiciones socioeconómicas y ambientales de la población vulnerable y con mayor riesgo de enfermar por leishmaniasis visceral humana. La mejora de esas condiciones contribuirá a los objetivos de la Agenda 2030, lo que redundará en salud y bienestar de calidad para la población, independientemente de la región brasileña.

Palabras clave: Leishmaniasis Visceral; Perfil Epidemiológico; Enfermedad Tropical Desatendida.

Introduction

Neglected Tropical Diseases (NTDs) consist of a group of diseases caused by infectious agents or parasites, and are strongly related with poverty, as they might affect individuals in a situation of vulnerability (Bodimeade; Marks; Mabey, 2019; Engels; Zhou, 2020). NTDs spread in areas where access to medical assistance, basic sanitation, and drinking water is limited (Bodimeade; Marks; Mabey, 2019; Engels; Zhou, 2020). According to the World Health Organization (WHO, 2022a), NDTs are prevalent in 149 tropical and subtropical countries, affecting more than 1 billion people, with high morbidity and mortality.

VL is among the 10 major NTDs and reaches approximately 80 countries in Asia, Eastern Africa, South America, and the Mediterranean region. Among the most affected countries are Brazil, Eritrea, Ethiopia, India, Kenya, Nepal, Somalia, South Sudan, and Sudan, which account for more than 90% of new cases (WHO, 2022a). In the Americas, this disease is endemic in 13 countries, and 97% of the total cases were reported in Brazil in 2020; the others were reported in Argentina, Bolivia, Colombia, Paraguay, Venezuela, and Uruguay (OPAS, 2021). It used to be considered a rural disease; however, due to the change in the environmental scenario caused by deforestation, urbanization, and migration

flow, the disease has become a public health issue with geographical expansion (Batista et al., 2021).

With the purpose of eliminating this disease, the Control Program for Visceral Leishmaniosis (CPVL) has been created, contemplating activities intended for the human population, for vector control, and urban reservoirs. The strategies and activities might reduce lethality rates and morbidity level through early diagnose and treatment of the cases (Brasil, 2019). The disease epidemiology is directly linked to social and infrastructure vulnerability, and environmental factors. Therefore, the aim of the present study is to analyze the spread of human visceral leishmaniosis in Brazil, based on the spatiotemporal and epidemiological behavior, incidence, and socio-environmental data.

Method

The present study is an ecological, temporal series, descriptive and quantitative study. Secondary data from the System of Information of Diseases and Notifications (SINAN) were used, which are available in the TABNET program of the IT Department of the Unified Health System of Brazil (DATASUS). The data collected refer to the total number of cases, by notification year between 2010 and 2020.

The variables analyzed provided information on patient profile: gender, age group, color/ethnicity, education, residence zone, and disease progression (cure and death). In the variable education, data referring to the levels of incomplete schooling and complete schooling were clustered, as well as the categories “ignored”, “blank”, and “does not apply”.

The Generalized Linear Model (GLM) with Poisson's distribution was used to understand the association between VL and epidemiological factors. For the variables education, age, gender, ethnicity, and residence zone the following were calculated: *Odds Ratio* and Confidence Interval (CI 95%) with their upper limit (UL) and lower limit (LL).

Incidence rate and lethality rate were calculated according to Brasil (2014). Population estimates for these calculations were obtained from the DATASUS. In order to compare average incidence among the regions of Brazil, a Repeated-Measures analysis of Variance was used, followed by Tukey's Test for individual differences. Sample normality was verified using the Shapiro-Wilk Test.

To analyze the Annual Incidence Rate (AIR), the Prais-Winsten regression was used to understand disease dynamics per variable over the years. Thus, it was possible to understand whether the disease tended towards increasing, decreasing, or reaching stability

over the period. AIR calculation was based on Antunes (2005) and applied by Böhm et al. (2016), based on regression data $[-1+(10b)]*100$, where b is the slope of the regression line. P-values of the regression that had $\alpha \leq 0.05$ were considered significant. The analyses were elaborated using the Statistical Program PAST 4.10.

The prevalence of domiciles with inadequate water supply and sanitary sewage and no waste collection system was calculated using data obtained from the National Institute for Applied Economic Research (IPEA, 2022). The Gini Index was used to evaluate income concentration (0 - equality; 1 = richness concentration). Both sanitation variables (basic sanitation, waste collection) and economic variables (income per capita, and Gini Index) were used in a Multiple Linear Regression model. The incidence was considered as a dependent variable, for each Brazilian region, from 2010 to 2019 (IPEA, 2022).

Maps were elaborated using QGIS, a free geoprocessing software. The table with incidence data was associated with the spatial representation file (shapefile), provided by IBGE - Map base - Territorial Grids - States <<https://www.ibge.gov.br/geociencias/organizacao-do-territorio/malhas-territoriais/15774-malhas.html?=&t=acesso-ao-produto>>. The maps were built using data on prevalence of urban domiciles with inadequate water supply, sanitary sewage, and waste collection, household income per capita and Gini index in the Brazilian regions.

It is worth noting that there was no need to submit the study to the Committee of Ethics in Research with Human Beings, as this is a study on official public domain secondary data, with no identification of subjects. This study complies with CONEP Resolution N° 466/2012.

Results

Human Visceral Leishmaniasis (HVL) is endemic in Brazil and 38,634 cases were reported over the period from 2010 to 2020. Comparing the total occurrences per notification year, 2011 (10.6%) and 2017 (11.5%) were the years with the highest number of people with the disease. This disease is notified in all Brazilian regions: Northeast (54.5%), Southeast (19.0%), North (18.1%), Midwest (8.2%), and South (0.3%). The highest number of cases reported, comparing notifications per year in each Brazilian region, was in 2011 in the Northern region (22.0%). In the Northeastern region, the disease was the highest in 2014 (64.9%), in the Southeast it was the highest in 2017 (24.6%), in the South it was the highest in 2020 (0.7%), and in the Mid-western region, it was the highest in 2012 (13.1%) (Table 1). It is noticeable that the behavior of the disease in the Northeast

has a small variability (47.0% - 64.9%), with a prevalence that represents nearly 50% of the sum of the other regions.

Table 1—Number of confirmed cases of HVL and Prevalence (%), from 2010 to 2020, per Brazilian region.

Year	North n (%)	Northeast n (%)	Southeast n (%)	South n (%)	Midwest n (%)	Brazil n (%)
2010	702 (19,0)	1845 (49,8)	810 (21,9)	7 (0,2)	340 (9,2)	3704 (9,6)
2011	902 (22,0)	2046 (49,9)	756 (18,4)	6 (0,1)	397 (9,7)	4107 (10,6)
2012	634 (19,4)	1537 (47,0)	664 (20,3)	7 (0,2)	427 (13,1)	3269 (8,5)
2013	572 (16,5)	1984 (57,1)	555 (16,0)	4 (0,1)	357 (10,3)	3472 (9,0)
2014	434 (11,6)	2422 (64,9)	591 (15,8)	6 (0,2)	280 (7,5)	3733 (9,7)
2015	506 (14,2)	2148 (60,4)	664 (18,7)	6 (0,2)	234 (6,6)	3558 (9,2)
2016	622 (18,0)	1828 (52,9)	756 (21,9)	17 (0,5)	232 (6,7)	3455 (8,9)
2017	861 (19,3)	2199 (49,3)	1096 (24,6)	17 (0,4)	283 (6,4)	4456 (11,5)
2018	836 (21,7)	2197 (57,1)	604 (15,7)	15 (0,4)	199 (5,2)	3851 (10,0)
2019	541 (19,1)	1603 (56,7)	456 (16,1)	16 (0,6)	211 (7,5)	2827 (7,3)
2020	366 (16,6)	1246 (56,6)	383 (17,4)	15 (0,7)	192 (8,7)	2202 (5,7)

Source: SINAN (2022).

Regarding the sociodemographic profile of the infected individuals concerning gender, the higher incidence was in the male gender in all Brazilian regions. Regarding age group, there was higher prevalence of pediatric and juvenile cases in the Northern and Northeastern regions, while the predominance in the Southeast, South, and Mid-west was in adults. The predominant ethnicity was brown skinned in most regions, except for the South. In the category of schooling, notwithstanding the categories “ignored”, “white”, “and does not apply”, over the 10 years of analysis, individuals with less than eight years of schooling represented the highest number of cases, with no differences between regions. The residence zone with the highest number of reports of this disease was the urban, with predominance in all Brazilian regions.

All variables related to HVL were significant in the Northern and Northeastern regions. On the other hand, for the Southern region, only the variable gender was not significant, as opposed to the South, where only gender was significant. The variables that stood out in the Midwestern region were schooling and ethnicity. Regarding the Annual Increase Rate (AIR), disease incidence had significant values only in the Southern and Midwestern regions. AIR in the Southern region increased (0.90%) whereas there was a drop in incidence in the Midwest, with a negative AIR (25.1%). The other regions had a steady situation (Table 2).

Table 2 - Epidemiological factors of the patients with HVL, in Brazilian regions and AIR, between 2010 and 2020.

Region	Variable	Category	Cases (%)	OR [95%IC]	p-value	TIA/p-value/status	
North	Gender	Male	60	0,846	0.001*		
		Female	40				
	Education	<8 years	75	1,384	0.001*		
		>8 years	25				
	Ethnicity	Brown	81	Reference category			
		Black	7	0.897	0.262		
		Yellow	3	10.106	0.001*		
		White	6	0.318	0.001*		
		Indigenous	2	0.631	0.010*		
		Pediatric and juvenile	62	Reference category			
	Age Group	Adult	32	1,467	0.001*		
		Elderly	5	1,878	0.001*		
	Residence Area	Urban	70	Reference category			
		Rural	30	0.829	0.001*		
	Periurban	1	0.978	0.944			
Northeast	Gender	Male	66	0.828	0.001*		
		Female	34				
	Education	<8 years	63	0.342	0.001*		
		>8 years	37				
	Ethnicity	Brown	82	Reference category			
		Black	8	1.096	0.08		
		Yellow	1	1.209	0.254		
		White	9	0.908	0.06		
		Indigenous	1	2.771	0.001*		
		Pediatric and juvenile	53	Reference category			
	Age Group	Adult	41	1.323	0.001*		
		Elderly	7	1.556	0.001*		
	Residence Area	Urban	66	Reference category			
		Rural	33	1.15	0.001*		
	Periurban	1	0.814	0.130			
Southeast	Gender	Male	65	0.991	0.868		
		Female	35				
	Education	<8 years	60	0.530	0.001*		
		>8 years	40				
	Ethnicity	Brown	54	Reference category			
		Black	14	0.679	0.001*		
		Yellow	1	0.534	0.010*		
		White	30	0.520	0.001*		
		Indigenous	1	3.911	0.001*		
		Pediatric and juvenile	39	Reference category			
	Age Group	Adult	47	1.057	0.274		
		Elderly	14	1.261	0.001*		
	Residence Area	Urban	87	Reference category			
		Rural	12	2.20	0.001*		
	Periurban	1	0.654	0.240			
South	Gender	Male	7	63.32	0.001*		
		Female	93				
	Education	<8 years	48	0.491	0.131		
		>8 years	52				
	Ethnicity	Brown	10	Reference category			
		Black	0	0.00	0.999		
		Yellow	1	0.00	0.999		
		White	20	1.117	0.813		
		Indigenous	0	0.00	0.999		
		Pediatric and juvenile	31	Reference category			
	Age Group	Adult	53	0.796	0.632		
		Elderly	16	0.370	0.090		
	Residence Area	Urban	95	Reference category			
		Rural	5	0.00	0.999		
	Periurban	0	0.00	0.999			
Mid-West	Gender	Male	65	0.966	0.662		
		Female	35				
	Education	<8 years	68	1.469	0.001*		
		>8 years	32				
	Ethnicity	Brown	36	Reference category			
		Black	6	0.973	0.129		
		Yellow	1	0.570	0.180		
		White	20	0.595	0.001*		
		Indigenous	1	0.671	0.238		
		Pediatric and juvenile	38	Reference category			
	Age Group	Adult	49	1.424	0.133		
		Elderly	13	1.251	0.060		

	Urban	90	Reference category	
Residence Area	Rural	9	1.20	0.177
	Periurban	1	1.80	0.128

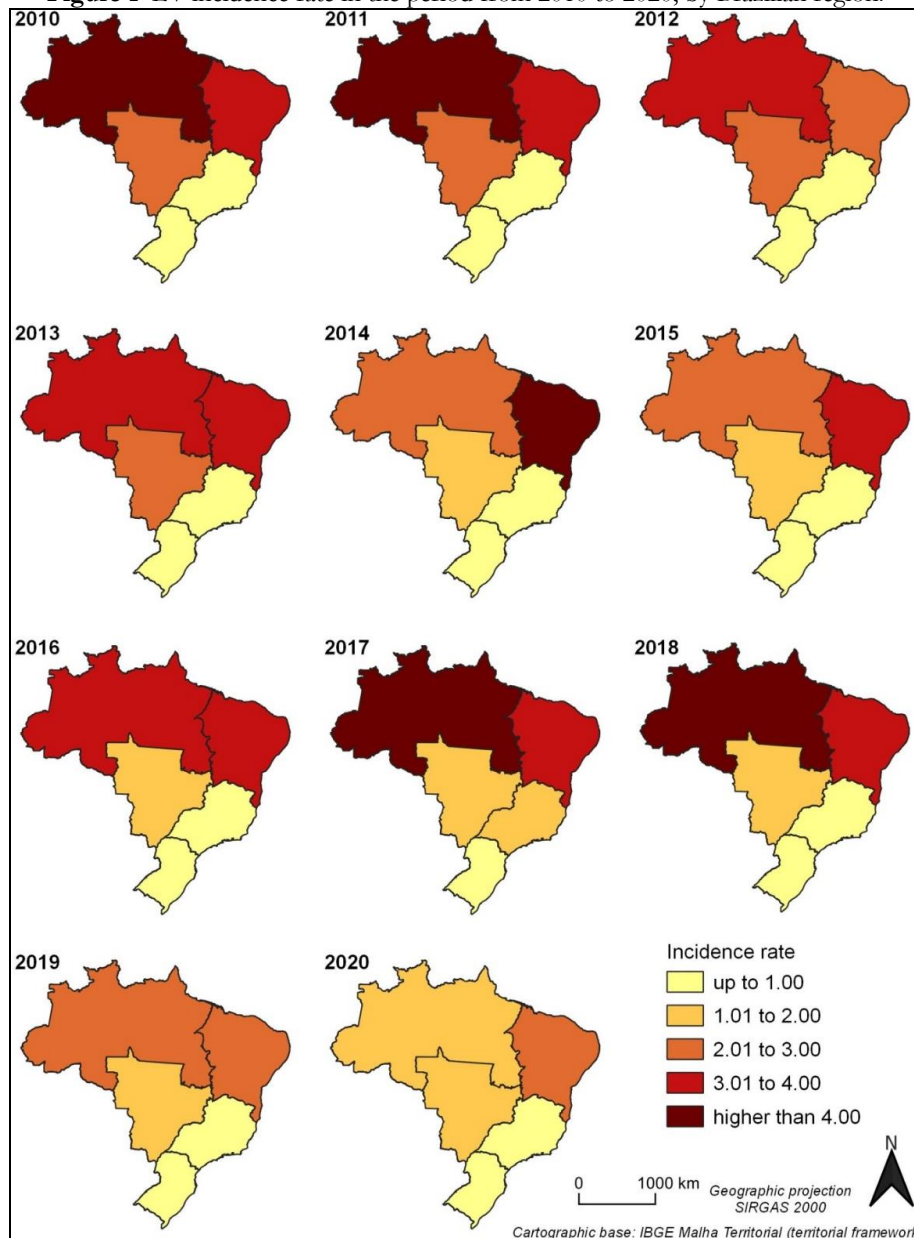
Obs.: Pediatric and juvenile (up to 19 years old); Adult (20 to 59 years old); Elderly (Above 65 years old)
Education: < 8 years (illiterate and elementary school); > 8 years (High School and Higher Education)

* significant $p \leq 0.05$

Source: Elaborated by the authors.

The HVL incidence rate varied quite a lot over the study period. Seven of the 10 years of the temporal series had an intensive incidence with variation between 3.26 and 3.90/100 thousand inhabitants. The Northern region had a high incidence rate in 2010, 2011, 2017, and 2018, with a maximum of 5.47/100 thousand inhabitants recorded in 2011. In the Northeastern region, a higher incidence rate was observed only in 2014, with 4.36/100 thousand inhabitants.

Figure 1–LV incidence rate in the period from 2010 to 2020, by Brazilian region.



Source: Elaborated by the authors.

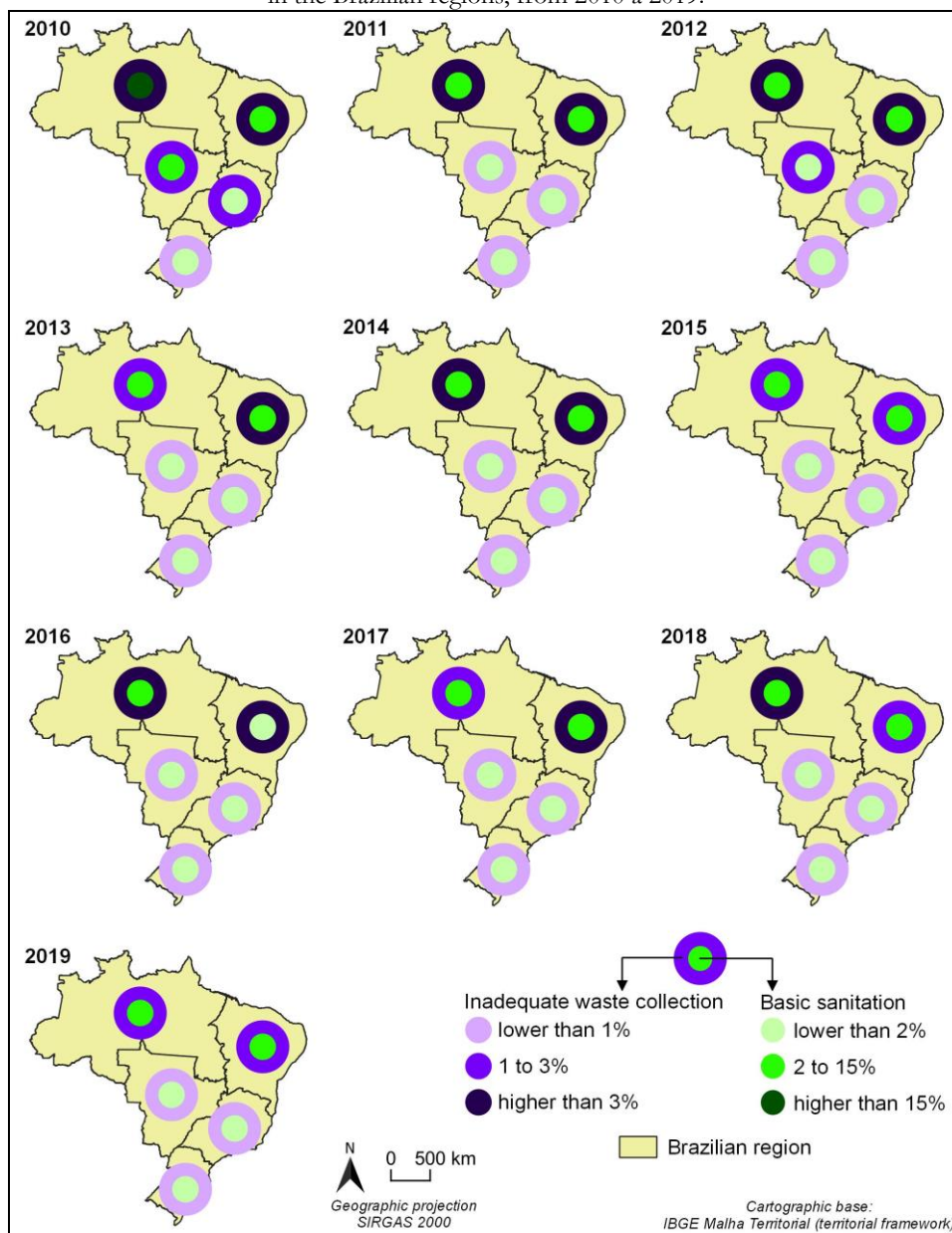
The World Health Organization defines Social Health Determinants (SHD) as the factors that will affect health outcomes, related primarily to the life conditions of each individual, how they live and work. Among the SHDs that might be connected to health equity, some worth noting are access to health social services, housing, sanitary sewage, income, and social protection, education, unemployment, work environment, among others, which are related to policies, economic systems, and social standards (WHO, 2022b).

Regarding urban sanitation infrastructure in the Brazilian regions, during the study period, the Northern and Northeastern regions had the worst basic sanitation and waste collection conditions. The year 2010 stood out with the highest prevalence of domiciles with these conditions (Figure 2).

Considering the environmental (sanitation) and economic variables for each region, the regression analysis indicated the following coefficients for p-value determination: North ($R^2 = 73.03\%$; $p = 0.0047$), Northeast ($R^2 = 15.52\%$; $p = 0.8232$), Southeast ($R^2 = 49.32\%$; $p = 0.2407$), South ($R^2 = 82.12\%$; $p = 0.00113$), Midwest ($R^2 = 70.04$; $p = 0.0616$). Income per capita was the variable with the highest weight for the Northern region (40.43%) and basic sanitation and Gini index were the highest for the South; the model with these two variables accounts for 72.40%. Incidence in the South is the lowest among the states (on average, 0.034 in the 10 years analyzed). In the Midwestern region, waste collection was the variable that most explained the model (52.50%).

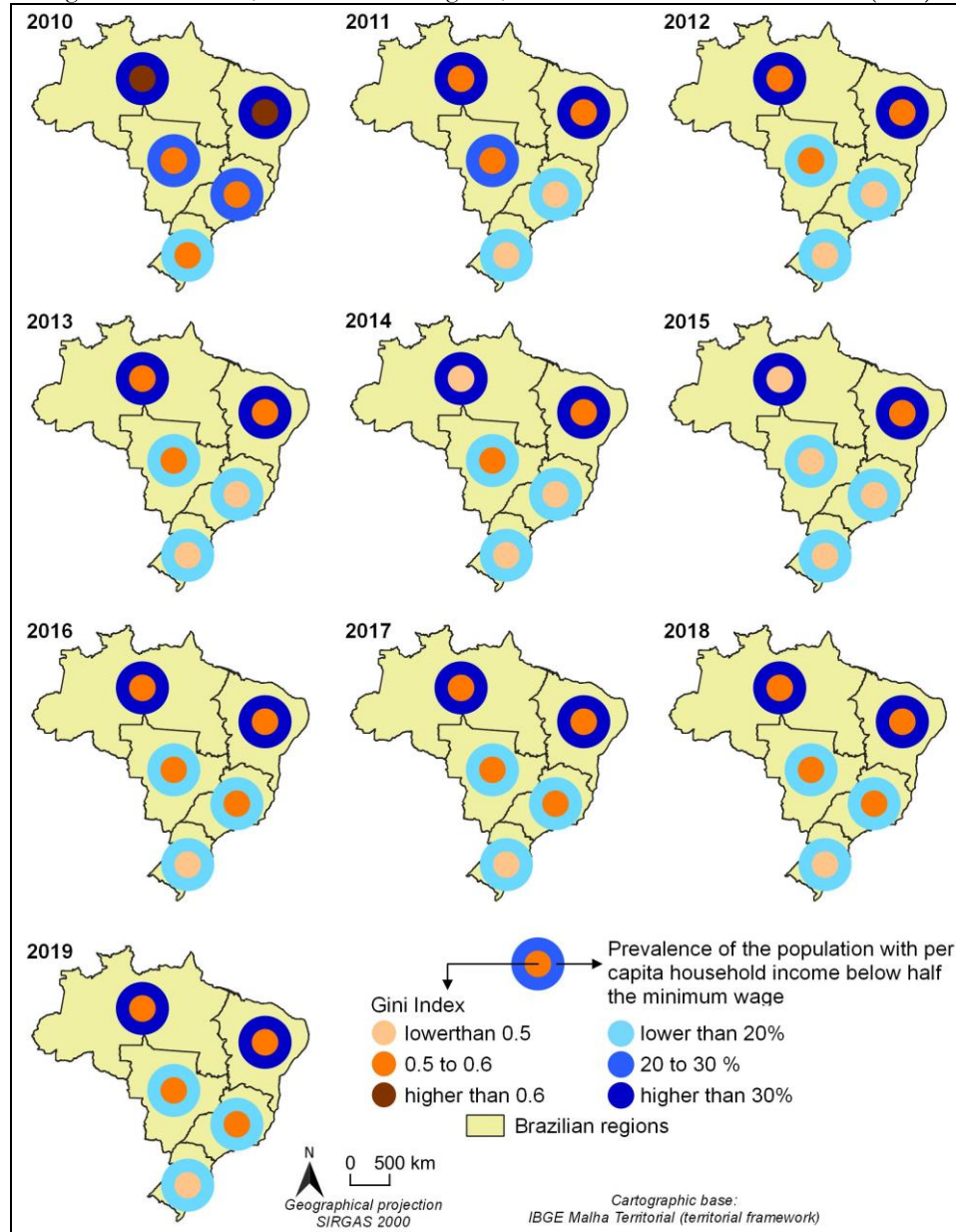
The Northern and Northeastern regions are identified as those with the highest prevalence of population with income equal to or lower than half the minimum wage. The Gini Index in 2010 was the worst in the historical series, indicating a situation of vulnerability and the worst household income per capita (Figure 3). It is noticeable that in both the Northern and in the Northeastern regions, more than 50% of the population is under this poverty condition. The region with the lowest inequality in Brazil is the Southern region.

Figure 2 - Prevalence of urban domiciles with inadequate water supply, sanitary sewage, and waste collection in the Brazilian regions, from 2010 a 2019.



Source: IPEA (2022). Elaborated by the authors.

Figure 3 - Prevalence of population with household income per capita equal to or lower than half minimum wage and Gini Index, in the Brazilian regions, from 2010 to 2019. Source: IPEA (2022).



Source: Elaborated by the authors.

Discussion

HVL is considered one of the five priority NTDs by the World Health Organization (OPAS, 2020), when considering its morbimortality. HVL is still a challenge for countries in the Americas. As a health policy, federal and regional governments have established programs for its surveillance and control, given its high incidence and wide geographic distribution (OPAS, 2018).

The lowest number of HVL cases recorded in the period was in 2020, which might be explained by the effect of the Covid-19 pandemic on surveillance and assistance activities. According to OPAS (2021), the fight against the Covid-19 pandemic became a

priority, and this affected the notification of NTDs, decreasing the activities for active search, early diagnosis, and treatments of the cases.

From the epidemiological aspect, HVL in Brazil attacks more the male gender, which corroborates other studies (Farias et al., 2019; Batista et al., 2021; Lima, et al., 2021; Chaves et al., 2022). The explanation for this occurrence might be related to a higher exposure to the virus, to physiological factors, and to an increase in susceptibility with aging (Reis, et al., 2017; Almeida et al., 2020; Cavalcante et al., 2022; Cezar et al., 2021; Pierote et al., 2022). This susceptibility in adults and the elderly is emphasized by the results of the present study. Studies conducted in Piauí (Chaves et al., 2022; Pierote et al., 2022) also showed a higher proportion of cases in adult individuals (20 to 59 years old), and might be associated to occupational hazards. The likeliness of being exposed to the risk of HVL infection might vary from one person to another due to differences in occupations, behavioral habits, and protection measures (Jiang et al., 2021). On the other hand, there are studies (Batista et al, 2021; Silva et al., 2022) that have recorded predominance in children. Susceptibility of children to HVL can be related to: immature immune system, inadequate nutrition, and higher exposure to the vector in the peridomicile area (Brasil, 2014).

Similar to the present study, brown skin color was the most prevalent (Cunha et al., 2020; Batista et al., 2021) in all Brazilian regions, except for the South. However, there is no explanation for a potential relationship between the disease and brown skin color (Souza et al., 2018). The predominance might be related to the fact that black individuals self-declare as brown skinned, which causes a bias towards the increased notification of this color/ethnicity (Cezar et al., 2022). In the Southern region, 73.2% of the population is comprised of white individuals, which might explain the predominance of the disease in this group (PNAD, 2019).

The higher number of HVL cases in individuals with elementary school may indicate that individuals with low education level are more susceptible (Reis, et al., 2017; Almeida et al., 2020; Cezar et al., 2021; Chaves et al., 2022; Silva et al., 2022). This scenario might be explained by the fact that individuals with lower schooling level have lower knowledge about disease control and prevention measures, which might be related to the incidence of cases.

In Brazil, the urban area represents the major endemic area of HVL. This behavior might be explained by inadequate urbanization (Reis et al., 2017). In addition, urban expansion to vegetated areas, associated with the adaptation of the vector insect to new habitats has contributed with leishmaniasis spatialization (Amaro; Costa, 2017).

Regarding clinical outcome, most cases evolved to cure, which suggests early diagnosis and treatment; similar data were found by Silva et al. (2022) and Cunha et al.

(2020). Regarding lethality rate, the Southern region had the highest percentage, even with the lowest number of notified cases and the lowest incidence. Having a late diagnosis and the presence of comorbidities are factors that might explain high lethality (Farias et al., 2019). These results were also reported by Cunha et al. (2020).

Brazil has different environmental, socioeconomic, and housing conditions. Sanitary conditions are determining factors for this disease, e.g., inadequate housing, lack of basic sanitation, improper waste disposal. On the other hand, inadequate sanitary conditions are observed to be related to low socioeconomic level. Moreover, these conditions allow the formation of breeding sites of vectors and infection of reservoirs, which provides opportunity for the disease to spread (Figueiredo et al., 2017). An estimated increase of 1% of individuals with domiciles with adequate waste collection might lead to a 4% decrease in HVL (Silva et al., 2021).

The highest incidence rates are present in the Northeastern and Northern regions, considered vulnerable, even though they have a steady Annual Increase Rate. Inadequate water supply and sanitary sewage, with no waste collection services and a higher rate of people with household income per capita equal to or lower than half of a minimum wage help keep these incidences steady. An estimated increase of one real in the income per capita might cause a decrease of 1% in HVL cases, which shows that disease permanence might be attributed to low socioeconomic level. This relationship might be associated with individuals residing in areas in the outskirts of cities and in precarious conditions (Sampaio et al., 2021; Silva et al., 2021). The probability that an individual is infected in an area without sewage system or waste collection (environment favorable to the presence of vectors) is estimated to be four to six-fold higher than in areas with adequate basic sanitation (Moura, Tallyta, Barreto, 2017). The lowest incidence rates of this disease were reported in the southern region, which had the lowest Social Vulnerability Index (SVI) and the lowest inequality in income (IBGE, 2020; IPEA, 2022).

Conclusion

The challenges of eradicating neglected diseases, as is the case of VL, goes through improving environmental, social, and economic conditions of the population, as well as meeting the goals of the 2030 Agenda. It is necessary to decrease vulnerability and social inequality providing health and quality of life to the population. In this respect, the spread of human visceral leishmaniasis in Brazil indicated that the endemic remains, and the risk of becoming ill Northeastern region was higher due to its incidence rate, in the period ranging from 2010 to 2020. Moreover, predominant epidemiological factors outlined the

following profile: males, pediatric and juvenile, brown colored skin, with elementary school, and residing in the urban zone.

HVL is an undernotified disease with high number of incomplete records, which hampers the actual situation. These factors indicate the need for assessing the completeness of the information, as well as monitoring the cases, thus preventing activities for assistance and reduction of the endemic from having flaws. A more effective surveillance and control of the disease in the country is essential, involving the vectors, the reservoirs, and environmental care, with the purpose of identifying the cases early on, decreasing transmission and reducing morbimortality.

From the environmental perspective, social public policies are required, aiming at improving the socioeconomic conditions of the vulnerable population, which is more exposed to the disease hazard. Other measures that are also required are control and entomological management measures to prevent vectors from developing, especially in endemic areas or in areas where the disease occurrence has grown. In addition, to perform the control measures of HVL throughout national territory, it is important that the municipalities are focused on three aspects: epidemiological surveillance, educational measures, and administrative measures. Moreover, research conducted at the academy - which involves socio-environmental and operational issues, as with any scientific, technological, and innovative production resulting from this process - must be considered as a path to improve prevention practices of neglected diseases.

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APA

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