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Temporal trend in the incidence of human visceral leishmaniasis in Brazil

Tendência temporal da incidência de leishmaniose visceral humana no Brasil

Claudio José dos Santos Júnior (https://orcid.org/0000-0002-2853-1968) [1]
Marquiony Marques dos Santos (https://orcid.org/0000-0001-5812-4004) [2]
Fabio Celso Cipriano de Oliveira Lins (https://orcid.org/0000-0003-4827-8506) [3]
Jackson Pinto Silva (https://orcid.org/0000-0002-9592-0840) [4]
Kenio Costa de Lima (https://orcid.org/0000-0002-5668-4398) [5]

Abstract *It is an ecological study that analyzed the time trend of visceral leishmaniasis incidence rates in Brazil using segmented time regression by joinpoints. There was a decreasing incidence rate of this disease in the country with an average annual percent change (AAPC) of -5 (CI95%: -9.1; -0.6) and a reduction of 1.69 cases/100 thousand inhabitants in 2007, and 0.91/100 thousand inhabitants in 2020. The Central-West region showed the highest reduction percent (AAPC: -9.1; CI95%: -13.8; -4.3), followed by the Southeast region (AAPC: -8.7; -14.6; -2.5). The North and South regions showed the largest number of joinpoints in the time series. The highest incidences were recorded in the male population, however, stable (AAPC: 2.14; CI95%: -8.3; 0). In the age group analysis, the trend was decreasing for the groups from 0 to 4 years old (AAPC: -7.7; CI95%: -12.6; -2.4), 5 to 9 years old (AAPC: -7.3; CI95%: -13.6; -0,4) and 10 to 14 years old (AAPC: -5.5; CI95%: -10.3; -0.3). It was found that although Visceral Leishmaniasis is an endemic disease in Brazil, there was a decrease in its incidence rate from 2007 to 2020.*

Key words *Visceral leishmaniasis, Epidemiological monitoring, Temporal distribution, Time series study, Ecological studies*

Resumo *Trata-se de um estudo ecológico que analisou a tendência temporal das taxas de incidência de leishmaniose visceral no Brasil mediante regressão temporal segmentada por pontos de inflexão. Observou-se tendência de decréscimo na taxa de incidência dessa patologia no país, com variação variação percentual média anual (average annual percent change – AAPC) de -5 (IC95%: -9,1; -0,6) e redução de 1,69 casos/100 mil habitantes em 2007, para 0,91/100 mil habitantes em 2020. A região Centro-Oeste apresentou a maior redução do AAPC (AAPC: -9,1; IC95%: -13,8; -4,3), seguida da região Sudeste (AAPC: -8,7; -14,6; -2,5). As regiões Norte e Sul apresentaram o maior número de pontos de inflexão (joinpoint) na série temporal. As maiores incidências foram registradas na população masculina, porém com tendência estacionária (AAPC: 2,14; IC95%: -8,3; 0). Na análise por faixa etária, a tendência foi decrescente nos grupos de 0 a 4 anos (AAPC: -7,7; IC95%: -12,6; -2,4), 5 a 9 anos (AAPC: -7,3; IC95%: -13,6; -0,4) e de 10 a 14 anos (AAPC: -5,5; IC95%: -10,3; -0,3). Verificou-se que, apesar de a leishmaniose visceral se tratar de uma doença endêmica no Brasil, houve declínio na sua taxa de incidência no período de 2007 a 2020.*

Palavras-chave *Leishmaniose visceral, Monitoramento epidemiológico, Distribuição temporal, Estudos de séries temporais, Estudos ecológicos*

[1] Programa de Pós-Graduação em Saúde Pública, Faculdade de Saúde Pública, Universidade de São Paulo. Av. Dr. Arnaldo 715, Cerqueira César. 01246-904 São Paulo SP Brasil. claudiojunior@usp.br
[2] Universidade Estadual do Rio Grande do Norte. Caicó RN Brasil.
[3] Universidade Estadual de Ciências da Saúde de Alagoas. Maceió AL Brasil.
[4] Instituto Federal de Alagoas. Maceió AL Brasil.
[5] Programa de Pós-Graduação em Saúde Coletiva, Universidade Federal do Rio Grande do Norte. Natal RN Brasil.

Introduction

Visceral leishmaniasis (VL) or kala-azar is a zoonosis of worldwide distribution caused by protozoa of the genus *Leishmania* that are transmitted by sandflies[1,2]. The main urban reservoirs of VL are dogs[3].

This disease is considered a problem of Public Health of international importance, especially affecting tropical countries, whose socio-environmental conditions favor the development and proliferation of *Lutzomyia longipalpis*, the main vector of *Leishmania chagasi*, the causative agent of VL in Latin America[2-5].

It is a disease of wide distribution in Asia, Europe, the Middle East, Africa, and the Americas, with the highest incidence in rural and suburban areas[6,7].

VL is the most severe form of leishmaniasis, being potentially fatal due to its multisystem involvement and the tropism of its agentS for hematopoietic organs, such as the spleen, liver, and bone marrow[3,8], and affects more frequently socially vulnerable populations and individuals with immunosuppression conditions, such as malnourished children, patients with HIV/Aids infection, elderly people with comorbidities, among other conditions that impair the host's immune response[3,4,9].

It is estimated that 400 thousand of new cases of this disease occur annually across the globe[1,10]. In the Americas, 13 countries are endemic, and from 2001 to 2020, 67,922 new cases were recorded, with an average of 3,400 occurrences per year. In 2020, of the total number of new cases in the American continent, 97% were reported by Brazil and the others by Argentina, Bolivia, Colombia, Paraguay, Venezuela, and Uruguay[4,11].

In the last three decades, however, many aspects of the VL ecoepidemiology were reviewed and enabled the development of surveillance measures by the control bodies, such as the incorporation of actions and activities in the Visceral Leishmaniasis Surveillance and Control Program (VLSCP). Since 2011, the Regional Leishmaniasis Program (RLP) by the Pan American Health Organization (PAHO)[11] has been monitoring the behavior of this disease in the Americas region with planning and control measures.

The identification of territorial units of greater epidemiological importance is a factor that needs to be considered in the planning of VL promotion, prevention, surveillance, and control measures by health agencies, especially in endemic regions, as is the case of the national territory. Despite this reality, no recent study was identified in Brazil on the behavior of the disease over the years in its different regions, Federation units, and according to sociodemographic characteristics. Therefore, this study sought to analyze the trends of VL incidence in the country from 2007 to 2020 by major national regions and Federation units, and according to the gender and age group of those affected.

Method

This is an ecological time series study to analyze the trends of VL incidence rates in the population of Brazil, from 2007 to 2020.

The study scenario is Brazil, the largest nation in South America in terms of land area and population. Information on new VL cases (CID 10 – B55.0) was collected from the Ministry of Health's Information System on Notifiable Diseases (SINAN Net) database, available on the website of the Department of Informatics of the Unified Health System (DATASUS; https://datasus.saude.gov.br/informacoes-de-saude-tabnet/).

The collection of data took place on March 20, 2022. SINAN Net is a system that aims to collect, transmit, and disseminate data routinely generated by the Epidemiological Surveillance System of the three levels of government in Brazil, through a computerized network, to support the investigation process and provide subsidies for the analysis of epidemiological surveillance information on compulsory notifiable diseases, as it is the case with VL[12].

Data on the population residing in the country by gender and group age were obtained through demographic information from the Brazilian Institute of Geography and Statistics (IBGE), which is information based on censuses and the inter-census population estimates (www.ibge.gov.br/estatisticas/sociais/populacao).

VL cases were tabulated using DATASUS Tabnet and Microsoft Excel Office 2013 was used to organize the database, build indicators, and create tables.

VL incidence rates were calculated as the number of new VL new cases reported to SINAN divided by the population residing in the location and year, multiplied by 100 thousand inhabitants. The rates were calculated for the country and according to regions North, Northeast, Central-West, Southeast, and South; federation units (FU – North Region: Rondônia, Acre, Amazonas, Roraima, Pará, Amapá, Tocantins; Northeast Re-

Ciência & Saúde Coletiva, 28(9):2709-2719, 2023

gion: Maranhão, Piauí, Ceará, Rio Grande do Norte, Paraíba, Pernambuco, Alagoas, Sergipe, Bahia; Central-West Region: Mato Grosso do Sul, Mato Grosso, Goiás, Distrito Federal, Southeast Region: Minas Gerais, Espírito Santo, Rio de Janeiro, São Paulo; South Region: Paraná, Santa Catarina, Rio Grande do Sul), gender, and age groups (in years, younger than 4; 5 to 9; 10 to 14; 15 to 19; 20 to 39; 40 to 59; 60 to 79; and 80 or older).

Then, a joinpoint regression analysis model was used for the time analysis. This model verifies if one line with multiple segments is statistically better to describe the time evolution of a data set than a straight line, or with fewer segments. In this way, it allows identify the trend of the indicator (increasing, stable, or decreasing) and the points where there is a change in this trend, allowing us to know the *annual percent change* (APC) and that of the entire period, called *average annual percent change* (AAPC)[13,14].

The incidence rates were considered a dependent variable (Y) and calendar years as an independent variable (X). For each trend detected, 95% confidence intervals (CI95%) and p values (5% significance level) were considered. Non-significant *p* values resulted in a stability trend (accepting the null hypothesis that the incidence rates have not changed over the years). On the other hand, significant *p* values resulted in a classification of growth trend (positive APC or AAPC) and decreasing trend (negative APC or AAPC)[13,14].

All tests were performed on Joinpoint Regression Program, version 4.9.0.1, and to minimize the effect of eventual autocorrelations, the option "fit an autocorrelated errors model based on the data" available on the software was used.

Results

Between 2007 and 2020, 45,270 new cases of VL were recorded, with a predominance in the Northeast region (52.78%). The male gender was responsible for 64.13% of the occurrences. As for age, the most affected group was from 1 to 4 years old (34.33%). The year with the highest incidence of VL was 2017, with 1.98 cases/per 100 thousand inhabitants.

The joinpoint regression analysis model pointed out, for the VL incidence rate in Brazil, a time behavior with two APCs: the first segment, stationary between 2007 and 2018 (APC:-0.5; CI95%: -2.6; 1.6; p > 0.05); the second also between 2018 and 2020 (APC: -26; CI95%: -45.9; 1.4; p > 0.05) (Figure 1). When analyzing the total period, however, there was a significant decreasing trend in the incidence of the disease in the national territory, with an average annual percent change (AAPC) of -5 (CI95%: -9.1; -0.6; p < 0.05), and a reduction from 1.69 cases/100 thousand inhabitants in 2007 to 0.91/100 thousand inhabitants in 2020 (Table 1).

In the time analysis, two major administrative regions presented decreasing trend, highlighting the Central-West region with the largest average annual percent change (AAPC: -9.1; CI95%: -13.8; -4.3; p < 0.05) and Southeast (AAPC: -8.7; -14.6; -2.5; p < 0.05) with the lowest. There was an increasing trend in the South region (AAPC: 21.7; CI95%: 5.7; 40.2; p < 0.05) and stability in the North (AAPC: -8.6; CI95%: -20.4; 5.0; p > 0.05) and Northeast regions (AAPC: -4.2; CI95%: -9.4; 1.4; p > 0.05) (Table 1). The regression model also showed that the North and Southeast regions were the ones that presented the highest number of segments in the time series (*joinpoints*), representing the greatest oscillation in rated over the years (Figure 1).

Concerning the analysis by federation unit (FU), the time modeling showed that five regions and the Federal District presented decreasing trend, with one from the North region, one from the Northeast, one from the Southeast, and tho from the Central-West (two states and the Federal District). On the other hand, 16 presented stationary patterns, with four in the North, seven in the Northeast, two in the Southeast, two in the South, and 1 in the Central-West; and four showed an increasing trend, one in each region (except for the Central-West region) (Table 1).

From 2007 to 2020, the autochthony of the disease was confirmed in 26 federation units, distributed in five Brazilian regions, with the Northeast region being responsible for the largest number of cases in the country (n = 23,893; 44.6%). Only the state of Acre, in the North region, did not present VL cases during the studied period. The state of Tocantins, in turn, concentrated the highest incidence of VL throughout the data series.

Higher VL incidence rates were observed in the male population. In this group, the incidence trend was stationary (AAPC: 2.14; CI95%: -8.3; 0); in females, in turn, there was a decrease (AAPC: -6.3; CI95%: -20.8; -1.5) (Table 2). When stratifying the indicator according to age group, a decreasing trend was observed in the groups from 0 to 4 years old (AAPC: -7.7; CI95%: -12.6; -2.4; p < 0.05), 5 to 9 years old (AAPC: -7.3;

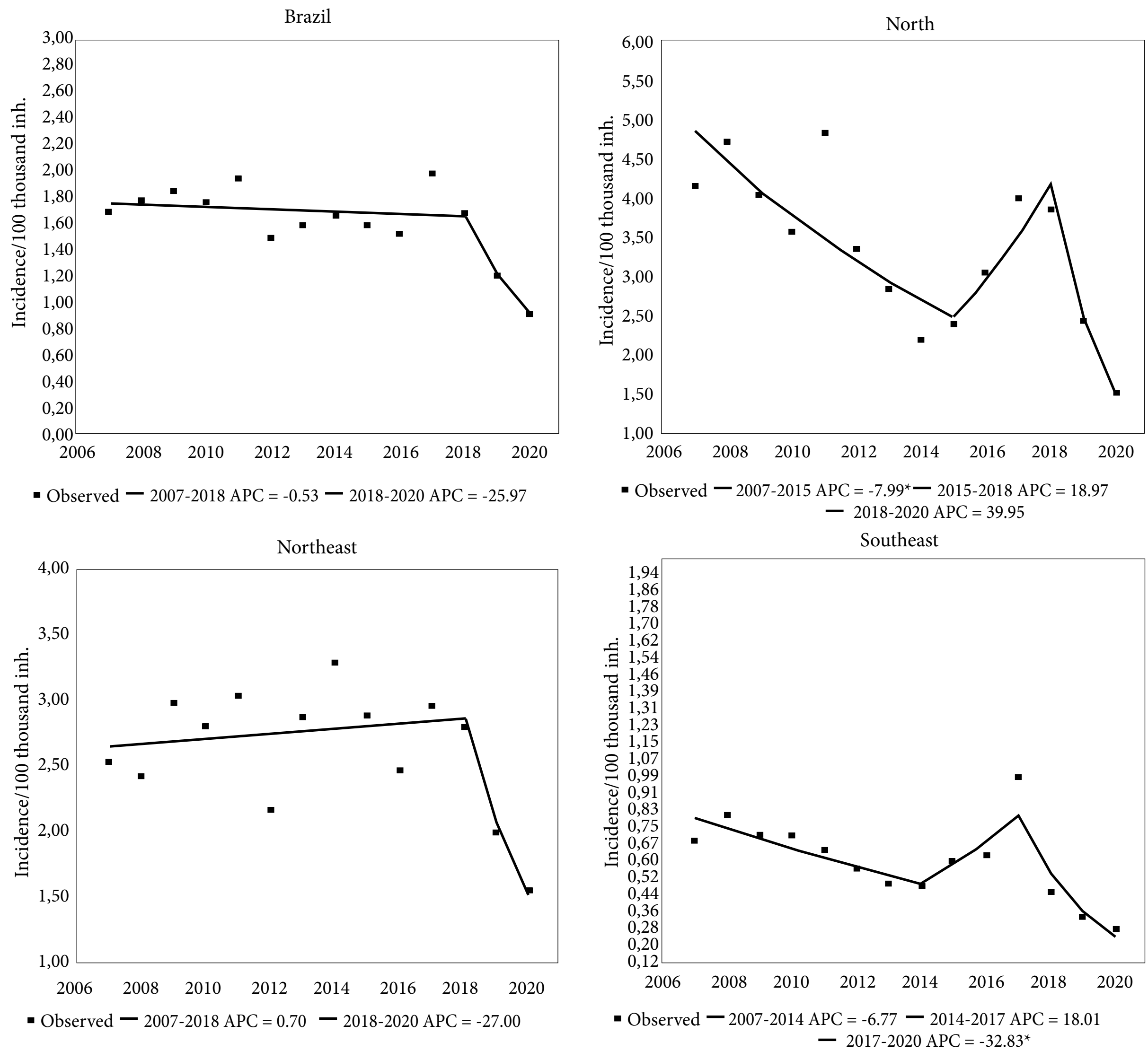

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Figure 1. Time evolution of VL incidence rate in Brazil and its administrative regions, 2007-2020.

CI95%: -13.6; -0.4; $p < 0.05$), and from 10 to 14 years old (AAPC: -5.5; CI95%: -10.3; -0.3; $p < 0.05$). In the other strata, the trends present a stationary behavior (Table 2).

Discussion

In Latin America, more than 95% of VL cases occur in Brazil, most of them in the Northeast region[1,11]. This scenario reflects that VL is a relevant public health problem in the national territory and makes the country a priority area for measures to monitor and control the disease, either through epidemiological or environmental surveillance actions.

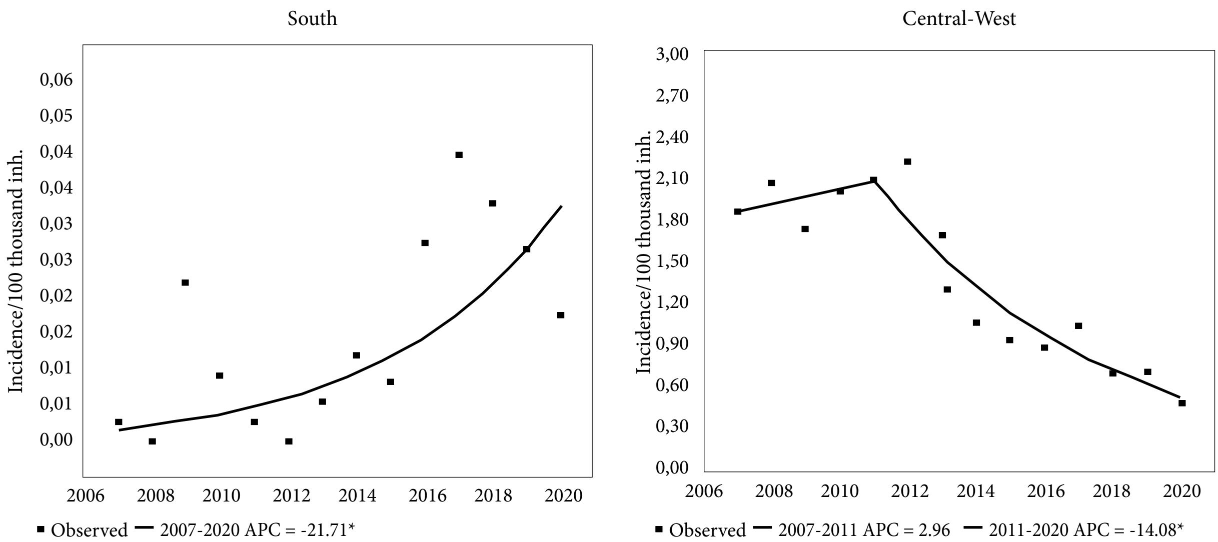

Figure 1. Time evolution of VL incidence rate in Brazil and its administrative regions, 2007-2020.

Caption: VL: Visceral leishmaniasis; inhh.: inhabitants; APC: *annual percent change*; inhab.: inhabitants; parameters used in the joinpoint analysis:minimum: 0; maximum: 3; model selection: test with 4,500 permutations; correlation of errors based on data; * statistical significance ($p < 0.05$).

Source: Authors.

In 2020, the lowest number of VL occurrences of the time series was recorded in the national territory, a phenomenon that was significantly reflected in the incidence of this disease (n = 1,933; 0.91 cases/100 thousand inhabitants). This significant decrease in the incidence of VL cases may represent an indication of the reduction in the force of morbidity and in the magnitude of the endemicity of this zoonosis nationwide, formerly treated as a disease of increasing incidence[15]. And it may also be one of the effects generated by the COVID-19 pandemic[16,17].

In analyzing the data, it is observed that there was a formation of an inflection point (*joinpoint*) in the time series of the incidence rate for the national territory in 2018. This behavior was influenced by the reduction in the number of cases at the level of states and regions, especially in the Northeast, which concentrates the greatest burden of the disease in the country and which, according to the data series, presented stability in seven of its Federation Units, decrease in Ceará, and increase only in the state of Alagoas.

Two studies carried out in Ceará indicated heterogeneity of VL in that state. In the first one, VL presented a trend of increase and expansion for the Central-West and East regions between 2003-2017, and a decrease from 2016 on[18]. In the second one, which also used segmented time regression, the global incidence rate of VL showed an increasing trend in the capital between 2007-2017 and a decrease for the interval 2015-2017[19]. These diverse findings possibly result from time frames and trend analysis adopted in the studies.

Another study, which had the state of Alagoas as its analysis space, confirms a progressive evolution of VL incidence rates in the Federation Unit, showing geographic expansion, a trend of zoonosis persistence in areas that already had reported cases, and overall strengthening of the endemic status of the disease in that territory between 2007 and 2018[20].

A historical series study of VL in the Northeast region developed by Batista *et al.*[21] highlighted the cyclical nature of the disease. The authors identified epidemic peaks in 1983-1984, 1993-1994, 2003-2004, and 2013-2014 in Piauí and a general trend of stability for VL incidence, mortality, and lethality rates between 1971 to 2018 in the state. Another study, in agreement with our findings, also indicated a decreasing trend of VL incidence for Tocantins[22].

Some national and Latin American studies also point to this cyclical behavior and the het-

Table 1. Percentage of annual average variation (AAPC) and percentage of annual variation (APC) of VL incidence rates in the regions and Federation units in Brazil (2007-2020).

Regions/ Federation Unit	Cases		Incidence		Joinpoint regression model									
	2007**	2020**	2007	2020	Period		APC	CI95%		Trend	AAPC	CI95%		Trend
Brazil	**3.204**	**1.933**	**1.69**	**0.91**	**2007**	**2020**					**-5***	**-9.1**	**-0.6**	**Decreasing**
					2007	2018	-0.5	-2.6	1.6	Stable				
					2018	2020	-26	-45.9	1.4	Stable				
North	637	285	4.14	1.53	2007	2020					-8.6	-20.4	5	Stable
					2007	2015	-8*	-13.9	-1.7	Decreasing				
					2015	2018	19	-35.1	118	Stable				
					2018	2020	-40	-67.2	10.1	Stable				
Amapá	1	1	0.16	0.12	2007	2020					4.1	-11.5	22.5	Stable
Amazonas	1	1	0.03	0.02	2007	2020					2.8	-19.5	31.3	Stable
Pará	281	175	3.81	2.01	2007	2020					-5.6	-13.5	2.9	Stable
					2007	2014	-6.9*	-12.6	-0.8	Decreasing				
					2014	2018	23.5	-2.5	56.4	Stable				
					2018	2020	-42.3	-64	-7.5	Decreasing				
Rondônia	1	0	0.06	0.00	2007	2020					-22	-41	3.2	Stable
Roraima	1	15	0.24	2.38	2007	2020					24.6*	4.8	48.2	Increasing
					2007	2010	148.5*	15.1	436.3	Increasing				
					2010	2020	1.3	-10.1	14.2	Stable				
Tocantins	352	93	26.08	5.85	2007	2020					-10.1*	-13.2	-6.9	Decreasing
Northeast	1.337	891	2.53	1.55	2007	2020					-4.2	-9.4	1.4	Stable
					2007	2018	0.7	-2	3.4	Stable				
					2018	2020	-27	-51	8.8	Stable				
Alagoas	28	56	0.90	1.67	2007	2020					6.2*	1	11.6	Increasing
Bahia	175	121	1.24	0.81	2007	2020					-0.8	-9.6	8.7	Stable
					2007	2010	31.5	-12.6	97.9	Stable				
					2010	2020	-8.9*	-14.5	-2.9	Decreasing				
Ceará	442	170	5.29	1.85	2007	2020					-6.3*	-9.1	-3.4	Decreasing
Maranhão	309	317	4.77	4.46	2007	2020					-1.7	-9.7	7	Stable
					2007	2018	5*	0.8	9.3	Increasing				
					2018	2020	-31.4	-62.3	24.6	Stable				
Paraíba	18	11	0.48	0.27	2007	2020					2.5	-3.3	8.7	Stable
Pernambuco	46	58	0.53	0.60	2007	2020					3.8	-0.3	8.1	Stable
Piauí	217	100	6.93	3.05	2007	2020					-4	-10	2.4	Stable
					2007	2017	1.5	-2.9	6.1	Stable				
					2017	2020	-20.1	-40	6.4	Stable				
Rio Grande do Norte	48	26	1.53	0.74	2007	2020					-4.7	-10.4	1.5	Stable
					2007	2011	10.8	-8.9	34.8	Stable				
					2011	2020	-10.8*	-15.7	-5.6	Decreasing				
Sergipe	54	32	2.66	1.38	2007	2020	-0.8	-4.4	2.9	Stable				

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erogeneous nature of VL transmission, which has varied between high and low incidences[19,23-25]. In a study developed by Servadio *et al.*[26], the asymmetry of VL distribution in the country is also revealed, with emphasis on the few states that followed the same trend of national incidence.

In this study, the trend for the Southeast regions and the state of São Paulo was decreasing.

Table 1. Percentage of annual average variation (AAPC) and percentage of annual variation (APC) of VL incidence rates in the regions and Federation units in Brazil (2007-2020).

Regions/ Federation Unit	**Cases**		**Incidence**		**Joinpoint regression model**									
Southeast	553	244	0.69	0.27	2007	2020					-8.7*	-14.6	-2.5	Decreasing
					2007	2014	-6.8*	-10.5	-2.8	Decreasing				
					2014	2017	18	-13.3	60.7	Stable				
					2017	2020	-32.8*	-42.4	-21.6	Decreasing				
Espírito Santo	0	0	0.00	0.00	2007	2020					13.6	-16.5	54.4	Stable
Minas Gerais	342	170	1.75	0.80	2007	2020					-8.3	-18.3	2.9	Stable
					2007	2014	-5.9	-12.4	1.1	Stable				
					2014	2017	26.5	-26	116.3	Stable				
					2017	2020	-37.4*	-52.1	-18.2	Decreasing				
Rio de Janeiro	1	3	0.01	0.02	2007	2020					24.9*	9	43.2	Increasing
São Paulo	210	71	0.51	0.15	2007	2020					-9.3*	-11.3	-7.3	Decreasing
South	1	6	0.00	0.02	2007	2020					21.7*	5.7	40.2	Increasing
Paraná	1	1	0.01	0.01	2007	2020					9.3	-48.8	133.3	Stable
					2007	2013	-27	-60.3	34.3	Stable				
					2013	2016	345.3	-87.9	16334.3	Stable				
					2016	2020	-30.2	-77.7	118.6	Stable				
Rio Grande do Sul	0	4	0.00	0.04	2007	2020					25.6*	5.1	50.3	Increasing
Santa Catarina	0	1	0.00	0.01	2007	2020					-9.4	-21.5	4.5	Stable
Central-West	254	81	1.86	0.49	2007	2020					-9.1*	-13.8	-4.3	Decreasing
					2007	2011	3	-12.7	21.4	Stable				
					2011	2020	-14.1*	-18.1	-9.9	Decreasing				
Distrito Federal	3	2	0.12	0.07	2007	2020					-11.7*	-20.4	-2.1	Decreasing
Goiás	13	22	0.22	0.31	2007	2020					0.7	-3.3	4.9	Stable
Mato Grosso	28	11	0.95	0.31	2007	2020					-15*	-19.7	-10.1	Decreasing
Mato Grosso do Sul	210	46	8.80	1.64	2007	2020					-11*	-14.7	-7.1	Decreasing

Caption: VL: visceral leishmaniasis; Incidence: Incidence rate/100 thousand inhabitants; APC: annual percent change; AAPC: average annual percent change; CI95%: confidence interval of 95%; **it covers all new cases confirmed in the national territory, including those with city blank/ignored; *statistical significance ($p < 0.05$).

Source: Authors.

In agreement, a survey that evaluated the space-time distribution of VL in the western region of that state, from 2004 to 2018, also indicated a decreasing trend in the number of cases of the disease, especially after 2010[27]. The authors of the study suggest that this phenomenon may be related to VLSCP settlement in that region[27].

During the time series, the state of Tocantins concentrated the highest burden of the disease in the country. Reis *et al.*[28] point out that such behavior takes place mostly in the north and south regions of that state, being influenced by high values of annual precipitation and humidity, in addition to high levels of vegetation and night

Table 2. Percentage of annual average variation (AAPC) and percentage of annual variation (APC) of VL incidence rates in Brazil by socio-demographic variables (2007-2020).

Gender	Cases		Incidence		Joinpoint regression model									
	2007**	2020**	2007	2020	Period		APC	CI95%		Trend	AAPC	CI95%		Trend
Male	1.984	1.325	2.14	1.28	2007	2020					-4.2	-8.3	0	Stable
					2007	2018	0.1	-1.9	2.2	Stable				
					2018	2020	-25	-44.6	1.6	Stable				
Female	1.220	608	1.27	0.56	2007	2020					-6.3*	-10.8	-1.5	Decreasing
					2007	2018	-1.7	-4	0.7	Stable				
					2018	2020	-28.1	-49.4	2.1	Stable				
Age group (years)	**Cases**		**Incidence**		**Joinpoint regression model**									
	2007**	**2020****	**2007**	**2020**	**Period**		**APC**	**CI95%**		**Trend**	**AAPC**	**CI95%**		**Trend**
0-4 years old	1.239	465	8.03	3.16	2007	2020					-7.7*	-12.6	-2.4	Decreasing
					2007	2018	-1.5	-4.1	1.1	Stable				
					2018	2020	-35.2*	-56.1	-4.4	Decreasing				
5-9 years old	399	127	2.36	0.87	2007	2020					-7.3*	-13.6	-0.4	Decreasing
					2007	2018	-2.2	-5.5	1.1	Stable				
					2018	2020	-30.8	-58.1	14.3	Stable				
10-14 years old	186	72	1.07	0.49	2007	2020					-5.5*	-10.3	-0.3	Decreasing
					2007	2018	-1	-3.4	1.6	Stable				
					2018	2020	-26.8	-49.5	6.1	Stable				
15-19 years old	183	87	1.05	0.55	2007	2020					-5.4	-14.4	4.6	Stable
					2007	2015	-2.9	-7.5	1.8	Stable				
					2015	2018	14.4	-26.2	77.5	Stable				
					2018	2020	-35.6*	-58.5	-0.2	Decreasing				
20-39 years old	663	514	1.06	0.75	2007	2020					-2.3	-4.7	0.1	Stable
					2007	2017	1.6	-0.1	3.3	Stable				
					2017	2020	-14.3*	-23.2	-4.4	Decreasing				
40-59 years old	374	470	0.92	0.88	2007	2020					-0.7	-4.1	2.7	Stable
					2007	2017	2.9*	0.5	5.4	Crescente				
					2017	2020	-12	-24.5	2.5	Stable				
60-69 years old	102	106	0.99	0.63	2007	2020					-2.5	-6	1.2	Stable
					2007	2017	2.8*	0.2	5.5	Crescente				
					2017	2020	-18.2*	-30.6	-3.5	Decreasing				
70-79 years old	40	60	0.69	0.66	2007	2020					-0.8	-5	3.6	Stable
					2007	2011	11.8*	2.8	21.7	Crescente				
					2011	2018	0.8	-3.6	5.5	Stable				
					2018	2020	-26.3*	-43.6	-3.8	Decreasing				
≥ 80 years old	18	32	0.73	0.72	2007	2020					0.6	-3.9	5.3	Stable

Caption: VL: visceral leishmaniasis; Incidence: Incidence rate/100 thousand inhabitants; APC: annual percent change; AAPC: average annual percent change; 95%CI: confidence interval of 95%; ** it covers all new cases confirmed in the national territory, including those with municipality blank/ignored; * statistical significance ($p < 0.05$).

Source: Authors.

Ciência & Saúde Coletiva, 28(9):2709-2719, 2023

temperature – environmental conditions favorable vector reproduction and to wild reservoirs of VL and that end up favoring the increase of the disease in this territory.

The differences between the behavior of national and federation units' incidence rates suggest that different factors can influence the risk of VL among states and regions of the country. Rocha *et al.*[29], Braz *et al.*[20,] and Ribeiro *et al.*[30] agree that the behavior of this zoonosis in the regions of the country is directly associated with the environmental and geographic conditions of the territory, where situations of high temperature and humidity predominate, which enable a good adaption and reproduction of the vector; and precarious socio-environmental issues such as lack of basic sanitation and water supply, poor housing conditions, accumulation of waste from the peridomicile both in an urban and rural area, the intense population of vectors and canine cases of the disease, presence of livestock close to residences and proximity of households to green areas, factors that directly interfere in the adaptation and reproduction of *L. longipalpis*.

It is worth noting in this area that the trends of incidence rates to remain stable, with no significant variations, in most federation units, may indicate the fragility of prevention and control measures, either due to lack of effectiveness or implementation difficulties in the VLSCP actions, or possible failures in the surveillance actions of this disease. This reality added to the high occurrence and burden of this disease still creates major challenges for health services, especially for the unified system, responsible for VL surveillance and control policies nationwide. On this topic, Werneck[31] highlights that despite the efforts and resources committed to the full functioning of VLSCP, the perception is consolidated that the actions aimed at reducing the transmission of VL have not had the desired effect of reducing the incidence of this disease.

Throughout the series analyzed, there was a higher incidence of cases among males and children under 5 years of age, with a record of stability for the occurrence in males and decreasing trend of cases in females and also in the group under 5 years of age. The specialized literature mentions that the greater the number of cases in a region, the greater the vulnerability of infected children, and when affecting the group of male adults or elderly[6,10,30].

In time, it is pertinent to consider that this work has all the limitations inherent to the fact that it is an ecological study, namely: the possibility of ecological fallacy, chance correlations, and difficulties in controlling confounding factors. It also has limitations arising from the use of secondary data, which, as is known, are subject to underreporting, eventual errors due to incompleteness, precision or inconsistency, or even underdiagnosis, a common phenomenon across the country[1].

Finally, it is important to have in mind that the data presented here, especially those concerning the last two years of the time series, may represent one of the indirect consequences generated by the COVID-19 pandemic[16,17]. Therefore, the number of cases and consequently, the VL incidence rate in the series analyzed may be higher than what was observed, wither because of the recognized impact of the SARS-CoV-2 public health emergency in the fight against neglected tropical diseases, including the VL, or throughout the series, due to deficiencies in health services, especially in locations where assistance and surveillance actions have operational problems linked to the chronic lack of inputs and financial, material, or personnel resources. It should be noted, however, that the results of this study were based on official sources of information, the same ones adopted for decision-making regarding public policies to combat and monitor VL nationwide.

Conclusion

Despite VL being an endemic disease in the national territory, there was a statistically significant decrease in the general incidence rate of this anthropozoonosis in Brazil for the period studied. It is important to consider, however, that this disease remains an important public health problem in the country and its regions, because, despite the verified trends of reduction in the general rate for the State, it is concomitantly observed inequalities in the epidemiological behavior of this indicator at the level of the political-administrative units, with an important portion of Federation units with incidence rates that remain on an increasing trend or in a stationary behavior. In this way, this study reaffirms the need to enhance effective measures to promote VL control in the country, with emphasis on the territories with the highest burden of this disease.

Collaborations

CJ Santos Júnior , KC Lima, MM Santos: conception and design of the study, analysis and interpretation of data, writing – original draft, final approval of the version to be submitted; KC Lima, MM Santos: project administration, writing – review e editing, final approval of the version to be submitted; FCCO Lins, JP Silva: funding acquisition, analysis and interpretation of data, final approval of the version to be submitted.

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