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Effect of environmental variables on the incidence of Visceral Leishmaniasis in Brazil and Colombia

Juan David Gutiérrez [a], Mariano Altamiranda-Saavedra [b], Julián Ávila-Jiménez [c], Iris Amati Martins [d], Flávia Virginio [e,*]

[a] Facultad de Ciencias Médicas y de la Salud, Universidad de Santander, Instituto Masira, Bucaramanga, Santander, Colombia
[b] Grupo de Investigación Bioforense, Facultad de Derecho y Ciencias Forenses, Tecnológico de Antioquia Institución Universitaria, Antioquia, Colombia
[c] Maestría en Ciencias Biológicas, Universidad Pedagógica y Tecnológica de Colombia, Tunja, Boyacá, Colombia
[d] Laboratório de Ecologia da Paisagem e Conservação, LEPaC, Universidade de São Paulo, Brazil
[e] Grupo de Pesquisa em Entomologia Médica, Instituto Butantan, São Paulo, Brazil

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ABSTRACT

Visceral Leishmaniasis (VL) is the most severe of the three forms of Leishmaniasis. In the Americas, Brazil and Colombia present more than 90 % of the cases in the region. Our aim in this research was to estimate the association of the incidence rate of Visceral Leishmaniasis with the following environmental variables: the percentage of area suitable for the vector *Lutzomyia longipalpis,* the episodes of La Niña and El Niño, the Brazilian and Colombian biomes. Epidemiological data were obtained from the Brazilian Notifiable Diseases Information System and the Colombian National Public Health Surveillance System. Environmental data were downloaded from the NASA Giovanni web app, the Modis Sensor database, and the meteorological agencies of Australia, Japan, and the United States of America. Records of the presence of *Lu. longipalpis* were obtained from public databases and previous studies. As a result, the incidence per 10,000 inhabitants with LEBS for each El Niño-Southern Oscillation (ENSO) episode showed the largest values during El Niño 2015–2016, mainly in Brazil's Northeast and Central regions and the Northeast region of Colombia. Compared with the Neutral 2012–2014 episode, the episodes of El Niño 2015–2016 and La Niña 2010–2011 showed an average increase in the monthly incidence rate of VL, and the average increase was higher during El Niño 2015–2016 (aIRR = 2.304 vs.1.453) We found a positive association between the incidence rate of VL and the El Niño 2015–2016 episode and an impressive% of area suitable for the vector *Lu. longipalpis* in the Amazon region.An increase of 1 % in the area suitable for the vector *Lu. longipalpis* leads to an average rise of 0.8 % in the monthly incidence rate of VL. Our study shows a possible association between VL incidence and ENSO, with the most considerable incidence rates observed during El Niño 2015–2016 in Brazil's Northeast and Central regions and the Northeast region of Colombia. The present study is very important to better understand the Visceral Leishmaniasis transmission dynamics.

1. Introduction

Visceral Leishmaniasis (VL) is a zoonotic disease, considered the most severe Leishmaniasis, potentially fatal with high mortality if not treated. In this context, 83 countries already had reported cases of VL (WHO, 2018), and currently, this disease is considered endemic in 13 countries of the Americas (MS, 2022; OPAS, 2021; PAHO, 2022b). Brazil and Colombia account for more than 90 % of the reported cases of VL in Latin America (Desjeux, 2001; Brasil, 2006; Wamai et al., 2020).

This disease is mainly caused by the etiological agent *Leishmania infantum* Nicolle, 1908 (Schwabl et al., 2021), which is vectored by Phlebotominae insects (Lozano et al., 2020). In the Americas, the primary vector responsible for the transmission of parasites that causes VL in humans is the complex *Lutzomyia longipalpis* (Lutz and Neiva, 1912) (Psychodidae, Phlebotominae) *sensu lato* (Lainson and Rangel, 2005; Bauzer et al., 2007; Souza et al., 2017). This vector is widely distributed from Mexico to Argentina (Moo-Llanes et al., 2013), and its distributional pattern is associated with geographic barriers that limit its

* Correspondent author.
E-mail address: flavia.virginio@butantan.gov.br (F. Virginio).

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establishment in some areas in the Neotropic (Arrivillaga et al., 2002).

All regions of the country currently have confirmed cases of human VL, of which 24 Brazilian States present autochthonous cases (SVS/MS, 2017). The Brazilian North's states, Amapá and Rondônia, present confirmed autochthonous cases of canine VL (SVS/MS, 2017). Furthermore, in the South region of Brazil, until 2008, there were no reports of human or canine cases of VL (Souza et al., 2009).

In Colombia, during the 1990s, an average of 6500 new cases of Leishmaniasis per year were notified. It has increased progressively to the point of passing 2005 and 2006 to about 20,000 cases each year, notified to the system SIVIGILA, the numbers include cases of visceral and tegumentary leishmaniasis and that the latter are predominant. In total, between 1943 and 2019 in Colombia, 697 cases of VL have been reported, occurring in 50 municipalities in 11 departments (Sánchez et al., 2020).

During the last two decades, in Brazil, some species of phlebotomine have been suggested as vectors of *Leishmania infantum* besides *Lutzomyia cruzi* (Mangabeira Filho, 1938; Falcão de Oliveira et al., 2017), such as *Pintomyia fischeri* (Pinto, 1926; Galvis-Ovallos et al., 2017), *Migonemyia migonei* (França, 1920; Guimarães et al., 2016) and *Nyssomyia neivai* (Pinto, 1926; Dias et al., 2013). Meanwhile, the second vector suggested in Colombia is *Pintomyia.evansi* (Nuñez-Tovar, 1924; Bejarano et al., 2001). However, besides these finds, *Lu. longipalpis* presents itself as a relevant link in the transmission chains of VL, and it is an essential biological risk factor in the transformation of the epidemiological profile and the increase in the urbanization of the disease.

Poor socioeconomic conditions, such as literacy rate, housing conditions, low socioeconomic status, households without sanitation, and population density, have been associated with the incidence of VL (Werneck et al., 2007; Sheets et al., 2010; Kolaczinski et al., 2008; Lima et al., 2017). Microhabitats with high moisture contribute to the presence of *Lu. longipalpis* (Ferro et al., 1997). Moreover, *Lu. longipalpis* has been associated with climatic and meteorological factors, particularly relative humidity, rainfall, wind speed, and temperature (Morrison et al., 1995; Oliveira et al., 2013; Ximenes et al., 2006). In this context, the most critical climatic anomaly in the Americas is El Niño-Southern Oscillation (ENSO) (Grimm et al., 2000; Wang and Fu, 2000), denoted by unusual temperatures in the Equatorial Pacific Ocean. The warm phase of the anomaly corresponds to El Niño and the cold phase to La Niña. Both phases can potentially change the atmospheric circulation and climate patterns along the continent (Cai et al., 2020; Holmgren et al., 2006; Infanti and Kirtman, 2016).

Several studies have evidenced that leishmaniasis vectors' distribution is influenced by climatic conditions (temperature and precipitation) and anthropogenic impact (loss of forest cover), and some changes in these variables directly disturb the association between disease and environment (Sharma et al., 2008; Artun and Kavur, 2017; Estallo et al., 2021). Thus, climatic variations caused by the ENSO episodes could affect the population dynamics and spatial distribution of the vectors and their relationship with the transmission peaks of the disease (Dutari and Loaiza, 2014).

Environmental niche models have been implemented to estimate the geographic distribution of Cutaneous and Visceral Leishmaniasis vectors and the effects of climate change scenarios in North, Central (Moo-Llanes et al., 2013; Peterson et al., 2017) and South America (Peterson and Shaw, 2003). A previous study has evidenced the effect of El Niño episodes on Cutaneous Leishmaniasis in zones with a more extraordinary potential richness of vectors in Northeast Colombia (Altamiranda et al., 2020). However, the effect of the episodes of El Niño and La Niña on the potential distribution of the vectors of VL has not yet been evaluated, nor has the association of this effect with changes in the incidence of cases of VL. In this sense, we aimed to assess the association between the incidence of VL and (a) the percentage of environmentally suitable areas for the potential distribution of *Lu. longipalpis*, (b) the episodes of the ENSO cycle, and (c) the Brazilian and Colombian biomes.

2. Material and methods

2.1. Data acquisition

2.1.1. Visceral leishmaniasis (VL) cases and vector records

Considering the uncertainties about the VL epidemiology and pathogen-vector interaction, this study was based on the human-confirmed (by parasitological test) autochthonous cases of VL from 2010 to 2016. Brazilian data were obtained from the Notifiable Diseases Information System, made publicly available by the Department of the Unified Health System of the Brazilian Ministry of Health (Tabnet, 2022). Brazilian estimated population data from 2011 to 2016, by the municipality and census tract information, were obtained from the Brazilian Institute of Geography and Statistics (IBGE, 2021). The same kind of data from Colombia was obtained from the National Public Health Surveillance System (INS, 2015) and the National Statistics Department of Colombia (DANE, 2011), respectively. Cases with inconsistencies in date or locality were excluded from the study. We regarded municipalities as the unit of the analysis and aggregated ENSO episode VL cases (see Section 2.1.3) in each of the municipalities.

The records of *Lu. longipalpis* were obtained from VectorMap, VectorBase, GBIF, and Peterson et al. (2017).

2.1.2. Environmental data

The monthly data to model the potential distribution of *Lu. longipalpis* corresponding to precipitation, soil temperature, wind speed, and minimum, maximum, and average air temperature were obtained from NASA Geospatial Interactive Online Visualization and Analysis Infrastructure web app (Acker and Leptoukh, 2007) (Table 1). Monthly data on land temperature and Enhanced Vegetation Index (EVI) were obtained from the Moderate Resolution Imaging Spectroradiometer (Modis) database using the R package MODIStsp (Busetto and Ranghetti, 2016).

Additionally, we downloaded raster layers, using MODIStsp (Busetto and Ranghetti, 2016) of land use and land cover (LULC) for the first year of each episode of the ENSO cycle analyzed. Besides, we downloaded a raster of altitude, available at http://srtm.csi.cgiar.org (Reuter et al., 2007). The Brazilian and Colombian biomes maps were downloaded from IBGE (2019) and IDEAM (2015), respectively (Fig. 1).

2.1.3. Cases of VL by ENSO episode

To perform this study, we included the episodes of La Niña, Neutral, and El Niño, with the most prolonged duration for 2010–2016. The kind of episode and its duration were defined by the complete consensus of the National Oceanic and Atmospheric Administration (NOAA, 2016), the Japan Meteorology Agency (Japan Meteorology Agency, 2018), and the Australian Bureau of Meteorology (Bureau of Meteorology of Australia, 2018).

Considering that the VL incubation period has an average of 2–6 months (PAHO, 2018), we included inside each ENSO episode the VL cases that occurred three months after the beginning and after the end of the ENSO episodes. Thus, the episodes selected for the study according to this criterion were La Niña 2010–2011 (from September 2010 to July 2011), Neutral (from July 2012 to August 2014), and El Niño

Table 1
Environmental data obtained from remote sensing for modeling the potential distribution of Lutzomyia longipalpis.

Variable	Product code
Precipitation	GLDAS_NOAH025_M
Land temperature	MOD 11C3v006
EVI	MOD13C2v006
Soil Temperature	GLDAS_NOAH025_3H
Minimum, maximum, and average air temperature	M2SDNXSLV
Wind Speed	M2TMNXFLX
Land coverage	MCD12C1V006

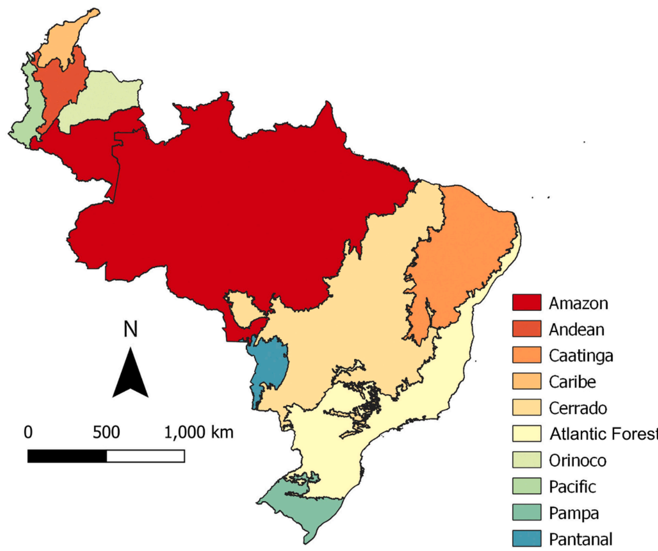

Fig. 1. Biomes from Brazil and Colombia.

2015–2016 (from July 2015 to April 2016). Daily cases were grouped by episode for each municipality in Brazil and Colombia.

2.2. Mapping incidence rates

Incidence rate data have an intrinsic variable instability because the estimation of the underlying risk is inversely proportional to the population at risk, implying that rates estimated for municipalities with small populations tend to have a significant standard error (Devine et al., 1994). To correct this bias, we implemented a Local Empirical Bayes Smoothing (LEBS) for the incidence rate to correct this bias. The method is based on the Bayesian estimation of the parameters for the shape and scale of a Gamma distribution of the incidence rate.

The method implies estimating a weighted average between the raw incidence rate for each municipality and the local average, with weights proportional to the population at risk (Anselin et al., 2006). We used the software GeoDa v. 1.18 (Anselin et al., 2006) to estimate the LEBS for the incidence rate of VL of each episode included in the study and in each municipality.

2.3. Potential distribution models of lutzomyia longipalpis

The potential distribution of *Lu. longipalpis* and the% of area suitable for this vector in each ENSO episode was estimated, and niche models were developed in Maxent 3.4.4. (Phillips et al., 2004), a presence-only Maximum Entropy Technique that uses presence data and environmental variables to model the potential distribution as a map of the estimated probabilities. A calibration area was defined using a dispersion, colonization, and extinction simulation method under the Grinnell R package V. 0.0.21 (Machado-Stredel et al., 2021) in order to carry out this process in a quantitative way and avoid estimates of the accessible area based-on subjective criteria.

To prevent Grinnell's algorithm from sampling cells with a low probability of occurrence of the species, we filtered the records outside the tropical belt (−15, 15° latitude). Additionally, we excluded records above 1750 m since the altitude is recognized as an environmental barrier for *Lu. longipalpis* and consequently to VL transmission (INS, 2015). Moreover, we extracted the minimum temperature of each occurrence point to find the lowest minimum temperature (12.43 °C). Finally, the raster of minimum temperatures was reclassified with "one" value for cells with temperatures higher than the minimum temperature found and "zero" values for cells with lower temperatures. Then, in Maxent under the KUENM R-package V. 1.1.5 (Cobos et al., 2019), 392 candidate models were built from the combination of a sequence of 14 regularization multipliers (0.1 0.2 0.3 0.4 0.5 0.6 0.7 0.8 0.9 1.0 2.0 3.0 4.0 5.0), seven feature class combinations ("lqp") and four different sets of environmental variables (Table 2) built from a collinearity analysis between them.

All candidate models were evaluated under three selection criteria: statistical significance (Partial ROC), omission rate below 5 %, and complexity (ΔAICc), and as a result of this evaluation, the model M_0.8_F_qp_Set3 was selected (Partial ROC 0, Omission rate 0.024, ΔAIC 0). A Mobility-Oriented Parity (MOP) analysis (Owens et al., 2013) was developed on the potential distribution maps resulting from the modeling process in each of the evaluated episodes to identify areas with strict extrapolation under a threshold that left out the most dissimilar environments of 5 % of the occurrences. Later, in the python-based ArcGIS v. 10.3 Toolbox SDMToolbox V. 2.4 (Brown, 2014), we reclassified the maps to binary with a threshold on environmental suitability for the lowest 10 % of the occurrences.

For each municipality, we estimated the% of area suitable for the vector based on the binary map of potential distribution and the municipality's area.

2.4. Regression analysis

Because we assume that the% of area suitable for the vector changes between the episodes of the ENSO cycle, we estimated for each episode the% of suitable area for *Lu. longipalpis* in each municipality, our goal was to estimate the association among the independent variables:% of suitable area for the vector in each municipality, the episode of the ENSO cycle (La Niña 2010–2011, Neutral 2012–2014, and El Niño 2015–2016), and the biome where the municipality is inserted, with the response variable: municipal incidence of VL, adjusted by LEBS and the months of duration of the episode (including the three buffer months after the beginning and after the end of the episode by incubation period).

We implemented a generalized linear model with a gamma response function and log link to estimate this relationship. The statistical model was based on the following equation:

$$Y_i = f(\beta_0 + \beta 1 * \%\ of\ area\ suitable + \beta 2 * episode\ ENSO + \beta 3 * biome) + \epsilon_i \tag{1}$$

Where Y_i denotes the incidence rate adjusted by LEBS per month for the observation *i*, $\beta 0$ is the intercept, $\beta 1$ is the association with the% of suitable area for the vector in the municipality of the observation, $\beta 2$ is the association with the episode ENSO, $\beta 3$ is the association with the biome of the municipality, ϵ_i is the random error term, and $f(.)$ is a gamma function response with a log link. The R package stats (R Core Team, 2013) were performed to implement the regression analysis. The marginal effects were estimated using the package ggeffects v.0.12 (Lüdecke, 2018). Finally, the incidence rate ratio (aIRR) and the 95 % confidence intervals (CI 95 %) were adjusted. The result of the potential distribution models and the statistical analysis can be reproduced with

Table 2
Environmental variable sets were used in the modeling process.

Set	Selection criteria	Variables
1	All variables	EVI, Land Cover, Minimum, Maximum, and Average temperature, Rainfall, Soil temperature and Wind
2	Corr < 60 %	EVI, Land Cover, Maximum temperature, Rainfall, Soil temperature and Wind Speed
3	Corr < 80 %	EVI, Land Cover, Minimum, Maximum, Rainfall, Soil temperature and Wind Speed
4	VIF <10	Land Cover, Maximum temperature, Rainfall, Soil temperature and Wind Speed

the data and scripts available at https://github.com/juandavidgutier/visceral_leish_Brazil-Colombia.

3. Results

A total of 4425 cases of VL in 6692 municipalities from Brazil and Colombia were reported during the three episodes analyzed. The top five municipalities with the highest number of cases were located in Brazil: Bauru (234; Cerrado Biome, the Brazilian savanna), Fortaleza (196; Caatinga Biome, a semi-arid environment), Teresina (149) and Campo Grande (149; Cerrado Biome, the Brazilian savanna), and Belo Horizonte (136; Atlantic Forest). These municipalities accounted for 19.5 % of the cases included in the study. The episode with the highest number of cases reported was Neutral 2012–2014, with 1510 cases, and the episode with the fewest cases reported was La Niña 2010–2011, with 799 cases.

The Brazilian Northeast and Midwest regions represented most cases, mainly during the Neutral 2012–2014 (Fig. 2B) and El Niño 2015–2016 (Fig. 2C) episodes. However, during the episode El Niño 2015–2016, the distribution of cases was the most comprehensive (Fig. 2C).

The incidence per 10,000 inhabitants with LEBS for each ENSO episode showed the largest values during El Niño 2015–2016 (Fig. 3C), mainly in Brazil's Northeast and Central regions and the Northeast region of Colombia. The lowest incidence per 10,000 inhabitants with LEBS were observed during La Niña 2010–2011 (Fig. 3A).

The potential distribution of *Lu. longipalpis* in the Neutral 2012–2014 episode was concentrated in the inter-Andean valleys of the Cauca and Magdalena rivers, the Pie de Monte Llanero (Eastern of Colombian Andes Mountain) at the east of the eastern cordillera and in the Urabá-Sinú and Bajo Magdalena regions of Colombia. In Brazil, in the Northern region of Roraima state, and all Brazilian extra-Amazônia regions. During El Niño 2015–2016, this potential distribution was preserved in the same regions with an expansion in Roraima and some Pará municipalities. In La Niña 2010–2011, the potential distribution covered majoritarian the same part of the Neutral 2012–2014 episode, besides the expansion to the southern Amazonia region, composed by Acre State, and advancing through the State of Mato Grosso. In addition, it is essential to mention that during La Niña 2010–2011, some municipalities - mainly of "Legal Amazonia" - can be considered suitable for the potential distribution of *Lu. longipalpis*, whereas Neutral 2012–2014 and El Niño 2015–2016 episodes can be considered unsuitable for the potential distribution of *Lu. longipalpis* (Fig. 4).

An increase of 1 % in the area suitable for the vector *Lu. longipalpis* leads to an average rise of 0.8 % in the monthly incidence rate of VL (Table 3 and Fig. 5). Compared with the Neutral 2012–2014 episode, the episodes of El Niño 2015–2016 and La Niña 2010–2011 showed an average increase in the monthly incidence rate of VL, and the average increase was higher during El Niño 2015–2016 (aIRR = 2.304 vs.1.453) (Table 3 and Fig. 6). When we compared the monthly incidence rate of VL per biome and took as reference the Amazon biome, most of the biomes (i.e., Andean, Atlantic Forest, Caribe, Orinoco, Pacific, and Pampa) had a lower incidence than the Amazon. Likewise, the relatively small number of observations in the Pantanal biome (n = 78) and the large confidence interval stands out (Table 3 and Fig. 7). Figs. 5 to 7 show the marginal effects of the regression model implemented.

4. Discussion

In this study, the association among the monthly incidence of VL in Brazil and Colombia, and (a)% in the area suitable for the vector *Lu. longipalpis*, (b) ENSO episodes, and (c) Biomes were estimated. To estimate the% of area suitable for *Lu. longipalpis*, previously, we estimated the potential distribution of the vector during the episodes of La Niña 2010–2011, Neutral 2012–2014, and El Niño 2015–2016. Considering that the rates estimated for municipalities with small populations tend to have a high standard error (Devine et al., 1994), to avoid bias related to that, we included the LEBS in the estimation of the monthly rate of incidence.

Despite the epidemiological complexity of VL, our results demonstrated that the VL incidence is possibly associated with the ENSO phenomenon. El Niño 2015–2016 presented significant positive associations with the VL incidence. The incidence rate with LEBS fo r each ENSO episode showed the most significant values during El Niño 2015–2016, mainly in Brazil's Northeast and Central regions and the

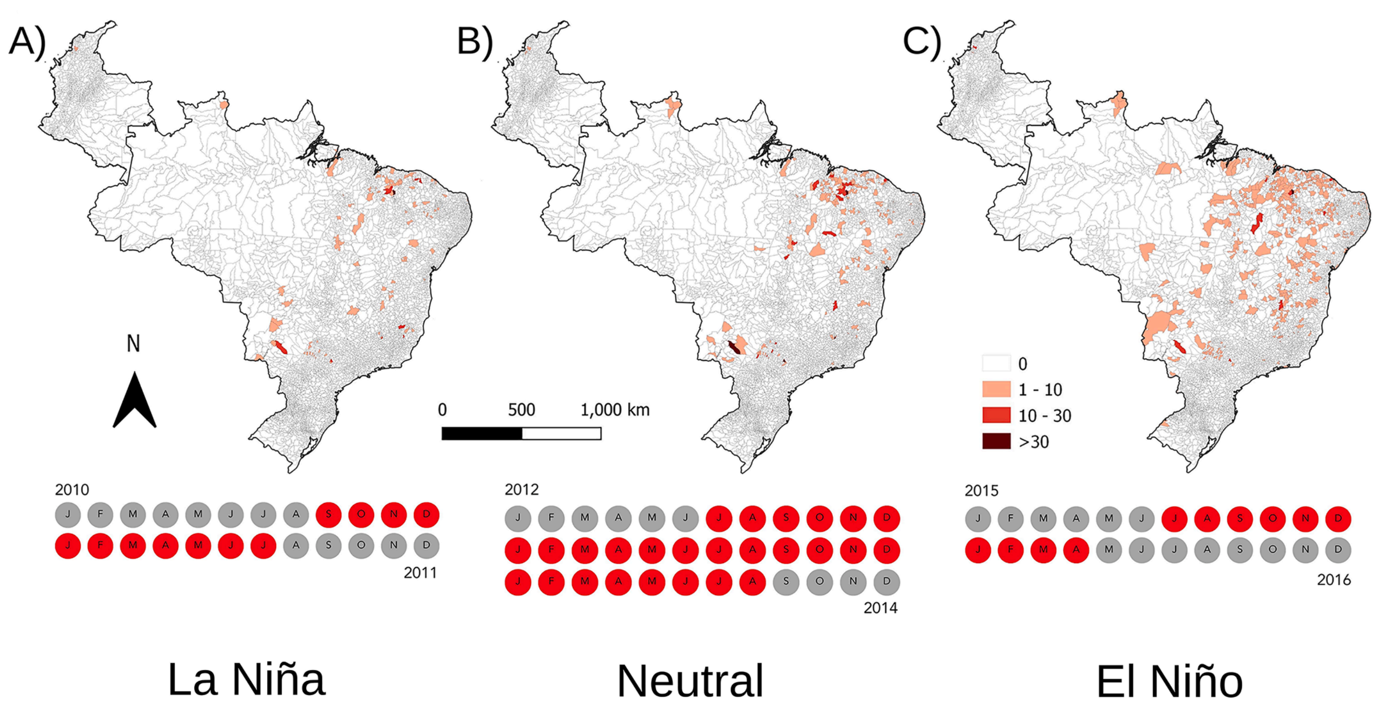

Fig. 2. Cases of VL reported during each ENSO episode: (A) La Niña 2010–2011, (B) Neutral 2012–2014, (C) El Niño 2015–2016. Red circles represent the months of each ENSO episode according to the consensus of meteorological agencies.

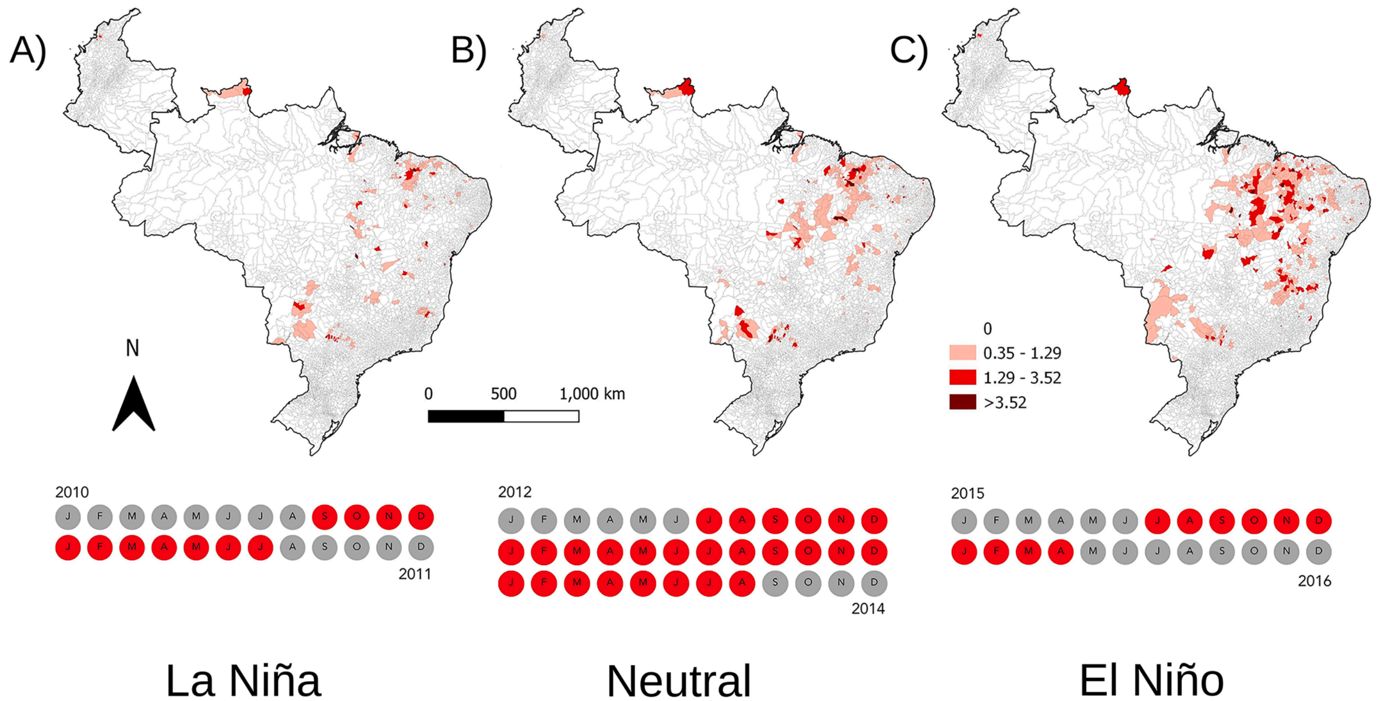

Fig. 3. Incidence per 10,000 inhabitants adjusted with LEBS of VL during each ENSO episode: (A) La Niña 2010–2011, (B) Neutral 2012–2014, (C) El Niño 2015–2016. Red circles represent the months of each ENSO episode according to the consensus of meteorological agencies.

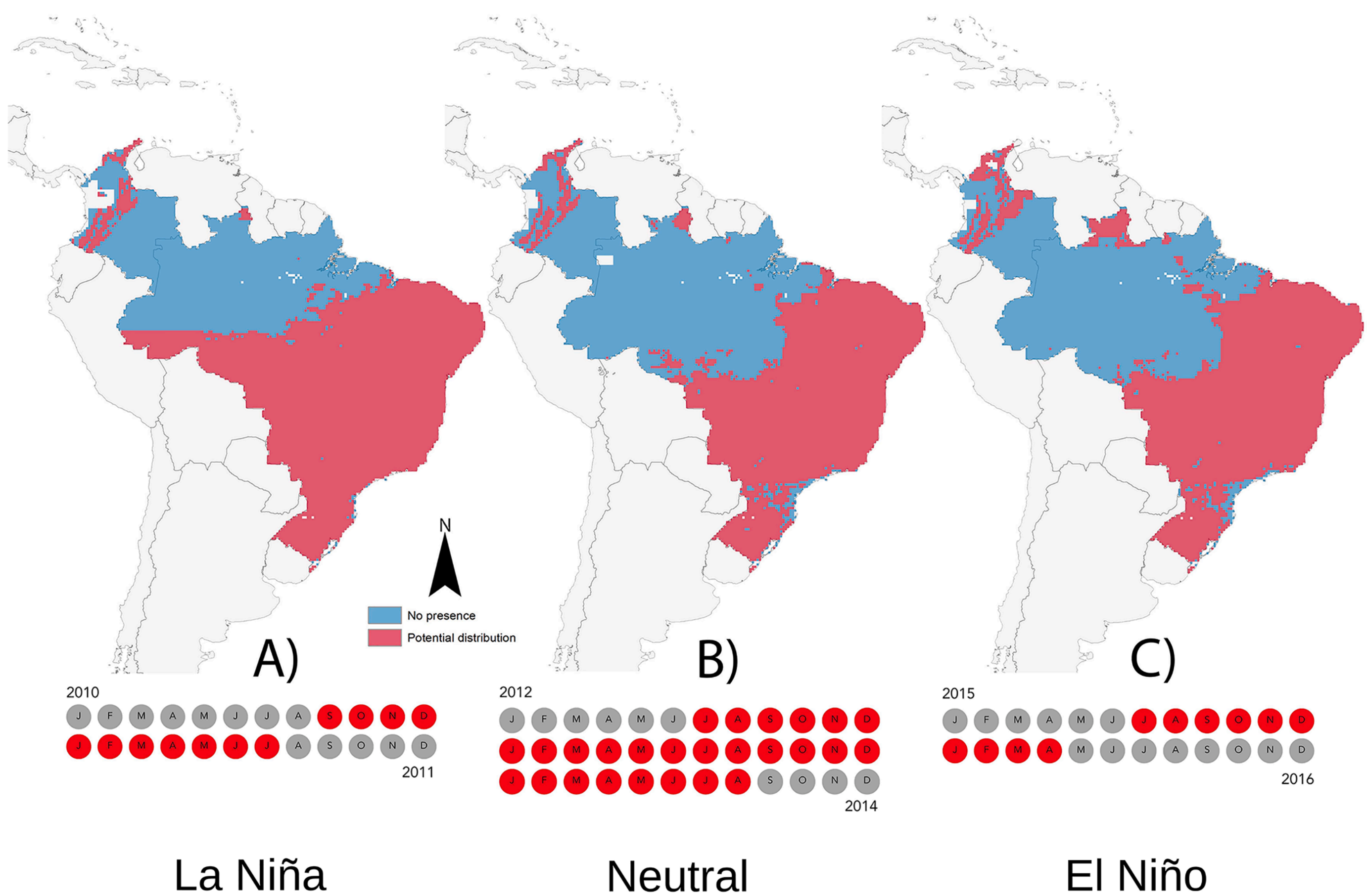

Fig. 4. Potential distribution of *Lu. longipalpis* in Brazil and Colombia during the episodes of La Niña 2010–2011 (A), Neutral 2012–2014 (B), and El Niño 2015–2016 (C).

Table 3
Result of regression analysis. ENSO episodes and environmental factors associated to the incidence of Visceral Leishmaniasis.

Variable	aIRR	95 % CI		p-value	Significance
Suitability	1.008	1.006	1.011		$< 2^{-16}$ ***
Episode Neutral 2012–2014	R				
Episode El Niño 2015–2016	2.304	2.048	2.593		$< 2^{-16}$***
Episode La Niña 2010–2011	1.453	1.291	1.637		$< 6.7^{-10}$***
Biome Amazon	R				
Biome Andean	0.146	0.115	0.185		$< 2^{-16}$***
Biome Atlantic Forest	0.39	0.317	0.482		$< 2^{-16}$***
Biome Caatinga	1.101	0.872	1.391		0.416
Biome Caribe	0.578	0.411	0.815		0.002**
Biome Cerrado	1.278	1.018	1.605		0.034*
Biome Orinoco	0.155	0.088	0.273		$< 1.6^{-10}$***
Biome Pacific	0.128	0.089	0.186		$< 2^{-16}$***
Biome Pampa	0.109	0.075	0.158		$< 2^{-16}$***
Biome Pantanal	1.242	0.537	2.871		0.612

ENSO Episode “Neutral” and Biome “Amazon” are the reference conditions for ENSO episodes and Biomes, respectively. aIRR = Adjusted incidence rate ratio, CI = Confidence interval, *R* = Reference value. Significance codes:‘***’ 0.001 ‘**’ 0.01 ‘*’ 0.05.

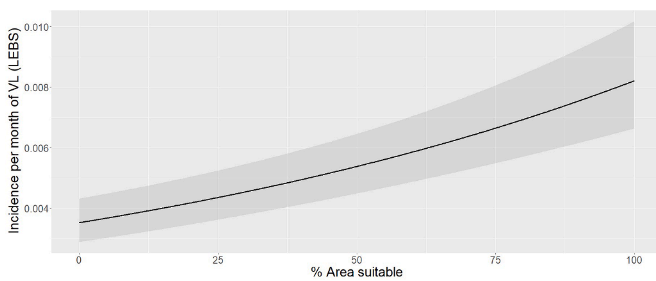

Fig. 5. Marginal effect of the association between% of area suitable for *Lutzomyia longipalpis* and incidence per 10,000 inhabitants of VL.

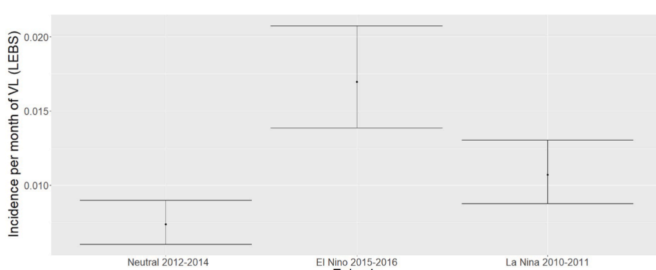

Fig. 6. Marginal effect of the association between episodes of the ENSO cycle and incidence per 10,000 inhabitants of VL.

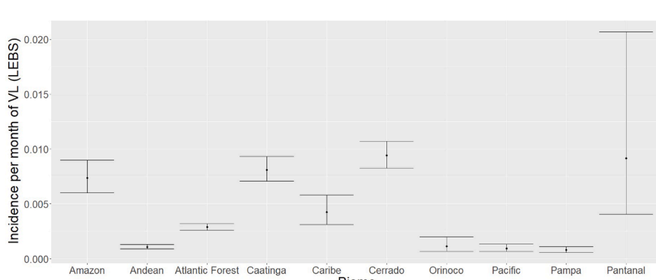

Fig. 7. Marginal effect of the association between biomes and incidence per 10,000 inhabitants of VL.

Northeast region of Colombia. Like the results presented in the literature on Leishmaniasis (Cabaniel et al., 2005; Chaves et al., 2014; Silva Neto et al., 2020; Altamiranda et al., 2020), the present study demonstrates a positive association between the VL incidence rates with LEBS during El Niño (2015-2016).

According to Minuzzi et al. (2007), there is a normal condition in the oceanic and atmospheric southern oscillation and an irregular variation that occurs around El Niño, which reveals an opposite phase of the phenomenon, represented by La Niña conditions. This condition is characterized by a cooling of the waters and increased atmospheric pressure in the eastern Pacific region (also called the “cold phase” or “positive phase”). Additionally, ENSO is considered the most significant example of quasi-periodic climate variability on an interannual scale that can affect weather worldwide (Kovats, 2000). In this context, an important point to be considered is that we included in each ENSO episode the VL-confirmed cases that occurred three months after the beginning and after the end of the ENSO episodes. It was done due to the VL incubation period which presents an average of 2–6 months (PAHO, 2018).

With the urbanization of VL, from 1980 to 2008, Brazil registered 59,129 cases of the disease, with an annual average of 2274 new cases, with 82.5 % (48,783) in the Northeast region (Maia-Elkhoury et al., 2008). The disease gradually spread to the Midwest, North, and Southeast, with an increase from 15 % of cases in 1998 to 44 % in 2005 (Martins et al., 1956; Magalhães et al., 1980; Marzochi et al., 1985; SVS/MS, 2017, 2022). Furthermore, in the South region of Brazil, until 2008, there were no reports of human or canine cases of VL (Souza et al., 2009). However, currently, all Brazilian regions have confirmed cases of human VL.

Ximenes et al. (2007) stated that VL underwent a process of geographic expansion from the 1980s onwards. Predominantly rural, in recent years, VL has undergone an urbanization process arising from migration and the disorderly growth of cities (Lacerda et al., 2021). Maia-Elkhoury et al. (2008) show that the expansion of VL in Brazil has been observed more effectively since the 2000s, with an observation of canine and human cases. Given its complexity, this infectious disease is challenging to control in Brazil. This difficulty is partly due to the diversity of vectors and reservoir’s characteristics and transmission cycle (Desjeux, 2004; Maia-Elkhoury et al., 2008). In addition to the conditions already mentioned for the spread of the disease, it is known that the climate directly influences epidemiology (Franke et al., 2002; Maia-Elkhoury et al., 2008).

Fortaleza, located in the Ceará State (Brazil, Caatinga Biome), was the most incident municipality in the present study. In this same State, the intensities of droughts, and decrease in heavy precipitation events, and the increase in Sea Surface Temperature (SST) anomalies in the Pacific and North of the Equator in the Atlantic Ocean lead to an increase in the number of consecutive dry days in the north of Ceará (Santos et al., 2011), which could contribute to these results. Studies related to ENSO episodes and Leishmaniasis generally observed a decrease in cases (Cabaniel et al., 2005; Chaves et al., 2014; Silva Neto et al., 2020). However, in the same Brazilian region of the most incident municipality of our study (Northeast), Bavia et al. (2005) demonstrated that in Bahia State between 1989 and 1995, after the El Niño phenomenon, there was a significant increase in the density of sandflies and the number of cases of human and canine VL.

In the same biome, the municipality of São João do Piauí, located in the Piauí State (Brazil, Caatinga Biome), was the third with significant VL incidence. Costa et al. (1990) show that the coastal region has a higher incidence of VL in this State. Corroborating that study, Tavares and Tavares (1999) show that the areas with the highest VL incidence geographically closely related to this municipality (Sergipe State) presented a humid coastal climate and accumulated precipitation superior to 1400 mm.

In this context, Pereira et al. (2020) demonstrated that precipitation reductions in the Caatinga strongly influence vegetation dynamics, with net primary production (NPP) remaining low throughout the droughts. Furthermore, the Caatinga acts as a carbon sink, even in years of severe drought. However, net ecosystem exchange (NEE) is lower in years of low NPP rates, resulting in long periods with limited ecosystem activity. The SST patterns indicate that extreme vegetation changes in the Caatinga are associated with the combination of ENSO events and North Atlantic SST warming.

Campo Grande, located in the Mato Grosso do Sul State (Brazil, Cerrado Biome), was the second municipality with a higher VL incidence in the present study. Silva Neto et al. (2020), in this same State, demonstrated that the years with the highest VL incidence coincided with a negative oscillation for ENSO, consistent with the La Niña years. Studies carried out in the urban area of Bonito, Mato Grosso do Sul, a region that has undergone intense environmental change revealed an increase in the density of *Lu. longipalpis* among human populations (frequency of 90.4 % in the home environment) and a progressive process of introducing VL in the urban area (Nunes et al., 2008). Our findings align with a recent study that sought to examine the spatio-temporal distribution of visceral leishmaniasis (VL) and identify high-risk areas within the Brazilian territory. This study identified Mato Grosso as one of the regions with a high risk of VL occurrence (de Melo et al., 2023).

In the present study, we observed a slight expansion in the potential distribution of *Lu. longipalpis* during El Niño and La Niña, compared to the predicted distribution for the Neutral episode. This expansion was mainly observed during El Niño in the states of Roraima and Pará and during La Niña in the southern region of the Amazonia, which includes the State of Acre and extends through the State of Mato Grosso.

Southern Brazil lies in a transition zone between two adjacent climatic regimes: the summer monsoon and midlatitude winter conditions; these regimes are responsible for peak rainy seasons in January (in the northern part) and July (in the southeastern part). Respectively, in this region, La Niña events are often associated with above-average rainfall (Githeko et al., 2000). These changes in precipitation can increase the availability of suitable habitats, favoring the distribution and abundance of *Lu. longipalpis* and influencing the availability of breeding sites and the abundance of potential hosts (De Oliveira et al., 2013).

On the other hand, regardless of the influence of the ENSO cycle, the states of Roraima, Pará, Acre, and Mato Grosso are currently undergoing an urbanization process; this could favor the presence of *Lu. longipalpis* because this synanthropic vector prefers areas with low vegetation cover (e.g., urban areas) (Casaril et al., 2014).

Our results about a more prominent association between the El Niño 2015–2016 episode and the incidence of VL, compared with the La Niña 2010–2011episode, is consistent with the report of Franke et al. (2002). However, these authors used the El Niño-3 index and not specific El Niño or La Niña episodes. Contrarily, Silva Neto et al. (2020) and da Silva et al. (2021) found that the leishmaniasis incidence increased during or after La Niña episodes. However, both studies have a minor geographic extension than our research, and the discrepancy could be related to a selection bias (Rousson et al., 2017).

To our knowledge, no previous studies have been developed that related a positive association between the% of area suitable for the vector *Lu. longipalpis* and the incidence rate of VL. However, a positive relationship between both variables sounds plausible because, in a municipality, a more significant% of the area suitable for the vector means a more significant probability of encounters between sand flies carrying the parasite and human hosts (de Santana Martins Rodgers et al., 2019).

It needs to be clarified why the biomes of Andean, Caribe, Atlantic Forest Orinoco, Pacific, and Pampa had a lower monthly incidence rate than the Amazon. However, it could be related to the implementation of the LEBS, which tends to balance the incidence rate, increasing the incidence rate in municipalities with a low population (most of them located in the Amazon) and decreasing the incidence in municipalities with a high population (Saravana Kumar et al., 2017).

Climate changes may alter temperature and precipitation and increase the variability of precipitation events, which may cause more intense and frequent floods and droughts (Dufek and Ambrazzi, 2008). Within this context, El Niño and La Niña directly influence frequent climatic events in Brazil and Colombia. Therefore, it is necessary to promote studies to predict possible extreme climatic events, such as heavy rains or prolonged droughts, and how they influence the spread of vector-borne diseases.

4.1. Limitations

We recognize some limitations in our study. We can highlight the assignment of the three months after the beginning and after the end of the episodes of La Niña 2010–2011, Neutral 2012–2014, and El Niño 2015–2016. The reason for this assignment is the necessity of including the disease's incubation period in the analysis. However, in that order of ideas, it would be possible to change the three months for any value between two and six months, which is the accepted range for the incubation period (PAHO, 2018). Additionally, several studies have demonstrated that local climate has a time-lag effect on vector-borne disease transmission in the short term (Ma et al., 2022).

Similarly, our results correspond to a non-causal association of the incidence rate of VL with a set of environmental variables (% of area suitable for the vector *Lu. longipalpis*, the ENSO episodes, and the main biomes in Brazil and Colombia). This non-causal association is related to the confusion bias and misspecification of the model. Additionally, the confusion bias is due to the nature of our research, which corresponds to an observational study, and the impossibility of including all the possible potential confounders (Freedman, 1997). The misspecification of the model is related to the assumptions of linearity and additivity in the form of the response of the dependent variable (incidence rate of VL) to the values of the environmental variables (predictors) when we implemented the statistical model of regression.

The models of potential distribution have intrinsic limitations to the methodology, some related to the sources of information. In the case of occurrences, the databases may have errors such as misidentification of the species, errors in the coordinates, or records duplicate or insufficient.

Moreover, even though we cannot control, other than the environmental/climate factors, such as improvement in diagnostic techniques, resources, governmental policies, can be able to influence the results. Regarding the environmental variables, the sources of bias can be found in the autocorrelation, the resolution of the variables, or that the extension of the projection area of the models does not capture the range of the variables for the species.

In addition, the modeling algorithms also may present biases in terms of their methodological application and the interpretation of the results (Feng et al., 2019; Sillero et al., 2021; Zurell et al., 2020). We took into account both the possible biases of the occurrences and the environmental layers, cleaning the databases of records of the modeled species (*Lu. longipalpis*) and eliminating records outside the projection area, proposing a calibration area of the model to start from an automaton algorithm that considers the values of the environmental layers in the occurrence cells and selecting sets of variables from correlation analysis of environmental variables to reduce autocorrelation and adjusting the resolutions of the environmental rasters.

However, we are aware that the distribution models are hypotheses built from the correlation of occurrences with environmental information and that they do not take into account other factors, such as biotic relationships or the influence of the presence of human settlements.

5. Conclusion

We discuss the relationship between the El Niño-Southern Oscillation (ENSO) phenomenon and the incidence of Leishmaniasis, a parasitic disease transmitted by sandflies. The study shows a possible association between VL incidence and ENSO, with the most considerable incidence rates observed during El Niño 2015–2016 in Brazil's Northeast and Central regions and the Northeast region of Colombia. Additionally, a significant positive association between VL cases and ENSO was observed, with many VL cases reported during El Niño

Environmental factors (temperature, humidity, luminosity, altitude, and vegetation cover), rainfall variations, droughts, and an increase in Sea Surface Temperature (SST) anomalies, and their particular differences between each Biomes, can influence parasite transmission and consequently affect VL development.

The potential distribution of *Lu. longipalpis* in Brazil expands during El Niño and La Niña episodes, especially in Roraima, Pará, Acre, and Mato Grosso. This expansion may be influenced by changes in precipitation, which can increase the availability of suitable habitats and influence the abundance of potential hosts. Additionally, the ongoing urbanization process in these states may also favor the presence of *Lu. longipalpis* due to its preference for areas with low vegetation cover. It is essential to continue monitoring this vector's potential distribution and implement effective control measures to prevent the spread of VL.

We found a positive association between the incidence rate of VL and the El Niño 2015–2016 episode compared to the La Niña 2010–2011 episode and an impressive% of area suitable for the vector *Lu. longipalpis* in the Amazon region. These results are consistent with previous studies and provide new insights into the potential influence of ENSO cycles and vector ecology on VL incidence. However, further studies are needed to understand better the mechanisms underlying these associations and their implications for VL control and prevention.

Furthermore, more studies on ENSO episodes, specific environmental conditions directly related to ENSO episodes and occurrence of Phlebotominae and Visceral Leishmaniasis, in the municipalities highlighted at the present study is very important to better understand the Visceral Leishmaniasis transmission dynamics.

CRediT authorship contribution statement

Juan David Gutiérrez: Conceptualization, Validation, Formal analysis, Methodology, Writing – original draft, Writing – review & editing. **Mariano Altamiranda-Saavedra:** Validation, Formal analysis, Methodology, Writing – original draft, Writing – review & editing. **Julián Ávila-Jiménez:** Validation, Formal analysis, Writing – original draft, Writing – review & editing. **Iris Amati Martins:** Validation, Formal analysis, Writing – original draft, Writing – review & editing. **Flávia Virginio:** Validation, Formal analysis, Writing – original draft, Writing – review & editing.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Data availability

Data will be made available on request.

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