Epidemiological Report

Human cases of Visceral Leishmaniasis
Historic Series 2010 – 2021

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BRIEF HISTORY OF INJURY/DISEASE

Visceral leishmaniasis (VL) is a neglected systemic disease that has an important association with social vulnerability.[1,2] In Brazil, it is considered a zoonotic disease, which involves the interaction of *Leishmania infantum*, sand fly vectors and dogs, which plays an important role as an urban reservoir.[1,3]

In the state of São Paulo (SSP), until the end of the 1990s, only imported human cases of VL were described.[4,5] Although the mosquito *Lutzomya longipalpis*, the main vector associated with the transmission of the disease, was identified in the 1970s in locations with basically rural characteristics, it was only in 1997 that the presence of this vector was confirmed in an urban area, in Araçatuba, located in the Northwest of São Paulo.[4-6] In the following year, 1998, the autochthonous transmission of canine VL was confirmed in this municipality[4-6] and, in 1999, the occurrence of autochthonous human cases was confirmed in Araçatuba and Birigui.[6]

Although more recently, the historical series of autochthonous human VL from São Paulo shows a reduction in cases,[7] the disease has become increasingly present in different epidemiological scenarios in the state, as a result of the interaction of several factors related to human interference.[1,2,5] This territorial expansion is perceived by the progressive number of municipalities with autochthonous human cases, from two in 1999 to 111 in 2020, while canine transmission was already registered in 176 municipalities in 2020.[8] The relevant data is that, although human and canine VL occur predominantly in the Midwest of the state,[7] the disease has been recorded in regions where secondary vectors have been associated with its occurrence, such as the immediate areas of São Paulo, where *Pintomyia fischeri* and *Migonemyia migonei* predominate, and the immediate region of Santos, where *Nyssomyia intermedia* predominates.[8-10]

Given this expansion, disease control remains a major public health challenge, given the complexity of the actions needed to reduce the risk of infection, which are related to the environment and the canine reservoir, for which there must be shared responsibility between the public sector and the community.

ETIOLOGICAL AGENT

In the Americas, the disease is caused by *Leishmania (Leishmania) infantum*, a protozoan of the *Trypanosomatidae* family, which has two evolutionary forms in its cycle: promastigote, which is the flagellated and extracellular form found in the digestive tract of the insect vector; and amastigote, a form that parasitizes cells of the mononuclear phagocytic system of vertebrate hosts.[3,11]

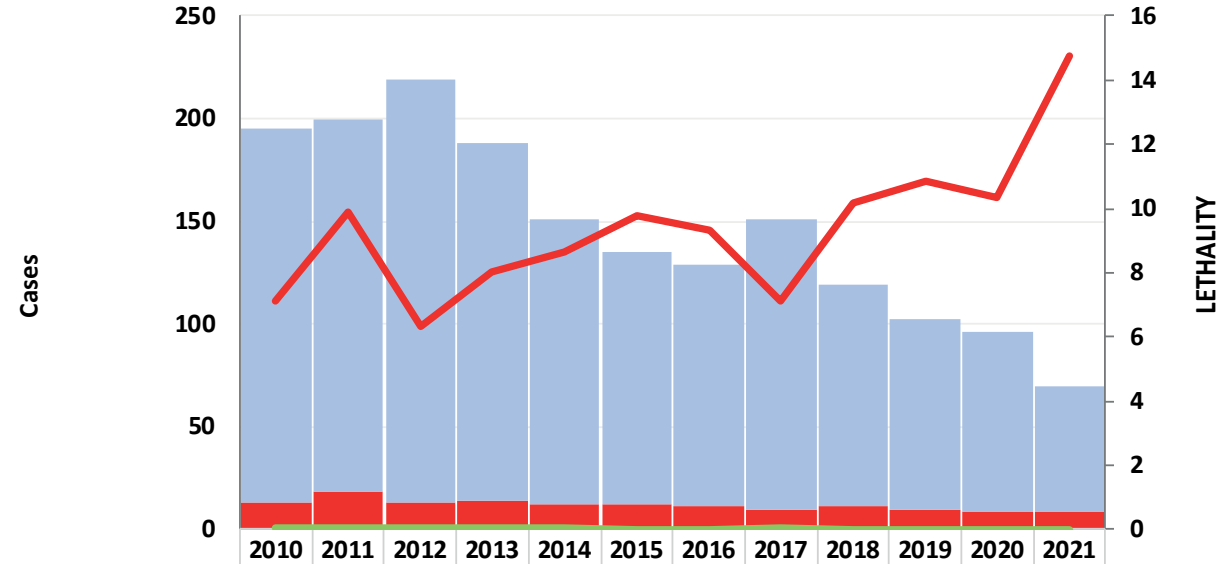
TRANSMISSION MODE

Transmission occurs through the bite of an infected female sand fly in the vertebrate host, when the promastigote form is inoculated and phagocytosed by macrophages. Inside the macrophages, they transform into amastigotes, multiply, and lead to cell rupture, when they enter the hematogenous route, infecting other mononuclear phagocytic cells.[3,11]

EPIDEMIOLOGICAL SITUATION

In the period from 2010 to 2021, 5,928 suspected cases of VL were reported in the state database of the Notifiable Diseases Information System, Net version (Sinan Net). Of these, 1,613 (27.2%) were confirmed as autochthonous human cases in the state, with an average of 134 confirmed cases, ranging from 61 cases in 2021 to 206 in 2012 (Graph 1). The number of deaths among the autochthonous cases was 142, resulting in an average lethality of 9.4% in the period (SD:±2.24).

Graph 1. Autochthonous cases of visceral leishmaniasis in the SSP, incidence coefficient (IC), deaths and lethality, according to year of notification, 2010 to 2021.*



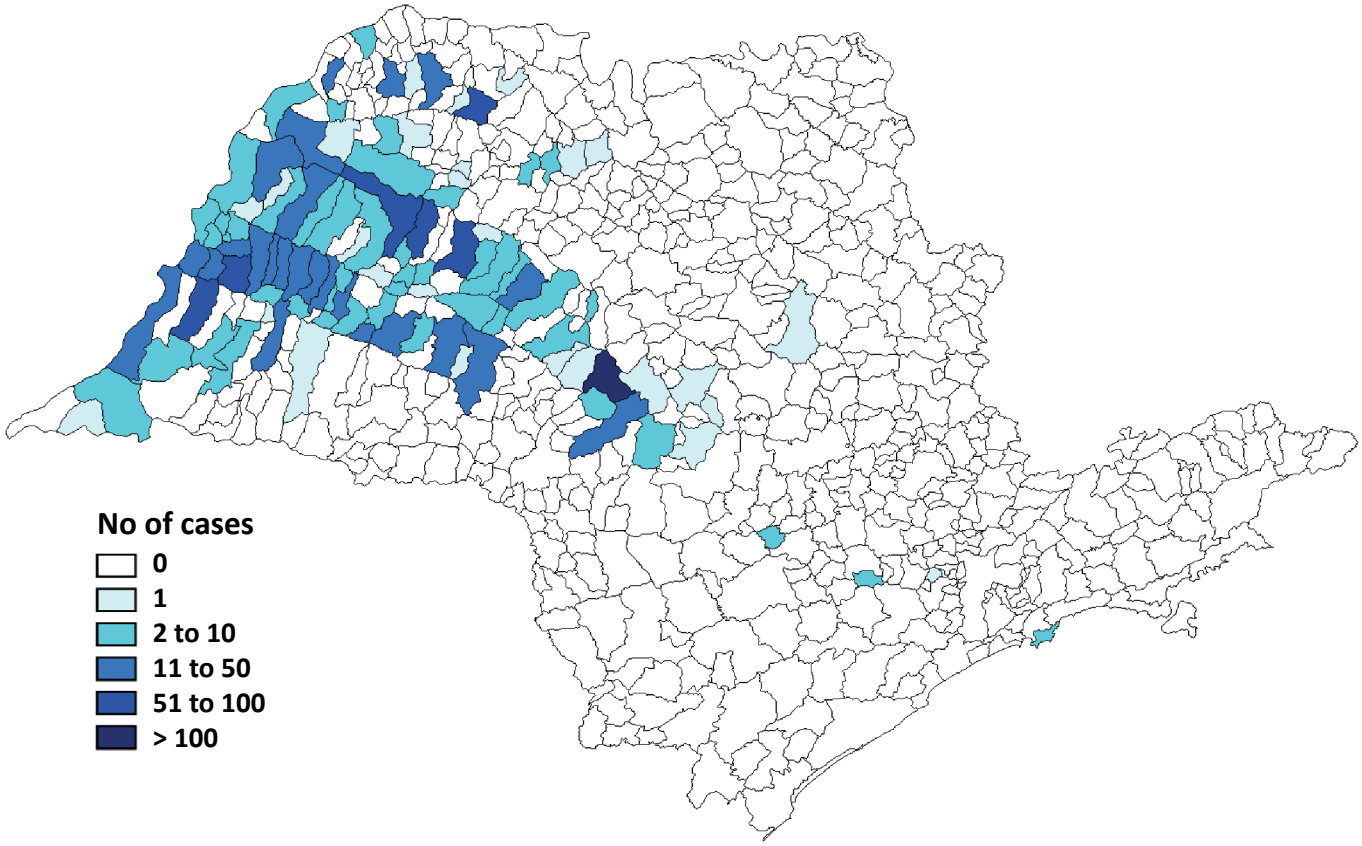
	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021
Cases	182	182	206	174	139	123	118	141	108	92	87	61
Deaths	13	18	13	14	12	12	11	10	11	10	9	9
CI/100,000 hab	0.43	0.43	0.48	0,40	0.32	0.28	0.26	0.31	0.24	0.20	0.19	0.13
Lethality	7.1	9.9	6.3	8.0	8.6	9,8	9.3	7.1	10.2	10.9	10.3	14.8

Source: Sinan Net, Division of Zoonoses/CVE/CCD/SES-SP. *Data extracted on June 28, 2022.

Data available on the Ministry of Health website until 2020[12] show an IC of visceral leishmaniasis in Brazil that ranged from 0.9 cases/100,000 inhabitants in 2020 to 2.0 cases/100,000 inhabitants in 2011 and 2017, while in the SSP the highest IC was 0.48 cases/100,000 inhabitants in 2012.

The spatial distribution shows the concentration of human cases of VL in municipalities in the Midwest region of São Paulo, with greater representation of the Epidemiological Surveillance Groups (ESG) in Araçatuba (23.6%), Bauru (21.8%), Marília (20.8%), PresidenteVenceslau (20.7%) and São José do Rio Preto (6.5%). Although the pattern of occurrence is related to municipalities/ regions already known to transmit the disease, from 2016 onwards, autochthonous transmission outside this axis was identified, as in the Santos, Osasco and Sorocaba ESG (Figure 1 and Table 1).

Figure 1. Distribution of autochthonous cases of visceral leishmaniasis according to municipality of infection, SSP, 2010 to 2021.



Source: Sinan Net, Division of Zoonoses/CVE/CCD/SES-SP. *Data extracted on June 28, 2022.

Table 1. Autochthonous cases of visceral leishmaniasis according to year of notification and municipality of infection, SSP, 2010 to 2021.*

Municipalities	2010		2011		2012		2013		2014		2015		2016		2017		2018		2019		2020		2021	
	Cases	Deaths	Cases	Deaths	Cases	Deaths	Cases	Deaths	Cases	Deaths	Cases	Deaths	Cases	Deaths	Cases	Deaths	Cases	Deaths	Cases	Deaths	Cases	Deaths	Cases	Deaths
ITAPEVI																	1							
ESG OSASCO	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0
ANDRADINA	1		3	1	9	2	3	1	7	1	8	4	3	1	3		5				3	1	1	
ARAÇATUBA	5	1	5		6	1	3		11		3		1		10	1	14	2	8	3			5	
AURIFLAMA							2																	
AVANHANDAVA											2	1			2						1			
BARBOSA																	1	1						
BILAC			1				1				1				1									
BIRIGUI	10	3	25	4	21	1	11	3	3	1	8		2		2	1	2		1		4		3	
BRAÚNA											1	1	1						2		2			
BURITAMA							1				2		1										1	
CASTILHO	2				1		1				1		1						1	1	1			
CLEMENTINA	1				1																			
GUARAÇAÍ			1								1				1	1								
GUARARAPES	1		1																1					
ILHA SOLTEIRA	1		1				1				1								1				1	
LAVÍNIA	1																				1		1	1

Municipalities	2010		2011		2012		2013		2014		2015		2016		2017		2018		2019		2020		2021	
	Cases	Deaths	Cases	Deaths	Cases	Deaths	Cases	Deaths	Cases	Deaths	Cases	Deaths	Cases	Deaths	Cases	Deaths	Cases	Deaths	Cases	Deaths	Cases	Deaths	Cases	Deaths
MIRANDÓPOLIS	1		2		1				3		1				2				3		3		1	
MURUTINGA DO SUL																							1	
NOVA INDEPENDÊNCIA													1											
PENÁPOLIS	4		3		8		9	2	6		4		2	1	7		6		3		2		5	1
PEREIRA BARRETO	3		1		3	1	4		1		1		1		2		2				3		6	1
PIACATU	1																							
RUBIÁCEA			1																					
SANTO ANTÔNIO DO ARACANGUÁ	2						1		1															
SANTÓPOLIS DO AGUAPEÍ																			2				1	
SUD MENNUCCI																					1	1		
TURIÚBA							1	1																
VALPARAÍSO			1								2				1	1	2						1	1
ESG ARAÇATUBA	33	4	45	5	50	5	38	7	32	2	36	6	13	2	31	4	33	3	22	4	21	2	27	4
SÃO CARLOS																			1					
ESG ARARAQUARA	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0
AGUDOS	4	1	1		2				3				1	1	1				1					
AVAÍ							1																	
BAURU	39	1	39	4	44	2	29	1	27	1	23	1	22		25	1	10	2	10	2	9	1	4	1
CAFELÂNDIA									1				1											

Municipalities	2010		2011		2012		2013		2014		2015		2016		2017		2018		2019		2020		2021	
	Cases	Deaths	Cases	Deaths	Cases	Deaths	Cases	Deaths	Cases	Deaths	Cases	Deaths	Cases	Deaths	Cases	Deaths	Cases	Deaths	Cases	Deaths	Cases	Deaths	Cases	Deaths
GETULINA	1		1		1						1						1	1						
GUAIÇARA	1				2																			
JAÚ																					1			
LENÇÓIS PAULISTA	1						1		1		1												1	
LINS	6		6		4				6				1	1	1		1							
MINEIROS DO TIETÊ							1																	
PEDERNEIRAS															1									
PIRAJUÍ																							2	
PIRATININGA	3						1																	
PRESIDENTE ALVES											1													
PROMISSÃO	2	1	1				1						1		1		1							
ESG BAURU	57	3	48	4	53	2	34	1	38	1	26	1	26	2	29	1	13	3	11	2	10	1	7	1
SÃO MANUEL																					1	1		
ESG BOTUCATU	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	1	0	0
ADAMANTINA	14		11		5		3		2		3		2		5		2	1	1				1	
BASTOS	2		6		9		4		4	1	1		3		3		1		4		1			
FLÓRIDA PAULISTA	3		3		1		3		1		2		4						1					
GUAIMBÊ	1																		2					
HERCULÂNDIA													2											

Municipalities	2010		2011		2012		2013		2014		2015		2016		2017		2018		2019		2020		2021	
	Cases	Deaths	Cases	Deaths	Cases	Deaths	Cases	Deaths	Cases	Deaths	Cases	Deaths	Cases	Deaths	Cases	Deaths	Cases	Deaths	Cases	Deaths	Cases	Deaths	Cases	Deaths
IACRI									1				4								1			
INÚBIA PAULISTA	1		1				1								1									
LUCÉLIA	2		1		6		1		3		1		3		1		2		1					
MARIÁPOLIS													2		1		1		1		3			
MARÍLIA			1						2	1	2		10	1	16		4		5	1	3		5	
ORIENTE																	1							
OSWALDO CRUZ	14	4	4		7		6		6		2		1		2		2	1	2		1	1	1	1
PACAEMBU	7				2		2		2		1													
PARAPUÃ			4		1										1				1		1			
POMPÉIA							1		3		3		2		1						1			
RINÓPOLIS	1	1	1		1				2															
SAGRES	2																		1					
SALMOURÃO	1		1				2		1		2	1			1				1					
TUPÃ					2	1	6		6	3	2		3		3		7	1	5	1	5		1	
ESG MARÍLIA	48	5	33	0	34	1	29	0	33	5	19	1	36	1	35	0	20	3	25	2	16	1	8	1
MARTINÓPOLIS																			1					
PRESIDENTE BERNARDES															1				1					
PRESIDENTE PRUDENTE							2				2	1	2	1	3	1	2		2		6		4	
SANTO ANASTÁCIO											2	1	2		1				2		2			

Municipalities	2010		2011		2012		2013		2014		2015		2016		2017		2018		2019		2020		2021	
	Cases	Deaths	Cases	Deaths	Cases	Deaths	Cases	Deaths	Cases	Deaths	Cases	Deaths	Cases	Deaths	Cases	Deaths	Cases	Deaths	Cases	Deaths	Cases	Deaths	Cases	Deaths
SANTO EXPEDITO							1																	
ESG XXI PRES.PRUDENTE	0	0	0	0	0	0	3	0	0	0	4	2	4	1	5	1	2	0	6	0	8	0	4	0
DRACENA	10		13		5		2		3		7		7		11		2		5		4	1	2	
EUCLIDES DA CUNHA PAULISTA																					1	1		
FLORA RICA	1								1	1	1													
IRAPURU	2		5		1		1				2		1				1							
JUNQUEIRÓPOLIS	6		4	1	1		4		2		4		4				1				1			
MARABÁ PAULISTA									1		1				1						1			
MONTE CASTELO	2						4								1									
NOVA GUATAPORANGA	1				1		2				1		2						1		2			
OURO VERDE			1		7	1	5		2		2		1		2		1							
PANORAMA	8		1		2		4		1		2		5	1	4	2	2				4	1		
PAULICÉIA	1		1		1		1								3									
PRESIDENTE EPITÁCIO									1		3		7		5		13		6		9	1	3	
PRESIDENTE VENCESLAU	1		4		14		12	1	6	1	4		1		2				3		1		3	2
SANTA MERCEDES					1		1																	
SÃO JOÃO PAU D'ALHO			5	1			1																	

Conclusion

Municipalities	2010		2011		2012		2013		2014		2015		2016		2017		2018		2019		2020		2021	
	Cases	Deaths	Cases	Deaths	Cases	Deaths	Cases	Deaths	Cases	Deaths	Cases	Deaths	Cases	Deaths	Cases	Deaths	Cases	Deaths	Cases	Deaths	Cases	Deaths	Cases	Deaths
TEODORO SAMPAIO																	1				1		3	
TUPI PAULISTA	4		6	1	3		4		2		1		2		2		1		1					
ESG XXII PRESIDENTE VENCESLAU	36	0	40	3	36	1	41	1	19	2	28	0	30	1	31	2	22	0	16	0	24	4	11	2
GUARUJÁ													2	2	1									
ESG XXV SANTOS	0	0	0	0	0	0	0	0	0	0	0	0	2	2	1	0	0	0	0	0	0	0	0	0
AMÉRICO DE CAMPOS																	1							
GENERAL SALGADO							1	1																
GUAPIAÇÚ																					1			
MIRASSOL													1	1			3							
MONÇÕES													1											
NEVES PAULISTA											1	1							1	1				
SÃO JOSÉ DO RIO PRETO													1	1										
VALENTIM GENTIL					1																			
VOTUPORANGA	1		6	3	28	3	22	4	14	2	6		2		5	2	4		2	1	2		1	
ESG XXIX SÃO JOSÉ DO RIO PRETO	1	0	6	3	29	3	23	5	14	2	7	1	5	2	5	2	8	0	3	2	3	0	1	0
APARECIDA D'OESTE			1																1					
ESTRELA DO OESTE													1											
FERNANDÓPOLIS											1				2		5	1	7		2		2	

Municipalities	2010		2011		2012		2013		2014		2015		2016		2017		2018		2019		2020		2021	
	Cases	Deaths	Cases	Deaths	Cases	Deaths	Cases	Deaths	Cases	Deaths	Cases	Deaths	Cases	Deaths	Cases	Deaths	Cases	Deaths	Cases	Deaths	Cases	Deaths	Cases	Deaths
JALES	3	1	5	2	3		6		2		2	1	1		1		2							
SANTA ALBERTINA																	1				1		1	1
SANTA FÉ DO SUL	4		4	1	1	1			1												1			
ESG XXX JALES	7	1	10	3	4	1	6	0	3	0	3	1	2	0	3	0	8	1	8	0	4	0	3	1
VOTORANTIM															1		1	1						
ESG XXXI SOROCABA	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	1	1	0	0	0	0	0	0
SP STATE	182	13	182	18	206	13	174	14	139	12	123	12	118	11	141	10	108	11	92	10	87	9	61	9

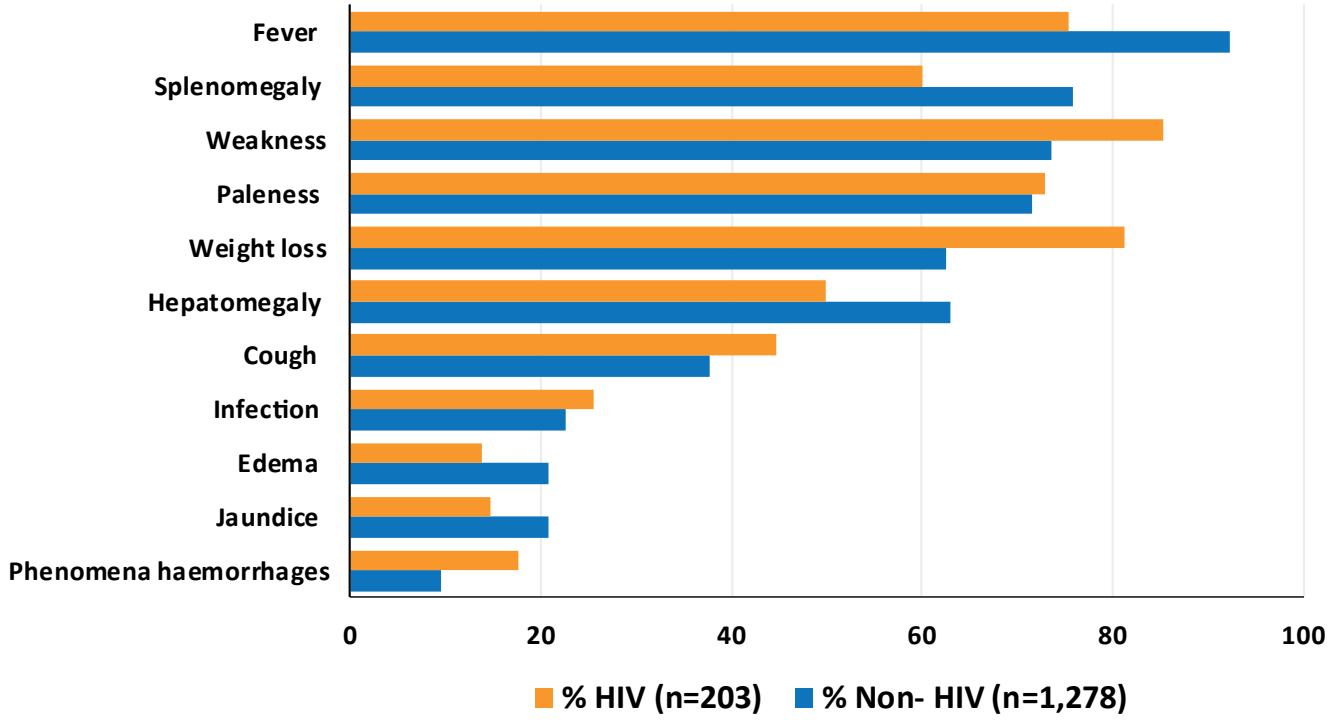
Source: Sinan Net, Division of Zoonoses/CVE/CCD/SES-SP. *Data extracted on June 28, 2022.

Regarding the cases, 1,481 (91.8%) had information regarding the presence or absence of co-infection with the human immunodeficiency virus (HIV), and these were the records considered valid for analysis.

Of the 1481 episodes, 1.278 (86,3%) were in non-HIV patients and 203 (13.7%) in HIV ones. When assessing the type of entry, the proportion of new cases in the non-HIV group was 92.3% (1,179/1,481), while in the HIV group it was 64.5% (131/203) and relapse was 35.5% (72/203), evidencing greater immunological vulnerability of this group to the disease (Table 2). Liposomal amphotericin b was the drug of choice in both groups for the treatment of VL, with laboratory criteria being the main form of diagnosis.

The most prevalent clinical manifestations in both groups were fever (non-HIV 92.2% and HIV 75.4%), splenomegaly (non-HIV 75.9% and HIV 60.1.3%), asthenia (non-HIV 73, 6% and HIV 85.2%), pallor (non-HIV 71.5% and HIV 72.9%) and weight loss (non-HIV 62.6% and HIV 81.3%) (Graph 2).

Graph 2. Clinical manifestations of visceral leishmaniasis cases according to the occurrence of co-infection with HIV or not, SSP, 2010 to 2021.



Source: Sinan Net, Division of Zoonoses/CVE/CCD/SES-SP. *Data extracted on June 28, 2022.

Considering only new cases, the average age in the non-HIV group was 27 years (interval from 1 month to 90 years) and in the HIV group, 41 years (interval from 2 to 80 years). In both groups, males, white race/color and urban residents were more prevalent (Table 3).

Table 3. Description of new cases of visceral leishmaniasis according to the occurrence of co-infection or not with HIV, SSP, 2010 to 2021.*

Variable	Non-HIV (n=1179)		HIV (n=131)	
	Average	Interval	Average	Interval
Age	**27**	**1 month - 90 years**	**41**	**2 - 80 years**
	n	%	N	%
Sex				
Male	761	64.5	93	71.0
Female	418	35.5	38	29.0
Race/Color				
White	682	57.8	72	55.0
Brown	311	26.4	36	27.5
Black	109	9.2	17	13.0
Yellow	22	1.9	1	0.8
Urbanarea				
Urban	1,132	96.0	127	96.9
Rural	24	2.0	0	0.0
Periurban	2	0.2	2	1.5

Source: Sinan Net, Division of Zoonoses/CVE/CCD/SES-SP. *Data extracted on June 28, 2022.

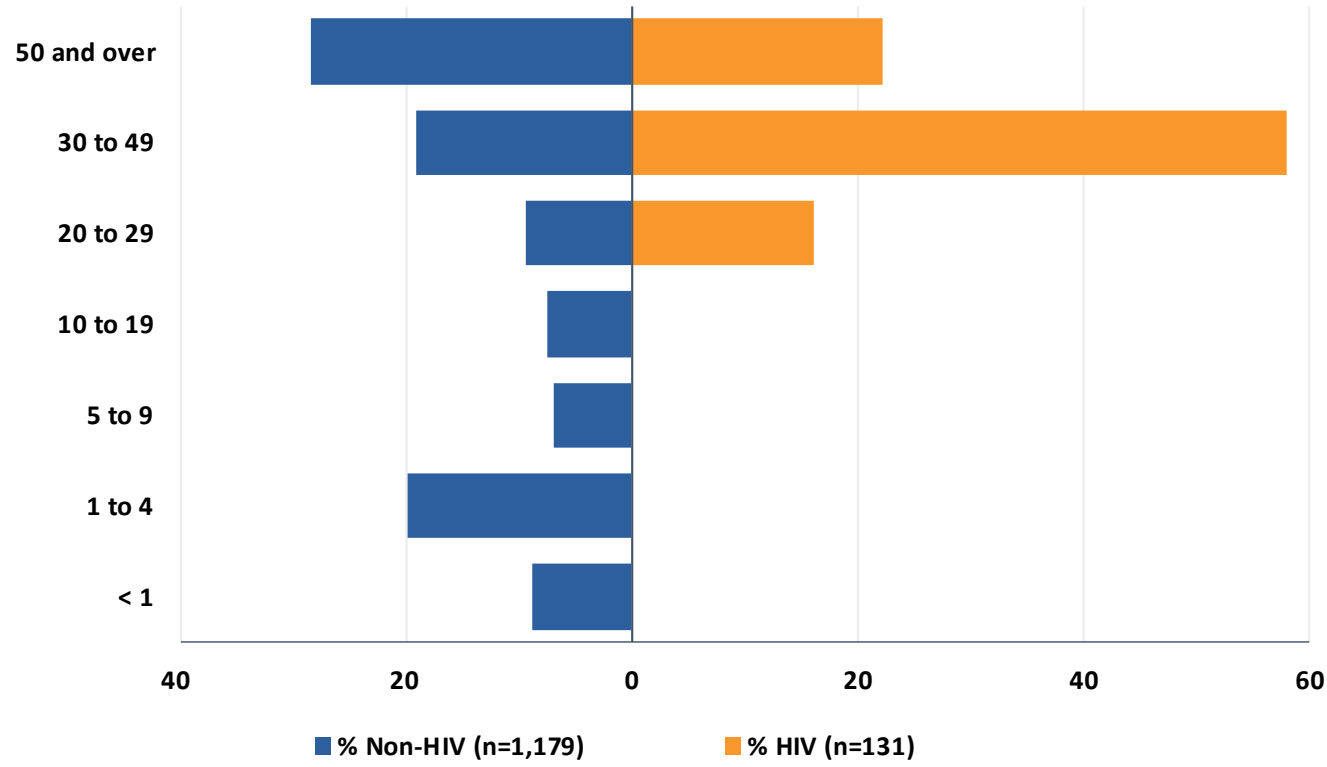
When we evaluated the age group of new cases, in the non-HIV group the most affected were patients ≥ 50 years old (28.4%), while in the co-infected group it was the age group from 30 to 49 years old (58.0%) (Table 4 and Graph 3). Regarding lethality, in the non-HIV group it was 8.7% (102/1,179), with the age group with the highest lethality being that of ≥ 50 years, with 18.5% (62/335). Among co-infected individuals, the overall lethality rate was 16.0% (21/131), with the 20-29 age group reaching 28.6% (Table 4 and Graph 3).

Table 4. New cases of visceral leishmaniasis according to age group and occurrence of co-infection or not with HIV, SSP, 2010 to 2021.*

Age group (in years)	New non-HIV cases				New HIV cases			
	Cases		Deaths		Cases		Death	
	n	%	n	Lethality	n	%	n	Lethality
< 1	104	8.8	3	2.9	0	0.0	0	0.0
1 to 4	234	19.8	5	2.1	1	0.8	0	0.0
5 to 9	81	6.9	2	2.5	0	0.0	0	0.0
10 to 19	88	7.5	2	2.3	4	3.1	0	0.0
20 to 29	111	9.4	8	7.2	21	16.0	6	28.6
30 to 49	226	19.2	20	8.8	76	58.0	12	15.8
50 and over	335	28.4	62	18.5	29	22.1	3	10.3
Total	**1,179**	**100.0**	**102**	**8.7**	**131**	**100.0**	**21**	**16.0**

Source: Sinan Net, Division of Zoonoses/CVE/CCD/SES-SP. *Data extracted on June 28, 2022.

Graph 3. Distribution of new cases of visceral leishmaniasis according to age group and occurrence of co-infection or not with HIV, SSP, 2010 to 2021.*

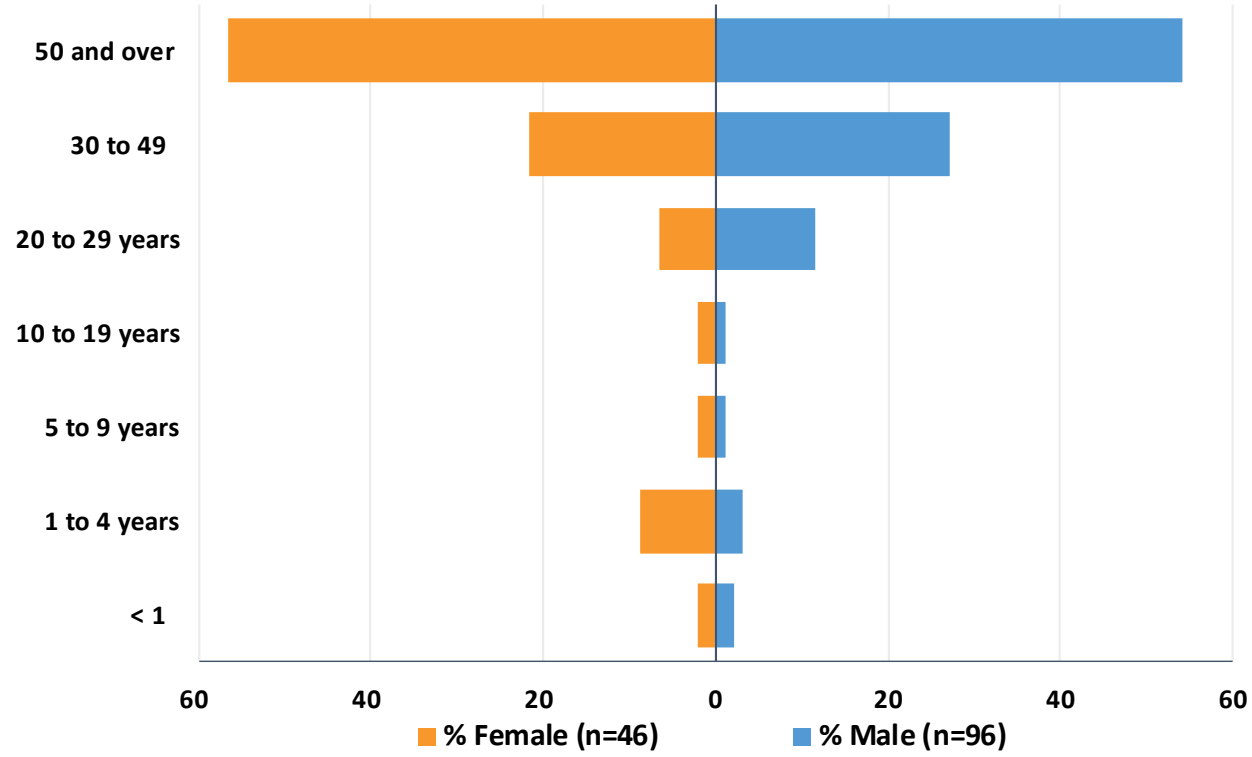


Source: Sinan Net, Division of Zoonoses/CVE/CCD/SES-SP. *Data extracted on June 28, 2022.

Regarding VL cases that died during the analysis period (n=142), male patients (67.9%) and aged ≥ 50 years (54.9%) were more frequent (Graph 4), with an average age of 55 years (range 8 months to 89 years). In 91.5% (130/142) of the cases, death occurred during the course of a first episode of the disease. LV-HIV coinfection occurred in 14.8% (621/142), laboratory diagnosis was the main diagnostic criterion (93.0%) and liposomal amphotericin b was the drug of choice for treatment (53.5%). It should be noted that in 30 cases (21.1%), the treatment was not carried out.

The interval between the onset of symptoms (OS) and treatment had an average of 27 days (interval from 2 to 311), while the interval between OS and the date of death was 31.5 days (interval from 2 to 809) (Table 5). However, the evaluations were carried out with secondary data, and therefore there may be bias in the recording of information.

Graph 4. Distribution of cases with evolution to death from visceral leishmaniasis according to age group, SSP, 2010 to 2021.



Source: Sinan Net, Division of Zoonoses/CVE/CCD/SES-SP. *Data extracted on June 28, 2022.

Table 5. Characterization of cases with evolution to death from visceral leishmaniasis, SSP, 2010 to 2021.*

Variable	Deaths (n=142)	
	Average	Interval
Age	**55 years**	**8 months- 89 years**
OS interval and treatment (n=101)	27 days	2 - 311 days
OS intervaland death	31.5 days	2 - 809 days
Variable	**Deaths (n=142)**	
	n	%
Sex		
Male	96	67.6
Female	46	32.4
Race/Color		
White	78	54.9
Brown	34	23.9
Black	17	12.0
Entry		
New case	130	91.5
Recurrence	12	8.5
HIV		
Yes	21	14.8
No	102	71.8
Diagnosticcriteria		
Laboratory	132	93.0
Parasitological	84	59.2
Quicktest	73	51.4
Medicine used		
Ampho b liposomal	76	53.5
Pentavalent antimonial	14	9.9
Ampho b deoxycholate	10	7.0
Notused	30	21.1
No information	11	7.7

Source: Sinan Net, Division of Zoonoses/CVE/CCD/SES-SP. *Data extracted on June 28, 2022.

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