

Update on *Dirofilaria immitis* epidemiology in South America and Mexico: literature review

Atualização sobre a epidemiologia de *Dirofilaria immitis* na América do Sul e no México: revisão de literatura

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Abstract

Dirofilaria immitis (LEIDY, 1856; RAILLET; HENRY, 1911) is a parasite that is widely disseminated around the globe, with a higher prevalence in warm, humid climates. The first report of its occurrence in South America is from 1878 in Brazil. At that time, reports were scarce and difficult to retrieve – therefore, gathering them will facilitate record-keeping over time. Four databases were searched (Scopus, MEDLINE, LILACS, and PubMed) and the search keywords were “Dirofilaria” or “heartworm” and the countries’ names. Four countries lacked reports (Bolivia, Ecuador, French Guiana, and Uruguay) and other three (Suriname, Guyana, and Paraguay) had only old reports. Chile was the only country in which studies were conducted over time, and no infected dogs were registered. For the other six countries (Mexico, Peru, Colombia, Venezuela, Argentina, and Brazil), reports showed that the infection frequency varied over time and with the surveyed area. Therefore, the information indicates that *D. immitis* is established, and veterinarians must institute preventive programs to optimally care for their patients and protect the health of their families.

Keywords: Heartworm. Dog. Prevalence. Diagnostic.

Resumo

Dirofilaria immitis (LEIDY, 1856; RAILLET; HENRY, 1911) é um nematoide de ampla distribuição geográfica, que ocorre com maior frequência em áreas quentes e úmidas do planeta. O primeiro registro de sua ocorrência na América do Sul foi realizado em 1878, no Brasil. Naquela época os registros eram poucos e raramente de fácil obtenção, razão pela qual reuni-los facilitará o acesso a tais informações. Quatro bases de dados (Scopus, MEDLINE, LILACS e PubMed) foram estudadas utilizando-se as palavras-chave “Dirofilaria” ou “heartworm”, os nomes dos países da América do Sul e o México. Nenhum registro foi encontrado para quatro países (Bolívia, Equador, Guiana Francesa e Uruguai) e para outros três (Suriname, Guiana e Paraguai) os registros eram antigos. Apenas o Chile é o território onde houve estudos registrados com ausência do parasita. Os outros países (México, Peru, Colômbia, Venezuela, Argentina e Brasil) apresentam registros com frequência variável no tempo ou no espaço. Assim, as informações reunidas indicam que infecções por *D. immitis* ocorrem na maior parte da América do Sul e no México e que os médicos veterinários devem instituir programas preventivos para garantir cuidados médicos de qualidade aos pacientes e para proteger a saúde destes e de suas famílias.

Palavras chave: Verme do coração. Cão. Prevalência. Diagnóstico.

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Introduction

Dirofilaria immitis was described by Leidy (1856), and the first report of canine infection in Latin America was published in 1878 by Silva Araújo in the State of Bahia, Brazil (PINTO, 1944). At that time, there were few publications on canine parasitosis. Since retrieving these publications is laborious, the information obtained from them is precious (Table 1).

Table 1 – *Canine Dirofilaria immitis* infection prevalence before 2003 in different South American countries and Mexico, according to the detection test

Country	Surveyed area	Prevalence (%)	Test used	Reference
Argentina		7.8	MK	BULMAN et al., 1989a, 1989b
		0	MK	LIGHTOWLER et al., 1992
		41.1	MK	MANCERO et al., 1992
		2	MK	ROSA et al., 1994
		23.5 (South)	Ag	ROSA et al., 2002
		17.7 (North)	Ag	ROSA et al., 2002
Brazil	Rio de Janeiro State	13.68	MK, Ag	LABARTHE et al., 1997
	Niterói, RJ	24.86	MK, Ag	
	Petrópolis e Teresópolis, RJ	25.6	MK, Ag	
	Santa Catarina State	12	MK	LABARTHE et al., 1992
	Rio Grande do Sul State	1.1	MK	
	Botucatu, SP	1	MK, Ag	YADA et al., 1994
	Paraíba State	12.4	Ag	ARCOVERDE et al., 1994
	Maceió, AL	12.5	MK, Ag	CALHEIROS et al., 1994
	Recife, PE	4.7	MK, Ag, Necropsy	ALVES et al., 1994
	Pará State	10.7	MC, MK, MT	SOUZA et al., 1997
	Bertioga, SP	45	MK	DUQUE-ARAÚJO et al., 1995
	Guarujá, SP	14.2	MK	
	Riviera de São Lourenço, SP	18	MK	
	Mairiporã, SP	17	MK	
	Cuiabá, MT	9.62	MK	FERNANDES et al., 1996
	São Luiz, MA	15	MK	AHID et al., 1999
		Cuiabá, MT	12.08	MK, Ac
	Bahia State	10	MK	ALMEIDA et al., 2001
	Paraná State	5.5	MT, MK, Ag	REIFUR et al., 2001
	Alagoas State	1.3	MK, Ag	BRITO et al., 2001
	São Paulo State	8	MK, Ag	SOUZA; LARSSON, 2001
Chile		0	MK	ALCAÍNO; GORMAN; PUELMA, 1984
		0	MK	ALCAINO et al., 1995
Colombia		0.25	MK	LITTLE et al., 1968
		7,3	MK	LITTLE et al., 1968
		4.8 – 8.4	MK, Ag	GUERRERO et al., 1992
Guiana		14.1	MK	ORIHÉL, 1964
Mexico		7.5	MK, Ag	GUERRERO et al., 1992
		6.2	MK	GUEVARA et al., 1996
Paraguay		4	Necropsy	MASI et al., 1967
Peru		4.7	MC, MK, Ag	ACUÑA; CHAVEZ, 2002
		12.8	MC, MK, Ag	BRAVO et al., 2002
		3.2	MC, MK, Ag	CHIPANA et al., 2002
		4.4	Ag	ADRIANZÉN, 2002
Suriname		22	MK	REP; HEINEMANN, 1976
		26	MK	PANDAY et al., 1981
Venezuela		4 – 29	MK	D'ALESSANDRO, 1971

MC: microfilaria detection by microcapillary, MK: microfilaria detection by the modified Knott's test, MT: microfilaria detection by thick blood, MF: microfilaria detection by filtration, Ag: detection of antigen, Ac: detection of antibody, PCR: polymerase chain reaction, RJ: Rio de Janeiro State, SP: São Paulo State, AL: Alagoas State, PE: Pernambuco State, MT: Mato Grosso State, MA: Maranhão State, PA: Pará State, BA: Bahia State, AM: Amazonas State, RO: Rondônia State, SC: Santa Catarina State, and PR: Paraná State

Until 1992, when the first macrocyclic lactone was launched in South America for the prevention of canine heartworm, information on the occurrence and distribution of canine *D. immitis* infections was scarce. Fortunately, the new medications the industry has launched in these countries in recent decades have promoted clinician's knowledge of the disease and scientists' interest in understanding heartworm epidemiology (LABARTHE; GUERRERO, 2005).

The new medications launched for chemoprophylaxis of heartworm are of the macrocyclic lactone class (ivermectin, milbemycin oxime, moxidectin, and selamectin) and are recommended since puppies are eight weeks of age. These drugs may be administered orally, topically, or parenterally. Ivermectin and milbemycin oxime can be found in oral formulations. Selamectin and moxidectin can be found in topical presentation. There are formulations of slow release of moxidectin for subcutaneous applications every 6 or 12 months (NELSON et al., 2005).

The internationally recommended drug for the elimination of the adult parasites is the organic arsenic Melarsomine Dihydrochloride (Immiticide® or Diroban®) by deep intramuscular route. This medication was once available in Latin American countries, but is no longer marketed in most of them. Therefore, adulticide treatments are currently performed with an alternative protocol. Although the alternative treatment protocol is not recommended by the American Heartworm Society, they recognize it as the only option to be used in countries where melarsomine hydrochloride is not available (NELSON et al., 2014). The alternative protocol should be carried out with monthly doses of preventive macrocyclic lactones associated with doxycycline (NELSON et al., 2014). The use of doxycycline is recommended because all *D. immitis* individuals harbor intracellular bacteria of the genus *Wolbachia*, essential for the maintenance of their basic functions. Therefore, the use of tetracyclines have a negative effect on the worms' embryogenesis and their survival (BANDI et al., 2001; MCCALL et al., 2004). The alternative protocol includes doxycycline at a dose of 10 mg/kg twice daily for four weeks and a macrocyclic lactone in monthly prophylactic doses (NELSON et al., 2014).

As interest in this area grew, canine vector-borne diseases have received increased attention as public health threats (COLWELL et al., 2011), especially because it is

well known that most human emerging or reemerging diseases have originated from animals (JONES et al., 2008). Among the vector-borne parasites, *D. immitis* has a special ability for dispersing once it is vectored by flying arthropods, such as one of the many mosquito species already identified as capable vectors (LUDLAM et al., 1970), resulting in high adaptation capacity to different environmental conditions.

Since a review in 2005 (LABARTHE; GUERRERO, 2005), 19 reports have been published in different countries in South America and Mexico. We decided to update the epidemiological information by incorporating newer publications into this review.

Material and Methods

Beginning in 2003, the keywords "Dirofilaria" or "heartworm" and the countries' names were used for searching the following databases: Scopus, MEDLINE, LILACS, and PubMed.

Results and Discussion

No information was found for Bolivia, Ecuador, French Guiana, and Uruguay, and the reports for Suriname (REP; HEINEMANN, 1976; PANDAY et al., 1981), Guyana (ORIHÉL, 1964), and Paraguay (MASI et al., 1967) were published before 1982, which limited updates on the present study (Table 1). The only country apparently free of *D. immitis* is Chile (ALCAÍNO et al., 1984, 1995; VEZZANI et al., 2006; LÓPEZ et al., 2012).

Early information from Mexico reported an overall prevalence of 6.2% to 7.5% (GUERRERO et al., 1992, GUEVARA et al., 1996). According to the necropsy results of stray dogs from Merida (Gulf of Mexico), 7.7% of the animals harbored worms (BOLIO-GONZALEZ et al., 2007), and 59.8% of the blood samples from Celestun (Gulf of Mexico) tested positive by PCR (CARO-GONZALEZ et al., 2011). A survey of 21 Mexican States (28 cities) showed a prevalence of 8.9% with a higher prevalence in the northeastern region (Gulf of Mexico) (MOVILLA et al., 2016).

In Peru no reports were published after 2004 because most veterinary practitioners consider *D. immitis* a minor problem. The prevalence rate for downtown Lima, San Martín de Porres, and the district of Rimac was 4.7%, as presented by Acuña and Chávez (2002). Additionally, in Chipana et al. (2002) reported results from a study performed in five districts from North of Lima, indicating

a mean prevalence of 3.2% (ranging from 0% to 5%). In Adrianzén (2002) demonstrated a mean prevalence of 4.4% in three districts of Lima (Chorrillos, La Molina and San Juan de Miraflores). In Adrianzén et al. (2003) reported the prevalence for three rural districts near Lima on the shores of the Lurin river: 12.5% for Cieneguilla, 7.5% for Lurin, and 2% for Pachacamac. In the most recent study from Corimanya et al. (2004) reported a 5.5% prevalence in the district of San Juan de Lurigancho near the Rimac river, which crosses the city of Lima.

Early information from Colombia showed a prevalence ranging from 0% to 8.4%, with an interesting presence of infected dogs at the high-altitude city of Bogota (2,650 meters above the sea level) (LITTLE et al., 1968; GUERRERO et al., 1989, 1992) (Table 1). In a recent survey conducted in three different cities, the detection of antigens in blood samples resulted in a prevalence range of 0% to 3% (Medellin 0/175; Barranquilla 4/223; Cartagena 3/100) (MCCOWN et al., 2015)(Table 2).

Table 2 – Canine *Dirofilaria immitis* infection prevalence starting in 2003 in different South American countries and Mexico, except Brazil, according to the detection test

Country	Prevalence (%)	Test used	Author
Argentina	2.28	MK	NOTARNICOLA, NAVONE, 2007
	2.3	MK	NOTARNICOLA, 2004
	14.41	Ag	VEZZANI et al., 2011
	1.63	MC	
	3.65	MK	
Chile	0	MK, PCR	LÓPEZ et al, 2012
Colombia	1.6	Ag	MCCOWN et al., 2015
Mexico	7.7	MK, Necropsy	BOLIO-GONZALEZ et al., 2007
	59.8	PCR	CARO-GONZALEZ et al., 2011
	8.9	Ag	MOVILLA et al., 2016
Peru	7.3	Ag	ADRIANZÉN et al., 2003
	5.5	Ag	CORIMANYA et al., 2004
Venezuela	15.2	MK, Ag	GUILARTE, 2011

MC: microfilaria detection by microcapillary, MK: microfilaria detection by modified Knott's test, Ag: detection of antigen, and PCR: polymerase chain reaction

Previous studies from Venezuela reported prevalence rates from 4% to 29% (D'ALESSANDRO, 1971) (Table 1). The only recent report found a prevalence of 15.2% at Sucre region (GUILARTE et al., 2011) (Table 2).

In Argentina, the presence of canine heartworm infections was confirmed in 1931 (MAZZA, ROMANA, 1931), and the known prevalence ranged from 0% to 60%, depending on the surveyed district and the diagnostic test utilized (BULMAN et al., 1989; GUERRERO et al., 1992; LIGHTOWLER et al., 1992; MANCEBO et al., 1992; ROSA et al., 1994, 2002; NOTARNICOLA, NAVONE, 2007). Two recent surveys have been published in Argentina. One reported a prevalence of 2.3% (6/256) (NOTARNICOLA, 2004), and the other was conducted from 2001 through 2006, which included 19,298 samples from the Province of Buenos Aires; the prevalence varied

depending on the test. The detected prevalence was 1.63% by micro hematocrit test, 3.65% by modified Knott's test, and when an antigen detection lateral flow test kit was used, the detected prevalence was 14.41% (VEZZANI et al., 2011) (Table 2).

Brazil is the South American country with the highest number of published papers on heartworm disease (VEZZANI et al., 2006) (Tables 1 and 3). Until the sharp decline in the national prevalence, when a survey registered a prevalence of 2% (LABARTHE et al., 2003), the known prevalence was 7.9% (GUERRERO et al., 1989). The reasons for this decline in canine *D. immitis* infection is thought to be due to multiple factors, most probably a result of chemoprophylaxis, widespread use of off-label injectable macrocyclic lactones, and extensive use of tetracyclines to treat ehrlichiosis (LABARTHE; GUERRERO, 2005).

Table 3 – Canine *Dirofilaria immitis* infection prevalence starting in 2003 in Brazil, according to the studied area and the detection test

Surveyed area	Prevalence (%)	Test used	Author
Florianópolis, SC	15	MK, MT	ARAÚJO et al., 2003
Ceará State	9.1	Ag	LABARTHE et al., 2003
Recife, PE	0	Ag	
Alagoas State	0	Ag	
Bahia State	4.3	Ag	
São Paulo State	2.7	Ag	
Rio de Janeiro State	3.8	Ag	
Minas Gerais State	0	Ag	
Paraná State	6.8	Ag	
Santa Catarina State	4.9	Ag	
Rio Grande do Sul State	0.3	Ag	
Mato Grosso do Sul State	0	Ag	
Distrito Federal State	0	Ag	
Itanhangá, RJ	2	MK, Ag	COSTA et al., 2004
Paraná State	5.5	MK, MT, MF, Ag	REIFUR et al., 2004
Florianópolis, SC	0	MK, PCR	MACHADO, 2005
Ilha de Marajó, PA	53.5	MT, MT, Ag	GARCEZ et al., 2006
Ilhéus-Itabuna, BA	0	Ag	CARLOS et al., 2007
Coari, AM	12.5	MT	SILVA et al., 2008
Ilha de Marajó, PA	32.45	MK, PCR	FURTADO et al., 2009
Porto Velho, RO	12.8	MT, Ag, PCR	OGAWA et al., 2013
Florianópolis, SC	2.1	Ag	LABARTHE et al., 2014
Araquari, SC	7.3	Ag	
Guaratuba, PR	24.5	Ag	
Guaraqueçaba, PR	31.8	Ag	
Pontal do Paraná, PR	26.3	Ag	
Guarujá, SP	2.8	Ag	
Bertioga, SP	7.6	Ag	
Mangaratiba, RJ	16.3	Ag	
Niterói, RJ	58.6	Ag	
Cabo Frio, RJ	27.5	Ag	
Armação de Búzios, RJ	62.2	Ag	
Lauro de Freitas, BA	20.3	Ag	
Salvador, BA	20	Ag	
Recife, PE	36.7	Ag	
Itamaracá, PE	49.5	Ag	
Lábrea, AM	44.4	PCR	SOARES et al., 2014
Cuiabá, MT	1	Necropsy	RAMOS et al., 2015
Recife, PE	11.54	MK	RAMOS et al., 2016

MC: microfilaria detection by microcapillary, MK: microfilaria detection by the modified Knott's test, MT: microfilaria detection by thick blood, MF: microfilaria detection by filtration, Ag: detection of antigen, Ac: detection of antibody, PCR: polymerase chain reaction, RJ: Rio de Janeiro State, SP: São Paulo State, AL: Alagoas State, PE: Pernambuco State, MT: Mato Grosso State, MA: Maranhão State, PA: Pará State, BA: Bahia State, AM: Amazonas State, RO: Rondônia State, SC: Santa Catarina State, and PR: Paraná State

As in other countries, in addition to the variations over time, there are areas in which the prevalence is high and others in which the parasite is rarely detected (LABARTHE et al., 2003). Years after the sharp decline in the Brazilian

prevalence, small animal veterinarians started to observe an upward trend in the number of heartworm-infected patients encountered in their practices. In an effort to confirm or disprove these reports, these endemic areas

were revisited in a new survey: A total of 1,531 canine samples was collected in Santa Catarina, Paraná, São Paulo, Rio de Janeiro, Bahia, and Pernambuco states, and 23.1% were found to be antigen positive (LABARTHE et al., 2014) (Table 3).

Local studies reported different prevalence rates according to environmental conditions, mosquito and canine density, as well as veterinary care dispensed to the dogs (CUMMINGS et al., 1995; WALTERS, 1995). Different percentages of canine infection were reported in several Brazilian regions. Since 2005 eight reports from Brazil have been published and demonstrated that there is an ample variety of epidemiological conditions that contribute to the different transmission rates among domestic dogs, resulting in a wide range of variation in prevalence. The areas vary from free of heartworm up to hyperendemic with infections registered at all five geographic regions of Brazil. In the Midwestern region, where the Brazilian Pantanal is located, only one survey was conducted, and it showed that 1% of the examined dogs were infected in the city of Cuiabá, MT (RAMOS et al., 2015). In the Northeastern region, where the climate varies from semiarid to tropical, the surveyed coastal cities have a tropical climate, and the warm temperatures are reduced by trade winds from the sea, reports ranged from 0% – 29.7%. In the coastal cities of the state of Bahia, the results were as follows: Ilhéus – no infected dogs detected (CARLOS et al., 2007); Lauro de Freitas – 20.3%; and Salvador – 20% (LABARTHE et al., 2014). In the coastal cities of the State of Pernambuco, the following results were reported: Itamaracá – 49.5% and Recife 36.7% (LABARTHE et al., 2014) or 11.54% (RAMOS et al., 2016). In the largest region, the tropical North, which is where the rainforest comprises approximately 75% of the territory, and on the coastal areas of the state of Pará, including Marajó Island, the largest fluvial-maritime island of the world, heartworms infected dogs at different rates, ranging from 32.5% (FURTADO et al., 2009) to 53.5% (GARCEZ et al., 2006). The states of Amazonas (AM) and Rondônia (RO) display favorable environmental conditions

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for the mosquito population to grow. Most areas are moist and warm, due to the influence of the flow rate of its large water bodies, such as the Amazon river. In Coari, AM, 12.5% (SILVA et al., 2008); in Lábrea, AM, 44.4% and in Porto Velho, RO, 12.8% (OGAWA et al., 2013) of the dogs were shown to be infected (Table 3).

In the Southeast region the uneven topography with anthropic disturbances contributes to the diverse climatic conditions, although most coastal cities are warm and humid during summer. The overall prevalence for the region was 26.3%. The prevalence rates in the state of Rio de Janeiro were as follows: Mangaratiba – 16.3%; Niterói – 58.6%; Cabo Frio – 27.5%; and Armação de Búzios – 62.2%. The prevalence rates in the cities of São Paulo State were: Guarujá – 2.8% and Bertioga – 7.6% (LABARTHE et al., 2014) (Table 3).

In the coolest region of Brazil, the South region, the prevalence detected in some coastal areas was impressively high. In the State of Santa Catarina the cities Florianópolis and Araquari had canine infection rates of 2.1% and 7.3%, respectively. In the State of Paraná the canine infection rates were as follows: Guaratuba – 24.5%, Guaraqueçaba – 31.8%, and Pontal do Paraná – 26.3% (LABARTHE et al., 2014) (Table 3).

Conclusion

The reviewed information indicates that *D. immitis* infections are present in most of the South American continent as well as in Mexico. There are obviously major differences regarding the different climatic and veterinary care conditions; however, heartworm infections are established and veterinarians must institute preventive programs to offer the best protection to their patients.

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