

Southern Brazilian geographic distribution of *Migonemyia migonei* (Diptera: Psychodidae), a putative vector of *Leishmania infantum* (Kinetoplastida: Trypanosomatidae): a systematic review

Distribuição geográfica sul brasileira de *Migonemyia migonei* (Diptera: Psychodidae), um vetor putativo de *Leishmania infantum* (Kinetoplastida: Trypanosomatidae): uma revisão sistemática

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Highlights

Migonemyia migonei is widely distributed in the state of Paraná.
There is a risk of receptivity in municipalities with *Migonemyia migonei*.
Further studies are required in Santa Catarina and Rio Grande do Sul.

Abstract

This systematic review gathered information on the spatial distribution in southern Brazil of the sandfly *Migonemyia migonei*, a possible vector of *Leishmania* species that cause visceral leishmaniasis (VL). Articles were searched from the PubMed, Scielo, Web of Science, and Scopus databases using the keywords: "Migonemyia migonei AND Paraná", "Migonemyia migonei AND Santa Catarina", "Migonemyia migonei AND Rio Grande do Sul", "phlebotomine AND Parana", "flebotomíneo AND Paraná" and "sandfly AND Paraná", "phlebotomine AND Santa Catarina", "flebotomíneo AND Santa Catarina" and "sandfly AND Santa Catarina", "phlebotomine AND Rio Grande do Sul", "flebotomíneo AND Rio Grande do Sul", and "sandfly AND Rio Grande do Sul". The initial search identified 322 articles that met the selection criteria. Empty files or duplicated were then excluded. The titles were screened, and the full texts were obtained. This review included 36 articles, covering 72 of the 399 (18.04%) municipalities in Paraná state, one of the

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295 (0.33%) in Santa Catarina, and two of the 497 (0.40%) in Rio Grande do Sul. *Mg. migonei* was found in 54 municipalities of Paraná state, in one municipality of Santa Catarina, and in one of Rio Grande do Sul. Based on the wide distribution of *Mg. migonei* in the municipalities of Paraná, greater monitoring is required regarding cases of VL in humans and animals in this region, in addition to epidemiological investigations of these cases of suspected autochthony, as well as increased prevention and control efforts. More studies on VL are required in Santa Catarina and Rio Grande do Sul.

Key words: Cutaneous leishmaniasis. Kala-azar. *Leishmania infantum*. Public health. Sandflies. Secondary vector.

Resumo

Esta revisão sistemática reuniu informações sobre a distribuição espacial no sul do Brasil do flebotomíneo *Migonemyia migonei*, um possível vetor de espécies de *Leishmania* causadoras da leishmaniose visceral (LV). Os artigos foram pesquisados nas bases de dados PubMed, Scielo, Web of Science e Scopus usando as palavras-chave: "Migonemyia migonei AND Paraná", "Migonemyia migonei AND Santa Catarina", "Migonemyia migonei AND Rio Grande do Sul", "phlebotomine AND Parana", "flebotomíneo AND Paraná" e "flebotomíneo AND Paraná", "flebotomíneo AND Santa Catarina;", "flebotomíneo AND Santa Catarina" e "flebotomíneo AND Santa Catarina", "flebotomíneo AND Rio Grande do Sul", "flebotomíneo AND Rio Grande do Sul" e "sandfly AND Rio Grande do Sul". A busca inicial identificou 322 artigos que atenderam aos critérios de seleção. Em seguida, arquivos vazios ou duplicados foram excluídos. Os títulos foram triados e os textos completos foram obtidos. Esta revisão incluiu 36 artigos, abrangendo 72 dos 399 (18,04%) municípios do Paraná, um dos 295 (0,33%) de Santa Catarina, dois dos 497 (0,40%) do Rio Grande do Sul. *Mg. migonei* foi encontrado em 54 municípios do Paraná estado, em um município de Santa Catarina e em um do Rio Grande do Sul. Com base na ampla distribuição de *Mg. migonei* nos municípios paranaenses, é necessária maior atenção quanto aos casos de LV em humanos e animais, além de investigações epidemiológicas desses casos de suspeita de autoctonia, bem como maiores esforços de prevenção e controle. Mais estudos são necessários em Santa Catarina e Rio Grande do Sul.

Palavras-chave: Calazar. Flebotomíneos. Leishmaniose cutânea. *Leishmania infantum*. Saúde pública. Votor secundário.

Introduction

Leishmaniasis is a neglected tropical zoonosis that is poverty-related, and is considered one of the six endemics of priority care. An estimated 30,000 new cases annually are reported worldwide, and millions of people are at risk of infection. This disease is therefore a serious worldwide public health issue (World Health Organization

[WHO], 2021). Leishmaniasis has two main clinical forms - cutaneous leishmaniasis (CL) and visceral leishmaniasis (VL). Brazil consistently reports the highest number of CL and VL cases in South America, with approximately 3,100 new cases reported annually (Ministério da Saúde, 2014, 2017; P. L. Costa et al., 2018b; WHO, 2021).

Sandflies are the only recognized biological vector for *L. infantum*; however, a

possible role of secondary vectors such as ticks and fleas has been suggested (Cecílio et al., 2022). To be considered a vector, a species must be anthropophilic and capable of being infected with a leishmanial parasite that has also been found in humans, in the same region where human infections have previously been reported (Cecílio et al., 2022; Killick-Kendrik, 1990).

In Brazil, VL is caused by *Leishmania (Leishmania) infantum* and is mainly transmitted by *Lutzomyia longipalpis* and *Lu. cruzi* (Araújo et al., 2013; van Griensven & Diro, 2012), which have predominantly rural distributions. However, cases in peri-urban and urban areas have also frequently occurred. The increasing urbanization of the epidemiological pattern of the disease favors transmission by other vectors (Ministério da Saúde, 2014; R. B. S. Silva et al., 2021).

Studies reporting VL in regions without *Lu. longipalpis* and *Lu. cruzi* corroborate the possibility of other sandfly species acting as vectors of *L. infantum* (Aguiar & Vieira, 2018; Carvalho et al., 2010; Steindel et al., 2013), such as *Migonemyia migonei* (Carvalho et al., 2010; P. L. Costa et al., 2018b; Moya et al., 2015). *Mg. migonei* is an important vector of *L. (Viannia) braziliensis*, one of the etiological agents of CL, and is considered a putative vector of *L. infantum*. This vector is widely distributed throughout South America and consistently found in areas where *Lu. longipalpis* are not (Aguiar & Vieira, 2018; P. L. Costa et al., 2018b; Marialva et al., 2020). As a result, this vector has attracted the attention of the scientific community, with several publications on whether or not its biology and environmental behavior is associated with cases of leishmaniasis. However, these studies have been directed to specific cities

or populations, without considering the distribution of this vector in larger Brazilian states or regions.

Geographic distribution has been shown to be important in the epidemiological study of several diseases, since patterns can be identified in each region and aid in the establishment of prevention measures. Thus, this work aims to study the geographic distribution of *Mg. migonei* in southern Brazil, through a systematic literature review.

Methodology

This study did not require ethics approval. A systematic review of literature based on the presence or absence of *Migonemyia migonei* in southern Brazil, published in the electronic databases PubMed, SciELO, Web of Science and Scopus, was performed from October 10th to November 1st, 2021, by two researchers (1 and 2). This systematic review followed the PRISMA guidelines (Page et al., 2021).

The keywords used were "*Migonemyia migonei* AND Paraná", "*Migonemyia migonei* AND Santa Catarina", "*Migonemyia migonei* AND Rio Grande do Sul", "phlebotomine AND Parana", "flebotomíneo AND Paraná", "sandfly AND Paraná", "phlebotomine AND Santa Catarina"; "flebotomíneo AND Santa Catarina" and "sandfly AND Santa Catarina", "phlebotomine AND Rio Grande do Sul", "flebotomíneo AND Rio Grande do Sul" and "sandfly AND Rio Grande do Sul".

The following inclusion criteria were adopted: (1) publications written in English or Portuguese; (2) publications that investigated phlebotomine fauna in Parana and/or Santa

Catarina and/or Rio Grande do Sul; (3) publications from 2008 to 2021; (4) original articles fully accessible through the portal of electronic journals of the Coordination for the Improvement of Higher Education Personnel (CAPES), a virtual library connected to the Brazilian Ministry of Education with content restricted to authorized users. The exclusion criteria were (1) repeated articles in different databases; (2) full text not available; (3) non-original studies; (4) author's name not disclosed; (5) studies carried out with specific phlebotomine fauna of other locations. The following grey literature sources were also searched using combinations of the key search terms: epidemiological bulletins from Brazilian Ministry of Health and/or State Health Department. These searches had no date restrictions and were updated in January 2022.

A combined database was generated with all potential studies using Mendeley software, and the publications were read in their entireties by two other researchers (3 and 4). Information about (1) city where the study was conducted, (2) cities where *Mg. migonei* was reported, and (3) year of study were extracted and tabulated in Microsoft Excel. Maps of the spatial distribution of *Mg. migonei* were created using QGis software 3.16.2 version.

Results and Discussion

The database and grey literature searches retrieved 322 citations and one epidemiological report from Rio Grande do Sul State Health Department, of which 284 met one or more exclusion criteria (Figure 1). A total of 39 relevant publications were identified.

The publications covered 72 of the 399 (18.04%) municipalities in Paraná, one of 295 (0.33%) in Santa Catarina, and one of 497 (0.40%) in Rio Grande do Sul. *Mg. migonei* was found in 54 municipalities of Paraná (Figure 2), in one municipality of Santa Catarina (Figure 3), and in one of Rio Grande do Sul (Figure 4).

Mg. migonei is often found in endemic areas. In a study carried out in Rio de Janeiro, a high frequency of captured *Mg. migonei* flies was reported. It was the second most captured vector in the 18 assessed endemic areas for VL; in some of these regions, *Lu. longipalpis* was not found at all (P. L. Costa et al., 2018b). The absence of the main vector in these regions shows the importance of secondary vectors in the transmission of leishmaniasis. Carvalho et al. (2010) detected *L. infantum* DNA in *Mg. migonei* in an endemic area for VL in the state of Pernambuco, where there were no reports of *Lu. Longipalpis*, suggesting a high adaptability of *L. infantum* to *Mg. migonei*. In the state of São Paulo, *Mg. migonei* is officially considered a secondary vector for the transmission of VL Leishmania species to humans and domestic animals, because disease transmission has been observed even in cases where the main vector was not detected (Aguiar & Vieira, 2018). The potential of *Mg. migonei* as a vector of *L. infantum* has been investigated not only in Brazil but also in South America as a whole (Moya et al., 2015; Salomón et al., 2010). A study in the city of La Banda, Argentina, reported cases of VL in humans and seropositive dogs, and the authors captured 151 sandflies, of which more than 90% were positive for *Mg. migonei*.

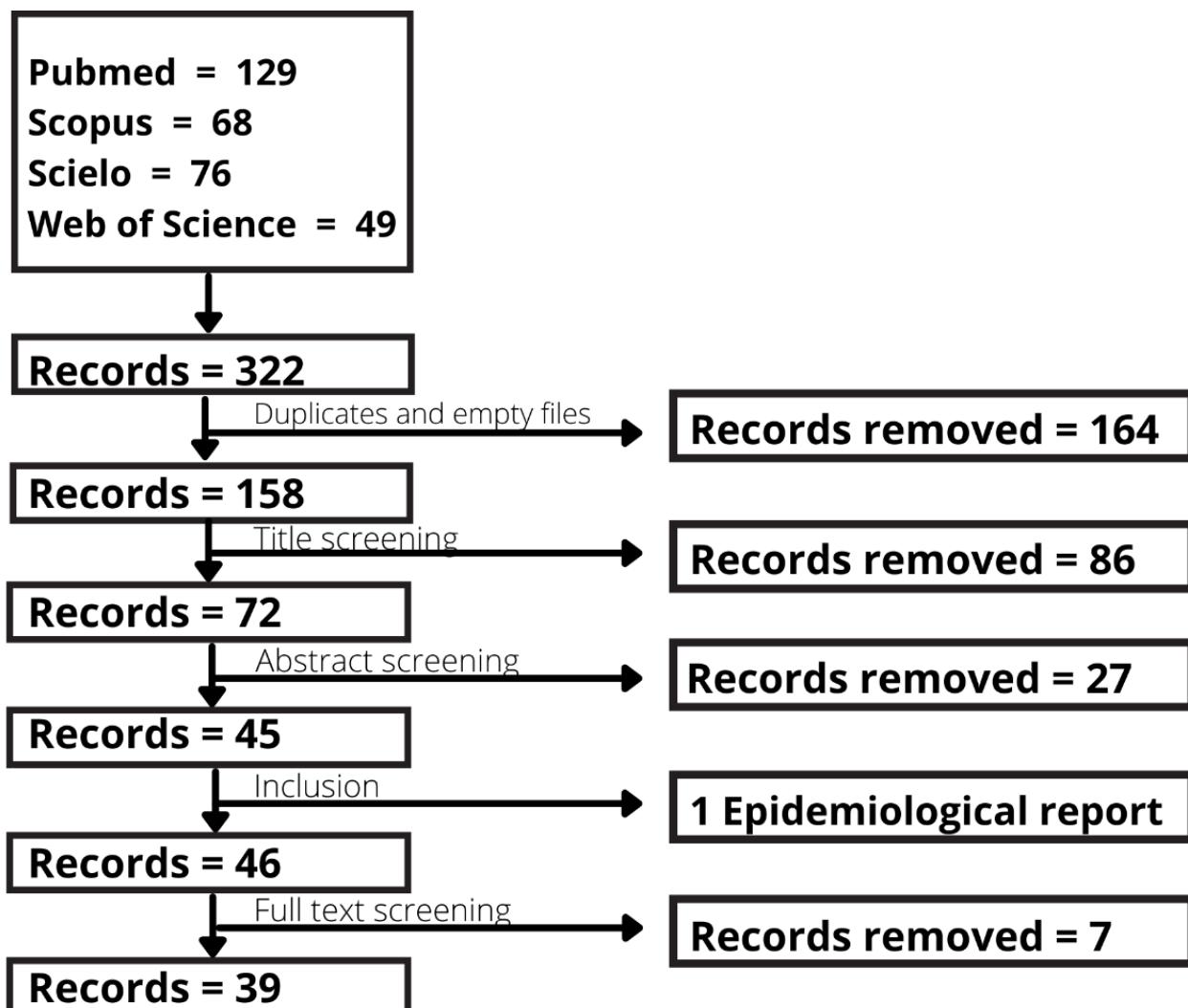


Figure 1. Flowchart showing article selection for the review

Experimental studies have not yet fully elucidated the infection characteristics and participation in the transmission of *L. infantum* protozoan by *Mg. migonei*, although this has been reported to be related to the development of the metacyclic forms of *L. infantum* in *Mg. migonei* (Guimarães et

al., 2016). The vectorial capacity among *Lu. longipalpis*, *Pintomyia fischeri* and *Mg. migonei* in transmitting *L. infantum* has been experimentally compared. Although *Mg. migonei* showed great blood meal capacity in dogs, *L. infantum* transmission was not observed (Ovallos, 2011).

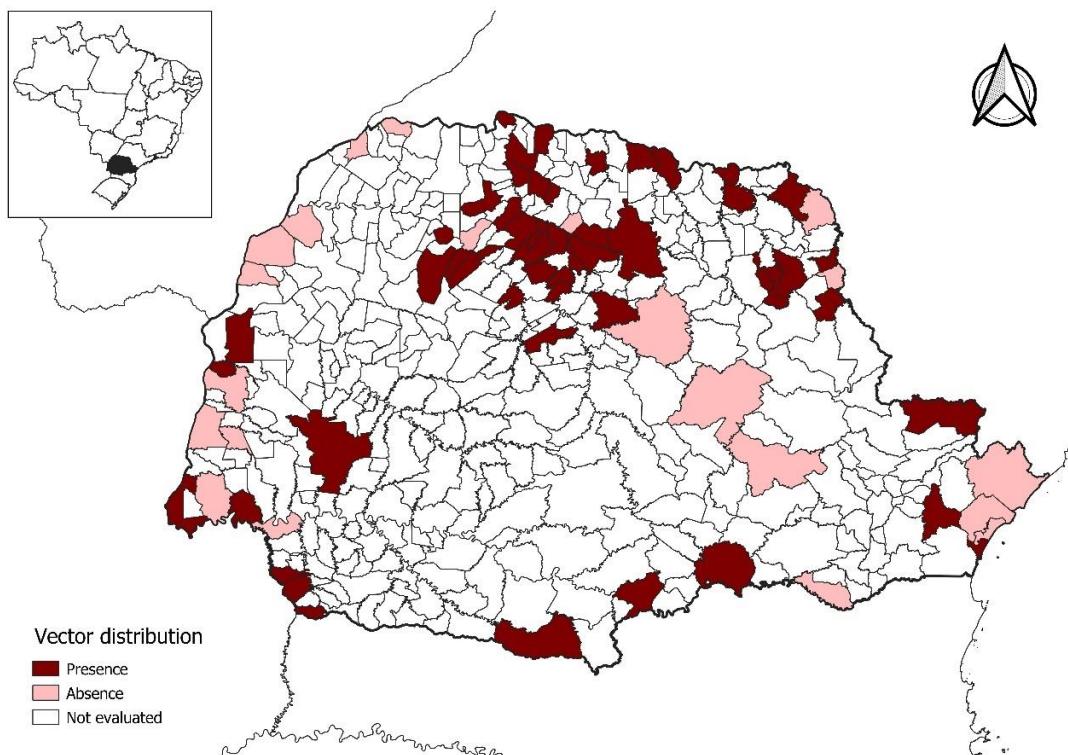


Figure 2. Spatial distribution of *Migonemyia migonei* in Paraná state, southern Brazil.

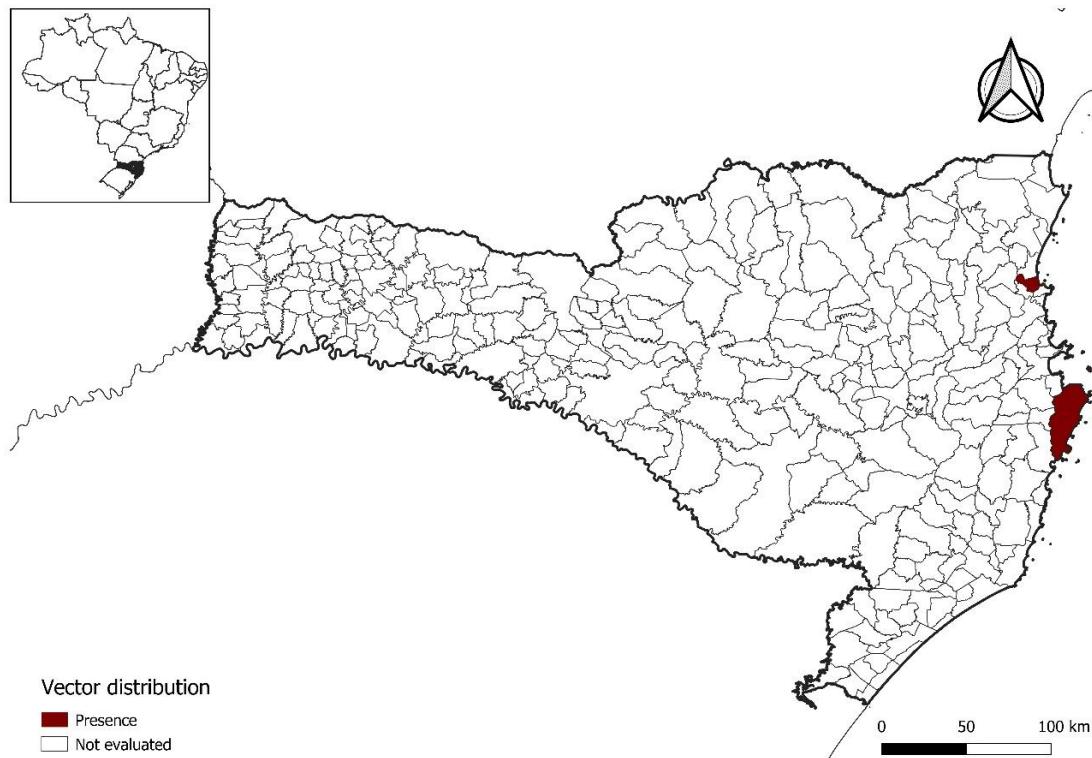


Figure 3. Spatial distribution of *Migonemyia migonei* in Santa Catarina state, southern Brazil.

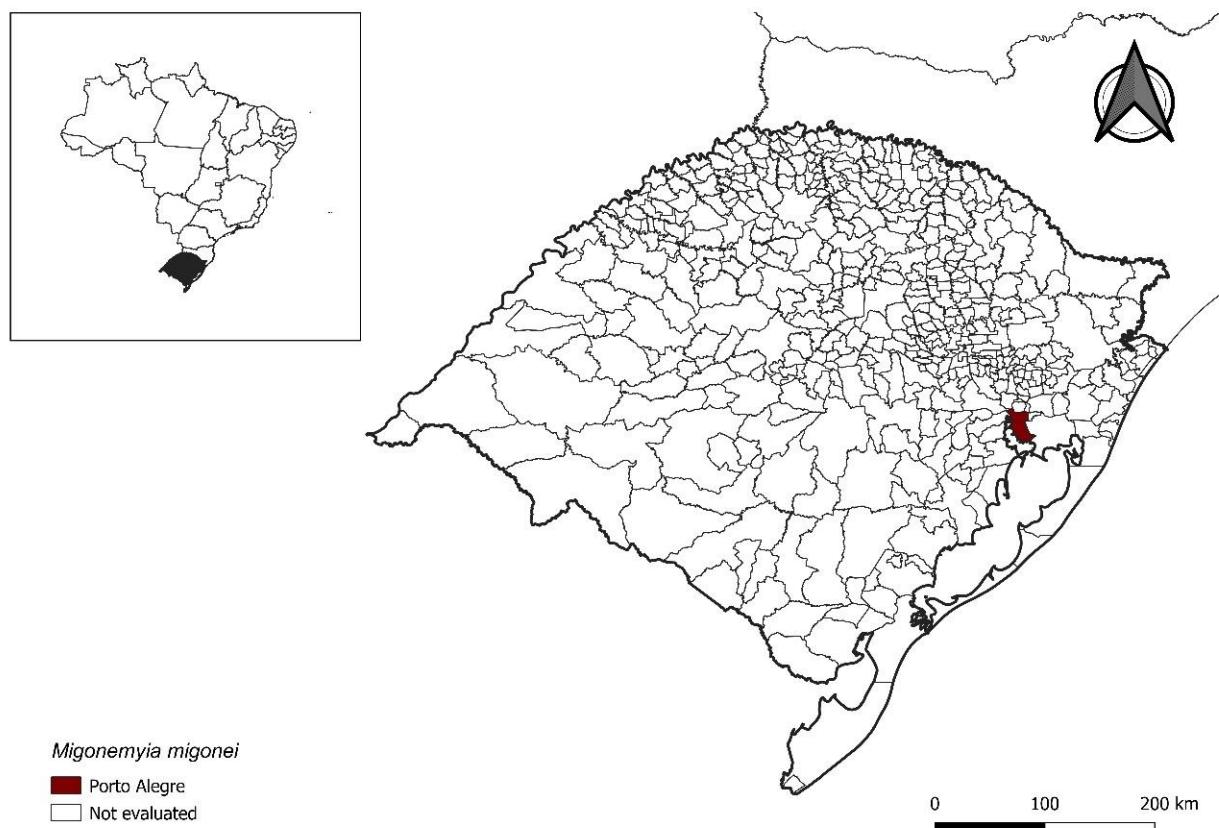


Figure 4. Spatial distribution of *Migonemyia migonei* in Rio Grande do Sul state, southern Brazil.

The possibility of *Mg. migonei* as a vector for *Leishmania* VL species is important to public health because it can favor the expansion of the disease to vulnerable silent receptor regions. These regions represent areas that have the vector and are geographically close to municipalities with canine and/or human transmission, but have not yet reported an autochthonous Leishmaniasis case (Chaves & Añez, 2004). These reports corroborate the need for constant surveillance on the spatial distribution of this potential vector and its possible association with VL cases (Salomón et al., 2010).

In Paraná, the primary Leishmaniasis vector has been chiefly detected; however the first sick dogs were only diagnosed in 2012 (R. C. F. Dias et al., 2020; Santos et al., 2012; Thomaz Soccoll et al., 2017). The first human case of VL was reported in 2016 in the western region of Foz do Iguaçu (Trench et al., 2016). The abundant presence of *Mg. migonei* in the state of Paraná has been observed since 1990 (Teodoro et al., 1991, 1993). In 37 municipalities in the state of Paraná, *Mg. migonei* was the third most abundant species of captured sandflies (A. M. Da Silva et al., 2008). Near the border between Paraná and São Paulo, 6.5% of 3,655 captured sandflies were *Mg. migonei* (Massafera et al., 2005).

In Santa Catarina, cases of VL started to receive greater attention from 2010 onwards with the emergence of autochthonous cases in dogs in the capital Florianópolis, including an outbreak in the region during this period (Figueiredo et al., 2012; Steindel et al., 2013). The hypothesis of *Mg. migonei* participation in VL cases in the state must be considered, because in a survey conducted by the State Health Department in 2015 of Florianópolis sandfly fauna, *Mg. migonei* was one of the most reported species (31.9%) of 1361 sandflies captured in regions with cases of the disease, but there was an absence of the main disease vector (unpublished data from Diretoria de Vigilância Epidemiológica, Santa Catarina). In another survey conducted by E. S. Dias et al. (2013), *Mg. migonei* was the second most reported sandfly, at 445 (30.21%) of 1,473 reported specimens.

In Rio Grande do Sul, autochthonous cases of VL in dogs emerged from 2008 in the São Borja municipality, including the capture of the primary vector *Lu. longipalpis*, and the first human case report in that municipality came the following year (Secretaria Municipal de Saúde de Porto Alegre, 2017; Secretaria Estadual de Saúde do Rio Grande do Sul, 2014). In this state there are also regions where, in addition to reported American cutaneous leishmaniasis, there have been confirmed cases of canine visceral leishmaniasis, all without the presence of the main disease vector - though *Mg. migonei* is one of the most abundant sandfly species in the area (Secretaria Municipal de Saúde de Porto Alegre, 2017; Rêgo et al., 2019; Secretaria Estadual de Saúde do Rio Grande do Sul, 2014). In Porto Alegre, the state capital, VL seropositive dogs were reported, and no primary vector was found, but *Mg. migonei*

was the most abundant sandfly identified, at 2,136 (62.88%) of 3,397 collected specimens. In an investigation conducted by the Municipal Health Department of Porto Alegre (2010), of 47 collected sandflies *Mg. migonei* (14.9%) was the third most abundant after *Nyssomyia neivai* (51.1%) and *Pi. fischeri* (34%). In all these studies, the secondary vector appears among the most captured (Secretaria Municipal de Saúde de Porto Alegre, 2010).

As the expansion and epidemiology of the disease unfolds, the emergence of cases of VL involving dogs and humans, in addition to the presence of the transmitting vector, is expected. It is naive to expect a complex disease to involve only one genus of vector in the southern region, so *Mg. migonei* must be considered as a potential part of the *Leishmania* life cycle. Knowing the spatial distributions of sandflies suspected to act as vectors of *L. infantum* can improve VL prevention and control in these regions (Brazil, 2014; D. N. C. C. Costa et al., 2018a; Sevá et al., 2016). It is critical to evaluate new patterns of transmission and the roles of these secondary vectors in the epidemiology of VL, and to strictly follow the plans of action, recommendations, and guidelines for the surveillance and control of leishmaniasis (Brazil, 2014, 2017).

Conclusion

Mg. migonei is widely distributed in the Paraná municipalities, with the northern region having the highest numbers in the state. Particular attention must be paid to the detection of VL in humans and animals where *Mg. migonei* is observed. Santa Catarina and Rio Grande do Sul may follow similar patterns of spatial distribution of *Mg.*

migonei; however, further studies are needed to confirm this hypothesis. Autochthonous cases of Leishmaniasis should be thoroughly investigated, as well as the distributions of sandflies in the vicinities of the cases, because different epidemiological approaches and prevention/control measures may be needed in each situation.

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