Evaluation of lymphatic filariasis in endemic area of Brazil where mass drug administration is not required

Ellyda Silva^a, Amanda Xavier^b, Elis Silva^a, Walter Barbosa Júnior^b, Abraham Rocha^{c,d}, Vania Freitas^e, Paula Oliveira^c, Ana Maria Aguiar-Santos^{b,c}, Cristine Bonfim^{b,f,g} and Zulma Medeiros^{b,a,b,c}

^aPrograma de Pós-graduação em Biociências e Biotecnologia em Saúde, Instituto Aggeu Magalhães (IAM), Fundação Oswaldo Cruz (FIOCRUZ), Recife, Pernambuco, Brasil; ^bPrograma de Pós-graduação em Ciências da Saúde, Universidade de Pernambuco (UPE), Recife, Pernambuco, Brasil; ^cServiço de Referência Nacional em Filariose, Departamento de Parasitologia, Instituto Aggeu Magalhães, Fundação Oswaldo Cruz (FIOCRUZ), Recife, Pernambuco, Brasil; ^dSecretaria de Saúde do Estado de Pernambuco, Laboratório do Hospital Otávio de Freitas, Recife, Pernambuco, Brasil; ^eSecretaria Municipal de Saúde de Jaboatão dos Guararapes, Diretoria de Vigilância em Saúde, Jaboatão dos Guararapes, Pernambuco, Brasil; ^fDiretoria de Pesquisas Sociais, Núcleo de Estudos em Estatísticas Sociais, Fundação Joaquim Nabuco (FUNDAJ), Recife, Pernambuco, Brasil; ^gPrograma de Pós-graduação em Saúde Coletiva, Universidade Federal de Pernambuco (UFPE), Recife, Pernambuco, Brasil

ABSTRACT

Mass drug administration (MDA) is the main counter-transmission strategy of the Global Programme to Eliminate Lymphatic Filariasis. In endemic countries, there are areas where MDA is not required. However, there is no standard approach in these areas, and studies are important to evaluate the epidemiological status. This study aimed to investigate lymphatic filariasis and strategies developed for its control in an area where MDA is not required. Together with the 2018 morbidity evaluation, a survey was conducted using point-of-care immunochromatographic test-AD12 tests for diagnostic screening in an area where MDA is not required. The methodology also included desk research based on Health Department reports of the control activities for lymphatic filariasis during 2003–2016. Among the 934 cases investigated in 2018, there was a 0.64% prevalence of circulating filarial antigen positive, comprising five adults and one 2-year-old child. Six patients aged 39–63 years had filarial disease. Fourteen surveys have already been conducted as control activities, and since 2009, there have been no positive cases. This study showed that the prevalence of antigenemia decreased from 2.97% in 2003 to 0.64% in 2018. Moreover, the transmission of filariasis infection was under control in this area. Our study provides insights into the surveillance phase by identifying areas of low transmission and where MDA is not required. Although we have not identified cases of filarial infection, there is a need to provide services that will provide assist those already affected with morbidity and help reduce and prevent disability.

KEYWORDS

Lymphatic filariasis;
Wuchereria bancrofti;
ICT card; mass drug
administration; Elimination;
Surveillance

Introduction

Lymphatic filariasis (LF) is a neglected tropical disease with chronic characteristics, with 1.4 billion people living in high-risk areas [1,2]. The International Task Force for Disease Eradication has defined LF as one of the six infectious diseases that are potentially 'eradicable.' The Global Programme to Eliminate Lymphatic Filariasis (GPELF) was therefore established in the early 2000s to prevent the spread of infection and reduce morbidity, thereby aiming to eliminate the disease by 2020 [3–5].

Mass drug administration (MDA) is GPELF's main strategy in interrupting the transmission of LF[6]. In 2017, the proportion of the population in endemic areas worldwide requiring MDA was 52.4%, with 465.4 million people treated in 37 countries with reported cases. Brazil is a GPELF signatory and conducted MDA between 2003 and 2017 in three municipalities of Pernambuco State: Recife, Olinda, and Jaboatão dos Guararapes, with the

exclusive use of diethylcarbamazine (DEC)[7]. Treatment was performed in focal areas, meeting the criteria established by each municipality [8–10].

In the municipality of Jaboatão dos Guararapes, socioenvironmental risk indicators (inadequate water supplies, inadequate sewage disposal and garbage collection, education and income level – S1) together with the prevalence of microfilaremia were described as tools for mapping areas to introduce GPELF strategies [11,12]. In 2002, 23,673 people were examined using the thick smear, and 14 priority districts for starting MDA were identified. The presence of family health units with trained professionals was also needed to conduct MDA[11].

In three of these priority districts, four locations were selected based on the highest rates of microfilaremia, poor sanitation conditions, and poverty: Cavaleiro (Alto da Colina and Baixa da Colina), Socorro (Quitandinha), and Sucupira (Retiro). Approximately 20,000 people

CONTACT Amanda Xavier ✉ amanda-xavier@hotmail.com Departamento de Parasitologia, Instituto Aggeu Magalhães, Fundação Oswaldo Cruz (FIOCRUZ), Av. Moraes do Rego, s/n, Cidade Universitária, Recife, Pernambuco 50670-420, Brasil

Supplemental materials data for this article can be accessed [here](#).

© 2019 Informa UK Limited, trading as Taylor & Francis Group

received treatment from 2006 to 2015. In the other 11 districts where MDA was not required, the strategy of surveys and individual treatment of microfilaremia was applied[11].

The number of districts receiving MDA in Jaboatão dos Guararapes was smaller than that initially mapped due to political decision supported by surveillance activities with individual DEC treatment for microfilaremia. Studies in these areas without treatment are necessary for continuous assessment of epidemiological status. Accordingly, this study aimed to investigate human LF infection by screening for circulating filarial antigen (CFA) for *Wuchereria bancrofti* using the point-of-care immunochromatographic test-AD12 (POC-ICT-AD12). Additionally, to understand the epidemiology of LF where MDA is not required, surveillance strategies developed by the Health Department to control this endemic disease were evaluated.

Materials and methods

LF survey

Jardim Jordão (8°08'43"S 34°56'12"W), a district of the municipality of Jaboatão dos Guararapes and an endemic area for LF in Pernambuco State, Northeast Brazil, was the location selected for the study. Here, there are 26,986 people living in 12,380 houses in an area of 3.97 km². Although this district has the highest rates of microfilaremia by the thick smear (2.78%) and the highest socioenvironmental risk in the study that set out the GPELF strategies in the municipality, MDA was not conducted because of technical difficulties such as the absence of family health units [11–13].

A cross-sectional study was conducted on residents aged > 2 years. The sample size was calculated based on an estimated microfilaremia prevalence of 2.78% [11], sampling error of 5%, and confidence interval of 95%, thus reaching 379 individuals. The houses were randomly selected using QGIS 2.18.

The rapid test used as diagnostic screening was POC-ICT (Alere, Inc., Scarborough, USA). According to the manufacturer's instructions, 100 µL of blood from fingerprick was transferred to the pad on the card, and the result was read after 10 min [14,15].

Positive results in the POC-ICT were investigated using circulating microfilariae and quantified using the polycarbonate membrane filtration technique with 3-mm pores (Nucleopore®) [16,17] and by searching for the 'filarial dance sign' using ultrasound [18,19]. To test for CFA, the enzyme-linked immunosorbent assay (ELISA) Og4C3-ELISA (TropBio® Pty Ltd, Townsville, Queensland, Australia) [20] and AlereTM filariasis test strip (FTS) [2,21,22] were used. For IgG4 detection through ELISA, two recombinant antigens were used: Wb123 [23] and Bm14 [14,24,25].

Estimation of morbidity load

All participants answered a questionnaire containing the following variables: age, sex, time of residence, previous use of DEC, and signs and symptoms of filarial disease. Individuals with any complaint of lymphedema, acute dermatolymphangioadenitis (ADLA), hydrocele, and chyluria were considered symptomatic[26].

Health Department database

Previous data were extracted from the Health Department reports of the municipality of Jaboatão dos Guararapes to understand activities aimed at LF surveillance in the Jardim Jordão district. Thick smear was performed in residents by spontaneous demand in mobile collection sites. We included surveys conducted between 2003 and 2016 and the vector control strategies, as well as the understanding of the epidemiology of LF.

Ethical considerations

The study was approved by the Research Ethics Committee of the FIOCRUZ-PE (CAEE: 65,910,217.8.0 000.5190).

Results

LF survey

A total of 934 POC-ICTs in 225 households were performed. Among those examined, 57.5% were female, with a mean age of 34.75 years (2–98), and 71.84% had lived in the municipality for more than 10 years. Table 1 shows the identification of six positive POC-ICT cases; hence, LF prevalence was 0.64%.

In the complementary research, six positive POC-ICT cases were amicrofilaremic and negative for the identification of adult worms through ultrasound and in the examinations for antigens by Og4C3-ELISA and FTS and for antibodies by Wb123-ELISA. Only one case was positive for Bm14-ELISA. No previous DEC treatment was reported in the positive cases.

Estimation of morbidity burden

Six presumed cases of filarial disease were identified among the 934 individuals examined. One man had acute dermatolymphangioadenitis (ADLA), and there were five cases of lymphedema (three women and two men), with ages from 39 to 63 years. Only one woman with lymphedema had already received previous DEC treatment. All morbidity cases were negative in the filarial infection investigation.

Table 1. Prevalence of lymphatic filariasis using POC-ICT, according to sex and age range in the district studied, Jardim Jordão, Jaboatão dos Guararapes, 2018.

Age range	Male			Female			Total		
	Number examined	Number of positive cases	%	Number examined	Number of positive cases	%	Number examined	Number of positive cases	%
2–4	28	0	0	14	1	7.14	42	1	2.38
5–9	36	0	0	34	0	0	70	0	0.00
10–14	49	0	0	49	0	0	98	0	0.00
15–19	36	0	0	46	1	2.17	82	1	1.22
20–29	36	1	2.77	68	0	0	104	1	0.96
30–39	54	1	1.85	84	0	0	138	1	0.72
40–64	128	1	0.78	189	1	0.53	317	2	0.63
≥65	30	0	0	53	0	0	83	0	0.00
Total	397	3	0.76	537	3	0.56	934	6	0.64

Health Department database

Between 2003 and 2016, the Health Department conducted 14 annual surveys and 10,769 (sample size range, 62–1,920) individuals were examined. The total number of examined individuals may include those who participated in the surveys twice or more. The highest prevalence was 2.97% in 2003, but after 2009, no positive LF cases were reported. All patients with microfilaremia received individual DEC treatment (Table 2).

As a vector investigation strategy, house visits were performed in time intervals of no more than 60 days to identify breeding sites for *Aedes* and *Culex* larvae. Such sites were treated with insecticides and bacteriological control of mosquito larvae. As the area is co-endemic for dengue and Zika virus, insecticides for adult mosquitoes have also been used during epidemics.

Discussion

The study showed a decrease in prevalence of microfilaremia from 2.97% in 2003 to 0.64% with POC-ICT in 2018. All POC-ICT positive cases were negative in the complementary investigation of circulating microfilariae, the ‘filarial dance sign’ using ultrasound, CFA (Og4C3- ELISA, FTS), and IgG4 detection (Wb123). Only one adult was Bm14 positive. These could be the result

of differences between antigen detection (activated by adult *W. bancrofti*) and antibody responses triggered by larval (Wb123) and adult worm (Bm14) exposures.

Studies suggest a loss of sensitivity to POC-ICT in low-endemicity settings, especially in individuals exhibiting low levels of CFA, which could hinder the monitoring of the LF elimination program[27]. Although there are limitations to the use of antigen markers during the surveillance period, the ability to monitor LF transmission status may be facilitated using more sensitive antibody markers [28]. However, the exclusive use of antibody markers creates difficulties in comparing information among the countries involved in the GPELF, since the main tools used in surveillance are antigen markers, especially in POC-ICT.

According to Braga et al [29], the interpretation of the POC-ICT result is observer dependent, which is the main confounding factor. Additionally, Simonsen and Mageša [30] suggest that POC-ICT provides false-positive results. The authors raise the issue that there is probably a ‘factor’ present in different concentrations in the blood of individuals aged ≥15 years living in LF endemic areas that contributes to the formation of the false positivity lines.

Pastor et al [31], indicated that the monoclonal antibody Bm14 can be a cross-reaction in individuals infected with *Strongyloides stercoralis* and *Ascaris lumbricoides*. As intestinal helminths are endemic in Brazil, with a high prevalence of *A. lumbricoides*, we can put forward the hypothesis that one or both of these parasites may produce positive Bm14 results in this case.

The area in question does not currently have a requirement for MDA, because the prevalence of the CFA is <1% [5]. However, there is a need for a surveillance model for the identification of new outbreaks or resurgence of infection [15,31, 32]. Since the reduction of the prevalence of microfilariae in this area means that mosquitoes can no longer transmit filariasis, to obtain definitive conclusions on this point, further studies, such as vector surveys, are needed. Molecular xenomonitoring can also be a useful tool for surveillance in areas where MDA is not required [33–35].

For the health services in areas of endemic filariasis, the thick smear is an economically feasible tool that is important in the present study. Antigen screening is the

Table 2. Surveys conducted using Health Department reports at the municipality of Jaboatão dos Guararapes for diagnosis of lymphatic filariasis in Jardim Jordão district, 2003–2016.

Thick smear	Number examined	Number of positive cases (%)	Number of positive cases in women	Number of positive cases in men
2003	908	27 (2.97)	—*	—*
2004	1914	26 (1.35)	06	20
2005	1542	22 (1.43)	03*	01*
2006	602	12 (1.99)	06	06
2007	526	4 (0.76)	01	03
2008	1920	7 (0.36)	02	05
2009	661	0	0	0
2010	543	0	0	0
2011	385	0	0	0
2012	520	0	0	0
2013	62	0	0	0
2014	114	0	0	0
2015	900	0	0	0
2016	172	0	0	0

most appropriate diagnostic tool for this evaluation, but PAHO/WHO (Pan Americana Health Organization/World Health Organization) donations are exclusively targeted on surveillance using a transmission assessment survey. Thus, there is also a need for additional donations for surveys in areas not requiring MDA, since endemic countries have economic difficulties in obtaining regular access to diagnostic kits.

The presence of lymphedema in the lower limbs was the most frequent complaint reported in this series of cases of filarial morbidity. Based on the prevalence of 0.64%, it could be inferred that there are approximately 170 individuals in the district who might need to participate in the program's morbidity management and disability prevention (MMDP) components, which are aimed at alleviating suffering among people with lymphedema and elephantiasis and improving their quality of life[36]. It is already established that initial acute attack of ADLA precipitates lymphedema for the first time in an affected limb (usually starting in childhood). Such repeated attacks later perpetuate and worsen lymphedema, leading to elephantiasis[37].

In this chronic phase, no filarial infection is detected since it may have developed as an initial precipitating factor. Moreover, similar recurrent infectious processes occurring in people in non-endemic areas are also causal agents in the progression of lymphedema. When there is advanced disease, these conditions are clinically indistinguishable from LF. Regardless of the certainty of the filarial etiology, the identification of cases of lymphedema in endemic areas is fundamental in the fulfillment of the strategies of the GPELF in the promotion of assistance to cases of morbidity.

The surveys conducted by the Health Department show that prevalence has decreased over the years to an absence of cases after 2009. This reduction was the result of the actions established by the Health Department, comprising annual surveys, treatment with DEC (6 mg/kg for 12 days) for microfilaremia, and the use of insecticide and biological control in the district for 14 consecutive years.

This study provides epidemiological information in areas where MDA is not required, including the identification of elderly individuals with positive antigen that may act as significant reservoirs of parasites, responsible for maintaining transmission[38]. However, the data on lymphedema and elephantiasis indicate the need to address individuals with this disease for MMDP components[39]. Based on this, Brazil can attempt to validate the elimination of LF as a public health problem.

Despite the decrease in prevalence of microfilaremia from 2.97% in 2003 to 0.64% with POC-ICT in 2018, the area still has a socioenvironmental risk for LF, an upsurge in the endemic disease being possible. Similar actions have been effective in arresting transmission in two endemic areas in Brazil: Maceió-AL [40] and Belém-PA

[41], highlighting the fact that there have also been major socioenvironmental improvements in both municipalities. Thus, there is a need for surveillance in areas where MDA is not required in GPELF countries with a socioenvironmental transmission risk.

Therefore, this study provides insights into the surveillance phase by identifying areas of lower transmission or areas where MDA is not required but which may be prone to the resurgence of LF transmission, owing to the existence of a socioenvironmental risk. Although we have not identified cases with filarial infection, there is a need to provide services to assist those already affected with morbidity and help reduce and prevent disability.

Acknowledgments

We would like to thank Alere Pty Ltd. for providing low-cost kits for this evaluation. The authors are grateful to the National Reference Center of Lymphatic Filariasis (NRCLF/IAM/FIOCRUZ) in Recife for their support in the laboratory procedures and the Health Department of Jaboatão dos Guararapes for the health system and fieldwork information.

Disclosure statement

No potential conflict of interest was reported by the authors.

Funding

This work was supported by the Coordenação de Aperfeiçoamento de Pessoal de Nível Superior [001]; Fundação de Amparo à Ciência e Tecnologia do Estado de Pernambuco [001]; Fundação de Amparo à Ciência e Tecnologia do Estado de Pernambuco [APQ 0359-4.06/13]- IBPG-0959-4.01/16.

ORCID

Amanda Xavier <http://orcid.org/0000-0001-9775-1078>
 Walter Barbosa Júnior <http://orcid.org/0000-0002-8301-6600>
 Ana Maria Aguiar-Santos <http://orcid.org/0000-0002-7243-7581>
 Cristine Bonfim <http://orcid.org/0000-0002-4495-9673>
 Zulma Medeiros <http://orcid.org/0000-0002-4434-955X>

References

- [1] World Health Organization. Global programme to eliminate lymphatic filariasis: progress report, 2016. *Wkly Epidemiol Rec.* 2017;92(40):594–607.
- [2] World Health Organization. Strengthening the assessment of lymphatic filariasis transmission and documenting the achievement of elimination: meeting of the neglected tropical diseases strategic and technical advisory group's monitoring and evaluation subgroup on disease-specific indicators. Geneva: 2016.

- [3] Ottesen EA, Duke BO, Karam M, et al. Strategies and tools for the control/elimination of lymphatic filariasis. *Bull World Health Organ.* **1997**;75(6):491–503.
- [4] Ottesen EA. The global programme to eliminate lymphatic filariasis. *Trop Med Int Health.* **2000**;5(9):591–594.
- [5] World Health Organization. Global programme to eliminate lymphatic filariasis: progress report. *Wkly Epidemiol Rec.* **2015**;91(39):489–504.
- [6] Ichimori K, King JD, Engels D, et al. Global programme to eliminate lymphatic filariasis: the processes underlying programme success. *PLoS Negl Trop Dis.* **2014**;8(12):e3228.
- [7] Aguiar-Santos AM, Medeiros Z, Bonfim C, et al. Epidemiological assessment of neglected diseases in children: lymphatic filariasis and soil-transmitted helminthiasis. *J Pediatr (Rio J).* **2013**;89(3):250–255.
- [8] Rocha A, Dos Santos EM, Oliveira P, et al. History of lymphatic filariasis control actions in Olinda, Pernambuco, Brazil. *Rev Patol Trop.* **2016**;45(4):339–348.
- [9] Center for Disease Control and Prevention. Lymphatic Filariasis: Elimination in the Americas. **2011**
- [10] Pernambuco. Secretaria Estadual de Saúde. Secretaria Executiva de Vigilância em Saúde. Plano Integrado de Ações para o Enfretamento às Doenças Negligenciadas no Estado de Pernambuco/ SANAR – 2015-2018 / Secretaria Estadual de Saúde. Secretaria Executiva de Vigilância em Saúde. Recife: Secretaria Estadual de Saúde. **2015**
- [11] Departamento de Saúde de Jaboatão dos Guararapes, unpublished data.
- [12] Bonfim CV, Netto MJE, Pedroza D, et al. A socioenvironmental composite index as a tool for identifying urban areas at risk of lymphatic filariasis. *Trop Med Int Health.* **2009**;14(8):877–884.
- [13] Brandão E, Bonfim C, Cabral D, et al. Mapping of *Wuchereria bancrofti* infection in children and adolescents in an endemic area of Brazil. *Acta Trop.* **2011**;120:151–154.
- [14] Weil GJ, Ramzy RMR. Diagnostic tools for filariasis elimination programs. *Trends Parasitol.* **2007**;23(2):78–82.
- [15] Rebollo MP, Bockarie MJ. Shrinking the lymphatic filariasis map: update on diagnostic tools for mapping and transmission monitoring. *Parasitology.* **2014**;141(14):1912–1917.
- [16] McMahon TF, Marshall JP, Vaughan DE. Bancroftian filariasis: a comparison of microfilariae counting techniques using counting chamber, standard slide and membrane (nuclepore) filtration. *Ann Trop Med Parasitol.* **1979**;73:457–464.
- [17] Rocha A, Lima G, Medeiros Z, et al. Circulating filarial antigen in the hydrocele fluid from individuals living in a bancroftian filariasis area - Recife, Brazil - Detected by the monoclonal antibody Og4C3-assay. *Mem Inst Oswaldo Cruz.* **2004**;99(1):101–105.
- [18] Dreyer G, Pimentael A, Medeiros Z, et al. Studies on the periodicity and intravascular distribution of *Wuchereria bancrofti* microfilariae in paired samples of capillary and venous blood from Recife, Brazil. *Trop Med Int Health.* **1996**;1(2):264–272.
- [19] Fox LM, Furness BW, Haser JK, et al. Ultrasonographic examination of Haitian children with lymphatic filariasis: A longitudinal assessment in the context of antifilarial drug treatment. *Am J Trop Med Hyg.* **2005**;72(5):642–648.
- [20] More S, Copeman D. A highly specific and sensitive monoclonal antibody-based ELISA for the detection of circulating antigen in bancroftian filariasis. *Trop Med Parasitol.* **1990**;41(4):43–46.
- [21] Chesnais CB, Missamou F, Pion SD, et al. Semi-quantitative scoring of an immunochromatographic test for circulating filarial antigen. *Am J Trop Med Hyg.* **2013**;89(5):916–918.
- [22] Weil GJ, Curtis KC, Fakoli L, et al. Laboratory and field evaluation of a new rapid test for detecting *Wuchereria bancrofti* antigen in human blood. *Am J Trop Med Hyg.* **2013**;89(1):11–15.
- [23] Kubofcik J, Fink DL, Nutman TB. Identification of Wb123 as an early and specific marker of *Wuchereria bancrofti* infection. *PLoS Negl Trop Dis.* **2012**;6(12):e1930.
- [24] Weil GJ, Curtis KC, Fischer PU, et al. A multicenter evaluation of a new antibody test kit for lymphatic filariasis employing recombinant *Brugia malayi* antigen Bm-14. *Acta Trop.* **2011**;120(1):S19–22.
- [25] Nunes LV, Rocha A, Araújo J, et al. Lymphatic filariasis: surveillance action among immigrants from endemic areas, Acre state, Brazilian Amazon. *Asian Pacific J Trop Dis.* **2016**;6(7):521–526.
- [26] Netto MJ, Bonfim C, Brandão E, et al. Burden of lymphatic filariasis morbidity in an area of low endemicity in Brazil. *Acta Trop.* **2016**;163:54–660.
- [27] Gounoue-Kamkumo R, Nana-Djeunga HC, Bopda J, et al. Loss of sensitivity of immunochromatographic test (ICT) for lymphatic filariasis diagnosis in low prevalence settings: consequence in the monitoring and evaluation procedures. *BMC Infect Dis.* **2015**;15:579–586.
- [28] Won KY, Robinson K, Hamlin KL, et al. Comparison of antigen and antibody responses in repeat lymphatic filariasis transmission assessment surveys in American Samoa. *PLoS Negl Trop Dis.* **2018**;12(3):e0006347.
- [29] Braga C, Dourado MI, Ximenes RA, et al. Field evaluation of the whole blood immunochromatographic test for rapid bancroftian filariasis diagnosis in the northeast of Brazil. *Rev Inst Med Trop Sao Paulo.* **2003**;45(3):125–129.
- [30] Simonsen PE, Magesa SM. Observations on false positive reactions in the rapid NOW filariasis card test. *Trop Med Int Health.* **2004**;9:1200–1202.
- [31] Pastor AF, Rocha A, Cassemiro KD, et al. Evaluation of the recombinant antigens Wb14 and WbT for the capture antibody diagnosis of lymphatic filariasis. *Memórias Inst Oswaldo Cruz.* **2018**;113(5):1–8.
- [32] Dorkenoo, Bronzan R, Yehadj D, et al. Surveillance for lymphatic filariasis after stopping mass drug administration in endemic districts of Togo, 2010–2015. *Parasit Vectors.* **2018**;11(1):244–252.
- [33] Sheel M, Sheridan S, Gass K, et al. Identifying residual transmission of lymphatic filariasis after mass drug administration: comparing schoolbased versus community-based surveillance - American Samoa. *PLoS Negl Trop Dis.* **2016**;12(7):e00006583.
- [34] Brant TA, Okorie PN, Ogunmola O, et al. Integrated risk mapping and landscape characterisation of lymphatic filariasis and loiasis in South West Nigeria. *Parasite Epidemiol Control.* **2018**;28(3):21–35.
- [35] Mehta PK, Rauniyar R, Gupta BP. Microfilaria persistent foci during post MDA and the risk assessment of resurgence in India. *Trop Med Health.* **2018**;46(25):1–6.
- [36] Chandrasena N, Premaratna R, Gunaratna IE, et al. Morbidity management and disability prevention for

- lymphatic filariasis in Sri Lanka: current status and future prospects. *PLoS Negl Trop Dis.* [2018](#);12(5): e0006472.
- [37] Shenoy RK. Clinical and pathological aspects of filarial lymphedema and its management. *Korean J Parasitol.* [2008](#);46(3):119–125.
- [38] Harris JR, Wiegand RE. Detecting infection hotspots: modeling the surveillance challenge for elimination of lymphatic filariasis. *PLoS Negl Trop Dis.* [2017](#);11(5): e0005610.
- [39] World Health Organization. Validation of elimination of lymphatic filariasis as a public health problem. WHO Guidance & Forms. [2017](#)
- [40] Fontes G, Rocha EM, Brito AC, et al. Lymphatic Filariasis in Brazilian Urban Area (Maceió, Alagoas). *Memórias Inst Oswaldo Cruz.* [1998](#);93(6):705–710.
- [41] Freitas H., Vieira JB, Braun R, et al. Workshop para avaliação da situação epidemiológica da filariose linfática no Município de Belém, PA. *Rev Soc Bras Med Trop.* [2008](#);41(2):212–216.