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Knowledge and practices on lymphatic filariasis in patients with filarial morbidity in an endemic area in Northeastern Brazil

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Background: Lymphatic filariasis (LF) is a stigmatizing and debilitating disease that represents a significant global public health challenge. Information regarding the knowledge and practices of individuals with filarial morbidities is limited, and this understanding is crucial for the implementation of effective control strategies. This study aimed to investigate the knowledge and practices of individuals with filarial morbidity residing in two intervention areas of the Elimination Program in the city of Olinda, Brazil.

Methods: A cross-sectional study was carried out with residents who reported filarial morbidity in 2010, four years after the start of mass drug administration, in the intervention areas of the LF Elimination Program in the city of Olinda, Brazil. The knowledge and practices of patients with reported filarial morbidity in an endemic area were scrutinized using a semi-structured questionnaire to collect pertinent information. Data were analyzed utilizing the R language version 3.6.1.

Results: Filarial morbidity was reported in 338 patients. Dermatolymphangioadenitis emerged as the most frequently reported clinical form (50.9%). Mosquito bites were the most commonly cited form of transmission, accounting for 296 cases (87.6%). Approximately 80% (266) confirmed the adoption of prevention measures. Participants reported that the treatment involved the administration of medication. The existence of a cure for parasitosis was indicated by 212 subjects (62.7%).

Conclusions: Individuals with reported filarial morbidity exhibit varying levels of conceptions, knowledge, and practices regarding the disease, despite residing in

an endemic area and receiving consistent visits from family health teams. Health services must identify shortcomings in this approach to minimize disparities, thereby enabling health education to effectively contribute to disease control and elimination in the municipality.

KEYWORDS

knowledge, practices, lymphatic filariasis, morbidity, Brazil

Introduction

Lymphatic filariasis (LF) is a neglected tropical parasitic disease caused by nematode helminths of the *Wuchereria bancrofti* and *Brugia* spp species. The disease is transmitted by the bite of different species of mosquitoes, mainly *Anopheles* in Africa and *Culex* in the Americas (1). It is estimated that around 882 million people are currently at risk of acquiring filarial infection because they live in 44 countries with active transmission. Approximately 36 million people remain with manifestations of chronic diseases. As part of the actions established by the Global Programme to Eliminate Lymphatic Filariasis (GPELF), the Mass Drug Administration (MDA) of around 9 billion doses has been performed since the beginning of the program, leading to a reduction in the number of infected people from 199 million in 2000 to 51 million in 2018 (1, 2).

Lymphatic filariasis is considered an important cause of physical disability because of its disfiguring and disabling sequelae (3) that lead to social stigmatization, reduced work opportunities (economic losses), and negatively affect the quality of life of those affected, in addition to increasing costs of health services (4). Filarial morbidity in chronic conditions most commonly leads to the development of swelling of the limbs (lymphedema or elephantiasis - acute dermatolymphangioadenitis—ADLA), testicles (hydrocele) and breasts. Other less commonly reported clinical expressions include swelling of the vulva and rheumatic and respiratory problems (5).

Considering the problem on a global scale, in 2000, the World Health Organization (WHO) launched the GPELF with the goal to eliminate LF by 2030 using strategies based on two main components: prevent the spread of infection through the large-scale annual treatment of all eligible people in an area or region where the infection is present; and alleviate the suffering caused by LF by providing the recommended essential package of care (2).

Faced with the challenge of ensuring the success of GPELF actions, the WHO draws attention to the importance of obtaining the knowledge, attitudes and practices (KAP) of the target population where the treatment intervention for a given endemic disease will be performed as a foundation for health promotion campaigns in the scope of public health (6, 7). Lack of knowledge about the disease and behavior of seeking to improve health conditions can improve or interfere with the effectiveness of

control measures. Thus, feedback from the population regarding knowledge and practices on LF can greatly enhance the coordination of National Elimination Programs. The information obtained through this tool would greatly help the GPELF to direct the actions and procedures to be adopted in the communities for a better adherence of the population to disease control interventions. Furthermore, National Programs to eliminate LF involving the management and care of those with morbidity increase the population's awareness about the disease and adherence to treatment (7).

In Brazil, LF is exclusively caused by W. bancrofti and transmitted by the Culex quinquefasciatus mosquito (8). Currently, the Recife Metropolitan Region, in the state of Pernambuco, is the remaining focus of LF in Brazil, and covers the cities of Recife, Olinda, Jaboatão dos Guararapes and Paulista (9, 10). The interventions to eliminate LF in these areas were implemented between 2003 and 2017 (11-13). Importantly, unlike most other LF-endemic countries, the Brazilian Ministry of Health decided to use only the single-dose diethylcarbamazine citrate (DEC) monotherapy for MDA, citing lack of evidence that DEC-albendazole coadministration was more effective than DEC alone (11, 14, 15). By 2018, these cities had halted MDA and implemented TAS 2 and TAS 3, during which no infected children were identified (15). Until the beginning of treatment implementation, there were no studies in Brazil evaluating knowledge and practices the KAP.

The goal of this study was to investigate the knowledge and practices of individuals with filarial morbidity residing in two intervention areas of the Elimination Program in the city of Olinda. The study data will contribute to improving strategic information, education and communication activities aimed at assisting patients in LF endemic areas.

Methods

Design and study area

A cross-sectional study was conducted with residents who reported filarial morbidity (RFM) in intervention areas of the LF Elimination Program in the municipality of Olinda, located in the

Metropolitan Region of Recife, state of Pernambuco, Brazil. It encompasses a territorial area of 41,300km² and is divided into 31 urban neighborhoods. As of 2022, the population was 349,976 inhabitants (16).

Actions to control LF transmission in the municipality commenced in 2005. Neighborhoods with microfilaremia prevalence exceeding 1% and a high socio-environmental risk of transmission were incorporated into the MDA. Treatment initiation took place in the Alto do Sol Nascente neighborhood, employing a door-to-door supervised treatment strategy that expanded across 17 neighborhoods (17–19). At the time, measures to identify and monitor morbidity cases had not yet been implemented in the municipality (20).

The study focused on the neighborhoods of Alto da Bondade and Alto da Conquista, characterized by a pre-MDA antigenemia prevalence of approximately 10% in schoolchildren who underwent MDA between 2007 and 2013, achieving treatment coverage exceeding 65% (18, 21). The inclusion criteria comprised patients with RFM (erysipelas-ADLA, lymphedema, elephantiasis, chyluria and hydrocele) identified and registered by Community Health Agents (CHA) during home visits conducted from 2007 and 2010 in all residences within the selected neighborhoods. The complaint of filarial morbidity was identified using a panel of representative images depicting various clinical manifestations related to filarial morbidity (22).

Data collection

Data collection took place in the months of April and May 2010, four years after the start of mass drug administration. Individual data concerning morbidity complaints were gathered using a semi-structured questionnaire adapted from the study with patients in Ghana (23). The questionnaire comprised both open-ended and multiple-choice questions. Information on interviewees' knowledge regarding the transmission, diagnosis, treatment, and cure for lymphatic filariasis, as well as practices related to individual measures to prevent mosquito bites and combating the vector was collected.

Variables were categorized as follows: information about transmission, diagnosis, treatment, and cure, classified as adequate (good), regular and inadequate (insufficient). The diagnosis and cure variables included only two dimensions; adequate (good) or inadequate (insufficient). Variables related to the identification of practices in seeking service, avoiding mosquito bites and combating the vector were comparatively described by sex, age group, and literacy status.

Data analysis

The frequency distribution of individual characteristics and knowledge about filariasis in the study population were outlined. The association of categorical variables with the type of morbidity was made using Pearson's Chi-square test. Descriptive levels were measured utilizing a Monte Carlo simulation with 10,000 replications, given that numerous cells in the contingency tables had values lower than 5.

Key questions pertaining to transmission, treatment, and protective measures, along with their relative frequencies, were considered in the knowledge measurement. The instrument for measuring knowledge about lymphatic filariasis (score) was developed through multiple correspondence analysis (MCA), utilizing the first dimension generated by the technique.

Multiple correspondence analysis is a multivariate statistical analysis technique facilitating dimensionality reduction for categorical data based on the association between the categories of analyzed variables (24). This reduction generates new variables (dimensions), representing linear combinations of weights assigned to each category of variables included. The application of MCA to variables yields dimensions to which the total variance of the original system is allocated in an ordinal manner, with dimension 1 having the highest quantity of general variance and dimension p having the smallest.

For an easier interpretation of the score, its scale was transformed to range from 0 to 100; 0 indicates high knowledge and 100 indicates low knowledge. The following formula was used to obtain the score on the new scale:

$$Y^* = \frac{Y - \min(Y)}{\max(Y) - \min(Y)}$$

Knowledge groups were created utilizing the k-means segmentation algorithm with the elbow method employed to determine the optimal number of groups.

Subsequently, after establishing the knowledge score groups, the behavior concerning various variables was investigated. The sample used to generate the knowledge score did not contain missing values for any of the questions, ensuring a consistent number of observations for all analyzed variables.

All computations were conducted using the R language version 3.6.1, placing emphasis on the FactoMineR package version 2.0 to perform the MCA and the Rcompanion package version 2.3.25 for the permutation median comparison test. Monte Carlo simulations and all calculations involving randomness were performed with seed 17052020.

Ethical considerations

The interviews for the questionnaire application were conducted following the participants' or their legal guardian's authorization and the signing of the informed consent form. In the case of minors, the information was conveyed to parents or the legal guardian, who responded on their behalf. The study received approval from the Research Ethics Committee of the Centro de Pesquisas Aggeu Magalhães - CEP/CPqAM/FIOCRUZ under number CAAE 0054.0.000.095–09.

Results

In this study, 338 individuals (229 from the Alto da Bondade and 109 from Alto da Conquista) of both sexes with an average age of 51.2 years, ranging from 17 to 92 years, were interviewed. Table 1 provides the characterization of interviewees, where 170 (50.3%) were male, the majority identified as mixed race/brown skin color (136 or 40.2%) and 213 (63%) were literate. The most frequently reported clinical form was Acute Dermatolymphangioadenitis (ADLA or erysipelas) at 50.9%, followed by hydrocele at 34.0% and lymphedema at 14.2%, all reported in females.

Knowledge of lymphatic filariasis

The primary mode of transmission reported by respondents was the mosquito bite, (296 or 87.6%). About 80% (266) adopted some preventive measure, the most common being the use of fans (244 or 91.7%). Concerning methods to prevent mosquito proliferation, care for the septic tank (292 or 86.4%) and the water tank (280 or 82.8%) predominated (Table 2). Regarding diagnosis, 292 (86.4%) respondents were aware that filariasis is diagnosed through a blood test (Table 2).

The knowledge and practices of interviewees related to the treatment of filariasis are presented in Table 3. Of the interviewees, 125 (37.0%) stated that filariasis can be treated and for 119 (95.2%) of them, this treatment can be done with medication. The existence of a cure for the parasitosis was reported by 212 (62.7%) individuals. Approximately 60% (198) of respondents had already undergone treatment. Among those who did not undergo treatment, the main reason given was not being able to schedule an appointment (37 or

TABLE 1 Sociodemographic and health characteristics of respondents.

Variable	Categories	N	%
Sex (n=335) ^a	Male	170	50.3
	Female	165	48.8
	White	90	26.6
Race/color (n=314) ^b	Black	88	26.0
	Mixed race/Brown	136	40.2
Able to read and write (n=314) ^c	Yes	213	63.0
	No	101	29.9
Type of morbidity (n=334) ^d	Lymphedema	47	13.9
	Hydrocele	115	34.0
	ADLA	172	50.9
Receives visits from CHAs (n=313) ^e	Yes	311	92.0
	No	2	0.6

ADLA, Acute dermatolymphangioadenitis; CHA, Community Health Agent. $^{a)}0.9\%$ (N = 3); $^{b)}7.1\%$ (N = 24); $^{c)}7.1\%$ (N = 24); $^{d)}1.2\%$ (N = 4); $^{c)}7.4\%$ (N = 25).

TABLE 2 Respondents' knowledge with filarial morbidity in an endemic area in northeastern Brazil, about transmission and ways to prevent lymphatic filariasis.

Transmission and prevention				
	Mosquitoes	296	87.6	
	Poor personal hygiene	130	38.5	
	Rats	122	36.1	
	Water	113	33.4	
Assumed method	Flies	107	31.7	
of transmission*	Excessive work	56	16.6	
	Birds	55	16.3	
	Food	35	10.4	
	Direct contact with people	35	10.4	
	Sex	19	5.6	
Did you use any	Yes	266	78.7	
preventive measures? (n=312)	No	47	13.9	
	Fan	244	91.7	
	Insecticide	111	41.7	
	Mosquito net	110	41.4	
Protection against	Moquito coil	75	28.2	
mosquito bites*	Repellent	52	19.5	
	Bonfire	16	6.0	
	Censer	6	2.3	
	Door and window screens	5	1.9	
	Keep the skeptic tank closed	292	86.4	
	Keep the water tank closed	280	82.8	
	Sand in plant pots	211	62.4	
	Gutter cleaning	155	45.9	
Control of mosquitoes*	Insecticide	147	43.5	
	Avoid construction and demolition debris around the home	138	40.8	
	Putting fish in reservoirs	24	7.1	
Diagnosis*	Blood test	292	86.4	
	Onset of swelling	118	34.9	
	Stool examination	116	34.3	
	Urine analysis	116	34.3	
	Heart examination	61	18.0	
	Endoscopy	43	12.7	
	Blood pressure test	39	11.5	
	Others	43	12.7	

*Multiple answers.
Missing values: a) 7.4% (N = 25).

TABLE 3 Respondents' knowledge and practices regarding the treatment of lymphatic filariasis.

Variable	Categories	N	%
Is there treatment?	Yes	125	37
is there treatment:	No	181	53.6
	Medication	119	95.2
	Physician	80	64
How can filariasis be	Medical exam	74	59.2
treated?*	Going to church	16	12.8
	Spiritual healer	9	7.2
	Tea	7	5.6
D (1)	Yes	212	62.7
Does filariasis have a cure?	No	126	37.3
Have you been treated or	Yes	198	58.6
are you undergoing treatment?	No	111	32.8
	Could not get an appointment	37	33.3
	Did not want to go	29	26.1
Reasons for not having	Does not have time	6	5.4
undergone treatment	Does not believe in healing	3	2.7
	Does not know	17	15.3
	Others	17	15.3
Have you searched any	Yes	158	46.7
services to undergo treatment	No	156	46.2
	Family Health Unit	89	56.3
	Hospital	87	55.1
	Medical center	31	19.6
	Self-medication	12	7.6
What type of service have you sought?	Spiritual healer	7	4.4
	Church	3	1.9
	African derived religion	2	1.3
	Spiritist center	1	0.6
Have you done	Yes	126	79.7
the treatment?	No 31		19.6
	Physician	120	95.2
Who prescribed	Nurse	2	1.6
the treatment?	Relative	1	0.8
	Other	1	0.8
Could the service accessed	Yes	90	71.4
treat the disease?	No	33	26.2

33.3%). When asked whether they had sought any health service, 46.7% (158) answered yes. Family health units (89 or 56.3%) and hospitals (87 or 55.1%) were the main health services mentioned. Almost 80% (126) followed the indicated treatment, which was prescribed by a physician (120 or 95.2%) and reported that the accessed health service was able to treat them (90 or 71.4%).

Table 4 displays how the knowledge score was formulated, segmented into four groups. The positive weights surpassed negative weights. Questions yielding higher scores for obtaining a low score (indicating high knowledge) were related to awareness of preventive measures, treatment availability, medication usage, and preventive actions like cleaning drains. Conversely, questions leading to higher scores (indicating low knowledge) related to actions like keeping the septic tank closed and taking steps to avoid mosquito bites.

The concentration of individuals in knowledge group exhibited homogeneity in frequency distribution. However, the knowledge group categorized as "bad" was approximately twice as extensive as the other groups. A significant association was observed between the variables: "sex", "literacy", "morbidity", and knowledge levels (Figure 1). Women outperformed in all knowledge groups. The morbidity variable also demonstrated a statistically significant association among different knowledge groups, suggesting a pattern where individuals with hydrocele are less likely to possess better knowledge, followed by those with lymphedema and ADLA. Additionally, respondents reporting ADLA displayed greater knowledge about filariasis (33.9%).

Discussion

The study demonstrated that individuals with RFM in an endemic area undergoing MDA in Brazil generally possess a good level of information about knowledge and practices related to the transmission, prevention, treatment, and diagnosis of LF. A subsequent study in the same study area supports these findings, since nearly all individuals recognized LF as a disease and associated it with chronic forms (21). This contrasts with studies conducted before MDA interventions, where individuals with clinical forms of FL often did not link them to filariasis, attributing them to heredity or supernatural factors, particularly "demonic spirits" (25–27).

In this study, hydrocele was the most frequently reported clinical form, differing from studies showing a higher frequency of lymphedema (27, 28). The prevalence of hydroceles was 2.45 times higher than reported lymphedema, aligning with the study by Machenzie and Mante in 2020 (29). These findings are significant for health services, as the psychosocial burden of hydrocele sufferers affects individuals, their family, and the community (28).

Regarding CHA visits, most interviewees reported receiving regular visits with CHA providing LF-related information. In many cases, these agents are acknowledged by community as "family members", instilling confidence, and sometimes they even have free access to homes. However, the periodic home visits by CHA were not sufficient to significantly influence the participants' knowledge levels about filariasis.

TABLE 4 Weights and questions relating to the knowledge score in conjunction with the score groups.

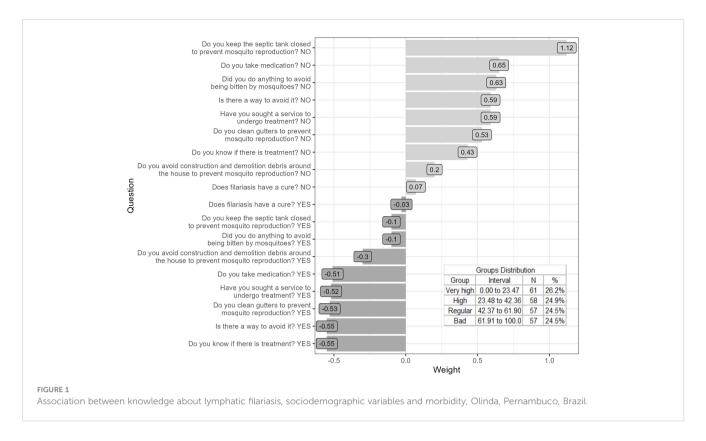
Questions			Answer	Weight	
Is there a way to avoid it?		Yes	-0.55		
		No	0.59		
			Yes	-0.52	
	Have you sought a service to undergo treatment?			No	0.59
	Do you know if there is treatment?			Yes	-0.55
				No	0.43
	Do you take medication?			Yes	-0.51
				No	0.65
	Does filariasis have a cure?			Yes	-0.03
	Does mariasis	s nave a cure:		No	0.07
	Did you do anything to avoid being bitten by mosquitoes?			Yes	-0.10
,				No	0.63
			Yes	-0.10	
Do you	Do you keep the septic tank closed to prevent mosquito reproduction?			No	1.12
				Yes	-0.53
Do you clean gutters to prevent mosquito reproduction?			No	0.53	
			Yes	-0.30	
Do you avoid constru	Do you avoid construction and demolition debris around the house to prevent mosquito reproduction?			No	0.20
Group	Group Interval			N	%
Very high	0.00	to	23.47	61	26.18
High	23.48	to	42.36	58	24.89
Regular	42.37	to	61.90	57	24.46
Bad	61.91	73.43	100.00	57	24.46

This study revealed that individuals with reported morbidity in the assessed areas had high understanding of how LF is transmitted. Most RFM in the present study knew that LF is transmitted through mosquito bites. Our findings align with some studies (26, 30, 31). The robust knowledge about LF transmission may result from the effective MDA coverage in the studied areas (21, 32). In contrast to these studies, a 2017 study in the same area reported that only 20% of those interviewed had knowledge about how LF is transmitted (21). Some other studies demonstrated the same (33, 34).

According to our findings, the majority of RFM used at least one means of protection to minimize or reduce human-mosquito contact. In our study the most cited means of protection were the fan, followed by insecticide and mosquito nets. However, a study in the Republic of Guinea (27) found an inverse order of the means of protection used by the population. This difference may be related to these populations' access to electronic equipment, as purchasing power is linked to their way of life, and the fan is more expensive than the mosquito net. Another hypothesis would be related to the lack of recognition of ways to minimize contact with the mosquito, reflecting a lack of interest and knowledge of the disease's implications (35).

In the present study, most interviewees (86.4% and 95.2%) knew that LF diagnosis involves a blood test, and its treatment typically includes medication, respectively. Furthermore, 62.7% believed in a cure, and 60.0% had already undergone treatment. In contrast to some studies, where 28.4% knew about the blood test for LF diagnosis and 96.1% were unaware of the treatment used for LF (30, 31), our study demonstrates higher awareness. Moreover, 80% of interviewees underwent treatment at the community's primary health care facility, unlike other endemic areas where patients face challenges traveling long distances to reach the health centers, leading them to resort to healers in many situations (34).

Individuals with hydrocele exhibited the least knowledge about LF among the identified clinical forms. A study in Nepal aligns with this finding, as hydrocele sufferers often did not attribute this clinical form to LF, nor recognize the mosquito as the disease transmitter (36). The authors also highlight that most hydrocele sufferers attributed the development of this clinical form to exhaustive physical work and sexual activity outside of marriage. Conversely, ADLA patients, mostly women, demonstrated greater knowledge about LF. The enhanced knowledge of ADLA patients



may result from women's presence at home, receiving constant visits from CHA, and women's increased health care-seeking behavior, especially during acute attacks when they receive health care and information about the disease.

Acute dermatolymphangioadenitis emerged as the most frequent complaint in the study, consistent with a morbidity report conducted in the municipality of Jaboatão dos Guararapes, Brazil (22). Similar results were observed in Haiti, particularly among women (14). The epidemiological association between the frequency/incidence of ADLA attacks serves as a sensitive indicator for the progression of lymphedema severity. A study by Dreyer and Addiss in 2000 in Brazil demonstrated that the management of lymphedema through hygiene, elevation of the affected limb, and treatment of interdigital lesions significantly reduces the frequency and duration of ADLA attacks (37). This was confirmed in a recent study, emphasizing the strong epidemiological association between repeated ADLA episodes and the progression of lymphedema, an important factor in disease progression (38). Consequently, it prevents the progression of lymphedema to severe forms (elephantiasis) and significantly improves the quality of life of patients with ADLA/lymphedema.

The National Filariasis Reference Service from the Oswaldo Cruz Foundation in Pernambuco, Brazil, emphasizes that in addition to the measures indicated by Dreyer and Addis 2000 to reduce ADLA episodes, continuous knowledge transmission about self-care is essential for individuals with ADLA/lymphedema. A recent study in Brazil during the COVID-19 pandemic observed that around 70% of patients evaluated reported maintaining daily hygiene of the limb affected by lymphedema. Despite this, there was

a higher presence of interdigital lesions, dermal ulcers, and number of ADLA attacks, possibly contributing to an increase in lymphedema volume (39).

Simultaneously, this knowledge must be coupled with adequate management involving physiotherapy through the complex decongestive therapy (CDT) technique (40, 41). This therapy comprises procedures such as hygiene, manual lymphatic drainage, compressive bandages, myolymphokinetic exercises, skin care, and precautions in daily activities, and appears to induce behavioral changes in treated patients. Patients instructed in self-care, observing significant improvement through therapy, play a decisive role in maintaining treatment continuity. The authors also highlight that CDT can be applied with low-cost materials, such as cotton fabrics. In Haiti (42), however, the incidence of ADLA episodes increased when using compressive bandages (Comprilan®, commercially available) to reduce lymphedema of the lower limbs in LF-endemic areas, possibly due a lack of prior hygiene of the affected limbs before applying the compression bandage.

The study presents notable limitations that warrant consideration and should be addressed in future research. These include: I) CHAs were trained to identify the clinical forms of LF but did not classify the reported degree of lymphedema; II) Despite the clinical form of ADLA being frequently mentioned, individuals were not queried about the frequency of ADLA episodes nor about the presence of interdigital lesions; III) The referred morbidity was identified by the CHA, and IV) No survey was carried out to evaluate the impact of MDA on the clinical forms of LF.

One of the limitations in this study is the lack of specific questions related to the flow that individuals with filarial morbidity should follow to manage their clinical condition.

In conclusion, the population in areas that received actions from National Programs to Eliminate LF demonstrated a high level of knowledge about filariasis and practices aiding in the prevention and treatment of the disease. Furthermore, it has been demonstrated that National Programs to Eliminate LF involving the management and care of those with morbidity increase awareness about the disease in the population, thereby enhancing residents' adherence to MDA. Given the high MDA coverage in the studied areas of AB and AC, despite periodic home visits from CHA, we believe their influence on individuals' knowledge in the present study was limited. Evaluation of post-intervention MDA is crucial to infer the impact on improving the quality of life of those with morbidity by the reduction of acute inflammatory episodes (ADLA), lymphedema, and/or or hydrocele.

Data availability statement

The original contributions presented in the study are included in the article/supplementary material. Further inquiries can be directed to the corresponding author.

Ethics statement

The study was approved by the Research Ethics Committee of the Centro de Pesquisas Aggeu Magalhães - CEP/CPqAM/FIOCRUZ under number CAAE 0054.0.000.095-09. The interviews for application of the questionnaire were performed after authorization by participants or their legal guardians and signature of the informed consent form. For minors, the information was transmitted to the parents or the legal guardian, who responded for them.

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Author contributions

MM: Writing – original draft, Writing – review & editing. EB: Writing – original draft, Writing – review & editing. PO: Writing – original draft, Writing – review & editing. CBo: Writing – original draft, Writing – review & editing. TM: Writing – original draft. HR: Writing – review & editing. CBr: Writing – original draft, Writing – review & editing. AR: Writing – original draft, Writing – review & editing.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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