BANCROFTIAN FILARIASIS IN TWO URBAN AREAS OF RECIFE, BRASIL: THE ROLE OF INDIVIDUAL RISK FACTORS

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SUMMARY

Bancroftian filariasis is spreading in towns of endemic areas as in Recife, northeastern Brazil, where it is a major public health problem. This paper deals with the prevalence of microfilaraemia and filarial disease in two urban areas of Recife, studying their association with individual characteristics and variables related to the exposure to the vectors. The parasitologic survey was performed through a "door-to-door" census and microfilaraemia was examined by the thick-drop technique using 45 µl of peripheral blood collected between 20:00 and 24:00 o' clock. 2,863 individuals aged between 5 and 65 years were interviewed and submitted to clinical examination. Males aged between 15 and 44 years old presented the greatest risk of being microfilaraemic. Microfilaraemia was also significantly associated with no use of bednet to sleep. The risk of being microfilaraemic was greater among those who had lived in the studied areas for more than 5 years. The overall disease prevalence was 6.3%. Males presented the greatest risk of developing acute disease. The risk of developing chronic manifestations was also greater among males and increased with age. We found no association between time of residence, bednet use, microfilaraemia and acute and chronic disease. We may conclude that in endemic areas there are subgroups of individuals who has a higher risk of being microfilariae carriers due to different behaviours in relation to vector contact.

KEYWORDS: . Bancroftian filariasis; Urbanization; Risk factors; Epidemiological pattern.

INTRODUCTION

Bancroftian filariasis is spreading in towns of endemic areas as in some Asian countries, like India where one meets half of the infected cases in the world, in Aegipt and eastern African coast ⁴.

This disease is characterized by a great variety of clinical manifestations, mainly those related to acute inflammation and chronic pathology of lymphatics. Some manifestations as the Tropical Pulmonary Eosinophilia, and others syndromes, generically known as occult filariasis are less frequent and probably related to host hypersensibility to microfilariae ²³. In spite of the low case-fatality rate, lymphatic filariasis is a major public health problem in endemic areas because of the great number of deformations occurring in the chronic disease. Besides that, the frequent episodes of acute disease interrupt the daily activities of patients keeping them out of work from 3 to 15 days.

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Nowadays, Recife, the capital of the state of Pernambuco, is the principal endemic area in Brazil, showing not only signs of a very intense transmission but also of its geographical spreading ⁷. In Recife, filariasis has a very heterogeneous distribution, occurring mainly in slums. In these areas the microfilaraemia prevalence may be as high as 14.9% ¹⁵ which highlights the failure of the selective treatment of microfilarie carriers as the unique control measure employed for decades.

In spite of the fact that the main goal of the filariasis control is to reduce or eradicate the clinical manifestations of filariasis, their prevalence within the areas which are highly endemic in Recife is unknown. In endemic areas exposed persons may or not become microfilaraemic or develop clinical manifestations of filariasis while some microfilariae carriers may remain assymptomatic or develop acute and chronic manifestations ^{19, 23}.

The great majority of research in this field, until recently, aimed to find a direct link between the development of clinical manifestations and the host immunological response. This assumption was based on the idea that there was a predisposition, perhaps a genetic one, that would modulate the immune response and consequently the clinical expression of infection ^{20, 24}. This concept is being substituted by a dynamic understanding of the involved immunological mechanisms that would be modified according to the exposure to infective larvae ^{3, 11}. This dynamic understanding emphasizes the role of environmental risk factors in the development of the infection and disease.

Nevertheless, there are very few field works studying the role of the individual behaviour as a risk factor to infection and disease ⁸. It should be important to the public health activities to identify the differences in risk amongst persons living in the same endemic areas that might be due to different behaviours regarding exposure to vectors. In this case a control program could stimulate behaviours that would reduce the risk of filariasis transmission.

With the aim to find more appropriated strategies to control Lymphatic Filariasis in Recife the Centro de Pesquisas Aggeu Magalhães/ Fundação Oswaldo Cruz (CPqAM) has developed a pilot project in two selected urban areas which presented similar socio-economic and environmental conditions. In a first moment

microfilaraemia and clinical surveys were made in order to identify the filarial morbidity pattern in the study areas and to establish a baseline for future evaluations of the control measures that will be implemented.

This paper deals with the prevalence of microfilaraemia and acute and chronic filarial disease, studying their associations with individual characteristics and variables related to the exposure to the vector. It would allow the identification of subgroups with different risks of filarial infection and disease. Control activities targeted to these groups could then be selected and implemented.

MATERIALS AND METHODS

Selected areas and population studied

Recife, capital of the State of Pernambuco, has an area of 219 km² and in 1991, 1,290,149 inhabitants. Up to 60% of the population has very low income and the majority live in slum areas ^{9,27}, where households are not connected to an underground piped sewerage system neither to a drainage system. Long periods of heavy rain that occur from March to August and high monthly average temperatures and atmosphere humidity ranging from 24° to 28° and from 60% to 80% respectivily, together with socio-economic circumstances, create the ideal conditions for vector proliferation.

Two districts were selected inside the urban area, Coque and Mustardinha, both slum areas, 6 km away from each other with similar environmental conditions and levels of microfilaraemia prevalence. Before performing the clinical and parasitological surveys the selected areas were mapped and social workers visited all the houses, in order to inform and explain in detail the purposes of the research, and to obtain the support of the population. It was offered a clinical and blood examination to every individual in the age-group of 5 to 65 years.

Parasitological and clinical surveys

The survey was performed through a "door-to-door" census between December 1990 and July 1991. Microfilaraemia was examined by the thick-drop technique using 45 µl of peripheral blood, collected between 20:00 and 24:00 o'clock.

All the subjects were invited to the out-patient units, one in each selected area, on the day following the blood collection. Medical staff from the CPqAM interviewed and examined the subjects, for signs and/ or symptoms of lymphatic filariasis. During the last month of the research, households visits were made in order to examine the people who did not come to the out-patient units.

The populations enrolled in the parasitological and clinical surveys were compared in relation to characteristics such as sex, age and prevalence of microfilaraemia as the non attendance of all subjects invited to the out-patients to perform the clinical examination could lead to an over or underestimation of the prevalence of clinical manifestation in the study areas. Besides that, the estimated association between microfilaraemia and the independent variables could be different in the two populations. We found no differences by age group and microfilaraemia prevalence. In relation to sex we observed a significant difference only in one of the areas, where the percentage of males was 45.1% in parasitological survey and 38.8% in the clinical survey. Thus, the similarity in relation to characteristics associated to filarial disease suggests that the proportions of filarial clinical manifestations are similar in the two populations.

Studied variables

The dependent variables were "microfilaraemia" defined as the presence of microfilariae in peripheral blood, and filarial clinical manifestations defined as "acute disease" and "chronic disease". Acute disease was identified when there had been one or more fever episodes (wheter or not followed by headache, nausea and vomiting) and by local disease (pain, heat, lymphangitis or adenolymphangitis on arms and legs, male genitalia or breasts) for at least three days. Chronic disease was identified according to WHO ^{30, 31} criteria for lymphoedema, elephantiasis, hydrocele or chyluria.

Isolated cases of adenitis were not included in the filarial disease prevalence calculations because they may be associated with other diseases. Respiratory disease that could suggest a tropical pulmonary eosinophilia, and haematuria were also excluded.

The independent variables studied were sex and age and vector exposure variables like "time of residence" in the areas categorized as "≤ 5 years" and "> 5 years" and "bednet use" categorized as "use" and "no use". To study filarial disease, "microfilaraemia" was considered an independent variable.

Data analysis

The logistic regression analysis was performed to study the association between microfilaraemia and each of the independent variables. The estimated "odds ratio" was calculated for each level of exposure in relation to the reference level. The confidence interval (95%), the p value and the likelihood ratio statistics (LRS) were also calculated. The multiple logistic regression analysis was used to control for several confounding factors simultaneously.

The EPI-INFO program version 5.1 was utilized to describe the distribution of variables studied, and the SPSSPC version 4.0 was utilized to made the logistic regression.

RESULTS

From the 4,597 persons that had their blood collected in parasitological survey, 2,863 (62.3%) aged between 5 and 65 years were interviewed and submitted to clinical examination, from which 1,193 (41.7%) were males and 1,670 (58.3%) were females. The prevalence of microfilaraemia among individuals that were submitted to clinical examination was 11.3%.

Recife, Jaboatão and Olinda are endemic areas for filariasis in the state of Pernambuco; the other "municipios" which belong to the metropolitan region of Recife as well as those out of the metropolitan area are considered nonendemic. 75.4% and 24.6% of the individuals interviewed were born, respectively, in the endemic and nonendemic areas. 76.2% of the latter had been living in the study areas for more than 5 years.

The univariate analysis showed that microfilaraemia was significantly associated with sex, the risk being higher for males (OR=2.27; 95% CI: 1.79-2.87; LRS: 46,82 on 1 d.f., p<0.001).

There was a statistically significant association between microfilaraemia and age-group (LRS=36.69 on 2 d.f.; p < 0.001). The risk for those aged 15 to 44 years was significantly increased (OR=2.27; 95% CI: 1.70-3.02). There was also an increase for those aged 45 to 65 years but the difference was not statistically significant (OR=1.36; 95% CI: 0.90-2.07; p > 0.05). When sex and age-group were adjusted for each other the association of both with filariasis remained significant (LRS=87.07 on 3 d.f.; p < 0.001).

When we evaluated whether the risk of

microfilaraemia varied according to the length of time individuals had lived in the area there was evidence of a time effect on risk, the risk was greater for those living for more than 5 years when compared to those living 5 years or less (OR=1.87; 95% CI: 1.25-2.79; LRS=10.68 on 1 d.f.; p=0.001).

It was of interest to explore the risk of infection in relation to the nocturnal use of bednets; when comparing those who do not use bednets with those who do, the former were at a significantly higher risk of microfilaraemia than the latter (OR=1.87; 95% CI: 1.47-2.38; LRS=26.79 on 1 d.f.; p < 0.001).

Sex was shown to be associated with microfilaraemia and therefore was a candidate for confounder of the association beetween microfilaraemia and the nocturnal use of bednet. After adjustment there was little change in the odds ratio estimated for bednet use, implying that the association occurs independently of sex (OR=1.74; 95% CI: 1.36-2.22; LRS=66.91 on 2 d.f.; p < 0.001).

A test of interaction between the variables, use of bednet and sex was performed; in other words, we examined whether the Odds ratios associated with use of bednet was homogeneous over the two levels of sex. To test for interaction two models were fitted; the first just adjusting the two variables for the effect of the other, and the second, including an interaction term. A likelihood ratio test was used to assess the significance of the addition of the interaction term; the following result was obtained: LRS=4.57 on 1 d.f.; p < 0.005. The LRS is statistically significant suggesting that the use of bednet and sex have an interactive effect on the risk of filariasis. Table 1 shows the stratum specific odds ratio for use of bednet at the two levels of sex.

The age and sex-adjusted odds ratio for the association between microfilaraemia and use of bednet was similar to that obtained before adjustment (OR= 1.76; 95% CI: 1.37-2.25; LRS= 106.49 on 4 d.f.; p < 0.001).

When the relation between microfilaraemia and the length of time living in the area was examined adjusting for age-group and sex, the odds ratio estimated did not change appreciably, suggesting that the association occurs independently of sex and age-group (OR=2.03; 95% CI: 1.33-3.08; LRS= 98.56 on 4 d.f.; p < 0.001).

TABLE 1
Odds ratios, confidence intervals and p values for the association of microfilaraemia and bednets use, for males and females

Variables	Odds Ratios	95% confidence interval		p - value
Males				
Bednets use				
Yes	1.00*			
No	1.38	1.00	1.90	0.050
Females				
Bednets use				
Yes	1.00*			
No	2.36	1.62	3.43	< 0.001

* Reference level

Total observations: 2.822

A multivariate analysis was carried out; we introduced all independent variables which had shown a statistically significant association with microfilaraemia and we used a step-down procedure. All the variables remained in the final model and are presented in Table 2. The effect of each variable is adjusted for the effect of the others.

The prevalence of filarial disease, either acute and chronic, among 2,863 subjects who were interviewed and had a clinical examination was 6.2%. Among those

TABLE 2
Estimated adjusted odds ratios, confidence intervals and p values for the association of microfilaraemia and bednets use, time of residence, age groups and sex

Variables	Odds Ratios	95% confidence interval		p - value		
Time of residence						
≤ 5 years	1.00*					
≥ 5 years	1.98	1.30	3.02	< 0.001		
Bednets use						
Yes	1.00*					
No	1.74	1.36	2.23	< 0.001		
Age groups						
(years)						
5-14	1.00*					
15 - 44	2.42	1.81	3.23	< 0.001		
45 - 65	1.61	1.05	2.47	< 0.05		
Sex						
Females	1.00*					
Males	2.22	1.74	2.83	< 0.001		

Likelihood ratio statistics on 5 d.f. = 118.27 p<0.001

* Reference level

Total observations: 2,822

examined, 54 (1.9%) had either symptoms or signs of acute filarial disease, while 123 (4.3%) had either symptoms or signs of chronic filarial disease.

Regarding sex and age-group a statistically significant association between acute disease and both factors was found. The risk of acute disease was approximately 3 times higher for males (OR=3.33; 95% CI: 1.84-6.01; LRS=17,61 on 1 d.f.; p < 0.001). In relation to the age-group those aged 15 to 45 years were at a significantly higher risk of acute disease (OR=4.72; 95% CI: 2.00-11.13); the individuals aged 45 to 65 years showed an increased risk but it did not reach statistical significance (OR=2.05; 95% CI: 0.62-6.75; p>0.05).

We assessed the risk of acute disease in those infected (microfilaraemic) as compared to those amicrofilaraemic and we found a significant increase in risk for the former (OR=2.10; 95% CI: 1.07 - 4.12; LRS=4.03 on 1 d.f.; p<0.05).

There was hardly any difference in the risk of acute disease between those who had lived in the area for 5 years or less and those who had lived there for more than 5 years (OR=0.94; CI: 0.50-2.28; LRS=0.03 on 1 d.f.; p>0.05).

Taking as baseline those who use bednet there was a slightly increased risk for those who do not use but the difference was not statistically significant (OR=1.11; 95% CI: 0.64 - 1.92; LRS=0.14 on 1 d.f.; p>0.05).

When sex and age-group were adjusted for each other there was evidence that the effect of each did not depend on the effect of the other (Table 3).

A multivariate analysis was conducted using the variables that had shown a statistically significant association with acute disease in the univariate analysis: sex, age-group and microfilaraemia. Using a step-down procedure just sex and age-group were retained in the final model suggesting that sex and age-group accounted for the association between microfilaraemia and acute filarial disease.

When the relation between chronic disease and sex was examined a statistically significant association was found (OR=2.30%; 95% CI: 1.58-3.34; LRS=19.70 on ld.f.; p<0.001).

TABLE 3

Estimated adjusted odds ratios, confidence intervals and p values for the association of acute filarial disease and sex and age groups

Variables	Odds Ratios	95% confidence interval		p - value
Sex	The second			
Females	1.00*			
Males	3.49	1.93	6.32	< 0.001
Age Groups				
(years)				
5 - 14	1.00*			
15 - 44	5.07	2.14	11.99	< 0.001
45 - 65	2.41	0.73	7.97	0.150

^{*} Reference level

Total observation: 2,822

When we analysed if chronic disease was associated with age-group a significant result was obtained (LRS=56.56 on 2 d.f.; p<0.001). Overall the odds ratios increases as the age increases, the subjects in the age-group 15 to 44 experiencing a 4-fold (OR=3.88 95% CI: 2.09-7.20) and those in the age-group 45 to 65 years a 9-fold increase (OR=9.23; 95% CI: 4.80-17.77).

There was no statistically significant association between chronic disease and microfilaraemia; there was a somewhat increased risk for those who were microfilaraemic but the confidence interval included 1 (OR=1.50; 95% CI: 0.90-2.48; LRS=2.26 on 1 d.f.; p>0.05).

When the association between chronic disease and length of time living in the area was tested there was an increased risk for those living for more than 5 years but the result was not statistically significant (OR=1.54; 95% CI:0.84-2.82; LRS=2.16 on 1 d.f.; p>0.05).

Regarding the use of bednet, the risk of chronic disease for both groups, those who use and those who do not, was found to be similar (OR=1.04; 95% CI: 0.72-1.50; LRS=0.05 on 1 d.f.; p>0.05).

When the variables sex and age-group were adjusted for each other the association of chronic disease with both remained statistically significant; thus, there is an association of chronic disease with sex which is independent of age-group and vice-versa (Table 4).

TABLE 4
Estimated adjusted odds ratios, confidence intervals and p values for the association of chronic filarial disease and sex and age groups

Variables	Odds Ratios	95% confidence interval		p- value
Sex				
females	1.00*			
Males	2.67	1.82	3.90	< 0.001
Age Groups				
(years)				
5 - 14	1.00*			
15 - 44	4.11	2.21	7.64	< 0.001
45 - 65	10.70	5.53	20.72	< 0.001

* Reference level Total observations: 2,822

DISCUSSION

The transmission of *Wuchereria bancrofti* is considered an "inefficient" process ¹². There is no animal infection reservoir, the infected vectors have a high mortality, the ingested larvae do not develop inside the vector and many of them do not survive while moving from human skin to the lymphatic system. Thus, the transmission of bancrofti filariasis occurs only where there are very high densities of infected vectors ¹⁷.

Its principal vector, Culex quinquefasciatus, the unique existing in Recife, proliferate mainly in stagnated and polluted water, a kind of breeding site found very frequently in towns of endemic areas. This characteristic of vector life cycle has led one to relate the endemic expansion to the kind of urbanization process, which is happening in most of the developing countries 10.16.

In Recife, 42.2% of the households are situated in slum areas ⁹, as a result of the distortion in the urbanization process which is occurring in this city. In these areas, the chronic deficit of urban infrastructure services, such as a underground piped sewerage and drainage systems, has contributed to create favourable conditions for mosquito breeding sites. This explain the heterogeneous distribution of filariasis whithin this city, the higher rates being found in the slums, a highly suitable environment for filariasis transmission.

In the communities studied the microfilaraemia prevalence of 11.3% classifies this areas as highly

endemic for filariasis according WHO criteria ¹⁸. Then non performance of clinical examination and interviews in 37.7% of the subjects enrolled in the parasitological survey does not seem to have introduced any bias in the results because of the similarity found between the two mentioned populations.

In relation to the morbidity pattern, we found that males aged between 15 and 44 years old presented the greatest risk of being microfilaraemic. This result agrees with the literature that frequently relates a greater microfilaraemia prevalence among males aged 15 or more 25, 31. BRABIN 1, for instance, in a recent review of parasitological surveys results from different endemic areas, has found that in the great majority of them females in reproductive years have lower microfilaraemia prevalence and parasitological densities than males. These observations are not still well elucidated and, as occurs with others parasites, one does not know whether the difference found between sexes is due to immunological mechanisms related to hormones or due to different vector exposure opportunities 2.

However, some authors believe that different levels of microfilaraemia prevalence whithin an endemic area are probably related to different exposure levels to infected vectors 8, that could result from different individual behaviours 29.

In the literature there is no evidence that people believe that they can prevent filariasis transmission by avoiding vector contact 8. CARME et al. 5, for instance, found that from 127 patients suffering from elephantiasis only 12.5% implicated the mosquito as a transmission agent of filariasis 5. Nevertheless bednets are largely used against mosquitos in endemic areas 6. We found that 49.6% of the subjects interviewed in the communities studied use bednet regularly to sleep. 54.1% out of them are females and 43.3% are males.

In our study we found a significant association between microfilaraemia and no use of bednet, which did not change after adjusting for sex and age-group, implying that there was no confounding effect of these variables. Nevertheless, there was an interaction between the variables "bednet use" and sex, that is, the risk of being microfilaraemic among individuals who do not use bednet to sleep is greater among females than males. In others words, among males bednet use seems to be a less important risk factor than among

females, suggesting others opportunities of exposure for the formers.

We observe that, at night, men stay out of the households for longer periods of time either playing domino or talking. Besides that, they wear fewer clothes than women due to the warm. Although *Culex quinquefasciatus* mosquito have endophilic habits one can found them around the households at night. Thus, different behaviours which are related to different levels of vector contact may be an explanation for the greater prevalence of microfilaraemia in males.

We also found a significant association between microfilaraemia and the length of time the individuals had lived in these areas, those who had lived there for more than 5 years, which means that they have been exposed to vector for a longer period of time, being at a greater risk.

The prevalence of clinical manifestations of 6.3% could be considered relatively low when compared with the prevalence of microfilaraemia in these two areas, as the prevalence of filarial disease is known to be always greater than microfilaraemia prevalence 3. In Recife, this observation could be a long effect result of selective treatment of microfilaraemic subjects, which was the control measure employed for decades. Between 1982 and 1993, for instance, 84,631 individuals were medicated with 5,277,201 tablets of Diethylcarbamazine (DEC). This kind of intervention has not interrupted or even diminished the infection transmission in Recife, however it may have reduced the prevalence of filarial clinical manifestations similarly to what has occurred in other endemic regions 26. In fact, a decrease in prevalence of severe chronic clinical manifestation had been reported by the Filariasis Control Program in Recife 14.

The other hypothesis is that immunological tolerance, specially neonatal immunological tolerance, may have a role in modulating the infection and disease dynamics. The hosts tolerance status is likely to prolong patent infection during which a strong immunity against infective larvae may be built. It would then inhibit further infections, and perhaps, reduce the probability of occurrence of subsequent immunopathological events ¹³.

The possible epidemiologic consequence from this observation is that, in an endemic community, the

disease prevalence in adults must increase as the infection prevalence increases until a determined level of infection prevalence, from which the disease prevalence will decline as a consequence of the increase in the proportion of neonatally-tolerized persons ¹¹.

In our study we found that the great majority (75.4%) of subjects interviewed and submitted to a clinical examination, were born in endemic areas to filariasis in Recife. This great proportion of authoctone subjects could have contributed to increase the relative importance of tolerant individuals and this would explain the low overall filarial disease prevalence in spite of the high level of infection transmission.

When we analyse the occurrence of chronic and acute disease we verify that the acute disease specific prevalence was 1.9%, a little higher than that one found in others endemic areas like India ²¹ and this prevalence can be considered a sign of the high transmission intensity. Males aged between 15 and 44 years old presented the greatest risk of developing acute disease. By the other hand the risk of developing chronic manifestations was also greater among males and increased with age. This kind of morbidity pattern is very similar to that found in Pondycherry, South India ²¹ and could be due to the accumulation of chronic cases whithin the population ²².

The observation of no significant association between time of residence, bednet use, microfilaraemia and acute and chronic filarial disease reflects the existence of host immune mechanisms involved in the disease process. It is well known that immigrants not previously exposed to filariasis when move to endemic areas develop clinical manifestation more frequently after infection. In our study, the great number of subjects born in other endemic areas within Recife and its metropolitan area, probably already exposed to filariasis, could explain the no association found between time of residence in the two areas studied and filarial clinical manifestation.

We may conclude that in highly endemic areas, as the studied ones, there are subgroups of subjects exposed to a higher risk of infection due to different behaviours in relation to vectors contact.

These results are very important as the Filariasis Control Program could also stimulated personal protection against vectors through health education. This could be done not only implementing vector control measures in the endemic urban areas but also stimulating the use of bednets to sleep. It is well known that the infection transmission requires a high rate of bites by person/time ²⁸, and this change in behaviour can contribute to reduce it.

RESUMO

Filariose bancroftiana em duas áreas urbanas do Recife, Brasil: o papel dos fatores de risco individuais.

A Filariose bancroftiana está se disseminando em áreas urbanas de regiões endêmicas como no Recife, nordeste do Brasil, onde se constitui em um problema de saúde pública. Este artigo descreve a prevalência de microfilaremia e doença filarial em duas áreas urbanas do Recife, estudando sua associação com características individuais e variáveis relacionadas ao contacto com vetores. O inquérito parasitológico foi realizado através de um censo "porta-a-porta" e a pesquisa de microfilárias foi efetuada pela técnica da gota espessa utilizando 45µl de sangue capilar entre 20:00 e 24:00 horas. Homens com idade entre 15 e 44 anos apresentaram o maior risco de microfilaremia. Microfilaremia esteve também associada com o não uso de mosquiteiros para dormir e um maior tempo de residência nas áreas de estudo. A prevalência total de doença filarial foi 6,3%. Os homens apresentaram o maior risco de desenvolver doença aguda. O risco de manifestações clínicas crônicas foi também maior entre os homens e aumentou com a idade. Não encontramos associação entre tempo de residência nas áreas, uso de mosquiteiros, microfilaremia e doença filarial aguda e crônica. Podemos concluir que em áreas endêmicas existem subgrupos de indivíduos que têm um maior risco de serem portadores de microfilárias devido a comportamentos diferentes em relação ao contato com o vetor.

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