

Evidence of continued transmission of *Wuchereria bancrofti* and associated factors despite nine rounds of ivermectin and albendazole mass drug administration in Rufiji district, Tanzania

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Abstract

Background: In most sub-Saharan Africa, the National Lymphatic Filariasis Elimination Programme (NLFEP) is based on annual mass drug administration (MDA) with ivermectin and albendazole. In order to interrupt transmission, 4–6 rounds of MDA are required with at least 60–70% minimum effective coverage. Children born since the introduction of the MDA programme are recommended for assessing the interruption of transmission. The objective of this study was lymphatic filariasis transmission status after nine rounds of MDA in Rufiji district, Tanzania.

Methods: This cross sectional survey involved 270 heads of household. Parents or guardians were interviewed on behalf of the schoolchildren about their participation in MDA programme. Status of LF prevalence was assessed by measuring *Wuchereria bancrofti* circulating filarial antigens (CFA) in blood samples from standard one school children (6 – 9 years) using immunochromatographic test cards.

Results: A total of 413 standard one schoolchildren were tested for CFA; 59 (14.3%) had CFA. Two thirds (66.8%) of the children did not participate in 2011 MDA round. Prevalence of CFA was significantly lower in younger (6.4%) than older children (40.4%) ($p < 0.05$). Participation in the last (2011) MDA did not significantly change the prevalence *W. bancrofti* CFA ($\chi^2 = 0.723$, $p = 0.4$). The recorded MDA coverage for 5 years including 2011 was above the 60–70 % minimum effective coverage. The community reported coverage was 40.4% for last MDA (2011), for previous MDAs was 53.0%; being far below the minimum effective coverage. Though the large majority (97.0%) of households had heard of LF, only about half (57.0%) knew it was transmitted by mosquitoes. Less than a half (43.6%) of households were aware of the adverse effects of LF, therefore motivated to participate in MDA.

Conclusion: The findings indicate that LF transmission has continued in Rufiji district despite nine rounds of MDA. Low compliance to MDAs due to community and programmatic factors were responsible for the continued LF transmission. Detailed entomological studies are required to establish LF transmission dynamics and the programmatic factors associated with MDA implementation in the area.

Keywords: Lymphatic filariasis, mass drug administration, schoolchildren, community compliance, Tanzania

Introduction

Lymphatic filariasis (LF) is a parasitic disease transmitted by mosquitoes and is ranked by the World Health Organization as a second leading cause of permanent disability worldwide (Mathieu et al., 2008). LF affects an estimated 120 million people in 81 countries, with over one-fifth of the world's population being at risk of infection due to their exposure to infective larvae through the mosquito vector (WHO, 2008). LF causes hydrocele in an estimated 25 million men and lymphedema or elephantiasis of the leg in 15 million people, mostly women (Ottesen et al., 2008). Microfilariaemia is indicative of the presence of motile larvae of the parasite (microfilariae) released by adult *W. bancrofti* in the blood stream. Individuals with microfilariaemia also have detectable circulating antigen (CFA), as well as do a proportion of those without microfilariaemia who have clinical manifestations of filariasis but no circulating microfilariae. In addition, some individuals in endemic areas appear normal but have cryptic infections and therefore detectable CFA (Turner et al., 1993; Satapathy et al., 2006).

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The Global Programme for Eliminating Lymphatic Filariasis (GPELF) was established in 2000 with the goal of eliminating the disease as a public health problem worldwide by 2020. The programme involves repeated annual mass drug administration (MDA) which are based on the community-wide distribution of albendazole plus either diethyl carbamazine (DEC) or ivermectin to all those at risk of infection in LF endemic communities (WHO, 2000). The drug combinations have microfilaricidal effect and thus suppress circulating microfilariae in the blood, thereby reducing the transmission potential of the parasite (Ottesen *et al.*, 1997). In order to interrupt transmission of LF in endemic countries, GPELF recommends the MDA with effective antifilarial drugs to the entire population at risk for a sufficient period of time. The objective of MDA is to reduce the level of microfilaremia in infected individuals so that transmission cannot be sustained, even after MDA has been stopped; in this way transmission is interrupted. The effectiveness of MDA in reducing the prevalence and density of microfilaria in the blood is directly related to the proportion of the population that receives antifilarial drugs every year (Michael *et al.*, 2004). The WHO recommends annual mass treatment in settings where the prevalence of CFA is $\geq 1\%$ (WHO, 2000). For endemic countries, it was thought that 4–6 rounds of MDA, with at least 60–70% minimum effective coverage of the total population would be adequate to interrupt transmission however five years later it was concluded that in many settings, more than 4–6 years of MDA will be required in order to interrupt transmission (WHO, 2005). GPELF has scaled up impressively since it began and by the end of 2007, 48 countries had implemented elimination programmes and approximately 570 million people had been treated (WHO, 2008).

The current benchmark for success, as defined by the WHO, is a *W. bancrofti* CFA prevalence of less than 1% in a community when transmission cannot be sustained and there should be few or no incident infections. A reduction in prevalence of CFA would be expected after the start of MDA campaigns since reduced transmission will lead to a reduced acquisition of infection in young children (Molyneux, 2009). Thus, children born since the MDA began are recommended for assessing LF transmission status, as this group will be the most sensitive in terms of exposure to infection after the initial MDA (Molyneux, 2009). The use of new sensitive and highly specific diagnostic tools detecting *W. bancrofti* CFA have shown that many children acquire the infection earlier than hitherto thought and that often a considerable proportion of young children are CFA positive (Lammie, 1994). Thus screening of young schoolchildren has successfully been used for mapping the distribution of LF and for assessing the impact of MDA on interruption of LF transmission (WHO, 2005; Ramzy *et al.*, 2006; Simonsen *et al.*, 2011).

Tanzania Mainland is endemic for LF with 34 million people at risk of infection and about 6 million people with debilitating manifestations of the disease. The endemicity varies from being highly endemic along the coast with CFA levels of 45–60%, to low endemicity in the areas of Western Tanzania with endemicity of 2–4% (Malecela *et al.*, 2009). Tanzania's National Lymphatic Filariasis Elimination Programme (NLFEP) began in 1997 following the World Health Assembly resolution that declared that lymphatic filariasis would be eliminated as a public health problem by 2020 (Malecela *et al.*, 2009). The Tanzania NLFEP launched its first MDA with ivermectin and albendazole in 2000 when 45,000 people were treated. Since then NLFEP covered six regions and 34 districts, with 9.2 million people having been treated in the nine years of its inception. NLFEP goal has been to apply annual MDA with a combination of ivermectin (150–200 µg/kg) and albendazole (400mg) to all individuals aged 5 years and above in selected programme areas; a regimen that had been shown to drastically reduce *W. bancrofti* microfilarial load (Simonsen *et al.*, 2004).

Early studies in Rufiji indicated that LF had a severe detrimental socioeconomic impact on patients, particularly when acute filarial fevers would keep them in bed for up to three days unable to work and, thus, adversely affecting their productivity (Gasarasi *et al.*, 2000). According to the Tanzania NLFEP reports, the prevalence of Lymphatic filariasis by

immunochromatographic test (ICT) prior to MDA implementation in Rufiji was 49.0% (MoHSW, 2012). Annual MDA in Rufiji district had gradually been scaled up from August 2002 and by September 2011 a total of nine rounds had been implemented. In order to measure the effect of the MDA rounds on LF transmission, a survey was conducted among schoolchildren born during the MDA implementation period. The programmatic factors associated with coverage and uptake of MDA was also assessed. The objective of this study was to assess LF transmission status following nine rounds of MDA, coverage, compliance and factors associated non-compliance.

Materials and Methods

Study area

The study was carried out in Rufiji district (7° 55'S; 38° 15'E) in south-eastern Tanzania. The district is characterised by flood plains situated on either side of the Rufiji River, the Rufiji inner, outer Delta and coastal belt zone and the North and South hill zone (the Matumbi Mountains). The Rufiji district is known to be highly endemic for LF with a prevalence of CFA of 49.0% prior to the MDA campaigns launched the NLFEP since 2002 (MoHSW, 2012). A quantitative cross sectional study to assess implementation status of MDA campaigns and associated programmatic factors; and whether there has been interruption of transmission following nine rounds of MDA was conducted from April to May 2012 in Rufiji district, Tanzania.

Prevalence of *W. bancrofti* CFA

This involved 413 standard one primary schoolchildren aged 6 – 9 years who were born during MDA implementation period. Demographic characteristics of each participant in the last MDA round were recorded. Each child was examined for *W. bancrofti* CFA so as to demonstrate any evidence of recent exposure to *W. bancrofti* infection, by the presence of CFA in the sample population. Prevalence of *W. bancrofti* CFA was determined by using immunochromatographic test (ICT) cards (Binax Now® Filariasis, Inverness Medical Innovations Inc., Scarborough, ME, USA). The test was run by taking 100 µL finger-prick samples of whole blood and placing this onto the sample pad of ICT card as described previously (Rawlins *et al.*, 2000). The numbered cards were stacked and taken to the Parasitology Laboratory of the Muhimbili University of Health and Allied Sciences for a second reading and quality control.

MDAs coverage, Community and Programmatic factors

Two different methods were used to assess the MDA treatment coverage. First, the official programme coverage for all administrative wards in Rufiji district was obtained from the Pwani Regional NLFEP office. These reported coverages had been calculated as the recorded number of treatments delivered in the wards divided by the eligible ward population (estimated as 80% of the total wards population).

A questionnaire was administered to 270 heads of household within the catchment of the primary school involved in the study. Each participant was asked to provide demographic information. Respondents were also asked questions regarding general knowledge of lymphatic filariasis, compliance with previous MDAs and, if noncompliant, reasons for noncompliance. For noncompliance, the respondents were asked if they had ever participated in an MDA, if they had participated in the previous MDA (2007) and the MDA before that (2005). Parents or guardians completed the questionnaire for their children.

Data analysis

All data were entered into SPSS Statistical Software Package Version 17.0. Prevalence rates were calculated using the descriptive options in SPSS. Association between independent variables (age

of the schoolchildren, possible community and programmatic factors) and dependent variable (infection status) was assessed by the chi-square test at the significance level of 0.05

Ethical considerations

This study received ethical approval from the Muhimbili University of Health and Allied Sciences Research Ethical Review Board. Informed verbal consent for participation in the study was obtained from each head of household. For schoolchildren this was obtained from parents on their behalf. The names and addresses of the children were taken so that if any child proved CFA positive would be referred for treatment. Permission to conduct the study was obtained from the Rufiji district administrative authorities.

Results

Socio-demographic characteristics

A total of 270 heads of households were interviewed of which 35.2% were males while 64.8% were females. The mean age was found to be 35 years (range= 21-60 years). Of the respondents, 41.5% had primary education, 31.9% had attained secondary education while 14.8% had not gone to school. Slightly less than half (46.7%) of the respondents were employed either in the formal or non-formal sector while 32.6% and 20.7% were farmers and business persons, respectively (Table 1).

Table 1: Socio-demographic characteristics

Attribute	Response	No (%)
Sex	Male	95 (35.2)
	Female	175 (64.8)
Age group	≤ 29	102 (37.8)
	30-49	128 (47.4)
	50-69	40 (14.8)
Marital status	Married	103 (38.1)
	Cohabiting	8 (3.0)
	Divorced	8 (3.0)
	Widow/widower	40 (14.8)
	Single	111 (41.1)
Education level	No formal education	40 (14.8)
	Primary education	112 (41.5)
	Secondary education	86 (31.9)
	Post-secondary education	32 (11.9)

Table 2: Relationship of age with the prevalence of *W. bancrofti* CFA (N = 413)

Age (years)	No. positive (%)		No. negative (%)
6	3 (9.7)	28 (90.3)	31
7	14 (9.6)	132 (90.4)	146
8	18 (14.9)	103 (85.1)	121
9	24 (20.9)	91 (79.1)	115
Total	59 (14.3)	354 (85.7)	413

Chi-square for trend = 5.84; p=0.016

Prevalence of *W. bancrofti* CFA

A total of 413 children were tested for *W. bancrofti* CFA. Of these, 236 (57.1%) were females; 31 (7.5%) were 6 years old, 146 (35.4%) 7 years old, 121 (29.3%) 8 years old and 115 (27.8%) were 9 years old. Of the 413 schoolchildren tested, 59 (14.3%) were positive for *W. bancrofti* CFA. The prevalence of *W. bancrofti* CFA increased significantly with increasing age, thus those 6 years old

were significantly less likely to be infected than those 9 years old (χ^2 -trend = 5.84; $p=0.016$) (Table 2). This indicates that the probability for *W. bancrofti* infection increases with age conceivably due to increasing risk of exposure to infection with increasing age.

Of the 413 children tested for *W. bancrofti* CFA, 139 (33.7) participated in the last (2011) MDA round while 252 (66.3%) did not participate. Of those participating, prevalence of CFA was 12.2%; in those not participating, prevalence was 15.3% thus participation in the last MDA did not significantly change the prevalence of *W. bancrofti* CFA ($\chi^2 = 0.723$, $P = 0.4$)

Programmatic factors

The programme coverage ranged from 54.3 to 88.0% between 2002 and 2011. In 2005 MDA was not implemented due to delayed funds from the donors, this led to poor performance in the 2006 since sensitization was not well done. There was fluctuation in annual programme coverage with the highest in 2004 (Table 3).

Table 3: Programme reported Mass Drug Administration coverage in Rufiji district, 2002 – 2011

Year	Targeted population	No. participants	Coverage (%)
2011	170606	150133	88.0
2010	166682	113677	68.2
2009	162848	130279	80.0
2008	159103	115350	72.5
2007	155443	116583	75.0
2006	151868	85046	56.0
2005	-	-	-
2004	144962	136267	94.0
2003	141628	123216	87.0
2002	138370	75135	54.3

The reported compliance with the last round of MDA (2011) was 40.4% while compliance to previous MDA rounds was 53.0% (Table 4). The reported community compliance coverage was far below the 60–70% minimum effective coverage required to interrupt transmission.

Table 4: Community compliance with MDA programme (N = 270)

Attribute	Responses	No. (%)
Ever swallowed Albendazole / Ivermectin in MDA rounds	Yes	143 (53.0)
	No	127 (47.0)
Frequency of swallowing Albendazole / Ivermectin in MDA rounds	Once	68 (25.2)
	More than once	75 (27.8)
Swallowing Albendazole / Ivermectin in (2011) last MDA round	Yes	109 (40.4)
	No	161 (59.6)

More than half (57.3%) of the respondents could attribute mosquito bites to the transmission of lymphatic filariasis. Generally the respondents were aware of scrotal and limb swelling as well as filarial fever attacks as being the common manifestations of lymphatic filariasis. Majority of the respondents were knowledgeable of the appropriate control measures which included anti-filarial drugs and mosquito control (Table 5).

Table 5: General awareness of lymphatic filariasis (N = 270).

Attribute	Responses	No (%)
Mode of transmission	Mosquitoes bites	150 (57.3)
	Sex during menses	48 (18.3)
	Others (stepping in polluted waters)	16 (6.1)
	Don't know	48 (18.3)
Lymphatic filariasis manifestations	Scrotal swelling	112 (42.7)
	Limb swelling	106 (40.5)
	Fevers & joint pains	44 (16.8)
Lymphatic filariasis control	Taking anti-filarial drugs	161 (61.4)
	Measures against mosquitoes	24 (9.2)
	Others (avoid sex in menses, quarantine)	27 (9.9)
	Don't know	51 (19.5)

A large percentage was aware of the MDA programme (71.9%) and frequency of MDA rounds (77.8%), while a large majority (90.7%) was aware of the eligibility for MDA rounds (Table 6).

A total of 270 community participants were interviewed on their willingness to participate in the MDA programme and reasons for participation. More than half (61.5%) of the respondents expressed willingness to participate in the programme. The reasons for willingness to participate included prevention of LF (55.4%), awareness of the programme (33.7%) or being affected by the disease (10.8%).

Table 6: General understanding of the NLFEP in Tanzania (N = 270).

Attribute	Responses	No (%)
Awareness of MDAs programme	Yes	194 (71.9)
	No	76 (28.1)
Awareness of eligibility for MDAs	All household member	245 (90.7)
	Persons with LF	25 (9.3)
Awareness of MDA frequency	Once every year	210 (77.8)
	Don't know	60 (22.2)
Awareness of community based LF control of chronic manifestations	Yes	144 (53.3)
	No	119 (44.1)
Sources of information on NLFEP	Don't know	7 (2.6)
	Radio	49 (25.3)
	Health workers	50 (25.8)
	Village leaders	45 (23.2)
	Television	23 (11.90)
	Leaflets / Newspapers	27 (13.8)

Discussion

The observed *W. bancrofti* CFA prevalence of 14.4% among schoolchildren born after the initiation of MDA indicates the likelihood that transmission is still ongoing and the children were harbouring adult worms as the CFA test detects antigens released by adult worms in human blood (Weil et al., 1997). The drop of CFA prevalence from 49.0% to 14.4% indicates that the 9 rounds of MDA had an impact on the prevalence of *W. bancrofti* though not to a level of interrupting transmission. If transmission had been interrupted there should be little to no infection in this age group as they were born after initiation of the MDA programme. Given the high levels of sensitivity and specificity (99%) for CFA reported for the ICT card test (Weil et al., 1997), the observed prevalence of *W. bancrofti* CFA indicates that transmission of *W. bancrofti* has continued. Transmission of *W. bancrofti* might have continued because of high endemicity as

reflected by the high baseline CFA prevalence of 49.0%. From mathematical models and program experience, the high baseline prevalence of infection might have caused transmission to continue despite 9 MDA rounds (Michael *et al.*, 2004).

A number of factors such as the initial level of LF endemicity (prevalence and density of microfilaremia), the competence and vectorial capacity of the local vector as well as population coverage and population compliance affect programme outcome (Kyelem *et al.*, 2008). Since this evaluation took place after the optimal 4-6 year rounds of MDA, it is unlikely that the observed CFA levels were due to persistent antigenaemia (Weil & Ramzy 2007). That LF transmission continued despite the 9 rounds of MDA is supported by the observation that older (9 years old) children were at increased risk of infection than their younger (6 years) children. This is further supported by the observation that participation in the last (2011) MDA did not significantly change the prevalence *W. bancrofti* CFA.

Findings from this study show that for four consecutive years to the last (2011) MDA round, the reported MDA coverage was optimal with at least 60–70% minimum effective coverage of the total population that is adequate to interrupt transmission (WHO, 2000; Michael *et al.*, 2004). This was also accompanied with a very high awareness of the MDA program itself, eligibility for MDA and frequency of MDA, thus more than half expressed their willingness to participate in the MDA programme. However there was a marked difference between the District reports and the community reported coverage. The reported community coverage was far below the 60–70% minimum effective coverage required to interrupt transmission (WHO 2005).

Community compliance plays an important role in MDA campaigns for LF elimination. The community is the main target for LF elimination because *W. bancrofti* does not multiply freely in the environment and the parasite has no significant non-human vertebrate host that could serve as a reservoir of infection for humans (Ottesen, 2006). Continuity of LF transmission might be explained by low community compliance to the MDA programme as less than a half reported to participate in the last (2011) MDA round while only about a half reported to have ever participated in the previous MDA campaigns. This indicates that non-compliance might be a major factor for the continued transmission of LF in this area. It has been shown that continuing transmission of LF seems to be associated with individual in the community who are persistently noncompliant to the MDA campaigns and these serve as reservoirs of infection to mosquito vectors (Boyd *et al.*, 2010). Moreover, the fact that the programme does not address the vector cannot be ignored. Population coverage and population compliance are among the most prominent factors that affect MDA programme outcome which are in turn heavily dependent on social mobilization, supervision and monitoring as well as the adequacy of resources, and the political commitment (Kyelem *et al.*, 2008).

LF has gender issues that may conceivably influence community compliance to MDA campaigns in different directions. Since the commonest clinical manifestation of LF is hydrocele associated with stigma and socio-economic disabilities in men, it is not surprising that significantly more men than women complied with the MDA campaigns (Talbot *et al.*, 2008). The lower participation in females might have resulted from the fact that pregnant women should not participate in LF MDA campaigns that makes non-pregnant women and women in general to have doubts about safety of the drugs used in the MDA campaigns (Mathieu *et al.*, 2004). Women have the general fear of drugs especially when pregnant; there is the general misconception that the drugs used in the LF MDA campaigns are meant for fertility control (Mathieu *et al.*, 2004).

It is unlikely that the observed level of CFA reflects persistent CFA, as this could only be the case in the early years of MDA implementation when many infected people remain antigen positive for the first two rounds of MDA after which a substantial and significant decline occur after the fourth MDA; thus following the 9 MDA rounds, the observed CFA level is likely to be due to new infection (Weil & Ramzy 2006; Simonsen *et al.*, 2011).

In conclusion, among children born during implementation of 9 rounds of MDA, the prevalence of CFA dropped by 70.6% but not to a level of interrupting transmission. Low community compliance and inadequate mosquito vector control were likely to be the main reasons for continued LF transmission. Further studies should assess compliance profiles of communities so as to identify those groups of individuals who remain persistently non-compliant during MDAs as well as the potential seasonal variations of relevance to LF transmission and quantifying the differences in vector competence among different mosquito vector species as this would better define the force of infection in the study area.

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