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Lymphatic filariasis in western Ethiopia with special emphasis on prevalence of *Wuchereria bancrofti* antigenaemia in and around onchocerciasis endemic areas

Welelta Shiferaw[a], Tadesse Kebede[a], Patricia M. Graves[b], Lemu Golasa[a], Teshome Gebre[c], Aryc W. Mosher[b], Abiot Tadesse[a], Heven Sime[a], Tariku Lambiyo[a], K.N. Panicker[a], Frank O. Richards[b], Asrat Hailu[a,*]

[a] *Department of Microbiology, Immunology and Parasitology (DMIP); Faculty of Medicine, Addis Ababa University, PO Box 9086, Addis Ababa, Ethiopia*
[b] *The Carter Center, Atlanta, GA, USA*
[c] *The Carter Center, Addis Ababa, Ethiopia*

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ABSTRACT

Lymphatic filariasis is known to be endemic in Gambella Region, western Ethiopia, but the full extent of its endemicity in other regions is unknown. A national mapping program for Ethiopia was initiated in 2008. This report summarizes initial data on the prevalence of *Wuchereria bancrofti* antigenaemia based on surveys carried out in a sampled population of 11 685 individuals living in 125 villages (112 districts) of western Ethiopia. The overall prevalence rate was 3.7%, but high geographical clustering and variation in prevalence (ranging from 0% to more than 50%) was found. The prevalence of hydrocele (in males) and lymphoedema of limbs was 0.8% and 3.6% respectively. Significantly higher ($\chi^2 = 49.6$; $P < 0.01$) prevalence of antigenaemia was noted in known onchocerciasis endemic districts (4.7%) compared to non-onchocerciasis endemic districts (2.3%). Thirty-four of the 112 districts, with a population of 1 547 685 in 2007, were found to be endemic. Of these, the numbers of districts with prevalence rates of >20%, 10–20% and 5–9% were nine, 14 and 20 respectively. Twenty-nine of these 34 endemic districts were found in three regions: Gambella Region (seven districts), Beneshangul-Gumuz Region (13 districts), and Southern Nations, Nationalities and Peoples' Region (SNNPR) (nine districts). The other five were from Amhara (two districts) and Oromia (three districts) regions. A tentative distribution map has been drawn to facilitate the launching of the Ethiopia LF elimination program.

1. Introduction

Lymphatic filariasis (LF) is a parasitic disease of man caused by three species of filarial parasites: *Wuchereria bancrofti*, *Brugia malayi* and *B. timori*, which are transmitted by anopheline and culicine mosquitoes.[1,2] Mosquitoes of the *Anopheles gambiae* complex[2–7] and *An. funestus*[2,5,6] are the vectors in rural Africa, while species in the genus *Culex* are involved in urban settings.[6]

Lymphatic filariasis is a cause of profound disability and stigma among millions of affected persons. The disability adjusted life years (DALY) burden due to LF is estimated to be 5.55 million.[8] So far, 120 million people living in 81 countries are known to be affected,[7] of which, 39 African countries carry over a third of the global burden of LF.[7]

While efforts to eliminate LF are continuing in many parts of the world, a few African countries have yet

* Corresponding author. Tel.: +251 1 115533197/911 480993.
E-mail addresses: hailu_a2004@yahoo.com, a_hailu@hotmail.com (A. Hailu).

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to complete mapping the geographical distribution of the disease.[8] Ethiopia is one of the African countries where LF is known to exist, yet data on its morbidity and geographical distribution are lacking. Studies carried out in the 1970s[9,10] and 1990s[11,12] have implicitly restricted the geographical limits of LF to the lowlands of southwestern Ethiopia, especially in Gambella Region. Elephantiasis of the feet, mostly considered to be of non-filarial origin (podoconiosis) is a common disease among poor rural communities of Ethiopia,[10,13–15] whose geographical overlap with LF has not been determined. A wider geographical distribution of LF was suggested by ecological indicators, including distribution of mosquitoes.[16]

To facilitate the launching of the LF elimination program in Ethiopia, a national survey was initiated in 2008 with the support of The Carter Center. This report summarizes initial data from surveys carried out in and around onchocerciasis endemic districts of western Ethiopia, where annual mass administration of ivermectin has been going on for several years through Community Directed Treatment with ivermectin (CDTI) program.

Regional states of western Ethiopia are divided into administrative zones (Figure 1), which are further subdivided into districts. There are a few exceptional 'Special Districts' that have the status of zones. Selection of districts for CDTI was done based on results of Rapid Epidemiological Mapping of Onchocerciasis (REMO) in Ethiopia completed in 2003.[17] Mass annual distribution of ivermectin (Mectizan® donated by Merck and Co, Whitehouse Station, NJ, USA) was targeted to all eligible persons (age 5 years or height 90 cm and above) in districts where the prevalence of onchocerciasis microfilariae was >40% (≥20% nodule rate). The REMO mapping identified districts needing CDTI within 10 administrative zones. The Carter Center and Lions Club partnered with the Federal Ministry of Health and the African Program for Onchocerciasis Control in 8 of these 10 zones, beginning with Keffa and Sheka zones in 2001. Since then, the program has expanded to include areas in Bench Maji, North Gondar, Illu Aba Bora, Jimma, Metekel and Gambella where all zones have had at least four annual distribution rounds. The other two zones, i.e., West Wellega (now split to West Wellega and Kelem Wellega) and East Wellega are similarly covered by 'Light for the World', a non-governmental organization working on disabilities and blindness. During 2009, in the Carter Center-assisted zones, 3 143 181 people were treated with ivermectin in 13 897 targeted villages through the work of 40 594 community-directed distributors (CDDs).

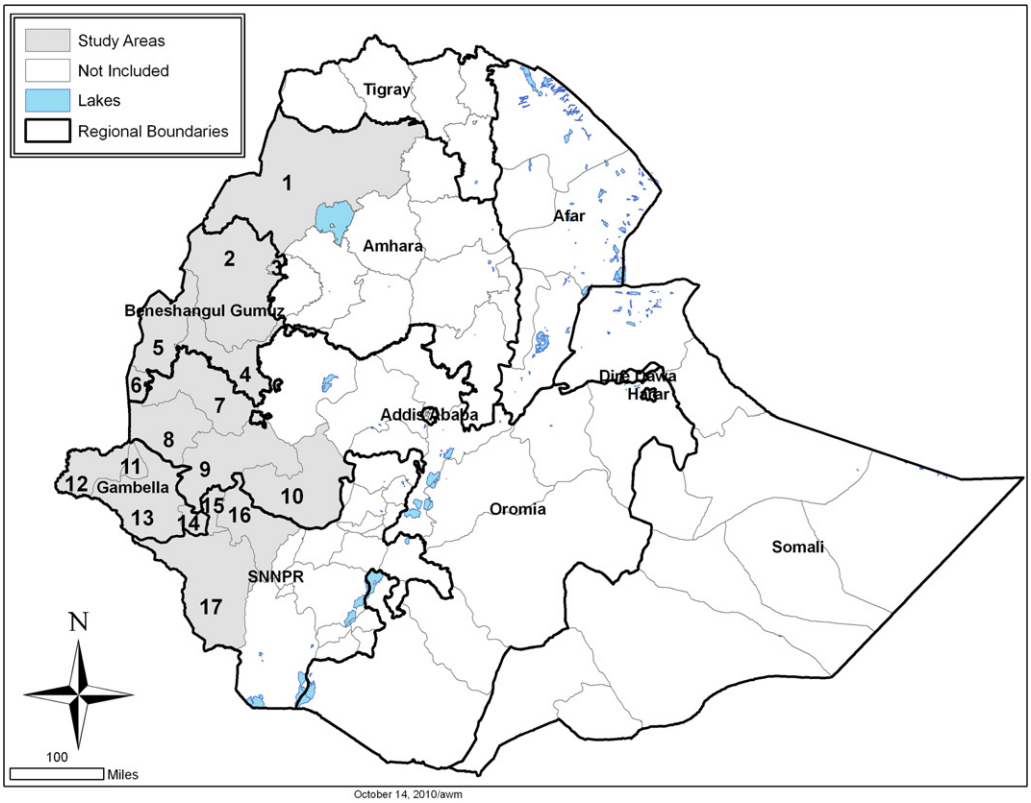

Figure 1. Map of Ethiopia showing lymphatic filariasis survey areas by administrative zones in western Ethiopia, January 2008–July 2010.
Zones: 1: North Gondar [*n* tested = 500], 2: Metekel [*n* = 300], 3: Pawe Sp.D [*n* = 100], 4: Kemashi [*n* = 500], 5: Asossa [*n* = 700], 6: Mao Komo Sp.D [*n* = 100], 7: West Wellega [*n* = 1261], 8: Kelem Wellega [*n* = 1047], 9: Illu Aba Bora [*n* = 2097], 10: Jimma [*n* = 1300], 11: Etang Sp.D [*n* = 102], 12: Nuwer [*n* = 309], 13: Agnewak [*n* = 472], 14: Mezhenger [*n* = 198], 15: Sheka [*n* = 499], 16: Keffa [*n* = 1100], 17: Bench Maji [*n* = 1100].
SNNPR: Southern Nations, Nationalities & Peoples Region; Sp.D: Special District. Special Districts are administrative units which stand above the level of districts, but lower than 'zones'. Each zone usually comprises many districts.

2. Materials and methods

2.1. Study areas

One hundred and twelve districts located in 17 administrative zones of five Regional States (Gambella, Beneshangul-Gumuz, SNNPR, Oromia and Amhara) were included in the survey (Figure 1). The total population of the 112 districts in 2007 was 7 086 473.[18] The majority of the surveyed localities were located in 67 districts included in the Community Directed Treatment with Ivermectin (CDTI) program for onchocerciasis. Forty-five non-CDTI districts were also surveyed.

2.2. Sampling strategy

The objective of the survey was to determine the presence or absence of LF infection in districts where transmission was suspected to take place. Thus, the selection of clusters (villages) from within the surveyed districts was biased towards finding LF infection. This entailed preliminary assessment of the ecological settings (such as altitude, mosquitoes present/absent, malarious/non-malarious,) and formal inquiries and discussions with health facility personnel and Heads and Experts of the Regional and District Health Bureaus.

The sampling procedures were modified from the WHO Operational Guidelines for Mapping of Bancroftian Filariasis in Africa,[19] in which districts were defined as implementation units. In each district, we aimed to test 100 individuals for *W. bancrofti* antigenaemia. Approximately 30 households per village (160–200 people) were randomly selected and invited to the surveys. If the selected village population was smaller than 100, the district showed large ecological variation, or there were many podoconiosis cases, an additional one or two sites in the district were selected. The average number of persons sampled in a district was 104.3; the minimum was 42 and the maximum was 200 (Supplementary Table 1).

Results are reported and mapped here both by district ($n = 112$) and by village site sampled ($n = 125$). Districts are classified into three endemicity levels using the upper 95% binomial exact confidence interval (CI) of the percent positive: Group 1 (non-endemic), upper 95% CI of <3% prevalence, Group 2 (endemic), upper 95% CI 3–10%, and Group 3 (highly endemic) upper 95% CI $\geq$10%. Districts with no positive individual out of 100 tested (upper 95% CI 2.99%) or one individual positive out of 200 tested (upper 95% CI 2.75%) were classified in Group 1. Four districts, where only one individual was positive out of 100 tested (Shay Bench district in Bench Maji zone; Sayo and Dale Wabera districts in Kelem Wellega Zone; and Assosa Zuria district in Assosa zone) were classified in Group 2 (upper 95% CI 5.45%).

2.3. Screening for Wuchereria bancrofti antigenaemia and clinical assessment

NOW® Filariasis Test, a rapid field-ready immunochromatographic test (ICT) was supplied by Binax Inc. (Winslow, ME, USA). This test detects antigen from adult worms of *W. bancrofti*. The test was performed as per manufacturers' instructions, using 100 μl of freshly collected capillary blood, with test results read in 10 minutes. Finger prick blood samples were taken from all persons except children under two.

Screening of the study population for the main signs and symptoms of LF, i.e. elephantiasis or lymphoedema in both sexes and hydrocele in men, was performed in a health facility setting (health center/health post) either by physicians or trained nurses. All men who reported having genital signs of LF agreed to genital examination. Less than 5% of those who did not report genital pathology were examined, and were indeed negative; in the others LF genital signs were considered to be absent based on self report. Physical examination of women's genitalia was not performed. Lymphoedema and hydrocele were identified only at advanced stages, using pitting edema and loss of contour as minimum criteria for lymphoedema diagnosis, and large fluid-filled scrotum for hydrocele. Signs of onchocercal skin disease (such as dermatitis, onchocercomata, lymphadenopathy, and pigmentary changes of skin) were documented. Final diagnosis of LF infection was based on finding of positive ICT. Specific treatment, i.e., a single dose of ivermectin combined with albendazole, was given to all individuals with positive ICT, regardless of whether or not the drugs were given to the communities prior to our LF survey.

2.4. Geo-referencing and mapping prevalence of lymphatic filariasis antigenaemia

The altitude and coordinates of latitude and longitude of all surveyed villages were documented using a global positioning system (12-Channel Garmin® E Trex™, Garmin International, Olathe, KS, USA). Locations of villages were plotted on a map showing altitudinal ranges, and actual prevalence of antigenaemia at individual sites.

2.5. Statistical data analysis

Prevalence of antigenaemia and clinical features are given along with the exact binomial 95% confidence limits. In making comparisons of prevalence data between groups (e.g., between CDTI and non-CDTI districts), Pearson χ^2 was utilized together with *P*-values. All comparisons were 2-tailed; and a *P*-value <0.05 was considered significant. Statistical analyses were performed using SPSS version 16 (SPSS, Chicago, IL, USA).

3. Results

3.1. Characteristics of sampled populations

Between January 2008 and July 2010, surveys of LF were carried out in 125 villages located within 112 districts of 17 administrative zones (Figure 1, Table 1). A total of 11 685 individuals (5686 males, 5994 females, five gender not recorded) were tested; almost half (5285, 45.2%) being between the ages of 15 and 34 years. The overall population of the 112 districts surveyed was 7 454 345, among

Table 1
Prevalence of *Wuchereria bancrofti* antigenaemia in Community Directed Treatment with Ivermectin (CDTI) and non-CDTI districts of western Ethiopia, by region and zone, January 2008–July 2010

Region/ Zone	CDTI status[a]	Total no. districts	No. districts surveyed	No. individuals examined	No. ICT positive (%)	No. endemic districts
Gambella/						
Agnewak	Y	3	3	215	28 (13.0)	3
	N	3	2	257	3 (1.2)	1
Nuwer	Y	0	NA	NA	NA	NA
	N	4	3	309	0	0
Mezhenger	Y	2	2	198	32 (16.2)	2
	N	0	NA	NA	NA	NA
Etang Sp.D.	Y	0	NA	NA	NA	NA
	N	1	1	102	4 (3.9)	1
Oromia/						
Illu Aba Bora	Y	12	12	1397	1 (0.1)	0
	N	12	7	700	0	0
Jimma	Y	4	4	400	0	0
	N	13	9	900	0	0
Kelem Wellega	Y	10	10	1047	2 (0.2)	2
	N	1	0	0	ND	ND
West Wellega	Y	3	3	361	1 (0.3)	1
	N	17	9	900	0	0
SNNPR/						
Keffa	Y	11	10	1100	1 (0.1)	0
	N	0	NA	NA	NA	NA
Sheka[b]	Y	5	5	499	0	0
	N	0	NA	NA	NA	NA
Bench Maji	Y	10	10	1000	155 (15.5)	8
	N	1	1	100	30 (30.0)	1
Amhara/						
North Gondar	Y	4	4	500	41 (8.2)	2
	N	17	0	0	ND	ND
Beneshangul-Gumuz/						
Metekel	Y	3	3	300	72 (24.0)	2
	N	3	0	0	ND	ND
Pawi Sp.D.	Y	1	1	100	0	0
	N	0	NA	NA	NA	NA
Asossa	Y	0	NA	NA	NA	NA
	N	7	7	700	21 (3.0)	5
Kemashi	Y	0	NA	NA	NA	NA
	N	5	5	500	40 (8.0)	5
Mao Komo Sp.D.	Y	0	NA	NA	NA	NA
	N	1	1	100	5 (5.0)	1
Total CDTI districts (Y)		68	67	7117	333 (4.7)	20
Total non-CDTI districts (N)		85	45	4568	103 (2.3)	14
Grand Total		153	112	11685	436 (3.7)	34

CDTI: Community Directed Treatment with Ivermectin; ICT: Immunochromatographic test; NA: Not applicable (no districts in this category); ND: Not done; SNNPR: Southern Nations, Nationalities and Peoples' Region; Sp.D.: Special District.
[a] Y (yes): CDTI districts, N (no): Non-CDTI districts.
[b] There were five districts in Sheka zone at the time of the survey and only three districts during the 2007 census.

which 4 640 776 (62.3%) resided in CDTI and 2 813 569 (37.7%) in non-CDTI districts.[18]

3.2. Prevalence of *Wuchereria bancrofti* antigenaemia by administrative zones and districts

Of the 112 districts studied, 34 were endemic for LF with 12.3% prevalence of *W. bancrofti* antigenaemia in these districts (Table 2). Of the 34 endemic districts, 14 had prevalence with upper 95% CI of 3–10%, and the other 20 were highly endemic (≥10% upper 95% CI; Table 2, Figure 2). The remaining districts ($n = 78$) were classified as non-endemic (Supplementary Table 1). The majority of the LF endemic districts (i.e., 29 of the 34) were found in three regions: Gambella Region (seven districts), SNNPR (nine districts), Beneshangul Gumuz region (13 districts). Two districts in North Gondar zone (Amhara region), one in Kelem Wellega zone and two in West Wellega zone (Oromia region) were also classified as endemic (Table 2). The overall prevalence of *W. bancrofti* antigenaemia in all 112 districts of the 17 zones was 3.7% (Table 1).

3.3. Comparison between districts inside and outside the onchocerciasis Community Directed Treatment with Ivermectin program

In the sampled zones, we surveyed 67 out of the 68 CDTI districts and 45 adjacent districts out of the 85 non-CDTI districts (Figure 2). Twenty of the 34 LF endemic districts were under CDTI compared to the other 14 which were found in non-CDTI districts. Significantly higher prevalence

Table 2
Prevalence of *Wuchereria bancrofti* antigenaemia in 34 lymphatic filariasis endemic districts of western Ethiopia, and endemicity classification, January 2008–July 2010

Region/ Zone	District[a]	Total population	Number of individuals examined	No. ICT positive (%)	95% CI for % ICT positive	Endemicity classification[b]
Gambella/						
Agnewak	Abobo	16 569	91	5 (5.5)	1.80–12.4	HE
	Dima	7996	82	13 (15.9)	8.70–25.6	HE
	Gambella Zuria	10 586	42	10 (23.8)	12.1–39.5	HE
	Gog	16 823	157	3 (1.9)	0.40–5.5	E
Etang Sp.D.	Etang Sp.D.	35 307	102	4 (3.9)	1.10–9.7	E
Mezhenger	Godare	38 763	98	3 (3.1)	0.60–8.7	E
	Mengesh	20 464	100	29 (29.0)	20.4–38.9	HE
Total of Gambella Region endemic districts		146 508	672	67 (10.0)	7.8–12.5	
SNNPR/						
Bench Maji	Bero	12 239	100	15 (15.0)	8.70–23.5	HE
	Guraferda	35 264	100	50 (50.0)	39.8–60.2	HE
	Maji	33 838	100	21 (21.0)	13.50–30.3	HE
	Meinit Goldeya	89 481	100	27 (27.0)	18.60–36.8	HE
	Meinit Shasha	44 766	100	31 (31.0)	22.10–41.0	HE
	Mizan Aman	34 491	100	4 (4.0)	1.10–9.9	E
	Shay Bench	116 682	100	1 (1.0)	0.03–5.5	E
	Debub Bench	109 282	100	6 (6.0)	2.20–12.6	HE
	Surma	24 595	100	30 (30.0)	21.20–40.0	HE
Total of SNNP Region endemic districts		500 638	900	185 (20.6)	18.0–23.4	
Beneshangul-Gumuz/						
Metekel	Dangur	40 781	100	17 (17.0)	10.2–25.8	HE
	Guba	14 901	100	55 (55.0)	44.7–65.0	HE
Asossa	Asossa Zuria	87 366	100	1 (1.0)	0.03–5.5	E
	Homesha	21 502	100	2 (2.0)	0.2–7.0	E
	Menge	40 129	100	5 (5.0)	1.6–11.3	HE
	Oda buldi Guli	43 868	100	5 (5.0)	1.6–11.3	HE
	Sherkole	19 992	100	8 (8.0)	3.5–15.2	HE
Kemashi	Agalo Meti	18 935	100	4 (4.0)	1.1–9.9	E
	Belojegonfoy	24 993	100	3 (3.0)	0.6–8.5	E
	Kamashi Zuria	16 380	100	2 (2.0)	0.2–7.0	E
	Sirba Abay	15 100	100	29 (29.0)	20.4–38.9	HE
	Yaso	12 619	100	2 (2.0)	0.2–7.0	E
Mao Komo Sp.D.	Mao Komo Sp.D.	42 050	100	5 (5.0)	1.6–11.3	HE
Total of B. Gumuz Region endemic districts		398 616	1300	138 (10.6)	9.0–12.4	
Amhara/						
North Gondar	Metema	110 231	200	24 (12.0)	7.8–17.3	HE
	Quara	93 629	100	17 (17.0)	10.2–25.8	HE
Total of Amhara Region endemic districts		203 860	300	41 (13.7)	10.0–18.1	
Oromia/						
Kelem Wellega	Seyo	117 511	100	1 (1.0)	0.03–5.5	E
	Dale Wabera	105 708	100	1 (1.0)	0.03–5.5	E
West Wellega	Gimbi Zuria	74 844	161	1 (0.6)	0.02–3.4	E
Total of Oromia Region endemic districts		298 063	361	3 (0.8)	0.2–2.4	
Grand Total		1 547 685	3533	434 (12.3)	11.2–13.4	

B. Gumuz: Beneshangul-Gumuz; ICT: Immunochromatographic test; SNNPR: Southern Nations, Nationalities & Peoples' Region; Sp.D.: Special District.
[a] Districts with *W. bancrofti* antigenaemia prevalence with upper 95% CI of 3% and above.
[b] E: Endemic and HE: Highly Endemic based on upper 95%CI of 3% and 10% prevalence cut-off respectively.

of antigenaemia was noted in CDTI (4.7%) compared to non-CDTI (2.3%) districts (Pearson χ^2 49.6; $P<0.01$) (Table 1). Coincidentally, 20 of the 34 endemic districts were classified as highly endemic (Table 2) and 20 of the 34 were in CDTI districts; however these 20 districts were not the same group. See Supplementary Table 1 for details of all districts. The overall prevalence of *W. bancrofti* antigenaemia among 3533 individuals of the 34 endemic districts was 12.3% (Table 2), and the population living in those districts was 1 547 685 individuals who could be considered to be at risk of LF infection.

3.4. Lymphatic filariasis morbidity

The prevalence of hydrocele (in adult males) and lymphoedema of limbs among adults (age ≥15 years) living in 34 LF endemic districts was 1.3% and 2.8% respectively (Table 3). In this age group, there were a total of 69 cases with advanced lymphoedema of limbs (elephantiasis), whereas only 14 cases of hydrocele were found. This finding was consistent with our in-depth surveys conducted in Gambella district (to be reported separately). Prevalence of ICT positivity was significantly higher in those with hydrocele, self-reported chyluria and onchocercal skin disease

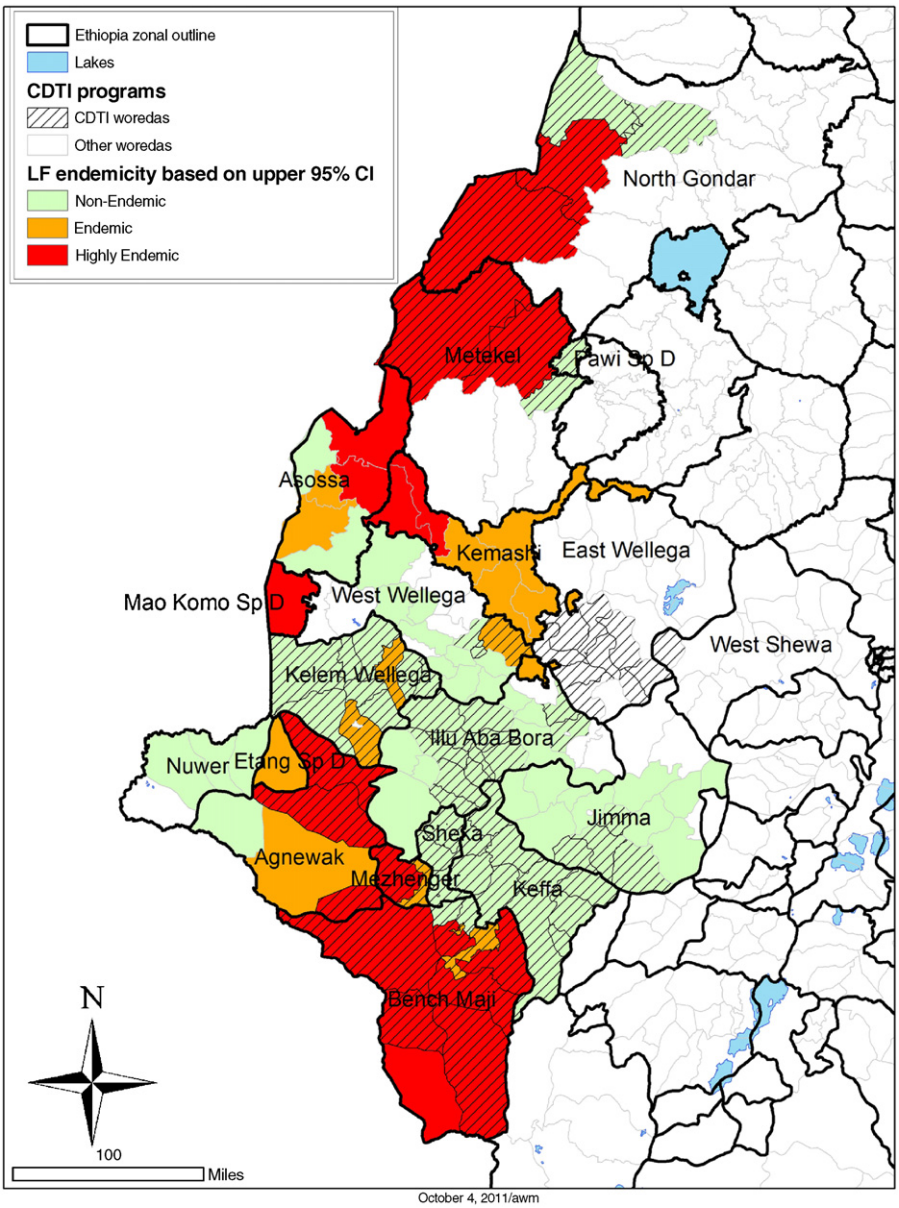

Figure 2. Classification of districts of western Ethiopia by LF endemicity January 2008–July 2010.
Districts are classified based on the upper 95% exact binomial CI of the percent positive, taking into account the number positive and number sampled.
Upper 95% CI <3%: non-endemic.
Upper 95% CI 3% to 9%: endemic.
Upper 95% CI ≥10%: highly endemic.

than in those without these symptoms (Table 3); ICT positivity did not differ significantly between those persons positive or negative for lymphoedema, lymphadenopathy or dermatitis.

Among the 69 cases of lymphoedema, 51 were from two zones: Bench Maji (23 of 650 examined) and Kelem Wellega (28 of 176 examined). All the 28 cases from Kelem Wellega were diagnosed as podoconiosis, i.e., lymphoedema of the lower legs (below knee), mossy foot and absence of genital lymphoedema. This was also supported by the low rate of *W. bancrofti* antigenaemia (two ICT positive out of 1047 tested in this zone). The prevalence of clinical filariasis and onchocerciasis related signs/symptoms in the sampled population of 11 685 individuals is shown in Supplementary Table 2.

3.5. Demographic and other risk factors

The majority of the persons examined (68%) were farmers. Others were children of farmers and young adults going to school (22%), civil servants (1.5%), and individuals involved in different economic activities

Table 3
Prevalence of filarial antigenaemia among adults (age ≥15) with and without clinical signs and symptoms associated with lymphatic filariasis and onchocercal skin disease in 34 LF endemic districts, western Ethiopia, January 2008–July 2010

Signs/symptoms	% showing signs/symptoms	No. ICT positive (%)	χ^2	*P*-value
Lymphoedema of limbs				
Present (*n* = 69)	2.8	10 (14.5)	0.01	0.93
Absent (*n* = 2432)	NA	343 (14.1)		
Total (*n* = 2501)	NA	353 (14.1)		
Hydrocele (in males)				
Present (*n* = 14)	1.3	5 (35.7)	4.5	0.05
Absent (*n* = 1098)	NA	166 (15.1)		
Total (*n* = 1112)	NA	171 (15.4)		
Chyluria				
Present (*n* = 18)	0.7	7 (38.9)	9.2	0.01
Absent (*n* = 2483)	NA	346 (13.9)		
Total (*n* = 2501)	NA	353 (14.1)		
Lymphadenopathy				
Present (*n* = 17)	0.7	3 (17.6)	0.18	0.72
Absent (*n* = 2484)	NA	350 (14.1)		
Total (*n* = 2501)	NA	353 (14.1)		
Dermatitis				
Present (*n* = 124)	5.0	25 (20.2)	4.2	0.12
Absent (*n* = 2377)	NA	328 (13.8)		
Total (*n* = 2501)	NA	353 (14.1)		
Onchocercal skin disease				
Present (*n* = 138)	5.5	30 (21.7)	7.0	0.01
Absent (*n* = 2363)	NA	323 (13.7)		
Total (*n* = 2501)	NA	353 (14.1)		

ICT: Immunochromatographic test; NA: Not applicable.
χ^2 used was either Pearson's χ^2 or Fisher Exact Test. The latter was used when one of the cells of a 2×2 table contained an expected value less than 5. *P*-values were 2-sided asymptotic (for Pearson's χ^2 or 2-sided Exact significance test for χ^2 derived from Fisher Exact Test).

(8.5%). The overall prevalence of antigenaemia was higher among farmers (4.0%) and their children (3.6%) compared to civil servants (0.6%) and traders (1.4%) (Pearson $\chi^2 = 15.5$; $P < 0.05$). More than 90% of the participants were life-long residents of the sampled villages. When asked about mosquito net use, 46% reported using nets often and the rest rarely or never.

Religion-wise, non-believers (13.0%) and minority Catholic Christians (13.6%) had higher prevalence of *W. bancrofti* antigenaemia compared to Moslems (3.2%), Protestant Christians (4.4%) and Coptic Orthodox Christians (1.2%). The number of ethnic groups identified in the survey was 24; but two were represented by one individual each. Six ethnic groups, namely Surma, Mezhenger, Meanit, Gumz, Dezzy and Mao were highly affected (prevalence ≥10%); while four (Agew, Agnewak, Bench and Berta) were moderately affected (prevalence 1–9%); and the other 12 (Amhara, Chara, Gurage, Kefa, Kulo, Menja, Nuer, Oromo, Shekecho, Tigre, Welaita, Yem) were unaffected. Since both religion and ethnic group are highly confounded with location of residence and also seasonal migration patterns, we defer analysis of these risk factors to a more extensive multivariate analysis that will be reported separately.

When antigenaemia prevalence data from 34 endemic districts were analyzed by age, the prevalence curve suggests a peak in the 35–49 age interval (Figure 3), which was significantly different from prevalence rates in the age intervals 0–4 (Kruskall-Wallis $\chi^2 = 4.8$; $P = 0.03$) and 50 and above (Kruskall-Wallis $\chi^2 = 5.7$, $P = 0.02$). Gender-wise, the prevalence of antigenaemia was 3.9% in males and 3.6% in females (Pearson $\chi^2 < 1.0$, $P = 0.5$).

The survey villages were located at altitudes ranging from 390 m in Jor district of Agnewak zone in Gambella Region to 2300 m in Gesha district of Keffa zone in SNNP Region. *Wuchereria bancrofti* antigenaemia was not found in locations above 1698 m; the majority of districts with

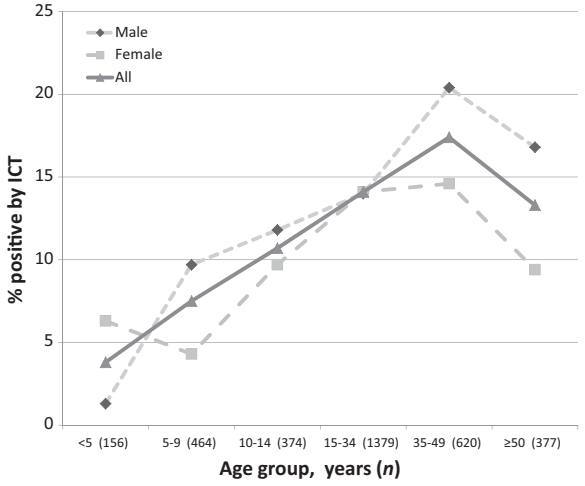

Figure 3. Age- and sex-specific prevalence of *Wuchereria bancrofti* antigenaemia in 33 endemic districts of western Ethiopia, January 2008–July 2010.
ICT: Immunochromatographic test.

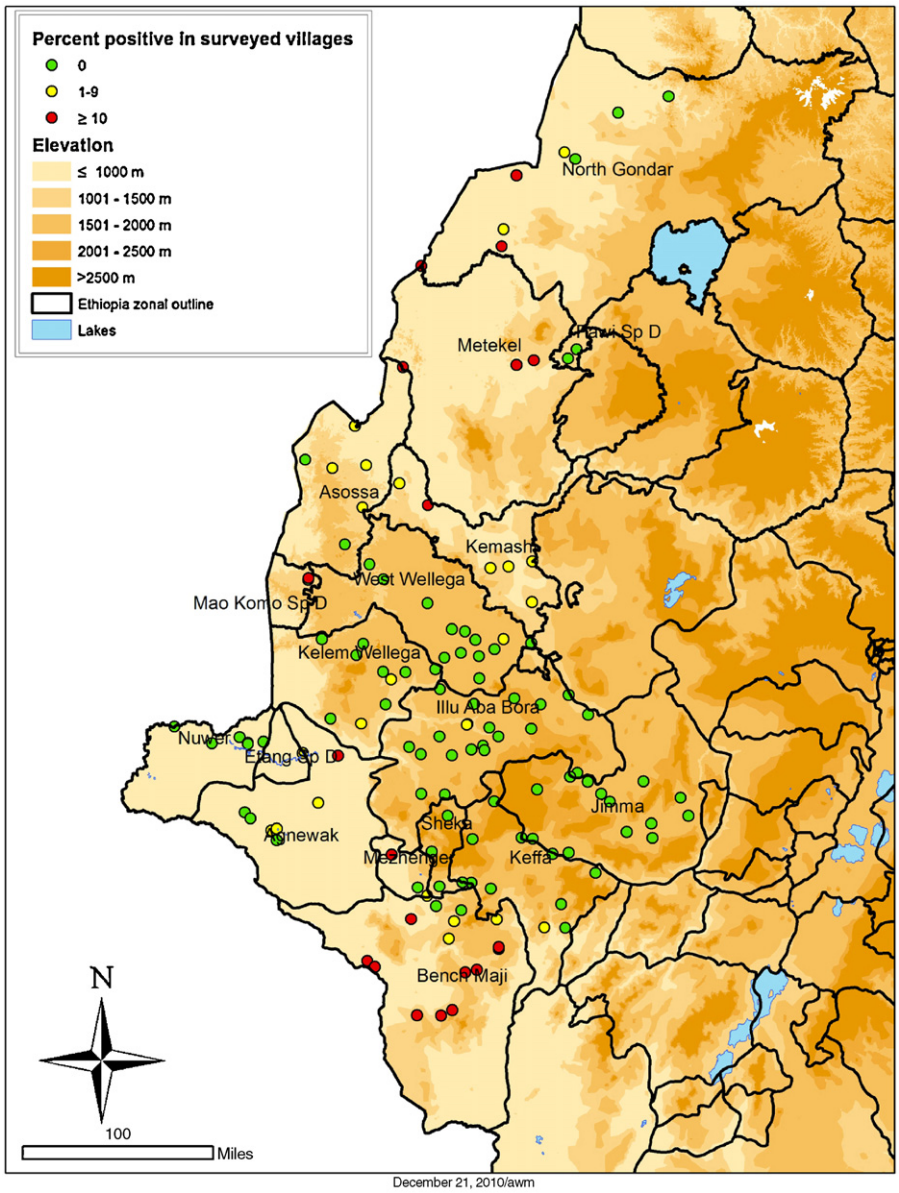

Figure 4. Raw prevalence of *Wuchereria bancrofti* antigenaemia in 125 survey villages located within 112 districts of western Ethiopia, January 2008–July 2010.
Each dot represents one individual village sampling site, showing raw prevalence computed as percent positive (no. positive divided by no. tested), and classified as shown in the legend.

positive antigenaemia were found below 1500 m. However, there were also many low altitude villages in which no positives were found. The village level results are shown on the map in Figure 4.

4. Discussion

This report confirms a much wider geographical distribution of LF in Ethiopia than previously thought (Figures 2 and 4), and also demonstrates wide geographical variability in the magnitude of its prevalence as reported elsewhere in other countries.[20] Since 12.3% of the population in the 34 LF endemic districts was positive for *W. bancrofti* antigenaemia, it can be inferred that up to 190 000 individuals in these districts are infected. This estimate is preliminary since we mostly sampled one village (sometimes two or three) per district.

Our data could not reveal the micro-level (village-level) variations in prevalence of infection in Ethiopia. In studies in Tanzania and Kenya, it was demonstrated that *W. bancrofti* transmission varied considerably within small geographical areas.[21] Ignoring such variation, at the macro-level, we found 11 out of 17 surveyed zones (Agnewak, Mezhenger and Etang Special District in Gambella Region; Bench Maji in SNNP Region; North Gondar in Amhara Region; Metekel, Asossa, Kemashi, and Mao

Komo Special District in Beneshangul-Gumuz Region; Kelem Wellega and West Wellega in Oromia Region) to be endemic for LF. In the endemic districts, a population of at least 1 547 685 persons need to be considered for planned mass drug administration (MDA) campaigns.

A recent report highlighted Ethiopia as a country with the fourth highest prevalence of LF in Sub-Saharan Africa, and puts 30 million of its people at risk of LF infection (reviewed in Hotez and Kamath, 2009).[22] The recent report of 23 parasitologically confirmed cases of LF from a dermatology clinic in Tigray Region in north Ethiopia[23] suggests the existence of yet unidentified endemic foci. Geographic Information Systems (GIS) and remote sensing should be utilized to guide the geographic mapping of 'risk' and 'non-risk' localities as has been done in India.[24] The analysis of geo-environmental variables by GIS, and the identification of significant risk factors could be key elements of the tools towards the completion of LF mapping in Ethiopia.

The age prevalence curve of filarial antigenaemia (Figure 3), depicting an increasing trend with age, is similar to reports from Malawi[25] and Papua New Guinea.[26] The relatively high prevalence of antigenaemia in young children indicates active transmission of LF taking place in the surveyed localities.

We found that CDTI villages had higher prevalence of filarial antigenaemia compared to non-CDTI villages (Table 1). Although sampling was biased towards surveying mostly CDTI districts, the surveyed non-CDTI districts were adjacent. The data suggest that the distribution of LF in western Ethiopia is spatially overlapping with onchocerciasis. Thus, the LF elimination program in western Ethiopia could easily be integrated with the ongoing onchocerciasis control program. However, several non-CDTI districts were also endemic for LF. We noted that the majority of non-CDTI LF endemic districts (11 of the total 14) were found in Beneshangul-Gumuz Region (Table 1). It is possible that some areas endemic for onchocerciasis were missed during the mapping for that disease. Initiation of MDA in districts not currently under CDTI will be more challenging, but should be started as soon as possible given the high LF antigenaemia prevalence in many of these areas.

The high prevalence of LF antigenaemia in CDTI districts raises a question about the effectiveness of CDTI in preventing LF transmission and highlights the challenges of effectively implementing CDTI. The impact of several rounds of ivermectin treatments on the levels of filarial antigenaemia is a subject of significant interest in LF elimination programs. A study in Kenya demonstrated a 43.5% decline of antigenaemia after two rounds of MDA,[27] while in Papua New Guinea three rounds of MDA decreased filarial antigenaemia by 64%.[26] Six rounds of MDA using diethylcarbamazine (DEC) or ivermectin in LF endemic communities of India did not have much effect on prevalence of filarial antigenaemia.[28] A recent report from Tanzania also confirmed the waning effects of MDA.[29] These observations leave much to be desired about the impacts of MDAs on LF antigenaemia prevalence. Thus, a critical appraisal of the coverage and effectiveness of CDTI is needed so as to illuminate whether adding albendazole to the CDTI programme would achieve the coverage necessary for LF elimination, or if not then what would be needed to improve the program.

Since the emphasis of the current survey was to detect LF antigenaemia and to map its spatial distribution, full morbidity assessments were deferred due to the impracticality of a full body clinical examination of 11 685 individuals, and the limitations of organizing night blood collections. Nonetheless, during the antigenaemia surveys, all individuals were prompted to answer questions about presence/absence of genital lymphoedema and hydrocele. The majority responded to the questions, but hesitated to show the private body parts. However, all male individuals who claimed to have hydrocele did indeed have it. Chyluria would have been difficult to observe by point prevalence survey, and thus questions about the presence or absence of it were not accompanied by physical examination. Consequently, the data on the prevalence of hydrocele and chyluria was likely to be grossly underestimated. Regarding women, due to the inadequacy of the facilities of rural health posts and cultural sensitivity, examination of women's genital parts was not undertaken. We found a higher prevalence of lymphoedema of limbs/elephantiasis than hydrocele, in spite of expecting a higher prevalence of the latter as seen in most LF endemic areas[20,27] but perhaps affected in Ethiopia by the occurrence of podoconiosis as possible causes of limb pathology. In Nigeria, prevalence rates of 1.9% and 0.4% were reported for hydrocele and lymphoedema respectively[8] cf. 0.8% and 3.6% in our current survey (Supplementary Table 2).

The main clinical signs/symptoms of LF, i.e., hydrocele and lymphoedema, were less frequent than we expected, given the relatively high prevalence of antigenaemia in some districts. If the argument that LF is a recent introduction to western Ethiopia is true,[9,10] the rarity of these chronic manifestations would not be surprising since repeated exposures to *W. bancrofti* are required for these clinical features to manifest. However, there could be other explanations for this, including human or parasite genetic differences or transmission-related factors. Given the limited amount of morbidity observed, the emphasis of the LF elimination program in Ethiopia will be the interruption of transmission, but efforts to alleviate morbidity and to curb the sufferings of affected individuals cannot be neglected.

The availability of base-line morbidity and parasitological data as provided here is crucial for planning of interventions and for monitoring impact. Entomological studies are recommended as part of the sentinel site based epidemiological studies so as to elucidate the spatial variations in vector identity, abundance and transmission intensity. The initial entomological report from the late 1960s, implicating *An. gambiae* and *An. funestus* as vectors of LF in Ethiopia[9] needs updating.

Due to the focal nature of LF infection, and owing to the possibly inefficient anopheline mosquito vectors and the recent massive scale up of long lasting insecticidal nets,[30] LF elimination in Ethiopia should be achievable with a reasonable effort. In 2007, 69.0% of households at <2000 m elevation owned at least one net and 65.6% owned an impregnated net.[31] More long lasting insecticidal nets have been distributed since 2007, although net use has not necessarily kept pace with ownership[32] and more

education and communication on net use, including risk and prevention of filariasis, is needed.

The geographic overlap of LF with onchocerciasis provides the opportunity of programmatic integration. Currently, of the 34 districts identified as endemic for LF, 20 are known to be onchocerciasis endemic and are under ivermectin distribution; while five in Gambella have received two years of albendazole and ivermectin. Following mapping of the remaining CDTI districts in East Wellega and West Shewa, addition of albendazole to ivermectin in the remaining LF endemic CDTI districts is the highest priority, followed by the initiation of both ivermectin and albendazole in the non-CDTI districts identified here, followed by other LF districts identified by future mapping in order to achieve LF elimination.

Authors' contributions: AH, KNP, TG, PMG and FOR were involved in the conception and design of the study. AH, KNP, WS, TK, LG, AT, HS and TL conducted the field surveys. Data were analyzed and interpreted by AT, PMG, WS, AWM, TK, LG, AT, HS, TL and AH. The maps were prepared by AWM. The draft manuscript was prepared by AH, PMG, FOR and WS. All authors critically revised the content of the manuscript and approved the final version. AH is guarantor of the manuscript.

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Conflicts of interest: None.

Ethical approval: Individuals participated in the survey after signing written consent forms. Individuals under 18 gave verbal assent, and their legal guardians signed the consent forms. The survey procedures and the study protocol were reviewed by Institutional Ethics Review Board of the Faculty of Medicine (Addis Ababa University), and approved by National Ethics Review Committee (NERC) of the Ethiopian Science & Technology Ministry (ESTM). Specific treatments for LF and onchocerciasis were given when diagnosis was confirmed by ICT and skin snip examination respectively.

Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.trstmh.2011.10.006.

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