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Chronic clinical manifestations related to *Wuchereria bancrofti* infection in a highly endemic area in Kenya

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Summary Clinical examinations were conducted in an effort to provide baseline data for a pilot filariasis elimination programme implemented in a *Wuchereria bancrofti*-endemic focus in Malindi district, Kenya. Of 186 males aged 15 years and above examined, 64 individuals (34.4%) had hydrocele, and the prevalence of the manifestation in those above 40 years old was 55.3%. The prevalence of leg lymphoedema in persons aged 15 years and above was 8.5%, with a higher rate in males (12.6%) than in females (5.7%). The overall prevalence of inguinal adenopathy was 8.6%, and males had a significantly higher (12.9%) prevalence of adenopathy than females (5.1%) ($P < 0.001$). The data in the present study provided support for consideration of filarial infection as a possible cause of inguinal lymphadenopathy in bancroftian filariasis-endemic areas. The results of this study also indicate that lymphatic filariasis is a serious public health problem in the northern coastal areas and morbidity control programmes should be implemented to alleviate the suffering of those affected.

1. Introduction

Lymphatic filariasis is a leading cause of permanent disability worldwide (WHO, 1995), and it is estimated that more than 40 million people are suffering from one or more of the overt manifestations caused by the disease (Molyneux and Zagaria, 2002; Ottesen et al., 1997). The clinical manifestations of lymphatic filariasis, however, vary from one endemic area to another and also differ to some extent on the species of the parasite involved (Sasa, 1976). Lymphatic filariasis caused by *Wuchereria bancrofti* infection is characterized by a wide spectrum of clinical manifestations, from clinically asymptomatic but infected individuals to patients with disfiguring chronic filarial disease. Hydrocele and lymphoedema are the most widely recognized clinical manifestations of the disease because of the gross

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disfigurement and disability that they cause in affected patients.

Although there are a few reports suggesting that chronic lymphadenopathy is an important presentation of lymphatic filariasis in *W. bancrofti*-endemic areas (Abdel-Hameed et al., 2004; Dreyer et al., 2001; Jungmann et al., 1991), the cause and significance of the manifestation has been a matter of considerable debate. Clinical studies conducted in paediatric populations in Haiti and Brazil have shown that lymphadenopathy, specifically crural and inguinal lymph node pathology, are manifestations of filarial infection in children (Dreyer et al., 1999; Fox et al., 2005). However, there are limited population-based reports on the importance of lymphadenopathy from many endemic areas.

In Kenya, hydrocele and lymphoedema have previously been reported as common chronic clinical manifestations related to *W. bancrofti* infection. A previous survey in Pate Island recorded a microfilaria prevalence of 32% and an 'elephantiasis' (lymphoedema) rate of 11% in 142 males that were examined in the study (Heisch et al., 1959). Between 1971 and 1973, a total of 5004 males aged 15 years and above was examined for clinical signs and symptoms of lymphatic filariasis in a cluster sample survey conducted in 73 sites in the Coast Province (Wijers, 1977). The overall prevalence of hydrocele alone was 29.9%, and 30.2% of those examined had either hydrocele or elephantiasis of the genitalia or limbs.

The area along the Sabaki River was previously identified to be a highly endemic focus for bancroftian filariasis during the cluster sample survey conducted in the early 1970s (Wijers, 1977), but since then there has been no report from this area and the north coast in general. In 2001, the *W. bancrofti*-endemic Sabaki River area was selected for a pilot lymphatic filariasis elimination programme using annual single dose co-administration of diethylcarbamazine (DEC) and albendazole under the Global Programme to Eliminate Lymphatic Filariasis (GPELF), which presented an opportunity to update the epidemiological data. The aim of the present study was to provide an update on the chronic clinical manifestations associated with *W. bancrofti* infection in this highly endemic area. The baseline clinical data could be used to provide supplementary information on the effect of an annual mass drug administration campaign during monitoring and evaluation of the pilot programme to eliminate lymphatic filariasis.

2. Materials and methods

2.1. Study area

In 2001, the previously known *W. bancrofti*-endemic focus along the Sabaki River in Malindi district, Kenya was selected for a pilot lymphatic filariasis elimination programme. The strategy employed for filariasis elimination in the area is annual single dose mass drug administration of DEC (6 mg/kg) plus albendazole (400 mg). The present study was conducted in 2002 during a baseline epidemiological survey in four sentinel communities: Jilore, Marikano, Magongoloni and Mkondoni, all in the Sabaki River area. A census including name, sex and age was conducted before the clinical study. The protocol for this study (KEMRI SSC No. 658) was reviewed and approved by both the Scientific Steering and Ethical Review Committees of the Kenya Medical Research Institute (KEMRI), Kenya and the Research Ethics Committee of Liverpool School of Tropical Medicine, UK.

2.2. Clinical examinations

All consenting individuals were examined clinically for chronic clinical manifestations related to bancroftian filariasis. The clinical examinations were performed during daytime in selected buildings within the study communities. A female nurse conducted examinations of females, while a male Clinical Officer conducted examinations of males.

In addition to examination for lymphoedema of the limbs, males were also examined for filarial-related lesions in the genitalia, including hydrocele and scrotal or penile lymphoedema. Hydrocele and scrotal lymphoedema were graded as previously described in a study conducted in this setting (Wijers and Kinyanjui, 1977) with few modifications. In the present study, true hydrocele was defined as a swelling of the scrotal sac at least 6 cm in longitudinal axis due to fluid accumulation. Thickening of the scrotal skin without hardening was not classified as true scrotal lymphoedema in the present study.

Females were examined for lymphoedema of the limbs and breasts, but unlike in males, examination of the female genitalia was not conducted. Lymphoedema of the legs was graded as previously described (Dreyer et al., 2002). During the physical examinations the individuals were also examined for inguinal lymphadenopathy, which was graded as previously described (Wijers and Kinyanjui, 1977).

2.3. Microfilaria and antigen testing

Blood samples were collected from consenting individuals between 20:30 and 24:00 hours. One hundred microlitre fingerprick blood samples were stored in tubes containing 0.9 ml of 3% acetic acid and used for microfilaria examination and counting the following day using the counting-chamber method (McMahon et al., 1979). Plasma samples were tested for circulating filarial antigen (CFA) using a commercial ELISA kit based on the monoclonal antibody Og4C3 following the manufacturer's instructions (TropBio Ltd, Queensland, Australia). Specimens with $\geq$128 antigen units were considered positive for CFA.

3. Results

3.1. Hydrocele and scrotal lymphoedema

Of the 348 males aged 5 years and above that were examined, hydrocele was detected in 66 individuals, with two cases found in boys below 15 years old (12 and 14 years old). The prevalence of hydrocele and scrotal lymphoedema in males aged 15 years and above in the four sentinel communities are summarized in Table 1. Of the 186 males aged 15 years and above that were examined, 64 individuals (34.4%) had hydrocele. Of the 348 males examined, 10 individuals had scrotal lymphoedema, and all cases were in persons aged 15 years and above. Of these 10 individuals with scrotal lymphoedema, four also had hydrocele. There were

Table 1 Prevalence of hydrocele and scrotal lymphoedema in males aged 15 years and above

Community	No. examined	No. (%) males with	
		Hydrocele	Scrotal lymphoedema
Jilore	42	17 (40.5)	4 (9.5)
Marikano	52	16 (30.8)	1 (1.9)
Magongoloni	39	16 (41.0)	3 (7.7)
Mkondoni	53	15 (28.3)	2 (3.8)
All	186	64 (34.4)	10 (5.4)

no significant differences in the prevalences of hydrocele and scrotal lymphoedema among the four communities.

The prevalence of hydrocele increased steadily with age. Males above 40 years old had a significantly higher prevalence of hydrocele (55.3%) than those in the 21—40 year (28.3%; $P = 0.003$) and 15—20 year (10.0%; $P < 0.001$) age groups. Similarly, males in the 21—40 year age group had a higher prevalence of hydrocele than those in the 15—20 year age group ($P = 0.017$).

A total of 144 males aged 15 years and above that were clinically examined for hydrocele also provided a blood specimen for microfilaria examination. The prevalence of microfilaraemia in 51 males with hydrocele was 35.2% compared to 24.7% in 93 individuals without the manifestation ($P = 0.284$). For 79 males aged 15 years and above who were examined for both hydrocele and antigenaemia, the prevalence of CFA in 34 males with hydrocele was 64.7% compared to 46.7% in 45 individuals without the manifestation, but the difference was not significant ($P = 0.164$).

3.2. Leg lymphoedema

Lymphoedema of the legs was detected in 42 of 782 persons examined, with two individuals below 15 years old (an 8-year-old boy and a 13-year-old girl). The prevalence of leg lymphoedema in persons aged 15 years and above among the four study communities is summarized in Table 2. The overall prevalence of leg lymphoedema in 469 persons aged 15 years and above was 8.5%. The prevalence of leg lymphoedema in males (12.9%) was higher than in females (5.7%) ($P = 0.006$).

A total of 370 individuals aged 15 years and above were examined for both leg lymphoedema and microfilaraemia.

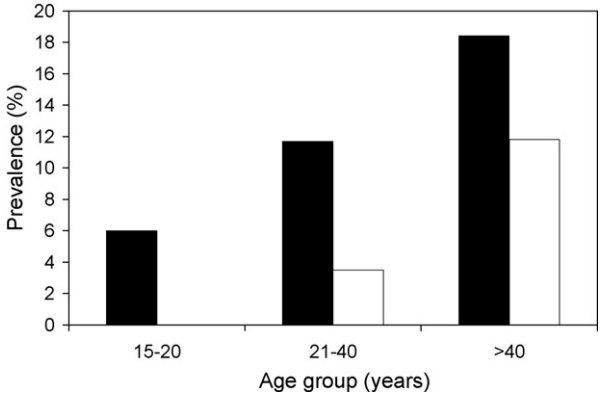

Figure 1 Prevalence of leg lymphoedema in males (■) and females (□) aged 15 years and above.

The prevalence of microfilaraemia in 29 individuals with leg lymphoedema was 31.0% compared to 25.5% in 341 persons without the manifestation ($P = 0.515$). Of 210 individuals aged 15 years and above examined for both leg lymphoedema and antigenaemia, the prevalence of CFA in 17 and 193 persons with and without leg lymphoedema was 41.2 and 47.7%, respectively ($P = 0.607$).

As for hydrocele, the prevalence of leg lymphoedema also increased with age (Figure 1). Of 50 males and 49 females in the 15—20 year age group examined, leg lymphoedema was detected in three males and no females. The majority of leg lymphoedema cases were in stage 1 (47.6%), which is mild and reversible at night. Of 11 persons with lymphoedema stage 3 and greater, eight (72.7%) were female.

3.3. Inguinal adenopathy

Of the total 782 individuals examined, 67 cases of inguinal adenopathy were detected. Of these, 45 (67.2%) and 22 (32.8%) were in males and females, respectively. The prevalences of inguinal adenopathy among the four study communities are summarized in Table 3. The overall prevalence of inguinal adenopathy was 8.6% and males had a significantly higher (12.9%) prevalence of adenopathy than females (5.1%) ($P < 0.001$).

The prevalence of inguinal adenopathy increased with age (Table 4). In general, the prevalence of adenopathy was lower in the 5—10 year age group (3.7%) and similar in the 11—20 (8.1%) and 21—40 (8.0%) year age groups. The

Table 2 Prevalence of leg lymphoedema in persons aged 15 years and above

Community	All		Males		Females	
	No. examined	No. (%) with lymphoedema	No. examined	No. (%) with lymphoedema	No. examined	No. (%) with lymphoedema
Jilore	95	6 (6.3)	42	4 (9.5)	53	2 (3.8)
Marikano	128	12 (9.4)	52	6 (11.5)	76	6 (7.9)
Magongoloni	112	12 (10.7)	39	8 (20.5)	73	4 (5.5)
Mkondoni	134	10 (7.5)	53	6 (11.3)	81	4 (4.9)
All	469	40 (8.5)	186	24 (12.9)	283	16 (5.7)

Table 3 Baseline prevalence of inguinal adenopathy in all persons examined

Community	All		Males		Females	
	No. examined	No. (%) with adenopathy	No. examined	No. (%) with adenopathy	No. examined	No. (%) with adenopathy
Jilore	174	18 (10.3)	83	12 (14.5)	91	6 (6.6)
Marikano	193	15 (7.8)	87	9 (10.3)	106	6 (5.7)
Magongoloni	201	19 (9.5)	82	11 (13.4)	119	8 (6.7)
Mkondoni	214	15 (7.0)	96	13 (13.5)	118	2 (1.7)
All	782	67 (8.6)	348	45 (12.9)	434	22 (5.1)

Table 4 Age-specific prevalence of inguinal adenopathy

Age group (years)	All		Males		Females	
	No. examined	No. (%) with adenopathy	No. examined	No. (%) with adenopathy	No. examined	No. (%) with adenopathy
5—10	214	8 (3.7)	107	5 (4.7)	107	3 (2.8)
11—20	198	16 (8.1)	105	16 (15.2)	93	0 (0.0)
21—40	201	16 (8.0)	60	8 (13.3)	141	8 (5.7)
>40	169	27 (16.0)	76	16 (21.1)	93	11 (11.8)
All	782	67 (8.6)	348	45 (12.9)	434	22 (5.1)

prevalence of inguinal adenopathy then increased two-fold in the above 40 years age group (16.0%). Males had a higher prevalence of adenopathy than females in all the age groups.

As for hydrocele and leg lymphoedema, the prevalences of active infection were compared for persons aged 15 years and above with and without inguinal adenopathy. Overall, there was a tendency toward higher prevalence of active infection in individuals with inguinal adenopathy than in those without. Microfilariae were detected in 30.2% of 53 individuals with inguinal adenopathy compared with 19.8% of 529 persons without the manifestations ($P = 0.077$). Similarly, CFA was detected in 51.3% of 39 persons with inguinal adenopathy compared with 36.3% of 339 individuals without the manifestation ($P = 0.067$).

3.4. Other clinical manifestations

Two males (aged 39 and 44 years) had penile lymphoedema. Lymphoedema of the arms was detected in six individuals, with two of the cases being bilateral. Of the six cases of lymphoedema of the arm, five were in males. All the individuals with penile or arm lymphoedema also had other clinical manifestations of bancroftian filariasis. The youngest person with lymphoedema of the arm was a 28-year-old male who had bilateral involvement.

4. Discussion

Although bancroftian filariasis was demonstrated to be highly endemic in coastal areas of Kenya through studies conducted in the 1960s and 1970s (Nelson et al., 1962; Wijers, 1977), there was a paucity in collection of epidemiological data in this region for more than 20 years. It was not until the mid-1990s that different groups started to conduct epidemiological studies in the country, but all the studies have been conducted in Kwale district on the southern coast (Estambale et al., 1994; Mukoko et al., 2004; Njenga et al., 2000; Wamae et al., 1998). The present study is the first to provide an update of epidemiological data on chronic clinical manifestations related to lymphatic filariasis on the northern coast since earlier surveys conducted in the 1970s.

Hydrocele was the most common chronic clinical manifestation of lymphatic filariasis observed in the present study. This observation is consistent with reports from most studies in sub-Saharan Africa (Estambale et al., 1994; Gyapong et al., 1993; Mukoko et al., 2004; Ngwira et al., 2002; Njenga et al., 2000; Simonsen et al., 2002; Wamae et al., 1998). The finding that hydrocele prevalence was more than 55% in males aged above 40 years indicates that bancroftian filariasis is a major cause of morbidity and disability in adult males in the northern coastal areas of Kenya. The GPELF has two major objectives: to interrupt transmission of infection by mass administration of antifilarial drugs, and to reduce suffering for those already with chronic disease. The current management of hydrocele in Kenya, as in many other parts of the world, is hydrocelectomy, but most of those affected cannot afford the cost of the operation. As the GPELF progress, it is important that ways of identifying and assisting those with hydrocele be developed.

The prevalence of hydrocele and lymphoedema in the present study was higher than reported in studies conducted in the southern coastal areas. The overall prevalence of leg lymphoedema was higher in males than in females, but fully developed non-pitting lymphoedema (stage 3 and above) was higher in females than in males. Although this finding may suggest that females had higher prevalence of advanced disease than males, it is also possible that the difference observed may be due to observer differences because different examiners examined females and males.

However, the finding that more males than females had lymphoedema of the arms suggests that the higher prevalence of leg lymphoedema in males than in females may not be an artefact. A study involving 12 communities in Kwale district also reported higher prevalence of lymphoedema in males than females (Mukoko et al., 2004). In many areas, however, the prevalence of lymphoedema is significantly higher in females than in males (Addiss et al., 1995; Njenga et al., 2000; Simonsen et al., 2002), but in other areas there is no significant difference between males and females (Gyapong et al., 1993; Supali et al., 2002). The reason for the differences in prevalence of lymphoedema between males and females among different studies is unclear, but host or parasite factors, or both, could play a role.

It is important for national filariasis elimination programmes under GPELF to include chronic disease rates during collection of baseline data before implementation of mass treatment, so that appropriate morbidity control can be incorporated into the programmes. The district hospitals have the capacity to perform hydrocelectomy, but the communities in many filariasis-endemic foci are often very poor and cannot afford to pay for the cost of the operation. To reduce the cost, arrangements could be made to provide the district hospital with materials required for the surgical operations. Simple improved hygiene practices using soap and water and skin care have been shown to result in significant reduction in lymphoedema (Addiss and Dreyer, 2000; McPherson, 2003). Thus, the implementation of chronic disease control programmes under GPELF might result in clinical benefits that could lead to increased motivation of the communities to participate in the elimination programme.

A relatively high prevalence of inguinal adenopathy was observed in the present study. A previous study demonstrated that the prevalence of inguinal adenopathy was significantly higher in communities with higher levels of infection (Wamae et al., 1998). It is possible that inguinal adenopathy is an important clinical manifestation of lymphatic filariasis in endemic areas, but it is currently underappreciated. For communities in which the majority of people walk barefoot, it has been suggested that a significant amount of lymph node pathology might be due to secondary infections obtained through injuries on the feet. This may explain why many studies have not previously reported data on prevalences of inguinal adenopathy. Nonetheless, data from histopathological and clinical studies have demonstrated that chronic lymphadenopathy is an important clinical manifestation in lymphatic filariasis-endemic areas (Abdel-Hameed et al., 2004; Dreyer et al., 1999, 2001; Jungmann et al., 1991).

The observation that inguinal adenopathy was also present in young children suggests that lymphatic pathology starts early in life. The recent application of ultrasonography to identify living adult worms presented the opportunity to localize the worms noninvasively in infected patients (Noroes et al., 1996). Ultrasonographic examination of amicrofilaraemic children presenting with chronic inguinal adenopathy in Brazil revealed the presence of living adult worms in their enlarged inguinal nodes (Dreyer et al., 2001). A recent clinico-pathological study of children infected with *W. bancrofti* demonstrated a predominance of lymph node involvement with adult worms detected in the afferent or efferent vessels of draining lymph nodes, predominantly in the inguinal region (Figueredo-Silva and Dreyer, 2005). In addition to demonstrating that lymphatic pathology occurs early in life, the studies provided evidence that living adult worms (or their products) in the inguinal glands may be involved in the development of adenopathy.

Inguinal adenopathy was significantly higher in males than in females in the present study. A similar observation was made in Haiti, where boys were found to be more likely than girls to have lymph node pathology (Fox et al., 2005). In addition, the prevalence of inguinal adenopathy also increased with age as for hydrocele and lymphoedema. Further, there was a tendency toward higher prevalence of active infection in individuals with inguinal adenopathy compared with those without the manifestation. These observations give support for consideration of filarial infection as a possible cause of inguinal lymphadenopathy in bancroftian filariasis-endemic areas.

The prevalence of active infection was similar in persons with and without lymphoedema in the present study. Previous reports on the association of lymphoedema and infection, however, have often been conflicting. Some studies have reported that persons with lymphoedema frequently have no detectable microfilaraemia (Addiss et al., 1995; Estambale et al., 1994; Lammie et al., 1993), whereas other studies have shown infection among individuals with lymphoedema (Alexander, 2000; Simonsen et al., 2002). There seems to be a general agreement that hydrocele is usually associated with infection, from studies conducted in other parts of East Africa (Meyrowitsch et al., 1995; Simonsen et al., 2002; Wamae et al., 1998) and other regions (Addiss et al., 1995; Lammie et al., 1993). However, in the present study, there was no significant difference in the prevalence of active infection in persons with hydrocele and those without the manifestation. Overall, contrary to the standard tenet in the epidemiology of lymphatic filariasis that active infection is negatively related to chronic disease, the results of the present study support a previous meta-analysis that showed no evidence for a negative association between infection and disease (Michael et al., 1994).

In conclusion, the prevalence of hydrocele (34.4%) and lymphoedema (8.5%) in the Sabaki River area are higher than reported in studies conducted on the southern coast (Estambale et al., 1994; Mukoko et al., 2004; Njenga et al., 2000; Wamae et al., 1998). This observation confirms the previous observation that lymphatic filariasis is a more serious public health problem in the north than in the south coastal areas (Wijers, 1977). It is of interest to note that the prevalence of clinical filarial disease in the area has not changed much since the 1970s. The data from our study provides justification for implementation of intervention programmes in the area to interrupt transmission and reduce morbidity and suffering related to clinical filarial disease. Similar studies to update the epidemiological data from other northern areas, including the Tana River and Lamu districts, are required.

Conflicts of interest statement

The authors have no conflicts of interest concerning the work reported in this paper.

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