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## Parasitological, serological, and clinical evidence for high prevalence of podoconiosis (non-filarial elephantiasis) in Midakegn district, central Ethiopia

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## Abstract

**OBJECTIVE**—Both podoconiosis (a geochemical non-filarial disease) and chronic filarial disease result in lower limb elephantiasis. The aims of the present study were to determine whether the elephantiasis in Midakegn district, central Ethiopia is filarial or non-filarial (podoconiosis) using serological, parasitological, and clinical examinations, and to estimate its prevalence.

**METHODS**—House-to-house visits were made in 330 randomly selected households. All household members that had elephantiasis were interviewed and clinically examined at the nearby health center to confirm presence of elephantiasis, check presence of scrotal swelling, and rule out other causes of lymphoedema. Midnight blood sample was obtained from each participant with elephantiasis for microscopic examination of *W. bancrofti* microfilaria. Day time blood sample was obtained from half of the participants for serological confirmation using the immuno-chromatographic test card.

**RESULTS**—Consistent with features of podoconiosis (non-filarial elephantiasis), none of the elephantiasis cases had consistently worn shoes since childhood; 94.3% had bilateral swelling limited below the level of the knees; no individual had thigh or scrotal elephantiasis; parasitological test for microfilariae and serological tests for *W. bancrofti* antigen turned negative in all samples. The prevalence of the disease was 7.4%. Prevalence peaked in the third decade of life, which also includes the most economically active age groups.

**CONCLUSIONS**—This study has shown high prevalence of podoconiosis (endemic non-filarial elephantiasis) and absence of filarial elephantiasis in Midakegn district. Prevention, treatment, and control of podoconiosis must be among the top priorities of public health programs in the district.

## Keywords

Podoconiosis; Non-filarial elephantiasis; Prevalence; Wuchereria bancrofti, Serology; Ethiopia

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## Introduction

Podoconiosis (endemic non-filarial elephantiasis) is a geochemical disease resulting in bilateral swelling of the lower legs in individuals with long term exposure to irritant red clay soil derived from volcanic rocks (Price, 1990). Mineral particles present in red clay soils are absorbed through the skin of the foot, are engulfed by macrophages in the lower limb lymphatics and induce an inflammatory response in the lymphatic vessels, leading to fibrosis and obstruction of the vessel lumen (Price, 1976). Podoconiosis is a common public health problem in tropical Africa, central and south America, and north India (Price, 1990). The World Health Organization has recently recognized the significance of the disease in endemic areas, and included podoconiosis in its list of Neglected Tropical Diseases (NTDs) (http://www.who.int/neglected\_diseases/diseases/podoconiosis/en/). In Ethiopia alone, podoconiosis affects up to 1 million people (Destas et al., 2003), and causes huge economic burden and social stigma (Tekola et al., 2006, Yakob et al., 2008).

Despite the significant public health burden of podoconiosis in Ethiopia, disease mapping has not been done at countrywide level. While filarial elephantiasis has been reported in the southwest low lands (Jemaneh and Kebede, 1995), recent evidence (clinical findings, absence of Wuchereria bancrofti microfilaria, and a geographic environment conducive to podoconiosis) indicates elephantiasis in the south and southwest highlands is due to podoconiosis (Desta et al., 2007, Destas et al., 2003, Alemu et al., 2010). In contrast, the type and prevalence of elephantiasis observed in Midakegn district in central Ethiopia has not been studied. Understanding the type of elephantiasis and estimating its burden in endemic areas is critical to better understand pathogenesis of the disease and for designing appropriate disease prevention, treatment and control strategies. The pathogenesis of podoconiosis mainly involves damage to lower limb lymphatic vessels, and unlike filarial elephantiasis lymph nodes are relatively intact (Price, 1977). Clinically, podoconiosis differs from filarial elephantiasis in that groin involvement and unilateral limb swelling are rare (Desta et al., 2007). As a consequence, unlike filarial elephantiasis that needs laboratory tests to detect filarial antigens, diagnosis of podoconiosis can be made at community level and progression of the disease can be curbed using footwear and personal hygiene that protects exposure to the irritant geochemical. The aims of the present study were to differentiate whether the type of elephantiasis in Midakegn district is filarial or non-filarial (podoconiosis) using clinical, serological, and parasitological methods, and to estimate its prevalence.

#### Methods

#### Study area

The study was conducted in Tulu Etaya and Ganbela *kebeles* (the lowest administrative unit in Ethiopia, equivalent to a village) of Midakegn district, central Ethiopia. Tulu Etaya and Ganbela *kebeles* are located within an altitudinal range of 1,420–1,740 meters above sea level. The population of the *kebeles* (n=5,590) is mainly engaged in subsistence agriculture, and the median age of the population is approximately 17 years. Elephantiasis was ranked as the third commonest cause of health facility visits in the district; yet there are no podoconiosis prevention and treatment services.

In the present cross-sectional study, 330 of the 1,077 households in the two *kebeles* were randomly selected. The selected households were visited to identify individuals that had elephantiasis. Written informed consent was obtained from each participant, and approval for the study was obtained from the ethics review board of the Faculty of Life Sciences, Addis Ababa University.

#### **Observation and interview**

During the house-to-house visits, observation of legs was done by four trained health extension workers (i.e., trained community health workers) to identify cases of elephantiasis. Identified cases were interviewed using an open-ended questionnaire to assess their knowledge and perception about elephantiasis, shoe wearing experience, age of onset (age at which the limb started to swell), and family history of the disease. Following this, participants were asked if they were willing to undertake physical examination and to give blood sample for parasitological and serological tests. All identified cases of lymphoedema consented to undertake the tests.

#### Clinical, parasitological, and serological examinations

All individuals that were observed and considered to have elephantiasis undertook physical examination of the legs by three clinical nurses at Midakegn Health Center to confirm presence of elephantiasis, check presence of scrotal swelling, and rule out other causes of lymphoedema. Next, approximately 20µl finger-prick blood was collected by using heparinized capillary tubes between 10 p.m. and 2 a.m. for parasitological examination. The blood sample was placed onto a microscopic slide to form thick blood smear which was hemolysed by using 0.85% physiological saline, fixed with pure methanol, and stained with 10% Giemsa stain (dilution: 1 in 20 of stock solution) for 15-20 minutes. Each slide was examined for W. bancrofti microfilaria at 100X magnification under a light microscope in the biomedical science laboratory, Addis Ababa University. Finally, day time finger-prick blood sample was obtained from 60 randomly selected participants with elephantiasis for serological examination. The immuno-chromatographic test (ICT) card was used to confirm presence of circulating *W. bancrofti* antigens according to the manufacturer's instructions (Binax, Inc., Scarborough, ME, USA). The control lines developed in the ICT test indicated that the cards were valid. Previous studies showed that the sensitivity and specificity of the ICT filariasis card test was 100% when compared with Knott's concentration and counting chamber methods (Sammy et al., 2001), and 85-100% and 96-100%, respectively when compared with three other tests (Phantana et al., 1999). The ICT card test is rapid, relatively simple to use in field settings, and can be used with day or night blood samples. It has been regarded by the World Health Organization as the "gold standard" for diagnosis of lymphatic filariasis (Nuchprayoon 2009).

## Results

Observation by the health extension workers and clinical examination by the nurses was done on a total of 1656 individuals found in the randomly selected 330 households, and revealed the prevalence of elephantiasis of the lower legs to be 7.4% (123/1,656). The prevalence of elephantiasis among men and women was almost identical. Characteristics of the identified cases and features of the disease are presented in the table below. The mean age of the identified cases was  $43.4 (\pm 15.9)$  years, and 78.0% belonged to the age group 20–60 years. The mean age of onset of the disease was estimated as  $25.8 (\pm 9.5)$  years. The majority of cases (94.3%) had bilateral swelling limited below the level of the knees. Seven individuals, all with early stages of elephantiasis, had unilateral swelling. No individual had thigh or scrotal elephantiasis. Parasitological test for microfilariae and serological tests for *W. bancrofti* antigen turned negative in all samples. The negative predictive value for physical examination (the proportion of those considered by physical examination not to have filarial disease; and who did not have filarial microfilariae by microscopy and filarial parasite antigens by serological tests) was 100%.

Most patients did not know the cause of the disease; yet, some associated the disease with - unidentified 'worm' in the water they consume from the nearby river, poverty, and evil

spirits. 30.1% of cases mentioned at least one first degree relative(s) (sibling, child, or parent) that had elephantiasis. The social stigma associated with the disease was highly evident from the public avoidance the affected displayed during the house-to-house survey. None of the patients had consistently worn shoes since childhood, and 60.2% had never worn shoes. Among those that wore shoes after onset of disease, 77.6% reported reduction in size of the swelling following use of footwear. Men and women had no statistically significant differences in these characteristics.

## Discussion

By using serological, and parasitological, and clinical investigations, this study provided compelling evidence that the elephantiasis in Midakegn district is a manifestation of podoconiosis (endemic non-filarial elephantiasis). Absence of the main clinical manifestations of lymphatic filariasis such as hydrocele in men and swelling of local glands that were observed in southwestern Ethiopia (Jemaneh and Kebede, 1995) substantiate the non-filarial basis of elephantiasis in the present study. Furthermore, limitation of the swelling below the level of the knees, bare-footedness in the majority of patients, high seasonal annual rainfall that would favor formation of the red clay soil that contains irritant inorganic mineral particles (Price, 1974, Price, 1976) indicate that the elephantiasis observed in Midakegn district is podoconiosis. This is in agreement with studies that indicated that podoconiosis is common in highland red clay soil areas of tropical Africa inhabited by poor barefooted farming communities (Davey et al., 2007b, Wanji et al., 2008).

The prevalence of podoconiosis in the present study area (central Ethiopia) was higher than that previously reported in south Ethiopia (Destas et al., 2003), and west Ethiopia (Alemu et al., 2010). The higher prevalence in Midakegn district may be because of high exposure of individuals to the irritant soil particles subsequent to extensive barefoot walking to distant marketplaces located in the highland areas of the district and during farming. Moreover, variations in the population-level frequency of genetic variants that confer susceptibility to podoconiosis (Tekola Ayele et al., 2012) may explain part of the difference in prevalence of disease in different endemic areas. Similar to most previous reports (Davey et al., 2007b, Alemu et al., 2010), the average age of highest prevalence is in the third decade of life, which also includes the most economically active age groups. About one-third of patients had affected close relatives which corroborates a previous segregation analysis that showed genetic predisposition to podoconiosis (Davey et al., 2007a, Price, 1972).

The serious economic effect of podoconiosis has been shown by a study in southern Ethiopia in which patients were half as productive as non-patients and the disease results is a loss of 45% of productive days per year (Tekola et al., 2006). Therefore, the predominance of the disease in the productive age group and its prevalence among multiple family members imply a huge economic burden to this mainly agricultural community. Shunning of patients observed in the present study concurs with a previous study finding that has showed that isolation is one of the coping mechanisms of podoconiosis patients to counter the severe social stigma (Tora et al., 2011, Yakob et al., 2008). Podoconiosis was reported to be the third common reason for health facility outpatient visits in Midakegn district and the present study showed high prevalence of the disease. However, there are no disease prevention and treatment programs in place. A simple lymphoedema management program, which was shown by a community-oriented nongovernmental organization in southern Ethiopia, to increase the quality of life of patients, and reduction in clinical stage disease and leg circumference (Sikorski et al., 2010), could be instituted through the health extension system in the district. This consists of use of simple and cheap footwear, washing feet with soap and water and elevation of limbs while sitting. In agreement with recommendations of use of footwear to prevent and treat early forms of the disease (Kloos et al., 1992, Davey et al.,

2007b), the present study also found that over three-quarters of patients that started wearing shoes reported a reduction in the size of the swelling. Community-level sensitization and health education programs in southern Ethiopia have reported qualitative reduction in social stigma against patients and families (Tekola et al., 2009).

Therefore, governmental health facilities, and non-governmental organizations must integrate prevention, treatment and control of podoconiosis with existing primary health care programs in the district. Accurate diagnosis of podoconiosis by health extension workers in the present study and by briefly trained non-health professionals in southern Ethiopia (Desta et al., 2007) shows the untapped role of the primary health care system of Ethiopia for prevention and control of the disease.

In conclusion, this study has shown high prevalence of podoconiosis (endemic non-filarial elephantiasis) and absence of filarial elephantiasis in Midakegn district. As a disease of high economic burden and social stigma, prevention, treatment, and control of podoconiosis must be among the top priorities of public health programs in the district.

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#### Table

Demographic characteristics of patients and clinical features of elephantiasis in Midekagn district, West Shoa Zone, Ethiopia

Characteristics		Number and %		
		Men (n=67)	Women (n=56)	All (n=123)
Age (in year)	14–19	4 (6.0)	8 (14.3)	12 (9.8)
	20-60	49 (73.1)	47 (83.9)	96 (78.0)
	61–70	14 (20.9)	1 (1.8)	15 (12.2)
Occupation	Farmer	64 (95.5)	55 (98.2)	119 (96.7)
	Student	3 (4.7)	1 (1.8)	4 (3.3)
Type of swelling	Bilateral below knees	62 (92.5)	54 (96.4)	116 (94.3)
	Unilateral below knee	5 (7.5)	2 (3.6)	7 (5.7)
Duration of swelling (in year)	<5	6 (9.0)	2 (3.6)	8 (6.5)
	5–9	8 (11.9)	10 (17.9)	18 (14.6)
	10–19	23 (34.3)	20 (35.7)	43 (35.0)
	20	30 (44.8)	24 (42.9)	54 (43.9)
Perception about cause of disease	Did not know	32 (47.8)	17 (30.4)	49 (39.8)
	Poverty	18 (26.9)	20 (35.7)	38 (30.9)
	Evil spirit	9 (13.4)	13 (23.2)	22 (17.9)
	'Worm' in water	8 (11.9)	6 (10.7)	14 (11.4)
Had affected first degree relatives		19 (28.4)	18 (32.1)	37 (30.1)
Worn shoes		27 (40.3)	22 (39.3)	49 (39.8)
Swelling decreased when wearing shoes (n=49)		20 (74.1)	18 (81.8)	38 (77.6)
Sought treatment		37 (55.2)	36 (64.3)	73 (59.3)