ISSN 2582 – 6050

Available Online at www.ijpba.info
International Journal of Pharmaceutical & Biological Archives 2023; 14(2):51-59

REVIEW ARTICLE

Podoconiosis, Epidemiology, Pathogenesis, Management, and Prevention Approaches with Special Focus in Ethiopia

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Received: 10 March 2023; Revised: 22 April 2023; Accepted: 05 May 2023

ABSTRACT

Podoconiosis is a condition brought on by exposing one's foot to irritable clay soil. The non-filarial endemic elephantiasis of the lower legs is hypothesized to be brought on by extended foot exposure to volcanic red clay soils. Poor agriculturalists frequently walk barefoot in the tropical highlands, which are a risk factor for exposure to irritating clay soil particles. The highlands of tropical Africa, Central America, and northwest India are typical locations for podoconiosis worldwide. African nations with a high prevalence of podoconiosis include Uganda, Tanzania, Kenya, Rwanda, Burundi, Sudan, and Ethiopia, according to data on the disease's global distribution. Podoconiosis was most prevalent in the Amhara, Oromia, and Southern Nations, Nationalities, and People regional states in Ethiopia's central highlands. Recent mapping in Ethiopia revealed that six regional states Amhara, Benishangul Gumuz, Oromia, SNNPR, Somali, and Tigray have high rates of podoconiosis. Podoconiosis is a completely preventable tropical non-communicable disease. Since wearing footwear has become customary, it has been eliminated from nations in northern Africa and Europe. Podoconiosis elimination has been given priority by the Ethiopian Federal Ministry of Health; however, the national program is struggling to stay on track for the goal.

Keywords: Control, epidemiology, Ethiopia, podoconiosis, prevention

INTRODUCTION

In the 1970s, British scientist Ernest Price identified a link between some occurrences of elephantiasis and volcanically produced soils. He named the illness podoconiosis, which is a mix of the Greek words for foot and dust. Due to the skin of the feet seeming mossy, it is also known as "mossy foot." It is a serious issue in tropical Africa where people who are extremely poor and unable to buy shoes or water for washing are cultivating soils that are irritated by environmental conditions of high altitude above 1000 m and excessive rainfall exceeding 1000 mm annually.[1]

Podoconiosis, also known as endemic non-filarial elephantiasis of the lower legs, is considered to be caused by a protracted exposure of the feet to red clay soils that have volcanic origins. Poor agriculturalists frequently walk barefoot, which exposes them to irritating clay soil particles. This practice is widespread in tropical highlands. When this extended exposure is combined with a genetic predisposition to the illness, the lymphatic capillaries are eventually damaged, resulting in edema in the lower legs.[4,5]

Ernest Price conducted in-depth studies on the etiology, natural history, distribution, and treatment of non-filarial elephantiasis in Ethiopia and throughout eastern Africa. His multidisciplinary approach to the research included clinical epidemiology, geology, pathology, and genetics. Price's groundbreaking research revealed a potential link between the disease and exposure to red clay soil.[2]

Gail Davey initially became aware of the podoconiosis epidemic in one of Ethiopia's

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southern areas. Since then, she has spearheaded podoconiosis research, describing the disease and its consequences using a multidisciplinary approach that includes epidemiology, immunology, mineralogy, genetics, bioethics, social sciences, and economics. In addition to approaching podoconiosis from a multidisciplinary standpoint, Price and Davey went above and above by collaborating with local and international organizations that converted the study into illness.[3]

The condition nearly often results in bilateral, although asymmetrical swelling of the lower legs. Scientific evidence now available suggests that genetic predisposition and exposure to irritating red clay soil in endemic locations play significant roles in the disease's etiology, despite the fact that the cause is still not fully understood.[14]

Podoconiosis is a serious yet underappreciated issue that has social, economic, developmental, and public health implications in areas where it is endemic. National and international attention has recently been drawn to the condition. The World Health Organization (WHO) has only recently recognized it as a neglected tropical disease (NTD); due to the incapacitating effects, it has on affected communities. Podoconiosis has also been approved for inclusion in the National Master Plan for NTDs by Ethiopia's Federal Ministry of Health (FMOH). It is a geochemical sickness that affects people who have been exposed to red clay soil that is made of alkalic volcanic rock. The condition, which results in significant impairment, is characterized by bilateral swelling of the lower legs and skin abnormalities that are mossy and nodular.[10,16]

EPIDEMIOLOGY

Throughout the world, podoconiosis is prevalent in the highlands of tropical Africa, Central America, and northwest India. Podoconiosis had previously been documented in various regions of Europe (France, Ireland, and Scotland) and North Africa (Algeria, Tunisia, Morocco, and the Canary Islands); but, at this time, there have been no reports of the disease in these nations, most likely due to the extensive usage of footwear. Africa is home to a number of nations with a high frequency of podoconiosis, including Uganda, Tanzania, Kenya, Rwanda, Burundi, Sudan, and Ethiopia. Equatorial Guinea, Cameroon, Chad, Niger, Nigeria, the islands of Bioko, Sao Tome and Principe, and Cape Verde are some other African nations where podoconiosis has been documented. Mexico and Guatemala, as well as the South American nations of Colombia, Ecuador, and Brazil, have podoconiosis cases documented in their highland regions. Sri Lanka and Indonesia also had it.[1]

Up to 1 million podoconiosis cases are thought to occur in Ethiopia alone, and the majority of these people fall into the economically active age range. In endemic parts of Ethiopia, the disease is present at a prevalence of more than 5%. Segregation analysis has been used to examine the genetic causes of podoconiosis in multiple affected families in Ethiopia. The study estimated a heritability of 0.63 (i.e., 63% of the variance in podoconiosis occurrence is explained by genetics), a sibling recurrence risk ratio of 5.07 (i.e., an individual with an affected sibling is 5 times more likely to develop podoconiosis than a randomly selected individual in the general population), and age and footwear were significant environmental covariates. Then, a genome-wide association research demonstrated that genetic variations in the HLA class II loci contribute to podoconiosis susceptibility.[3,5,17]

The WHO included podoconiosis to the lists of NTDs because of its significance for public health. As a result, it is currently recognized as a significant NTD in East Africa, South America, and Asia. After lymphatic filariasis (LF), podoconiosis is the second most frequent cause of tropical lymphedema. The number of people who have podoconiosis worldwide is estimated to be 4 million. According to other research, most patients experience at least five episodes of recurrent inflammatory swelling in their lymphedematous legs ("acute attacks"), which result in lost workdays. 12–14 patients encounter extreme stigma and discrimination. According to estimates, one million persons in Ethiopia have podoconiosis, making it the nation with the disease's projected highest burden.[4,16]

Ethiopia has the largest number of podoconiosis patients. It is estimated that approximately 1 million individuals are affected, with an additional 19.2 million people (22–24% of the population) at risk

from exposure to red-clay soils 23, 26, and 29, compared to 30 million from LF. Furthermore, the prevalence estimates from 56 market counts ranged from 0.4 to 3.7% 27, which are likely underestimated because to patients' limited mobility and stigma. More recent Ethiopian research estimated a frequency of 5.5% in southern Ethiopia. 5.2% in western Ethiopia, 7.4% in Central Ethiopia, 15% in Northern Ethiopia, and 3.3% in Southern Ethiopia. In Ethiopia, the prevalence of podoconiosis showed significant geographic variation, which suggested that there may be spatial patterns to the spread of diseases [Figure 1].[5,6]

Prevalence estimates based on attendee counts at fifty-six markets ranged from 0.42% to 3.73%, and subsequent analysis in Wollamo zone, southern Ethiopia, revealed a prevalence of 5.38% across five marketplaces. The southern Ethiopian settlement of Ocholo is located at 2000 m altitude in the mountains west of Lake Abaya. Elephantiasis was found in 5.1% of long-term residents, and 5.2% of those resettled 7–8 years ago in two resettlement schemes in Ilubabor, western Ethiopia. More recent population-based surveys in northwest, southern, and western Ethiopia (personal communication), as well as northern Cameroon (personal communication), have found prevalence rates of 6%, 5.4%, 2.8%, and 8.1%, respectively.[9]

Podoconiosis is a common disease in Ethiopia, according to current mapping. There are 345 districts with a prevalence of >1%, as seen on the national map of podoconiosis. Oromia, Amhara, and SNNP regional states are home to the majority of these districts. These regions where podoconiosis is endemic are home to 35 million people overall. Six regional states (Amhara, Benishangul Gumuz, Oromia, SNNPR, Somali, and Tigray) in the nation are affected by podoconiosis on a widespread basis.[9]

Although it seldom results in death, podoconiosis is a crippling and severely disfiguring disorder that throws a significant mental burden on each patient. Implementing disease prevention strategies and programs require a thorough understanding of the sociocultural environment in which patients with podoconiosis live and the effects the disease have on them. Patients with podoconiosis endure severe stigma in their societies. According to earlier qualitative research, the disease's hereditary propensity adds to the social burden it places on society. Similarly severe podoconiosis-related stigma has also been described in later trials conducted in Ethiopia [Figure 2a-c].[6]

PATHOGENESIS

The etiology of podoconiosis has not yet been completely understood. Based on existing evidence, the most accepted cause of podoconiosis is inorganic particle-induced inflammatory response on a background of genetic susceptibility.[3] Mineral particles, absorbed through the skin of the foot, are taken up into macrophages in the lower-limb lymphatics and induce an inflammatory response in the lymphatic vessels, leading to fibrosis and obstruction of the vessel lumen [Figure 3a-c]. This leads initially to edema of the foot and the lower leg, which progresses to elephantiasis: Gross lymphedema with mossy and nodular changes of the skin.[2]

A study by Price and Pitwell about the mineral content of the lymph nodes in barefoot people with and without elephantiasis of the legs confirmed the presence of elements including silicon, aluminum, and iron in all barefoot people, with slightly higher amount in those with elephantiasis suggesting the etiological significance of these particles. In addition, endemic areas were free of filariasis; footwear had a protective effect; birefringent silica particles were found in the lymph node macrophages; and the dermal content of various mineral elements was consistent with local soils, leading to the postulation of soil-induced disease. After he conducted epidemiological and geological studies, Price indicated that silicate particles cause subendothelial edema, endolymphangitis, collagenization, and obliteration of the lymphatic lumen. Biopsies from inguinal and femoral lymph nodes of affected individuals have shown the presence of birefringent particles and foreign body granuloma. Electron microscopy of the lymph node biopsy and micro-analysis showed that the particles are found inside the macrophages and consist dominantly silica with varying amount of

Figure 1: Podoconiosis; nodular form of podoconiosis of an adult patient in North Ethiopia[21]

Figure 2: (a) Early edema of the foot with splaying of the big toe. (b) Lichenification on the dorsum of the anterior foot. (c) Mossy growth on the lateral part of the foot in slippery distribution[21]

Figure 3: (a) Water bag pitting. (b) Fibrotic swelling with nodularity. (c) Oozing and maceration on skin folds[22]

Figure 4: Treatment and prevention of podoconiosis. (a) Washing (b) Bandaging (c) Shoe wearing from childhood as prevention method[21]

aluminum, titanium, and iron oxide.[2]

Histopathological examination of the lymph nodes showed that they contained birefringent minerals which, by microanalysis, were identified as sub-micron particles of kaolinite and small amounts of quartz, hematite, goethite, and gibbsite. When crystalline silica was injected into lymphatic vessels in the legs of rabbits, it resulted in macrophage

Figure 5: Use of elastic bandage to treat podoconoisis[21]

Figure 6: Simple treatment can use for podoconoisis[21]

proliferation followed by lymphatic fibrosis and blockage similar to that seen in podoconiosis. Price hypothesized that individual difference in the tissue handling of absorbed minerals plays a role in the development of full-blown podoconiosis. It is probable that certain minerals reach the nodes by transit through the afferent lymphatics after being absorbed through the plantar skin. Because of the known fibrogenic potency of silica, the hypothesis has emerged that the disease is an obstructive lymphopathy caused by fibrotic response to silica of soil origin. Animal study of injecting silica particles has shown that the obstructive effect of silica within the lymphatic system is on the lymphatics themselves and not on the draining lymph nodes.[17,11]

Histological examination of the lymphedematous skin shows epidermal hyperkeratosis, acanthosis, and hypergranulosis. This may be a consequence of growth factors released by the inflammatory cells, which are attracted to the irritant. The papillary dermis shows fibrosis and a perivascular infiltrate of lymphocytes, mast cells, and plasma cells plus coarse, wiry bundles of collagen. The deeper dermis shows sclerosis, reflecting temporal progression of the fibrosis. The presence of dilated blood vessels with surrounding fibrosis mimics the findings of stasis. However, there is no hemosiderin deposits. This feature, together with dermal sclerosis, contributes to the hardness and irreversibility of lesions. A recent study in northern Ethiopia has indicated that patients with podoconiosis have significantly lower stratum corneum hydration in the skin of their lower legs and feet than unaffected individuals from the same community, suggesting increased risk of cracking, susceptibility to infection, and lymphedema (Ferguson *et al*., 2013) [Figure 4a-c]. By comparing cases of podoconiosis at early and advanced disease stage and unaffected controls from the same area, a study has found differences in serum levels of oxidative stress biomarker levels and TGFβ1, suggesting their role in the pathogenesis of podoconiosis.[18]

Early Symptoms

The main presentation of the patient early on the course can be burning sensation or/and itching on the foot. The burning foot is characterized by patients, as on and off burning sensation on the foot following a day-long barefoot exposure on the farm or field. Occasionally, the patient may associate the condition with traditional beer consumption or for females with menstruation. Sometimes, the burning pain may extend into the lower leg and be associated with fever and a tender femoral lymph node. In most patients, this may continue for several years affecting one limb. Onset in the other limb may not occur for many months or years. Each episode of attacks resolves spontaneously or after a few days of rest and elevation of the affected limb. The itching on foot is described by the patient as persistent or intermittent itching of the dorsum of the foot, often over the dorsum of the anterior one-third and in the first or second web space. Constant rubbing leads to a reactive thickening of the skin (lichenification) suggesting chronic eczema. Repetitive scratching may lead to a breach in barrier function of the skin, which may lead to recurrent cellulitis or lymphangitis.[13]

The clinical picture and course of podoconiosis vary based on the time of presentation (early and late) and type of the lymphedema (water bag versus sclerotic or both) (1).

Early Signs

Identification of the earliest signs of podoconiosis is helpful for timely intervention which will have the potential to halt progression of the disease. The three key early signs are as follows:

Leg swelling

A transient edema of the lower leg especially the foot which increases following long working day and disappears in the morning after overnight rest (leg elevation). At this stage, the edema can be pitting. The unilateral foot edema can be associated with pitting on the anterior foot pad and splaying of the forefoot, widening of the forefoot with separation of the toe, particularly between the first and the second toes. The swelling of the forefoot may cause the toes to lack their usual curvature, appearing as sausages. The deep edema of the plantar foot may lift the toe off the ground.

Thickening of the skin

The skin over the anterior and dorsum one-third of the foot becomes lichen feed and thickening can occur which renders the skin particularly overlying the first toe web space, stiff, and unable to be pinched (positive Stemmer's sign). The increased skin markings, usually longitudinal, may be evident and exaggerated by squeezing together the toes; it is significantly visible between the first and second toes.

Mossy foot

Warty and papillomata's growth with rough surface are usually seen on the foot involving the dorsum of foot in the anterior one-third and the sole of foot in slippery distribution accentuating lateral side of sole and the heel of foot. This hyperkeratosis and wart growth looks like a "moss" but it is rough to touch [Figure 3c]. Patients who have started to wear shoes usually do not have the hyperkeratosis lesion. A mismatched and asymmetric enlargement of the second toe on the affected foot is a common finding.[3,7,8,14]

Later Symptoms

Following the recurrent burning episodes associated with transient swelling, the leg diameter progressively increases and establishes a persistent lymphedema. The late clinical picture can vary greatly. Conventionally, three main forms of lymphedema are distinguished in podoconiosis.

Soft and pitting ("water bag" type)

Subdermal edema that is soft to the touch and pits with pressure; it has little dermal fibrosis. Usually, the swelling has a narrow neck around the knee and wider base on the foot. The skin will have a smooth and dumpy surface, with occasional lymphorrhea, especially on the foot which attracts flies. Often there is loss of normal hair. With time, the foot and lower leg become large and flabby with elevation; there is considerable reduction in size. Swelling may lead to redundant skin folds around the ankle joint and ballooning over the toes. The disability to the patient is due to the great size of the limb and heaviness.

Hard and sclerotic/fibrotic or leathery leg "elephantiasis"

Sclerosis governs the changes in the skin and subcutis, which become woody hard and grossly thickened. The overlying epidermis on the foot takes on a sandpaper-like appearance which eventually, due to increasing hyperkeratosis, takes on the so-called "mossy" appearance.

Under areas of compression, such as a sandal strap, the skin remains smooth and dumpy. The stiff, sclerotic nature of this altered skin especially on the ankle compromises the normal flexibility of the ankle and toe which makes it vulnerable to cracking and trauma, in addition to ankylosis of the joints.

Mixed elephantiasis

Characterized by grossly swollen limb below the knee and non-pitting edema, not reducible overnight (leg elevation) and no sclerotic change. There may be variation in the compressibility between the lymphedema below the ankle and above the ankle.[12,19]

Other Clinical Features Associated with Podoconiosis

Fibrous nodules

These lumps of redundant skin with subepidermal fibrosis occur mostly on the dorsum of the toe and

foot; they tend to occur mostly with the fibrotic (sclerotic) and the mixed lymphedema. The nodules can start as smooth surface skin folds and progress to timorous growth which considerably inhibits footwear.

Interdigital and skin fold maceration

Whitish and wet patches on the interdigital space with occasional fissuring. The maceration is associated with oozing (lymphorrhea) and usually has bacterial and fungal infections. Dumpy foot from the lymphorrhea with microbial super-infection leads to the foul smell which adds to the stigma and social isolation of the patient.

Acute lymphangio-adenitis (ALA) or cellulitis

In general, lymphedematous limb is said to have compromised immunologic clearance mechanism which leads to recurrent infection. One of the most common causes of morbidity in podoconiosis is ALA affecting about 97% patients with a recurrence rate of 5 to 5.5 times/year and in each attack, the patient becomes bedridden for 4 days. ALA manifests as acute pain on the limb with fever, chills, and rigor. The limb becomes reddened, hot, and tender with tender swelling in the draining femoral lymph node.

Fusions of toes

Some podoconiosis patients present with toe fusions which starts on the fourth and second inter-digital spaces forming a web-like skin growth connecting the toe from proximal and extending distally.

Scaring and de-pigmentation

Recurrent itching and ulcerative skin on the dorsum of foot results in scarring and de-pigmentation of the skin on the distal foot. The scarring causes toe resorption which confuses with leprosy.

Price classified the clinical type of podoconiosis lesion based on the degree of fibrosis as the soft "water bag" or more fibrotic nodular "wooden" types. Recently, a validated podoconiosis clinical staging system that enables clinicians to assess the results of medical and surgical treatment, and investigators to document the effects of public health preventive interventions, has been developed. The staging system helps grade the severity of the disease and monitor treatment outcome. Investigators in Ethiopia developed a staging system with the aims of enabling disease burden to be measured and interventions to be assessed based on the staging:

- Stage 1- Swelling that is reversible overnight
- Stage 2- Swelling below knee that is not completely reversible overnight and if present, knobs/bumps are below ankle only
- Stage 3- Swelling below knee that is not completely reversible overnight and knobs/bumps are above ankle
- Stage 4- Swelling above knee that is not completely reversible overnight knobs/bumps are located anywhere in the foot or leg
- Stage 5- Joint fixation - swelling anywhere in the leg or foot.[2,14]

Differential Diagnosis

The differential diagnosis for podoconiosis includes other causes of tropical lymphedema, such as filariasis or leprosy and mycetoma pedis. Podoconiosis begins almost exclusively in the foot, as opposed to filariasis, where the initial edema can appear anywhere in the lower extremities. Podoconiosis is usually asymmetrically bilateral, whereas filariasis and mycetoma are usually unilateral. In addition, groin involvement with podoconiosis is extremely rare and is usually indicative of filariasis. If a clinical distinction between podoconiosis and filariasis cannot be made based on history and examination alone, blood smears and ELISA antigen testing can be useful to screen for filariasis.[19]

The disfigurement associated with podoconiosis can include soft or firm edema, and in later stages, firm nodules and a mossy appearance, whereas mycetoma is characterized by firm nodules and edema, usually without the mossy appearance of podoconiosis. In addition, the edema of podoconiosis is typically more striking and extends more proximally than the edema of mycetoma. Radiology can help distinguish between podoconiosis and mycetoma if the diagnosis is

questionable. Local epidemiology can also be a clue to diagnosis, as podoconiosis is typically found in higher altitude areas with volcanic soils, whereas mycetoma is found along the "mycetoma belt" between latitudes 15 south and 30 north, and filariasis is uncommon at higher altitudes and other environments in which the mosquito vector is less prevalent. Podoconiosis can be distinguished from leprosy by the preservation of sensation in the affected limb and the isolation of disease to the lower extremities.[20]

TREATMENT, MANAGEMENT, AND PREVENTION APPROACHES

Podoconiosis is an entirely preventable non-communicable disease. It has been eradicated from countries in northern Africa and Europe since footwear use has become standard.[14]

Although the Ethiopian FMOH has prioritized podoconiosis for elimination by 2020, the national program is faced with significant challenges to stay on track for the 2020 target.[15]

The key strategies for podoconiosis control are prevention of contact with irritant soil (primary prevention) and lymphoedema morbidity management (secondary and tertiary prevention) The primary prevention of podoconiosis includes using footwear, regular foot hygiene, and covering the house floor. These measures will prevent contact between the foot and the minerals triggering the inflammatory process. Secondary and tertiary prevention of the disease is based on lymphoedema management which consists of foot hygiene, foot care, wound care, compression, exercises and elevation, treatment of acute attack, and use of shoes and socks to reduce further exposure to the irritant soil. In some cases with nodules, surgical excision of the nodules may be recommended.

Price described the objectives of secondary and tertiary prevention as:

- To arrest the progress of early disease
- To reduce the frequency of acute attack
- To reduce the swelling of the limbs, and
- To maintain reduction of the swelling.

The first proof-of-concept study of podoconiosis lymphoedema morbidity management indicated modest clinical improvement and significant improvements in quality of life. At present, there is an ongoing randomized controlled trial which is aimed at measuring the effectiveness and cost-effectiveness of morbidity management [Figures 5 and 6].[2,11]

Podoconiosis Treatment

- Avoiding or minimizing exposure to irritant soils by wearing shoes
- Covering floor surfaces inside traditional huts
- Wash feet daily with soap and water
- Foot hygiene: Daily washing with soap and water (diluted bleach is also useful in the early stages of treatment)
- Skincare: Use of simple ointment/moisturizer
- Daily use of socks and shoes
- Use of elastic bandage
- Elevation and movement
- Minor surgery to remove nodules.

Podoconiosis Treatment Helps to

- Eliminate the bad odor
- Prevent and heal entry scratch
- Help patients self-confident
- Reduce the size of the lymphoedema
- prevent disability
- Prevent economic loss
- Make the foot fit for a shoe.

CONCLUSION

Podoconiosis is an endemic form of non-filarial elephantiasis of the lower legs that has been suggested to be brought on by prolonged foot exposure to red clay soils of volcanic origins. In Ethiopia, there have been incidences of podoconiosis, with the majority of those affected being in their prime working years. The highlands of tropical Africa, Central America, and northwest India are the regions of the world where podoconiosis is most common. Podoconiosis is a non-communicable disease that is entirely preventable.

As conclusion widespread usage of shoes is recommendable and has made it extinct in some of northern African and European nations. Preventing

contact with irritating soil (primary prevention) and managing lymphedema morbidity (secondary and tertiary prevention) are the main methods for controlling podoconiosis. The three main methods of preventing podoconiosis are wearing shoes, maintaining good foot cleanliness, and covering the floor.

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