



Review article

Epidemiology and sex differences of podoconiosis in Ethiopia: A systemic review and meta-analysis



Brhane Berhe^{a,*}, Haftom Legese^b, Fitsum Mardu^a, Kebede Tesfay^a, Gebre Adhanom^b, Tsega Kahsay^b, Getachew Belay^c, Hadush Negash^b

^a Unit of Medical Parasitology, Department of Medical Laboratory Sciences, College of Medicine and Health Sciences, Adigrat University, P.O. Box: 50, Adigrat, Ethiopia

^b Unit of Medical Microbiology, Department of Medical Laboratory Sciences, College of Medicine and Health Sciences, Adigrat University, P.O. Box: 50, Adigrat, Ethiopia

^c Unit of Clinical Chemistry, Department of Medical Laboratory Sciences, College of Medicine and Health Sciences, Adigrat University, P.O. Box: 50, Adigrat, Ethiopia

ARTICLE INFO

Keywords:
Determinants
Epidemiology
Ethiopia
Podoconiosis
Prevalence

ABSTRACT

Objectives: Podoconiosis is a poorly understood neglected tropical disease which results in a high socio-economic burden. In Ethiopia, despite the high prevalence, morbidity, and socio-economic impacts, little information is available about the disease. Thus, this review aimed to assess the effect of sex differences and pooled prevalence of podoconiosis in Ethiopia.

Study setting: Ethiopia is a country located in East Africa.

Methods: Published literature on the prevalence of podoconiosis in Ethiopia was searched through MEDLINE/PubMed, Cochrane Library, Goggle scholar, and Global Health. Studies conducted in humans, open access, and met 50% threshold on the quality assessment checklist score adopted from Joanna Briggs Institute were eligible for inclusion. Data were extracted using first author, year of publication, participants' population, setting (urban/rural), study design, podoconiosis infection among males, the total number of males, podoconiosis infection among females, the total number of females, and context using Microsoft™ Excel. R statistical software version 3.6.1 was utilized to carry out the meta-analysis. The protocol of this review is registered in the PROSPERO international prospective register of systematic reviews and assigned a registration number of CRD 42020154697.

Results: We performed heterogeneity, sensitivity, and publication bias analysis for the included articles. We identified 229 records, of which 11 studies met the inclusion criteria. The pooled prevalence of podoconiosis in Ethiopia was 6% [95% CI: 5%; 6%]. Subgroup analysis by setting indicated slightly higher prevalence in rural settings. The odds of podoconiosis infection among female is 1.15 times that of males. The effect of sex on podoconiosis was sub-grouped by study setting and the odds of females were 1.29 times at increased risk of acquiring podoconiosis than males ($p < 0.01$) in rural settings.

Conclusions: The prevalence of podoconiosis in Ethiopia is high. This review suggested that females are at higher risk of developing podoconiosis than males, particularly in rural communities which has health promotion and awareness implications regarding protective wear.

1. Introduction

Podoconiosis is a neglected tropical disease (NTD) manifesting as swelling of the lower legs most often in individuals having prolonged barefoot exposure, and predominantly farmers working in red clay soil covered highland areas are affected [1, 2]. It affects about four million people globally [2] and, in Africa, the epidemiology is variable with an overall prevalence of 7.8%. Prevalence reports by country include Burundi (1%) [3], Rwanda (0.6%) [3] and Ethiopia (0.4%–3.7%) [4].

Although the World Health Organization (WHO) launched efforts towards the elimination of podoconiosis in 2016, the global burden of the disease is poorly understood and its socio-economic and social stigmatization remains high [5].

It is estimated that up to 1 million cases of podoconiosis exist in Ethiopia [6]. The disease occurs in highland red clay soil areas, mainly among poor and barefooted rural dwellers. This soil type is estimated to cover 18% of the surface area of Ethiopia, on which an estimated 22–25% of Ethiopia's population (19.3 million) lives. In endemic areas of

* Corresponding author.

E-mail address: birhaneberhe54@gmail.com (B. Berhe).

<https://doi.org/10.1016/j.heliyon.2020.e05446>

Received 19 June 2020; Received in revised form 10 August 2020; Accepted 3 November 2020

2405-8440/© 2020 Published by Elsevier Ltd. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

Ethiopia, the prevalence of podoconiosis is high; 9.1% in Illubabor Zone, Oromia Region; 6% in the Pawe resettlement area, northwest Ethiopia; 5.5% in Wolaita zone, Southern Ethiopia; 2.8% in Gulliso Woreda, West Wollega zone, Oromia region; 7.4% in Midakegni, West Shewa Oromia region; 3.3% in Debreelias and Dembecha, East and West Gojjam, Amhara region [6, 7].

The economic burden of podoconiosis was also estimated in endemic areas of Ethiopia and it indicated that the total productivity loss for a patient per year amounted to 45% of total working days which corresponds to 63 US dollars, and the direct cost per patient per year was 143 US dollars, giving a total loss of 206 US dollars per patient per year. In a zone of 81,000 podoconiosis affected patients, the total overall annual cost of the disease was estimated to be exceeded 16 million US dollars per year [8]. Social stigma towards people with podoconiosis is common with patients being excluded from school, discriminated from participation in local meetings, churches, and mosques, and barred from a marriage with unaffected individuals [9].

Despite the high prevalence, morbidity, and socio-economic impact [8, 9], little information is available about the disease burden is available from the Ethiopian context. Consequently, little effort has been made at federal, regional, or zonal levels to control podoconiosis. Through a nationwide podoconiosis mapping and study to assess the effectiveness of lymphedema management and behavioral studies to increase shoe-wearing practices, preventive activities include health education and provision of locally produced shoes at subsidized prices as well as treatment efforts including the use of a package of items (foot hygiene, soap, antiseptic, ointment, pressure bandages, socks, and shoes) began [10]. However, podoconiosis remain a persisted community and national concern. Due to low awareness and inadequate attention to podoconiosis, many challenges exist, which can be categorized as clinical, prevention/control, and community-level challenges. For example, from a clinical perspective, there is a lack of access to prevention, diagnostic, and treatment services, gaps in service referrals, and, most importantly, limited knowledge of health professionals about the causes and clinical management of podoconiosis and differential diagnosis from other causes of lymphedema. From a prevention/control perspective, there is a lack of updated data on the geographic distribution and epidemiology of the disease, shortage of funding, absence of comprehensive data on the distribution and burden of podoconiosis. At the community level, podoconiosis is often neglected by the support of nongovernmental organizations and global health advocates due to its non-infectious and non-fatal disease progression, perpetuating this socio-economically devastating disease of the poor, which requires low-cost interventions such as access to water for food hygiene and decent foot ware [6, 11, 12, 13]. So, this systemic review provides insights into the pooled prevalence of podoconiosis and the difference in the likelihood of podoconiosis in men and women in Ethiopia.

2. Methods

2.1. Study setting

This systematic review and meta-analysis were conducted in Ethiopia which is the second most populous nation in Africa with over 102 million population divided into nine regions and two self-administrative states [14].

2.2. Protocol design and registration

A systematic review and meta-analysis of observational studies were conducted. This review is appropriate for summarizing and synthesizing research evidence to inform policymakers and practices by integrating results from several independent primary studies. Procedures for the review were done in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-analysis Protocol (PRISMA-P) and checklists [15] and Meta-analysis of observational studies in epidemiology

guidelines [16]. The protocol was registered in the International Registration of Systematic Reviews (PROSPERO), a platform for the international registration of prospective systematic reviews [17] with a registration number of CRD 42020154697.

2.3. Search strategy and searching sources

A search strategy was developed using specific key concepts in our research question: Epidemiology, Podoconiosis, Non-filarial elephantiasis, Determinants, and Ethiopia. For each key concept, appropriate free-text words and Medical Subject Headings (MeSH) was developed. The free-text words (truncated or with wildcards) and MeSH terms were combined using Boolean logic operators: “AND” and “OR” appropriately. We comprehensively searched MEDLINE/PubMed, Cochrane, Goggle scholar and Global Health. The search strategy for each database was validated by three authors independently. We used the following search words; (((((((“Prevalence”[Mesh]) OR “Epidemiology”[Mesh]) AND “Elephantiasis”[Mesh]) AND “Epidemiologic Factors”[Mesh] OR “Determinants” [Mesh])))). Besides, we also used keywords: “Prevalence and associated factors of podoconiosis in Ethiopia”, “Epidemiology and determinants of podoconiosis in Ethiopia”. We have also used “non-filarial elephantiasis” as a synonymous for podoconiosis. To avoid missing relevant studies and grey literature, we searched other sources by looking through reference lists of relevant reviews and selected studies, searching websites of relevant organizations (i.e., WHO, CDC, FMOH), and searching of relevant articles using the PubMed-related article feature, Google Scholar, World Health Organization, and Centers for Disease Control and Prevention websites, as well as proceedings of the International Union Against Podoconiosis conference proceedings (Conference Proceedings Citation Index-Science (CPCI-S), Dissertations & Thesis (www.proquest.com) and expert information.

2.4. Study selection and data extraction

After the literature search, all references were imported to EndNote X7 (endnote.com). The collected data were imported into Microsoft™ Excel. Two researchers (BB and HN) independently screened studies for eligibility. Following the screening, selection of studies was carried out, irrespective of their design and publication date. A prespecified criterion was used to screen articles by title, abstract and full text read. The data extraction checklist was developed from literatures. The researchers autonomously reviewed titles and abstracts against eligibility criteria to categorize the article as either ‘include’ or ‘exclude’ to avoid selection bias of searched articles. A third researcher (GA) was consulted for discrepancies at each stage of the selection. We resolved differences in opinion through discussion. Data were extracted by BB and HN from each selected study using a predetermined list of categories/characteristics: First author, year of publication, participants/population, setting (urban/rural), study design, podoconiosis infection among females, the total number of females, podoconiosis infection among men, the total number of men and context using Microsoft™ Excel.

2.5. Handling of missing outcome data

In the case of missing outcome data on select articles, we initiated e-mail requests through the first authors. The attempts to contact the authors were not successful and we excluded these articles from the review and meta-analysis.

2.6. Eligibility criteria

Studies conducted among human participants, found in open access, and meeting or exceeding a 50% quality assessment score was eligible for inclusion.

2.7. Quality assessment and critical appraisal

The quality of each study included in the review was assessed using a critical appraisal tool adopted from Joanna Briggs Institute checklist to assess the validity and quality of studies, the recommended tool for evaluating primary studies for the inclusion in systematic reviews for etiology and risk review [18]. A third researcher (GA) was consulted for resolution of the discrepancies that occurred while appraising the quality assessments. The items used for quality assessments are presented in (Table 1).

2.8. Data analysis

The R statistical software version 3.6.1 (Rx64 3.6.1, R-3.6.1-win.exe) was utilized to carry out the meta-analysis. During the meta-analysis, potential sources of heterogeneity were investigated using sub-group analysis.

2.9. Subgroup analysis

Due to the significant heterogeneity of the studies included in this review, subgroup analysis was conducted by study setting to identify the source of heterogeneity using the inverse variance method, DerSimonian-Laird estimator for tau² and Clopper-Pearson confidence interval for individual studies.

2.10. Assessment for heterogeneity, sensitivity, and publication bias

We assessed the extent of heterogeneity among studies with forest plots with 95% prediction regions and statistically with chi-squared (χ^2), p-value, and I-squared (I²) tests [19]. A sensitivity test was performed using influential analysis by the Mantel-Haenszel method. Publication bias for the sex difference on podoconiosis was assessed using the Egger test [20] by Mantel-Haenszel, DerSimonian-Laird, and p-value. Symmetry was screened using funnel plot test. Further in the Egger test, a p-value less than 0.05 was considered to demonstrate statistically significant publication bias.

Table 1. JBI Quality appraisal checklists.

JBI Checklist, 2017 (cross-sectional studies)	Degen F	Oli G	Alemu G	Deribe K	Elias A	Destas K	Yordanos M	Bekelle K	Tekola F	Mengstu G	Kloops H
1. Were the criteria for inclusion in the sample clearly defined?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
2. Were the study subjects and the setting described in detail?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
3. Was the exposure measured in a valid and reliable way?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	No
4. Were objective, standard criteria used for measurement of the condition?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
5. Were confounding factors identified?	Yes	No	No	Yes	Yes	No	No	Yes	Yes	No	No
6. Were strategies to deal with confounding factors stated?	Yes	No	No	Yes	Yes	No	No	Yes	Not	No	No
7. Were the outcomes measured in a valid and reliable way?	Yes	No	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes
8. Was appropriate statistical analysis used?	Yes	No	No	Yes	Yes	No	No	Yes	No	No	No
Overall appraisal:	8/8 (100%)	4/8 (50%)	5/8 (62.5%)	7/8 (87.5%)	8/8 (100%)	5/8 (62.5%)	5/8 (62.5%)	8/8 (100%)	6/8 (75%)	4/8(50%)	4/8(50%)
Including reason for exclusion	Included	Included	Included	Included	Included	Included	Included	Included	Included	Included	Included

2.11. Outcomes of interest

We have two outcomes. The primary outcome was prevalence of podoconiosis in Ethiopia measured by proportion which is chosen due lack comprehensive data in Ethiopia though it is public health concern. The second outcome was to determine sex difference of podoconiosis in Ethiopia measured by odds ratio (OR). Sex difference was chosen rather than other factors contributing for podoconiosis due to discordant findings. i.e. different studies reported differently. Besides, other factors contributing for the disease is not well studied.

3. Results

Our systematic review identified 229 records through the database search and 3 additional records through the manual search. After duplicates were removed, 200 studies were screened based on their titles and abstracts. Thirty-three articles were assessed as eligible for full text reviews. After the comprehensive reading of the articles, 11 studies met the inclusion criteria and were included in the systemic review. The list of studies included is provided in (Table 2). A total of 11 papers that showed the prevalence of podoconiosis and sex differences towards podoconiosis were reviewed. The review selection process was illustrated below using a PRISMA diagram (Figure 1).

3.1. Prevalence of podoconiosis in Ethiopia

Out of 146,120 study participants from 11 articles, the pooled prevalence of podoconiosis is 6% at 95% CI using random effect model (Figure 2). To resolve the heterogeneity, we performed subgroup analysis by setting. Finally, the prevalence was 6% and 5% among studies conducted in rural and urban dwellers respectively (Figure 3).

3.2. Effect of sex difference on the odds of podoconiosis infection

The odds of podoconiosis infection among female is 1.15 than male (p < 0.01) (Figure 4). The effect of sex on podoconiosis was sub-grouped by study setting and females were 1.29 times at increased risk of acquiring

Table 2. Result of different Ethiopian study sites.

Author	YP	Country	Setting	Design	LM	Sample	Positive	Event ♀	Total ♀	Event ♂	Total ♂	QS (%)
Degen F [21]	2019	Ethiopia	Rural	CS	ICT & clinical	638	40	25	400	15	238	100
Oli G [22]	2013	Ethiopia	Urban	CS	ICT & clinical	1656	123	56	824	67	832	50
Alemu G [23]	2011	Ethiopia	Rural	CS	Clinical	2991	335	243	1691	92	1300	62.5
Deribe K [24]	2015	Ethiopia	Rural	CS	ICT & clinical	5253	333	216	3045	117	2208	87.5
Elias A [25]	2016	Ethiopia	Rural	CS	Clinical	1483	80	33	708	47	775	100
Destas K [26]	2002	Ethiopia	Urban	CS	Clinical	33678	1890	937	16669	953	17009	62.5
Yordanos M [2]	2012	Ethiopia	Urban	CS	Clinical	51017	1704	838	25766	866	25251	62.5
Bekelle K [27]	2016	Ethiopia	Rural	CS	Clinical	39256	1197	733	19968	464	19288	62.5
Tekola F [28]	2013	Ethiopia	Rural	CS	Clinical	6710	379	222	3377	157	3333	75
Mengistu G [29]	1993	Ethiopia	Rural	CS	Clinical	3022	153	-	-	-	-	50
Kloops H [30]	1992	Ethiopia	Rural	CS	Clinical	416	31	-	-	-	-	50

YP = Year of publication, CS = cross-sectional, CC = Case-control, LM = Laboratory method, ♀ = female, ♂ = male, QS = Critical quality appraisal of the included articles, “-” = Missing data.

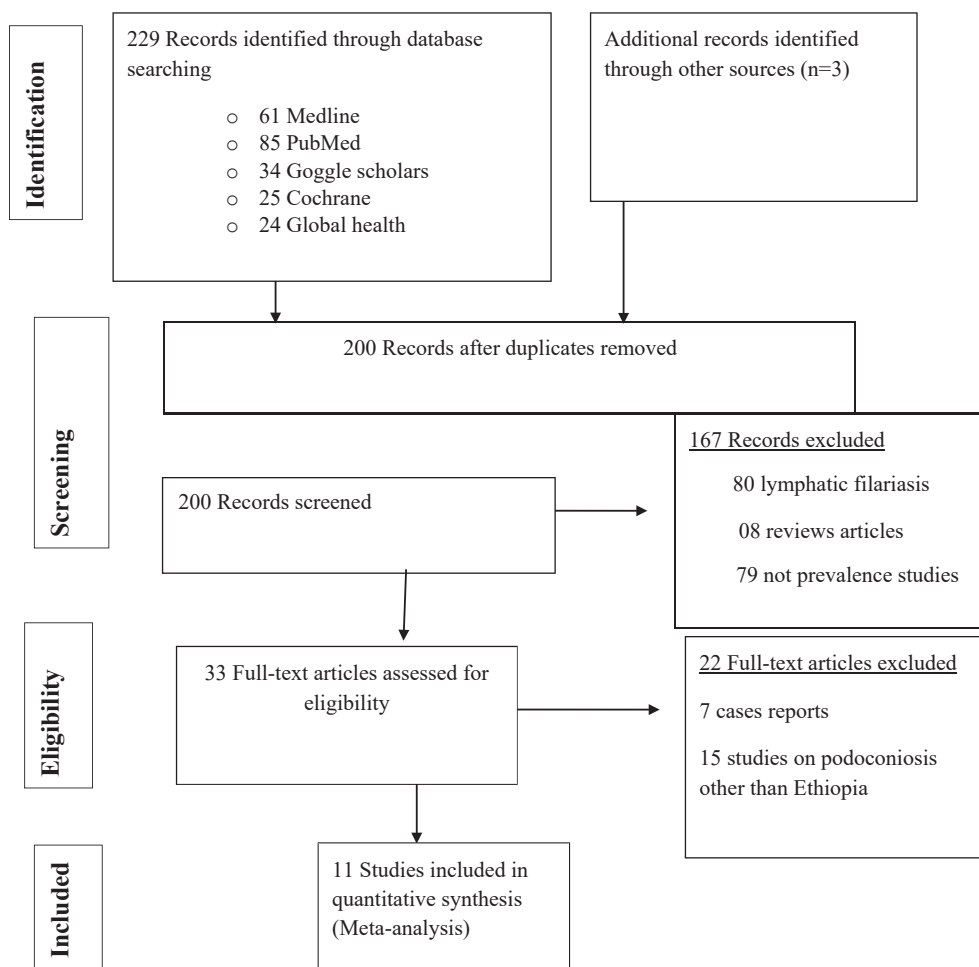


Figure 1. Flow diagram that showed selection process.

podoconiosis than males ($p < 0.01$) in rural settings. On the other hand, there was almost no significant difference in sex on podoconiosis infection among urban dwellers ($p = 0.49$) (Figure 5).

3.3. Sensitivity, publication bias and symmetry of data

A sensitivity analysis was performed and summarized (Figure 6). Publication bias was also done using the Egger test with an efficient bias

score of 0.217 and 2.28 standard error. Publication bias was not significant (p -value = 0.9267).

4. Discussion

Determining the point estimate of podoconiosis in Ethiopia is difficult due to poor reliable epidemiological data, being disease of voiceless and the absence of diagnostic instrument. Data on people having the disease

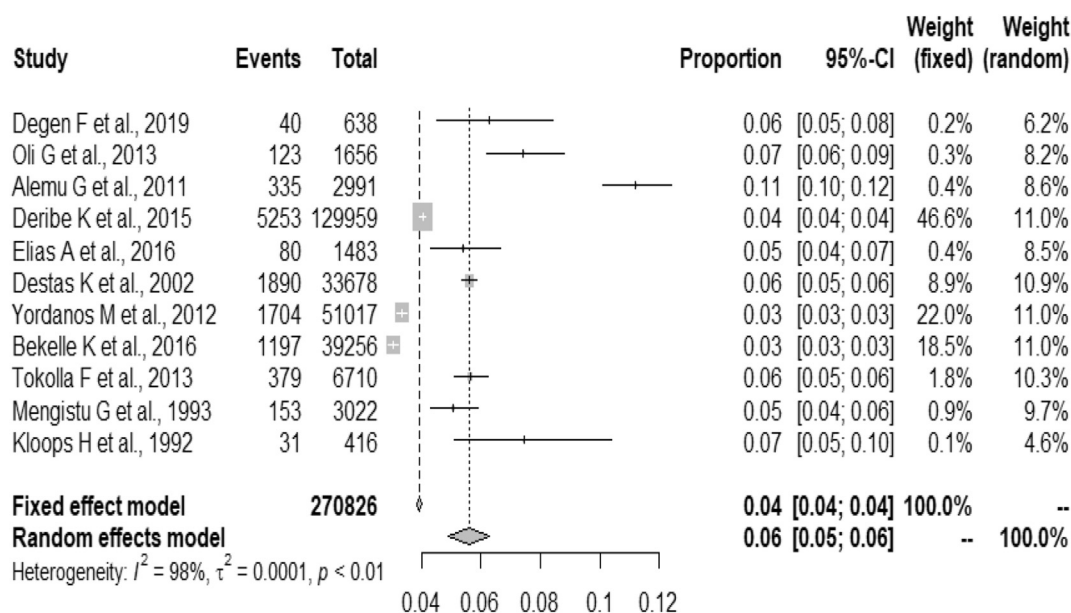


Figure 2. The pooled prevalence of podoconiosis in Ethiopia.

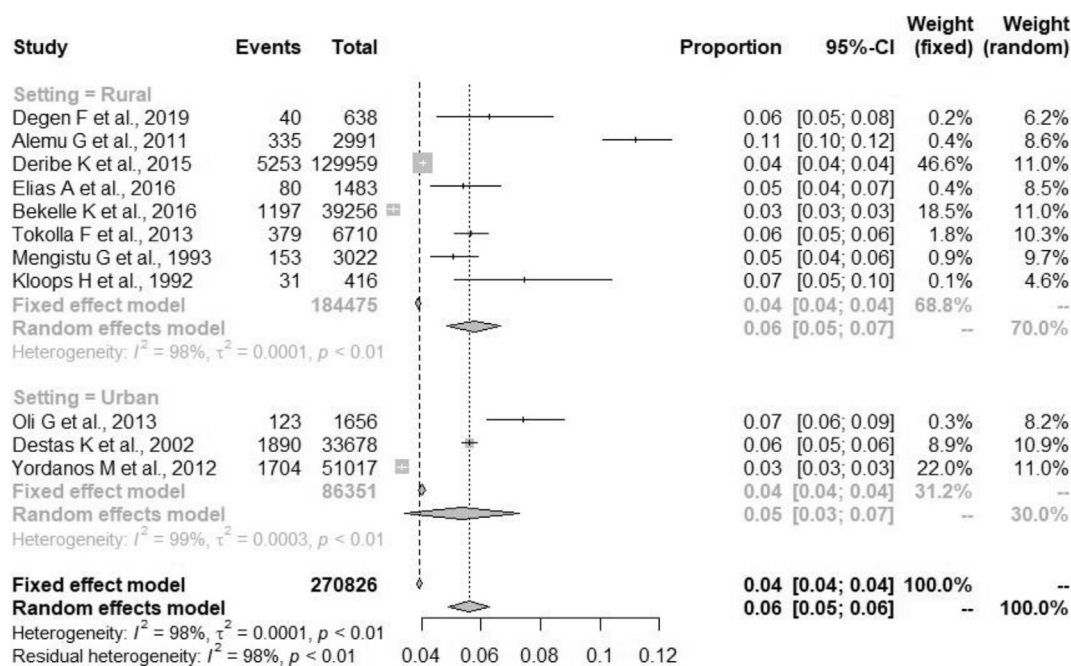


Figure 3. Subgroup analysis by study setting on the prevalence of podoconiosis in Ethiopia. Keys: Experimental events = Female, Control events = Male.

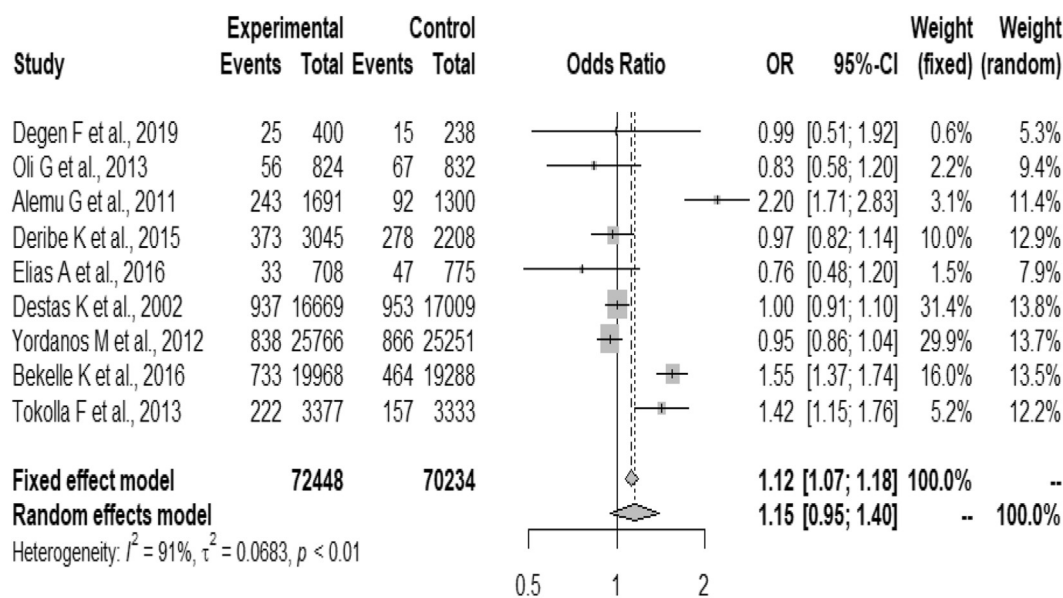
remain rare in Ethiopia partly because of the challenges of differential diagnosis from other types of elephantiasis [31]. Here, we have gathered available reliable epidemiological data to generate pooled prevalence of podoconiosis in Ethiopia. So, podoconiosis is one of the persistent major causes of lymphedema in Ethiopia [31]. Assessing the prevalence and effect of sex on podoconiosis is important for clinicians, epidemiologists, and policymakers to inform evidence-based management and treatment of the disease. It will also assist local and regional health policymakers to design appropriate methods of prevention and control of podoconiosis in Ethiopia. There are a few primary studies on podoconiosis in Ethiopia. However, the prevalence and determinant factors of the disease in the studies have not been systematically reviewed yet."

This systematic review aimed to synthesize the quality of available evidence on the pooled prevalence and effect of sex on podoconiosis. To

the best of the researchers' knowledge, this review is the first systematic review and meta-analysis of the epidemiology and effect of sex on podoconiosis in Ethiopia.

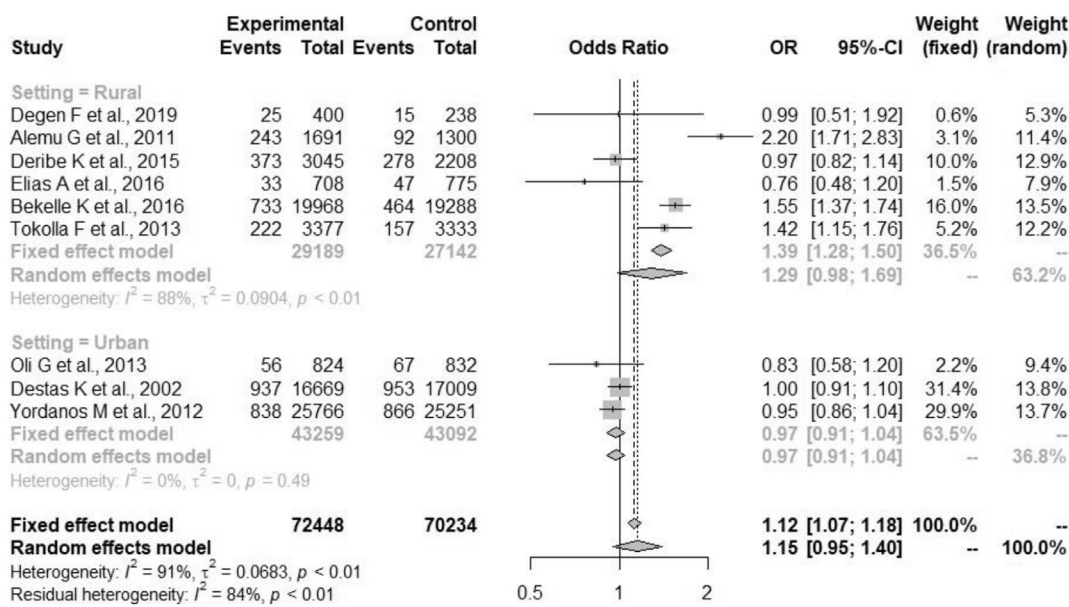
This systematic review has assessed all available literatures regarding the prevalence of podoconiosis and included 11 prevalence studies in Ethiopia. Out of the 11 eligible articles, the overall pooled prevalence of podoconiosis was 6% [95% CI: 5%; 6%]. This is consistent with articles included in this systemic review reporting 6% [26, 28] and 5% [25]. But some studies have reported lower prevalence, 3% [2, 27] and 3.4% [32] than the pooled prevalence.

Additionally, this review revealed lower prevalence than studies like 6.3% [21], 7% [22], 7.4% [24] and 11% [23]. These variations might be due to differences in hygiene practices, shoe-wearing practices, and family history.



Keys: Experimental events = Female, Control events = Male

Figure 4. Effect of sex difference on the odds of podoconiosis infection. keys: Experimental events = Female, Control events = Male.



keys: Experimental events = Female, Control events = Male

Figure 5. Subgroup analysis by the setting of sex differences on podoconiosis in Ethiopia.

Compared with other African studies, the present pooled prevalence is lower than a report from Cameroon (8.1%) [33] but higher than other studies conducted in Kenya (3.4%) [34] and Cameroon (0.4%–0.5%) [35, 36]. This variation might be due to climatic conditions, hygienic practices, socio-economic differences, and social rationales for barefoot and shoe wearing practices, and washing hands with water only.

As per the present review, the prevalence of podoconiosis in a rural setting is 6% which is relatively higher than urban areas, (5%). This is consistent with a previous study carried out in Ethiopia [37]. This might be due to lack of awareness of the diseases, lack of practical experience of

foot hygiene, frequent exposure to the irritant clay due to farming activities, socioeconomic status, and lack of clean water in a rural community.

There was variability in reporting of female/male risks of developing podoconiosis. Some studies reported females are at greater risk of developing podoconiosis [24, 27]; other indicated males were more affected [32]; still, others showed no sex differences [22, 26, 28, 29, 30, 31, 33]. Our systematic review revealed that being female increased the risk of developing podoconiosis. The finding of this review is consistent with studies conducted in Ethiopia [24, 27]. This finding might relate to

	OR	95%-CI	p-value	tau ²	I ²
Omitting Degen F et al., 2019	1.1230	[1.0674; 1.1815]	< 0.0001	0.0698	91.9%
Omitting oli G et al., 2013	1.1287	[1.0724; 1.1879]	< 0.0001	0.0691	91.7%
Omitting Alemu G et al., 2011	1.0871	[1.0321; 1.1449]	0.0016	0.0468	87.8%
Omitting Deribe K et al., 2015	1.1391	[1.0801; 1.2014]	< 0.0001	0.0771	91.6%
Omitting Elias A et al., 2016	1.1278	[1.0717; 1.1868]	< 0.0001	0.0681	91.7%
Omitting Destas K et al., 2002	1.1766	[1.1075; 1.2500]	< 0.0001	0.0953	91.2%
Omitting Yordanos M et al., 2012	1.1970	[1.1277; 1.2705]	< 0.0001	0.0828	90.2%
Omitting Bekelle K et al., 2016	1.0412	[0.9842; 1.1014]	0.1600	0.0507	86.3%
Omitting Tokolla F et al., 2013	1.1056	[1.0494; 1.1649]	0.0002	0.0707	91.4%
Pooled estimate	1.1222	[1.0668; 1.1805]	< 0.0001	0.0683	90.8%

Details on meta-analytical method:
- Mantel-Haenszel method

Figure 6. Influential analysis included studies of podoconiosis in Ethiopia.

females being traveling barefoot than their male counterparts [27]. In this review, the effect of podoconiosis with subgroup analysis by setting indicated that females living in a rural community were 1.29 times more likely to acquire podoconiosis than males, but, in urban communities, there was an almost equal risk across both sexes.

4.1. Limitations of the study

While searching literatures we could not get covariates for subgroup analysis (environmental factors like annual precipitation and soil content) to resolve heterogeneity for the included articles. Besides, we used only articles retrieved from open access sources.

5. Conclusions and recommendation

Our review revealed that the prevalence of podoconiosis in Ethiopia is high. Additionally, this review suggested that females are at higher risk of developing podoconiosis than males, particularly in rural communities. This evidence is important in informing the planning and implementation of podoconiosis prevention and control programming in Ethiopia including incidence case surveillance. The government should give attention and link to the existing health system of Ethiopia to help the limited knowledge of health professionals regarding the cause, management, prevention, and differential diagnosis of podoconiosis from other causes of lymphedema. Besides, civil society and other concerned bodies should support Ethiopia in terms of awareness creation in health professionals, introducing diagnostic kits and institutionalizing bureau to support the community of Ethiopia.

Declarations

Author contribution statement

All authors listed have significantly contributed to the development and the writing of this article.

Funding statement

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Data availability statement

Data will be made available on request.

Declaration of interests statement

The authors declare no conflict of interest.

Additional information

No additional information is available for this paper.

Acknowledgements

We would like to thank for academic with borders for providing editing services.

References

- [1] K. Deribe, S. Tomczyk, E. Mousley, A. Tamiru, G. Davey, Stigma towards a neglected tropical disease: felt and enacted stigma scores among podoconiosis patients in Northern Ethiopia, *BMC Publ. Health* 13 (2013) 1178.
- [2] B.M. Yordanos, A.W. Nicola, S.B. Jennifer, P. Baxter, M.J. Newport, P.M. Atkinson, G. Davey, Modeling environmental factors correlated with podoconiosis: a geospatial study of non-filarial elephantiasis, *Int. J. Health Geogr.* 13 (2014) 24.
- [3] E.W. Price, Endemic elephantiasis of the lower legs in Rwanda and Burundi, *Trop. Geogr. Med.* 28 (4) (1976) 283–290. PMID: 1014068.
- [4] A.P. Oomen, Studies on elephantiasis of the legs in Ethiopia, *Trop. Geogr. Med.* 21 (3) (1969) 236–253. PMID: 5361766.
- [5] WHO, Accelerating Work to Overcome the Global Impact of Neglected Tropical Diseases: A Roadmap for Implementation, 2016. Geneva.
- [6] E.W. Price, The association of endemic elephantiasis of the lower legs in East Africa with soil derived from volcanic rocks, *Trans. R. Soc. Trop. Med. Hyg.* 70 (1976) 288–295.
- [7] The Federal Democratic Republic of Ethiopia Ministry of health, A National Master Plan for Neglected Tropical Diseases (NTDS) 2013–2015, June 2013. Addis Ababa, Ethiopia.
- [8] F. Tekola, D.H. Mariam, G. Davey, Economic costs of endemic non-filarial elephantiasis in Wolaita Zone, Ethiopia, *Trop. Med. Int. Health* 11 (7) (2006) 1136–1144.
- [9] E.G. Hanna, The Social burden of Podoconiosis and Familial Occurrence in its Development, Addis Ababa University, Addis Ababa, 2005.
- [10] K. Deribe, K. Meribo, T. Gebre, A. Hailu, A. Ali, A. Aseffa, G. Davey, The burden of neglected tropical diseases in Ethiopia, and opportunities for integrated control and elimination, *Parasites Vectors* 5 (2012 Oct 24) 240.
- [11] K. Deribe, S. Tomczyk, F.T. Ayele, Ten years of podoconiosis research in Ethiopia, *PLoS Neglected Trop. Dis.* 7 (10) (2013), e2301.
- [12] WHO, The global atlas of podoconiosis, *Lancet* 5 (2017) 3.
- [13] D. Korevaar, B. Visser, Podoconiosis, a neglected tropical disease, *Neth. J. Med.* 70 (2012) 210–214.
- [14] Ethiopian population, World parameters, Available: <http://www.worldometers.info/world-population/ethiopia-population>, 2018. Accessed on. (Accessed 11 October 2019).
- [15] L. Shamseer, D. Moher, M. Clarke, Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015: elaboration and explanation, *BMJ* 349 (2015), e7647.

- [17] D.F. Stroup, J.A. Berlin, S.C. Morton, et al., Meta-analysis of observational studies in epidemiology: a proposal for reporting. A meta-analysis of observational studies in epidemiology (MOOSE) group, *JAMA* 283 (2000) 2008–2012.
- [18] P.F.W. Chien, K.S. Khan, D. Siassakos, Registration of systematic reviews: PROSPERO, *BJOG An Int. J. Obstet. Gynaecol.* 119 (2012) 903–905.
- [19] J.B. Institute, Joanna Briggs Institute Reviewers' Manual: 2014 Edition, The Joanna Briggs Institute, Australia, 2014.
- [20] J.P. Higgins, S. Green, *Cochrane Handbook for Systematic Reviews of Interventions*, 2011. Retrieved, <http://handbook.cochrane.org/handbook>. (Accessed 11 October 2019).
- [21] M. Egger, G.D. Smith, M. Schneider, C. Minder, Bias in meta-analysis detected by a simple, graphical test, *BMJ* 315 (7109) (1997) 629–634.
- [22] F. Dejene, H. Merga, H. Asefa, Community based cross-sectional study of podoconiosis and associated factors in Dano district, Central Ethiopia, *PLoS Neglected Trop. Dis.* 13 (1) (2019), e0007050.
- [23] G.G. Oli, F.T. Ayele, B. Petros, Parasitological, serological, and clinical evidence for the high prevalence of podoconiosis (non-filarial elephantiasis) in Midakegn district, central Ethiopia, *Trop. Med. Int. Health* 17 (6) (2012) 722–726.
- [24] G. Alemu, F. Tekola Ayele, T. Daniel, C. Ahrens, G. Davey, Burden of podoconiosis in poor rural communities in Gulliso woreda, west Ethiopia, *PLoS Neglected Trop. Dis.* 5 (6) (2011) e1184.
- [25] K. Deribe, S.J. Brooker, R.L. Pullan, H. Sime, A. Gebretsadik, A. Assefa, et al., Epidemiology and individual, household, and geographical risk factors of podoconiosis in Ethiopia: results from the first nationwide mapping, *Am. J. Trop. Med. Hyg.* 92 (1) (2015) 148–158.
- [26] A. Elias, H. Yemane, M. Meskele, Podoconiosis prevalence and its associated factors in sodd zuria district, Wolaita zone, south Ethiopia, *J. Pharm. Alt. Med.* 13 (2016).
- [27] K. Destas, M. Ashine, G. Davey, Prevalence of podoconiosis (endemic non-filarial elephantiasis) in Wolaita, Southern Ethiopia, *MRCGP, Trop. Doct.* 32 (2002) 217–220.
- [28] K. Bekele, K. Deribe, T. Amberbir, G. Tadele, G. Davey, A. Samuel, Burden assessment of podoconiosis in Wayu Tuka woreda, East Wollega zone, western Ethiopia: a community-based cross-sectional study, *BMJ Open* 6 (2016), e012308.
- [29] F. Tekola, G. Alemu, G. Davey, C. Ahrens, Community-based survey of podoconiosis in Bedele Zuria woreda, west Ethiopia, *Int. Health* 5 (2013) 119–125.
- [30] D. Frommel, B. Ayranci, H.R. Pfeifer, A. Sanchez, A. Frommel, G. Mengistu, Podoconiosis in the Ethiopian rift valley role of beryllium and zirconium, *Trop. Geogr. Med.* 45 (4) (1993) 165–167.
- [31] K. Deribe, F. Tekola-Ayele, G. Davey, Podoconiosis: endemic non-filarial elephantiasis, in: J. Gyapong, B. Boatin (Eds.), *Neglected Tropical Diseases Sub-Saharan Africa 1st Ed 2016 Edition*. 1, Springer International Publishing, Switzerland, 2016, pp. 231–249.
- [32] K. Deribe, S.J. Brooker, R.L. Pullan, A. Hailu, F. Enqueslassie, R. Reithinger, et al., Spatial distribution of podoconiosis in relation to environmental factors in Ethiopia: a historical review, *PLoS One* 8 (7) (2013), e68330.
- [33] S. Wanji, N. Tendongfor, M. Esum, J.N. Che, S. Mand, T. Mbi, et al., Elephantiasis of non-filarial origin (podoconiosis) in the highlands of northwestern Cameroon, *Ann. Trop. Med. Parasitol.* 102 (6) (2008) 529–540.
- [34] J. Muli, J. Gachohi, J. Kagai, Soil iron and aluminum concentrations and feet hygiene as possible predictors of Podoconiosis occurrence in Kenya, *PLoS Neglected Trop. Dis.* 11 (8) (2017), e0005864.
- [35] K. Deribe, A.A. Beng, J. Cano, A.J. Njouendo, J. Fru-Cho, A.R. Awah, et al., Mapping the geographical distribution of podoconiosis in Cameroon using parasitological, serological, and clinical evidence to exclude other causes of lymphedema, *PLoS Neglected Trop. Dis.* 12 (1) (2018), e0006126.
- [36] K. Deribe, J. Cano, A.J. Njouendo, M.E. Eyong, A.A. Beng, E. Giorgi, et al., Predicted distribution and burden of podoconiosis in Cameroon, *BMJ Glob. Health* 3 (2018), e000730.
- [37] H. Sime, K. Deribe, A. Assefa, M.J. Newport, F. Enqueslassie, A. Gebretsadik, et al., Integrated mapping of lymphatic filariasis and podoconiosis: lessons learned from area (Kapchorwa District) of Uganda, *Acta Trop.* 78 (2001) 171–176.