Epidemiology of podoconiosis in Ethiopia: a systematic review and meta-analysis protocol

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ABSTRACT

Introduction Podoconiosis is a non-filarial swelling of the lower extremity endemic in tropical regions, North America and India. The aetiology and pathophysiology of the disease remain unknown. We propose conducting a systematic review and meta-analysis to evaluate the burden and risk factors of podoconiosis in Ethiopia reported in studies from 2009 to 2019.

Methods and analysis We will search the following electronic databases: PubMed (MEDLINE), EMBASE, Hinari, Cumulative Index to Nursing and Allied Health Literature, ISI (Web of Science) and Google Scholar. Medical subject headings will be used to extensively search relevant literature on electronic databases using related keywords such as epidemiology or prevalence, magnitude or burden, podoconiosis, and Ethiopia. Grey literature and manual search will also be performed to retrieve unindexed research articles. Two reviewers will screen all retrieved articles, conduct data extraction and then critically appraise all identified studies. We will analyse data using STATA V.14 statistical software. We will demonstrate pooled estimates of podoconiosis and associated factors with effect size and 95% CI. The presence of heterogeneity among studies will be examined by forest plot as well as the I² heterogeneity test. Potential causes of heterogeneity will be explored by carrying out sensitivity and subgroup analyses. The presence of publication bias will also be examined by observing funnel plots and objectively by Egger’s regression test. If the funnel plot is asymmetric and/or Egger’s test was found to be statistically significant (p<0.05), the trim and fill (Duval and Tweedie’s) analysis will be performed.

Ethics and dissemination The study will use publicly available data and will not identify the authors of the publication by name. In light of these and as has been indicated, research ethics clearance is not required for evidence syntheses in such reviews. The results of this study will be published in a peer-reviewed journal and presented at national and international conferences.

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INTRODUCTION

Podoconiosis is a non-filarial elephantiasis and a non-infectious geochemical disease caused by exposure of bare feet to red clay soil derived from volcanic rocks. Mineral particles from the soil penetrate the skin and are taken up by the macrophages of the lymphatic system, causing inflammation and fibrosis of the vessel lumen, leading to blockage of the lymphatic drainage.1–3 A major and serious complication of podoconiosis is acute adenolymphangitis, which presents as a warm, painful sensation in the limbs, accompanied by fever.2 In addition to prolonged exposure to soil, many studies have shown that the prevalence of podoconiosis is associated with feet hygiene, shoe-wearing habit, gender, age, occupation, housing condition and income status.4–7

Podoconiosis imposes huge economic burden that worsens the prevailing poverty and results in considerable social stigma associated with the belief that the condition is familial and incurable.13 In Cameroon, podoconiosis imposed financial burden on affected households through direct treatment cost and reduced ability to work.14 Similarly, food insecurity was reported...
higher among households of Ethiopian patients with podoconiosis.15

Podoconiosis is endemic in 345 districts of Ethiopia, the majority of cases being in Oromia, Southern Nations, Nationalities and Peoples’ and Amhara regional states.16 In Ethiopia, studies have shown that podoconiosis is significantly associated with soil texture and land topography,17 washing practices and frequency of shoe-wearing,4 18 family history, and being barefoot.5 Although simple and effective treatment strategies are available in Ethiopia, patients with podoconiosis tend to discontinue their treatment. Some of the factors for discontinuation were remoteness from treatment sites, stigma and misconceptions about the treatment.19 On top of this, in Ethiopia, patients with podoconiosis suffer from stigma,20 depression21 and lower quality of life.22

A systematic review and meta-analysis showed that the use of footwear was associated with decreased risk of neglected tropical diseases (NTDs).23 The WHO has underscored the importance of integrated control of NTDs, including podoconiosis.24

Despite many remarkable achievements in the reduction of the public health problem of podoconiosis in Ethiopia, there are several important challenges that still exist and need special consideration at the national and international levels. Hence, comprehensive figure and continued updates with regard to the burden of the disease are warranted to boost the existing strategy and to design a new approach to eliminate podoconiosis. The purpose of this study is to demonstrate the pooled prevalence of podoconiosis in the country within the last 10 years.

During the last decade, the Ethiopian Federal Ministry of Health has prioritised and has been working to eliminate podoconiosis by 2020, in collaboration with international agencies, non-governmental organisations and the WHO; the national podoconiosis elimination programme, however, is now out of track for the 2020 target. The authors designed this systematic review and meta-analysis to determine the overall pooled prevalence of podoconiosis for the duration of the second millennium development goal, particularly after 2009, using available epidemiological studies. Moreover, identifying the predictors of podoconiosis is the first essential step to controlling the contributing factors. The findings from this systematic review will highlight the pooled prevalence and associated factors of podoconiosis, with implications to improve interventions, to ensure cost-effectiveness and to accelerate the reduction of podoconiosis cases.

**Specific objectives**

- To review and estimate the pooled prevalence of podoconiosis in Ethiopia.
- To review and estimate the pooled prevalence of podoconiosis in different regions of the country.
- To review and determine the pooled effect sizes of the determinants of podoconiosis in Ethiopia.

**METHODS AND ANALYSIS**

**Protocol and registration**

This protocol was developed following the Preferred Reporting Items for Systematic Review and Meta-Analysis Protocols guideline (online supplementary file 1),25 and the review that is to be guided by this protocol will be carried out following the guidelines of the Meta-analysis Of Observational Studies in Epidemiology (MOOSE).

The protocol was registered with the PROSPERO International Prospective Register of Systematic Reviews in 2019. The full documentation is available online (http://www.crd.york.ac.uk/PROSPERO/display_record.php?ID=CRD42019127459).

**Literature search**

We will systematically conduct a comprehensive literature search using different bibliographic databases. We will search the following online databases: PubMed (MEDLINE), EMBASE, Hinari, Cumulative Index to Nursing and Allied Health Literature, International Scientific Indexing (ISI) (Web of Science) and Google Scholar. We will use medical subject headings, keywords and free-text search terms. An extensive and comprehensive search will be performed using alternative terms such as epidemiology, magnitude, burden, prevalence, podoconiosis and Ethiopia. This search strategy will be performed by combining the above terms using Boolean operators. An example of the search strategy that will be used in PubMed will be as follows: (prevalence OR population OR magnitude OR epidemiology OR burden OR “public health” OR (public AND health) AND (podoconiosis OR “mossy foot” OR (mossy AND foot) OR “non-filarial” OR (non AND filarial) OR elephantiasis) AND (Ethiopia)). To check that the searches are exhaustive, we will use snowballing to screen the references of identified articles for potentially relevant studies. Furthermore, grey literature and manual search will be performed to retrieve unindexed research works. During the search process, to suppress the number of irrelevant studies, the search will be restricted to ‘human studies’ and ‘English language’ in the advanced search. Authors’ profiles will also be searched to ensure that other relevant articles are captured. The search activity will be done by BA, AD and SE, and the whole process is expected to be completed by 4 October 2019.

**Objectives**

**General objective**

The objective of this study is to conduct a systematic review and meta-analysis of studies assessing the prevalence and associated risk factors of podoconiosis in Ethiopia.
Criteria for considering studies for the review

Inclusion criteria
- Studies describing the prevalence of podoconiosis as well as associated factors across all age groups and regions within Ethiopia will be included.
- Articles published in the English language will be eligible for inclusion.
- This review will account for all observational and population-based studies reporting the incidence or prevalence of podoconiosis.

Exclusion criteria
- Studies conducted before 2009 and conducted outside of Ethiopia will be excluded.
- Narrative reviews, expert opinions, case reports and case series will be excluded.
- Articles without full text and data that are difficult to extract, despite contacting the corresponding author(s), will be excluded.

Study selection and data extraction

First, systematic search will be conducted in all identified databases, search engines and additional references that will be retrieved from other published articles. Second, studies conducted before 2009, conducted in countries other than Ethiopia and unrelated articles based on their title will be excluded. Third, those potentially eligible for inclusion will be imported to EndNote V.8, and duplicates will be removed by screening the de-duplicated citations by hand and will be recorded on a Microsoft Excel spreadsheet. To be considered duplicates, two or more citations had to share the same author, title, publication date, volume, issue and start page information. The full-text versions of the citations were consulted when we were in doubt. In such cases, we also checked the population size, methodology and outcomes to determine whether the citations were duplicates. Conference abstracts were deemed to be duplicates if full-text articles that shared the same study design, sample size and conclusion were retrieved, even if their publication dates varied. Lastly, the studies will be screened and selected for full-text review based on the inclusion criteria. MOOSE will be used to present the study inclusion, exclusion and reason for exclusion in a diagram. In conclusion, the following data will be abstracted using a structured data abstraction form and presented in a prepared format using Microsoft Excel spreadsheet. Information such as the primary investigator’s name, year of publication, region, residence, study design, sample size and the tool used to diagnose podoconiosis will be extracted. Moreover, prevalence and adjusted associated factors with their effect size (OR) and 95% CI (lower and upper CIs) will be extracted. Before analysis, a transformation of OR and prevalence will be made. For any difficulties that might be encountered during data extraction, the corresponding author(s) will be contacted by any means of communication.

Risk of bias (quality) assessment

Once all searches have been completed, the included studies will be assessed independently by three researchers (BA, SE and AD) using a quality assessment tool. The Newcastle-Ottawa Scale will be used to assess the quality of included observational cohort and cross-sectional studies. Study quality will be assessed using a quality assessment tool. Based on this tool, studies are rated as low risk, moderate risk and high risk with scores ≤5, 6–8 and >8, respectively. Discrepancies will be discussed and resolved by consensus between the authors and an independent reviewer. In addition to quality assessment, the reporting of the results of the systematic review and meta-analysis will be based on MOOSE statement (online supplementary file 2). All tools have ‘Yes’ and ‘No’ types of questions, and scores will be 1 and 0 for ‘Yes’ and ‘No’ responses, respectively. Scores will be summed and transformed into a percentage. Only studies that scored ≥50% will be considered for both systematic review and meta-analysis of prevalence. For any scoring disagreements, which might happen between the assessors, the sources of discrepancy will be investigated by a thorough revision. For persistent disagreements in spite of the detailed review, the average scores of the reviewers will be calculated. Similarly, for determinants, each factor with each outcome variable will be critically appraised. Similar cut-off point that will be used for prevalence studies will be applied to factors. The quality of results of the primary studies will be placed in a separate column in the data extraction form.

Data analysis and assessment of publication bias

The extracted data will be exported to STATA V.14 software for further analysis. The prevalence of podoconiosis in Ethiopia will be pooled from each study and determined as a single estimate. The existence of heterogeneity among the included studies will be examined by forest plot and I² heterogeneity test. I² values greater than 75%, 50%–75%, 25%–50% and less than 25% will be interpreted as the presence of considerable, substantial, moderate and low heterogeneity, respectively. An I² heterogeneity test of ≥50% and a p value of <0.05 will be declared as the presence of heterogeneity. Thus, the DerSimonian and Laird random-effects model will be employed. To identify influential studies that resulted in variation, sensitivity analysis will be carried out using the ‘metaninf’ command. Similarly, subgroup analysis will be employed by considering the year of the study, region and sample size as a source of variation. Moreover, the funnel plot and Egger’s regression test will be conducted to check for potential publication bias. Accordingly, asymmetry of the funnel plot and/or statistical significance of Egger’s regression test (p<0.05) will be suggestive of publication bias. In case of minor publication bias, using the ‘metatrim’ command, a non-parametric trim and fill (Duval and Tweedie’s) method of analysis will be performed.
DISCUSSION

There is paucity of data addressing the epidemiology of podoconiosis in Ethiopia, and we intend to fill this gap by reviewing available literature as outlined in this protocol. The findings of this systematic review and meta-analysis will have implications for stakeholders that work on NTDs, including podoconiosis. We also anticipate that the findings of this review will have many contributions to the development of strategies for the prevention of podoconiosis and its associated factors in the country.

Ethics and dissemination

No formal ethical review was required as the systematic review will use publicly available data and will not identify authors of the publication by name. In light of these and as has been indicated, research ethics clearance is not required for evidence syntheses in such reviews. The findings of this systematic review will be published in a reputable peer-reviewed journal and presented at scientific national and international conferences.

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