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Subcutaneous mycoses in Peru: a systematic review and meta-analysis for the burden of disease

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Abstract

Background There is a worrying lack of epidemiological data on the geographical distribution and burden of subcutaneous mycoses in Peru, hindering the implementation of surveillance and control programs.

Objectives This study aimed to estimate the disease burden of subcutaneous mycoses in Peru and identify which fungal species were commonly associated with these mycoses.

Methods We performed a meta-analysis after a systematic review of the published literature in PubMed, LILACS, and SciELO to estimate the burden of subcutaneous mycoses in 25 regions in Peru. The disease burden was determined in terms of prevalence (number of cases per 100,000 inhabitants) and the number of reported cases per year per region.

Results A total of 26 studies were eligible for inclusion. Results showed that sporotrichosis was the most common subcutaneous mycosis (99.7%), whereas lobomycosis, chromoblastomycosis, and subcutaneous phaeohyphomycosis were rare. Cases of eumycetoma and subcutaneous zygomycosis were not found. Of the 25 regions, the burden of sporotrichosis was estimated for four regions classified as endemic; in nine regions, only isolated cases were reported. The highest burden of sporotrichosis was in Apurimac (15 cases/100,000 inhabitants; 57 cases/year), followed by Cajamarca (3/100,000 inhabitants; 30/year), Cusco (0.5/100,000 inhabitants; 4/year), and La Libertad (0.2/100,000 inhabitants; 2/year). In two regions, the mycoses predominantly affected children.

Conclusions Sporotrichosis is the most common subcutaneous mycosis in Peru, with a high disease burden in Apurimac. Chromoblastomycosis, lobomycosis, and subcutaneous phaeohyphomycosis are rare mycoses in Peru.

Subcutaneous mycoses (sporotrichosis, chromoblastomycosis, lobomycosis, subcutaneous phaeohyphomycosis, and zygomycosis) are a group of chronic diseases of the subcutaneous tissue caused by a heterogeneous group of fungi commonly found in soil, leaves, and organic material. They are mostly caused by traumatic inoculation with thorns or any other material contaminated with these fungi[1–4] and carry a high morbidity. They are endemic in many tropical and subtropical countries and are most commonly reported in Africa, Central and South America, and India. Although these infectious diseases are considered "neglected" tropical diseases, they represent an important health problem in Latin American countries.[2–15]

These mycoses share many common features, including their epidemiological profile, mode of transmission, indolent chronic presentation, and the presence of pyogranulomatous lesions on histopathology.[1,4,5,13] Although they rarely cause severe or invasive disease, subcutaneous mycoses have an important impact on public health, as their spread may be difficult to control and can have high recurrence rates.[2–5] These mycoses are most severe in adults with outdoor occupations that bring them into contact with soil, plants, or plant materials.[1–5,16] Compared with major diseases, such as tuberculosis, malaria, and HIV, subcutaneous mycoses have lower incidence rates and produce less disease burden. However, we must bear in mind that subcutaneous mycoses are not communicable diseases and hence are subject to possible under-reporting, and therefore they remain socioeconomically important and clinically relevant.

In Peru, reported subcutaneous mycoses include sporotrichosis,[17–22] chromoblastomycosis,[23] and lobomycosis.[24] Among these, sporotrichosis represents a major health issue and occurs almost exclusively in childhood.[16–20,25] In recent decades, concerns of sporotrichosis have been heightened by the persistent existence of cases in some provinces in southern and northern highlands of Peru, such as Abancay,[17] Cajamarca,[20] Cusco,[22] and Otuzzco,[21,25] and it has been estimated that the incidence has increased in some regions.[26] It has been hypothesized that climatic factors could play an important role in the epidemiological heterogeneity of sporotrichosis,[1,2,4,17] since in Peru, climate conditions

range from subtropical in the south to arid in the north.[27] Although previous studies have mainly focused on local case reports and the incidence and temporal distribution of sporotrichosis, little has been reported about subcutaneous chromoblastomycosis, lobomycosis, or phaeohyphomycosis. Despite the significance of these subcutaneous mycoses to public health, their geographical distribution and burden of disease remain poorly understood, most likely because they are not notifiable diseases. Awareness of the prevalence and geographical distribution of these mycoses is important for their prevention, surveillance, and diagnosis, based on an accurate assessment of the burden of disease. Additionaly, in Peru there is no control or prevention programs for subcutaneous mycoses, therefore to estimate the disease burden is essential to health education, implementation of medical and health facilities in hyperendemic and non-hyperendemic areas, and to avoid the disease and its high morbidity and complications.

This study aimed to estimate the disease burden of subcutaneous mycoses in Peru and to identify which fungal species were commonly associated with these mycoses. We performed a meta-analysis after a systematic review of the published literature. We calculated pooled estimates of prevalence rates and cases per year per region, and we also described the characteristics of infected cases.

Materials and methods

This systematic review was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines (Table S1).[28]

Literature review

A comprehensive search using PubMed and regional databases (Latin American and Caribbean Health Sciences Literature [LILACS] and Scientific Electronic Library Online [SciELO]) was undertaken to identify original studies, case reports, and case series of subcutaneous mycoses in Peru published between 1965 and 2015. The following search terms were used: "subcutaneous mycosis," "sporotrichosis," "chromoblastomycosis," "eumycetoma," "subcutaneous phaeohyphomycosis," "subcutaneous zygomycosis," and "Peru." Each of these search terms was combined with the names of 25 geographical regions in Peru: "Amazonas," "Ancash," "Apurimac," "Arequipa," "Ayacucho," "Cajamarca," "Callao," "Cusco," "Huancavelica," "Huanuco," "Ica," "Junin," "La Libertad," "Lambayeque," "Lima," "Loreto," "Madre de Dios," "Moquegua," "Pasco," "Piura," "Puno," "San Martin," "Tacna," "Tumbes," and "Ucayali." We applied no language restrictions.

Upon review of the titles and abstracts of potentially eligible articles, duplicate studies were discarded. If multiple studies were reported in the same region, the study with the longest follow-up period was selected. Additional studies were identified by screening bibliographic references of relevant articles and meeting abstracts.

Inclusion and exclusion criteria

Studies eligible for inclusion were those that reported cases of subcutaneous mycosis diagnosed on the basis of histological analyses or positive cultures (recovery of isolates from clinical samples) for sporotrichosis, chromoblastomycosis, subcutaneous phaeohyphomycosis and subcutaneous zygomycosis, a positive test for lobomycosis either from biopsy or direct examination (20% potassium hydroxide [KOH]) and a clearly-defined source population. We excluded review articles, articles with data already published in another paper, reports of clinical images, incomplete case reports, and articles where the source population was unclear (e.g., the geographical boundary of the study area was poorly-defined).

Data extraction

For each included study, the following data were extracted: study population and enrollment time, the region in which the disease was reported, key demographic characteristics of study participants (i.e., age and gender), and characteristics of the infection (including infectious agent, methods of diagnosis, clinical forms, and sites of infection). Geographical variation was assessed using the altitude of the study region and the number of cases reported in that region.

Estimating the burden of subcutaneous mycoses

The burden of disease was determined in terms of prevalence and the number of reported cases per year per region. We estimated the prevalence rates (number of cases per 100,000 inhabitants) according to the region, age (i.e., under 15 years, ≥15 years), and general population. To determine the prevalence, the number of reported cases for each year in a region was divided by the total population of that region for that year. Population figures were obtained from statistical data available from INEI (National Institute for Statistics and informatics; http://www.inei.gob.pe/estadisticas/indice-tematico/poblacion-y-vivienda). We then used this adjusted estimate to calculate the prevalence rate per 100,000 inhabitants in each age/region stratum and the number of reported cases per year per region, as described previously.[6]

$$\text{Prevalence} = \left[\left(\frac{\text{Number of cases/Population by region}}{\text{Number of years}}\right) \times 100,000\right]$$

$$\text{Cases per years} = \left(\frac{\text{Number of cases}}{\text{Number of years}}\right)$$

To estimate the prevalence and number of reported cases per year in each region, articles with 10 or more cases were included. Articles with fewer than 10 cases were included to give an indication of the geographical location and characteristics of the study population.

Statistical analysis

Categorical variables were expressed as proportions and percentages. The χ^2 test was used to compare patient outcomes where relevant. Differences with $P < 0.05$ were considered significant. Data were analyzed using SPSS 19.0 software for Windows (SPSS Inc, Chicago, IL, USA).

Results

Characteristics of included studies

A total of 36 eligible studies were initially identified. Of these, 10 articles were excluded: three reviews, three containing duplicated data, two due to clinical images, and two containing data that could not be retrieved. After screening, 26 articles met the inclusion criteria (Fig. 1).[16–26,29–43]

Distribution of subcutaneous mycoses in Peru

The total study population from all 26 articles included 1970 cases: 1964 (99.7%) sporotrichosis cases, three lobomycosis cases, two chromoblastomycosis cases, and one subcutaneous phaeohyphomycosis case (Fig. 2a). Cases of eumycetoma and subcutaneous zygomycosis were not reported in Peru. Most cases of sporotrichosis were reported in Apurimac (75%), followed by Cajamarcan (19%), La Libertad (3%), and Cusco (2.9%). Regions with isolated cases only included Ayacucho, Arequipa, Amazonas, Ica, Lima, Loreto, Ancash, Junin, and Puno (Fig. 2b). The geographical distribution of sporotrichosis was focused in the southern highlands and north of Peru, whereas lobomycosis distribution was focused in the Peruvian jungle in the region of Madre de Dios, chromoblastomycosis in the highlands in the region of Cusco and the Peruvian jungle in the region of Ucayali, and subcutaneous phaeohyphomycosis on the coast in the region of Lima (Fig. 2c).

Studies were also analyzed according to the altitude of the geographical regions. A greater number of cases were reported in regions found at higher altitudes (Fig. 3). However, there was no association between the altitude and incidence rates despite the higher number of sporotrichosis cases in Peru found at altitudes higher than 2300 m.

Burden of subcutaneous mycoses in Peru

To estimate the burden of disease, 12 studies of sporotrichosis were included.[16–22,25,29,31,42,43] As a result of the limited number of cases of the other types of mycoses, it was not possible to estimate their burden of disease. The highest prevalence of sporotrichosis and the greatest number of reported cases per year were recorded in Apurimac (15 cases/100,000 inhabitants; 57 cases/year), followed by Cajamarca (3 cases/100,000 inhabitants; 30 cases/year), Cusco (0.5 cases/100,000 inhabitants; 4 cases/year), and La Libertad (0.2 cases/100,000 inhabitants; 2 cases/year) (Fig. 2c).

The burden of sporotrichosis by age was estimated for the Apurimac and Cajamarca regions only. The prevalence among children aged <15 years from Apurimac was 22.5 cases per 100,000 inhabitants (33 cases/year) and six cases per 100,000 inhabitants (21 cases/year) among those aged ≥15 years.

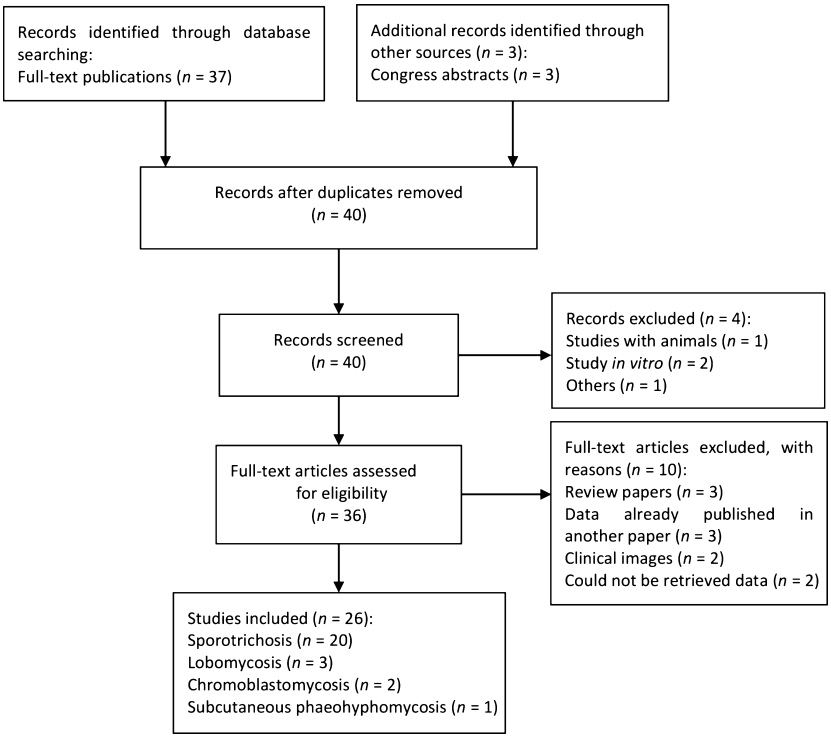

Figure 1 Flow diagram of the literature search

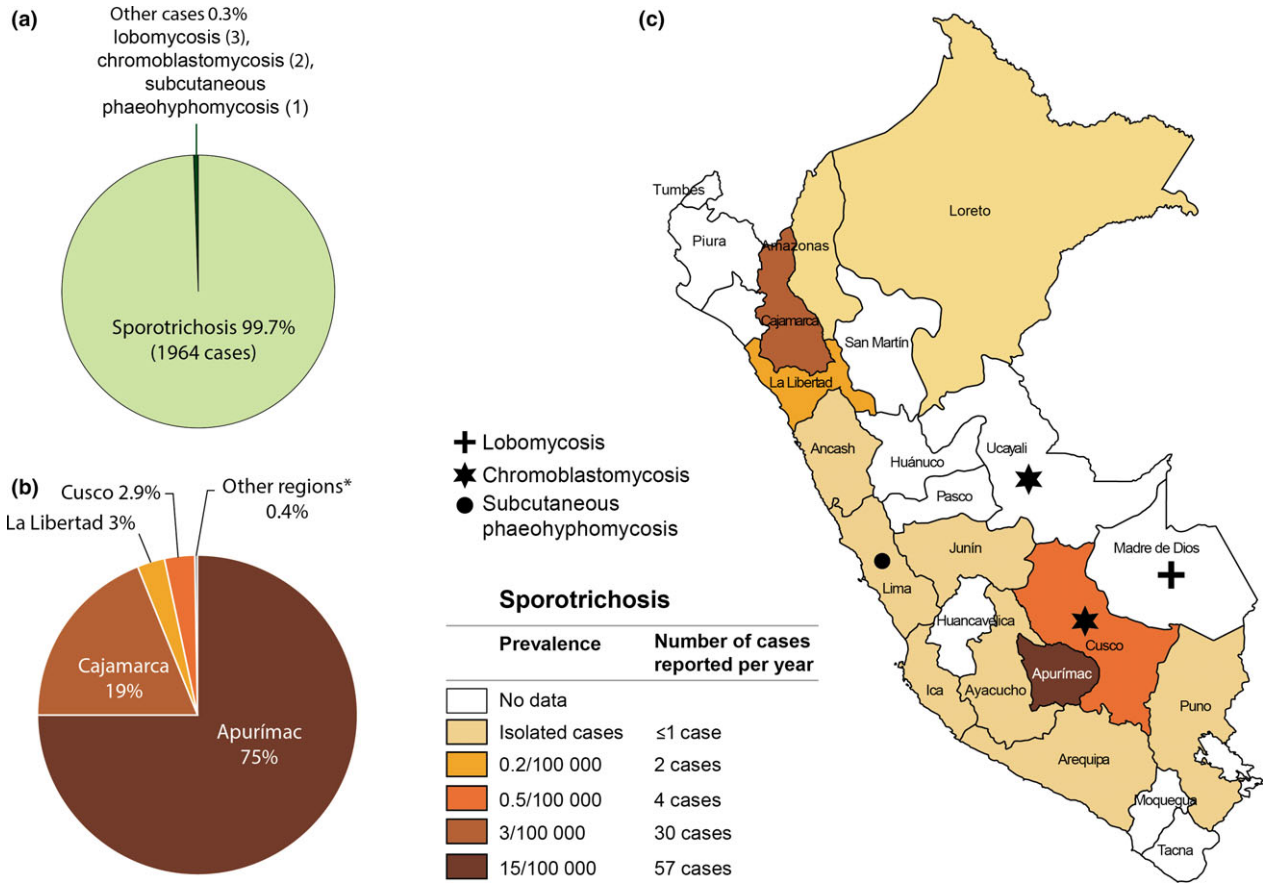

Figure 2 Subcutaneous mycoses in Peru. (a) Types of subcutaneous mycosis in Peru. (b) Geographical distribution of sporotrichosis in Peru. Numbers are percentages of cases by regions; the distribution of cases was as follows: 1463 cases in Apurimac, 372 in Cajamarca, 60 in La Libertad, and 58 in Cusco; (*) four cases in Junin, three in Amazonas, two in Ayacucho, two in Arequipa, two in Ancash, one in Ica, one in Iquitos, one in Lima, and one in Puno. (c) Prevalence and number of reported cases per year per region

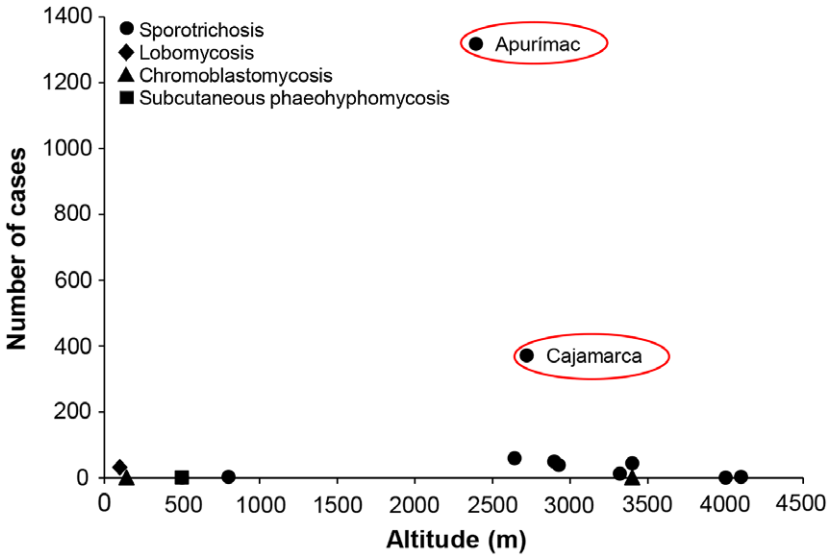

Figure 3 Relationship between cases of subcutaneous mycosis and altitude

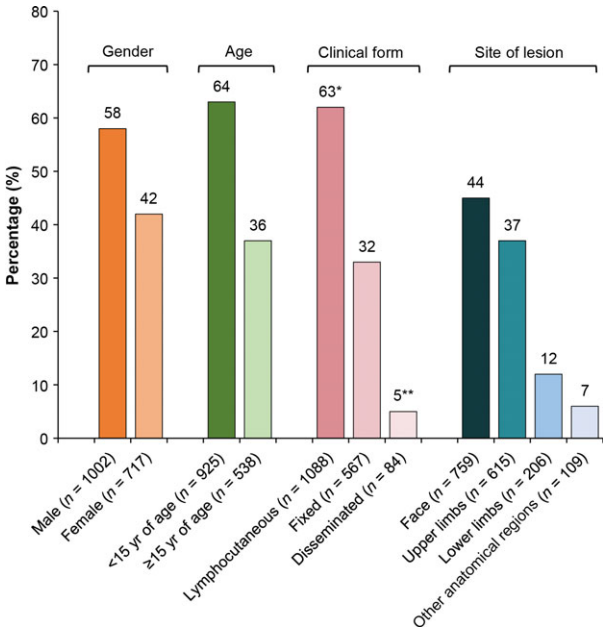

Figure 4 Distribution of demographic and clinical characteristics of sporotrichosis cases in Peru. *indicates two cases of coinfection with *Sporothrix* and HIV. **indicates one case of diabetes with disseminated sporotrichosis

Among children from Cajamarca, the prevalence was four cases per 100,000 inhabitants (20.5 cases/year). Overall the prevalence of sporotrichosis was approximately five times higher among children from Apurimac, compared with that among children from Cajamarca.

Demographic and clinical characteristics of the study population

For sporotrichosis cases, the age was recorded in 1463 cases, the gender in 1797 cases, the clinical form of the lesions in 1739 cases, and the lesion site in 1689 cases; 64% were children aged <15 years, and 58% were male. The lymphocutaneous clinical form (63%) was the most common, and the face was the most commonly affected site (44%) (Fig. 4). Diagnosis of sporotrichosis was made by fungal isolation and identification from cultures of biological samples. Using the morphophysiological method of Marimon *et al.*,[44] macroscopic and microscopic culture examinations revealed 99.6% of fungal isolates were *Sporothrix schenckii*, and only two isolates were identified as *S. schenckii* (*sensu stricto*).[17]

Demographic and clinical characteristics of cases of chromoblastomycosis, lobomycosis, and subcutaneous phaeohyphomycosis included in the study are described in Table 1.

Discussion

Since the overall burden of subcutaneous mycoses in Peru is currently unknown, we performed a meta-analysis after a systematic review of the published literature to estimate the burden of disease. The findings of this review should assist clinicians in making decisions, providing health education, and may also help in surveillance and diagnosis about the implementation of screening and management programs of this disease in hyperendemic and non-hyperendemic areas. Previous "non-systematic" reviews had reported sporotrichosis as endemic in 13 of the

Table 1 Cases of lobomycosis, chromoblastomycosis, and subcutaneous phaeohyphomycosis in Peru

Study	Location	Age/Gender	Clinical form	Site of lesion	TE	Laboratory diagnosis	Pathogen
Lobomycosis							
Bustamante *et al.* 2013[38]	Madre de Dios	29 yr, M		Left earlobe	12 yr	Direct microscopic examination, histopathological	*Locazia loboi* (synonym: *Lobomyces loboi*)
Talhari *et al.* 1985[37]	Madre de Dios	NA, M		Left earlobe		Histopathological	
Romero OR 1972[24]	Madre de Dios	NA, M		Left earlobe		Direct microscopic examination	
Chromoblastomycosis							
Cavero *et al.* 2004[23]	Ucayali	66 yr, M	Verrucous plaque	Back	16 yr	Culture, histopathological	*Cladosporium* sp.
Solórzano *et al.* 2011[39]	Cusco	51 yr, M	Verrucous plaque	Limb upper Limb lower	6 yr	Histopathological	Not identified (confirmed by observation of fumagoid cells or medlar bodies with biopsy)
Subcutaneous phaeohyphomycosis							
Vilcahuamán *et al.* 2010[40]	Lima	55 yr, F	Cystic lesion	Hand	1 yr	Culture, histopathological	*Exophiala jeanselmei*

yr, years; M, male; F, female; TE, time evolution; NA, not available.

25 regions we studied,[17,20–22,26,45] with lobomycosis, chromoblastomycosis, and subcutaneous phaeohyphomycosis being rare in Peru.[23,24,37–40] In our study, we found that, among the subcutaneous mycoses found in Peru, sporotrichosis was the most common and mainly located throughout highlands of Peru (Apurimac, Cajamarca, La Libertad, and Cusco). There is little doubt that sporotrichosis remains a major cause of morbidity in developing nations, such as Peru,[16–18,26] Mexico,[2,5,46] Brazil,[2,5,47] Colombia,[2,5,48] and Venezuela,[7,49] and our study here of sporotrichosis in Peru confirms the known distribution of sporotrichosis as well as the geographical areas where sporotrichosis has historically been a health problem. Therefore, healthcare providers should remain alert to the possibility that sporotrichosis may occur in 13 geographic foci in Peru, particularly in the regions of Apurimac, Cajamarca, La Libertad, and Cusco.

In this meta-analysis, all cases of lobomycosis were reported from the Peruvian jungle in Madre de Dios,[24,37,38] a poorly developed and low-altitude (183–500 m) region which has a tropical climate with an average temperature range between 10–27 °C and periods of intense precipitation of 1000 mm of rainfall per year.[27] It is likely these conditions favor the growth and spread of the fungus *Lacazia loboi,* given that this pathogen is found in forest areas with dense vegetation and large rivers, with intense precipitations of 2000 mm of rainfall per year, an average temperature of 24 °C and relative humidity of 75%.[13,50] Lobomycosis is endemic in the Amazon region of Central America (Panama, Costa Rica, and Mexico) and South America (Brazil, Colombia, Suriname, Venezuela, Guyana, French Guiana, Ecuador, and Bolivia) and predominates in Brazil.[2,12,13,51] However, it is rare in Peru where it is seen only in the region of Madre de Dios and usually affects adult males.

Chromoblastomycosis is a prevalent mycosis in Southern Africa[10,52] Latin America (Mexico, Brazil, and Venezuela),[2,7,9] and in the hyperendemic regions in the arid parts of Venezuela,[53] whereas it is rare in Peru with sporadic cases in the regions of Ucayali and Cusco.[23,39] Chromoblastomycosis is commonly caused by two fungal genera, *Cladophialophora* and *Fonsecaea*, which are found in arid climates and in the tropical rainforest, respectively.[1,2,10] Although *Cladophialophora carrionii* is the predominant agent of the disease in arid, desert-like climatic conditions,[2,10] in Peru, a *Cladosporium* species (synonym: *Cladophialophora* sp.) was reported in Ucayali, a region with a tropical climate with relatively higher levels of humidity.[23] In addition, members of *Cladophialophora* sp. are responsible for sporadic cases of chromoblastomycosis in the subtropical humid rainforest region. Therefore, it can be speculated that, in Peru, *Cladophialophora* species have adapted to the tropical humid conditions of Ucayali.

Subcutaneous phaeohyphomycosis targets primarily immunocompetent individuals, especially in warm and humid tropical climates,[2,14] and it is usually caused by the genera *Exophiala* and *Phialophora*.[2,14,54] To the best of our knowledge, in Peru, to date, only one case of subcutaneous phaeohyphomycosis caused by *Exophiala jeanselmei* has been reported in an immunocompetent individual in the region of Lima.[40] Compared to sporotrichosis, chromoblastomycosis, and lobomycosis, subcutaneous phaeohyphomycosis is the rarest mycosis in Peru.

Although there is ample evidence to support our findings that sporotrichosis produces a major burden of disease in Peru, the prevalence rates in our study may be explained, in part, by eco-climatic factors. Indeed, the highest prevalence of sporotrichosis was recorded in Apurimac, which comprises five provinces (Abancay, Andahuaylas, Antabambas, Ayamaraes, and Grau) known to have high rates of sporotrichosis[16,17,19] and where the climate is characterized by relatively higher levels of humidity and periods of intense precipitation (700 mm of rainfall per year),[27,55] followed by Cajamarca, where the climate is characterized by intermediate humidity levels,[27] and Cusco and La Libertad, which have relatively lower humidity levels.[27,55] These four regions represent historically endemic regions for sporotrichosis, although there is increasing evidence of sporadic cases occurring in other regions of Peru. Furthermore, the occurrence of the weather change may have had a significant impact on rainfall patterns and consequently in the spread of *Sporothrix* species in the Peruvian regions. It may have also contributed to the high burden of sporotrichosis in Apurimac. Therefore, taken together, the observed geographical differences in sporotrichosis burden may be attributed to variations in the local environment, specifically eco-climatic differences, which would favor fungal growth and spread, thereby predisposing populations to various skin diseases, including sporotrichosis, as reported by previous studies showing an increase in sporotrichosis cases during periods of increased rainfall.[56,57]

Furthermore, the high prevalence of sporotrichosis found in this study was lower than that previously reported in the Jalisco and Puebla mountain ranges in Mexico, an area known to have a high rate of sporotrichosis, with a prevalence of 25 cases per 1000 inhabitants.[2,5] The reasons for these differences are unclear, although geo-climatic variations could be an etiological possibility. To the best of our knowledge, there have been no other studies of sporotrichosis prevalence that would allow comparisons with international data; this is perhaps a reflection of sporotrichosis being considered as a "neglected" tropical disease. In order to address this issue, future research should focus on determining and comparing disease rates among people living in regions with high and low incidence of sporotrichosis.

We estimated the prevalence rates of sporotrichosis in the pediatric population from two regions, that is, Apurimac and Cajamarca. Our results indicate that the prevalence of sporotrichosis was much higher among children from Apurimac than those from Cajamarca. This high prevalence of sporotrichosis observed in children may be the result of age-dependent likelihood of exposure to soil or other environmental risk factors that harbor these endemic pathogens. Thus, children are more likely

to be exposed to these pathogens through recreational activities (e.g., playing in crop fields or on dirty floors in houses), particularly through the contact with cats, which is a risk factor of significance to sporotrichosis in an endemic region in Peru.[16,17] On the other hand, adults are more likely to be exposed through occupational activities. These factors increase the risk of infection and therefore the burden of disease. Although all age groups are susceptible to sporotrichosis,[5] several previous regional studies have documented a rapid increase in the incidence of sporotrichosis in the Peruvian children population.[16,19] However, studies in certain hyperendemic regions were not performed in the entire study population or in a regional sample to estimate the burden of disease. Therefore, the true magnitude of the prevalence of sporotrichosis in children remains uncertain.

According to Peruvian literature, *S. schenckii* is the most common causative agent of sporotrichosis, but identification of these species was made only by culture. Although in the current time, the identification and classification of the *Sporothrix* species are based on molecular characters, and there are now five pathogenic species whose epidemiology appears to vary.[44] The predominance of the pathogenic *Sporothrix* species and its epidemiology is still not known. The distribution of these causative agents is not equal around the globe and can vary between countries and regions. For example, *S. brasiliensis* is more commonly found in Brazil and is associated with zoonotic transmission through scratches and bites from infected cats, while *S. mexicana* is more commonly found in Mexico, and *S. globosa* and *S. schenckii* (*sensu stricto*) are cosmopolitan pathogens more common in Latin America, Europe, and Asia and are associated with traumatic inoculation with contaminated environmental materials.[44]

In this meta-analysis, the demographic and clinical characteristics of sporotrichosis cases were consistent with those described in the literature, with lymphocutaneous sporotrichosis most commonly affecting the facial region, albeit in an increased proportion of pediatric cases.[16–19] The predominance of the lymphocutaneous form affecting the facial region in children is generally attributed to the fact that the face is an exposed area with delicate skin and therefore susceptible to inoculant trauma or contact with cats during the children's recreational activities.[16,17] Although the "fixed form" is less common[1,2] and the disseminated form occurs in patients with diabetes, HIV/AIDS, and hematological malignancies,[1,58] in this meta-analysis, we identified only two cases of coinfection with *Sporothrix* and HIV[33] and one case of diabetes with disseminated sporotrichosis.[32]

Limitations of this study should be considered when interpreting the findings here. Firstly, according to used methods, these findings only provide an approximate estimate of prevalence in a certain regions, but the true figure may be higher or lower particularly as hyperendemic zones are confined to small provinces but may not reflect actual prevalence of sporotrichosis in the region. Therefore, these data can constitute gross underestimations or overestimations of the true prevalence of sporotrichosis in Peru. Secondly, although we are confident that the cases reported are representative of the region within the cases' catchment areas, they may not be representative of the region of study, because most of the cases reported were from a single hospital or a regional referral center. Third, only 12 studies with 10 or more cases from four regions, out of a total of 25, in Peru were included to determine the prevalence of sporotrichosis. Therefore, it is likely the prevalence of sporotrichosis was underestimated because only a few studies on sporotrichosis in Peru were published. Fourthly, the baseline surveys conducted in Peru included little information about subcutaneous mycoses, which limits our ability to determine the burden of chromoblastomycosis, lobomycosis, and subcutaneous phaeohyphomycosis in terms of prevalence and the number of reported cases per year per region. Finally, it is possible that a large number of patients had a subcutaneous mycosis but remained undiagnosed because their symptoms were less severe. Despite these limitations, we believe our presented results are valid and provide strong evidence for estimating the burden of sporotrichosis in Peru.

Findings from our study help to provide a better understanding of the burden and distribution of subcutaneous mycoses in Peru that may be useful for identifying at-risk population groups and developing appropriate intervention, surveillance, and prevention strategies. Moreover, early recognition of these diseases is important and can be achieved through education of the population and healthcare professionals in order to raise awareness of the diseases. Therefore, we propose that surveillance of mycoses of implantation in Peru should be improved through the implementation of a national survey and studies of fungal isolates causing clinical disease in order to mitigate the consequences of these diseases. In addition, healthcare professionals should be obligated to notify cases of sporotrichosis in endemic areas of Peru rather than considering it as a "neglected" disease as is currently the case.

In conclusion, sporotrichosis is the most common subcutaneous mycosis in Peru, with a high prevalence and high burden of disease, especially in the region of Apurimac. In contrast, chromoblastomycosis, lobomycosis, and subcutaneous phaeohyphomycosis are rare in Peru. Sporotrichosis affects primarily the pediatric population, and the most common presentation in children is the lymphocutaneous form affecting the facial region. Taken together, our results indicate that sporotrichosis has become a major public health challenge in Apurimac and underscore the need for strategies aimed at prevention, early detection, and treatment of this mycosis.

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Supporting Information

Additional Supporting Information may be found in the online version of this article:

Table S1. PRISMA 2009 checklist.

