Epidemiological aspects of patients with ungual and cutaneous lesions caused by *Scytalidium spp*

Aspectos epidemiológicos de pacientes com lesões ungueais e cutâneas causadas por *Scytalidium spp* *

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Abstract: BACKGROUND – Dermatomycoses caused by non-dermatophyte filamentous fungi are rare infections, except for onychomycosis, whose prevalence has increased over the past few years. Among these etiologic agents, we highlight Scytalidium dimidiatum and S. hyalinum, emergent fungi that cause mycoses that affect the nails and skin.
OBJECTIVE – To investigate the characteristics of onychomycosis and other mycoses caused by the fungi *Scytalidium spp*, using sex, age and site of infection as parameters.
METHODS – Eighty-one samples were evaluated showing positive culture for Scytalidium spp, obtained from 74 patients referred to the Laboratory of Investigation in Dermatology (ID) located in the city of Rio de Janeiro, RJ, between 1997 and 2006. The samples were submitted to diagnostic confirmation through direct exam and culture.
RESULTS – The prevalence of onychomycosis caused by *Scytalidium spp*. was of 0,87%. The most prevalent age was between 41-60 years (48.64%). Regarding the site of infection, the feet (91.36%) were most affected, with predominance of the left hallux. Hyaline hyphae were the most common structures in direct examination and the species S. dimidiatum was the most frequent in culture.
CONCLUSION – Onychomycosis caused by *Scytalidium spp*. is rare and S. dimidiatum was the most isolated species in this laboratory during the period of the study.
Keywords: Dermatomycosis; Epidemiology; Fungi; Onychomycosis

Resumo: FUNDAMENTO - As dermatomicoses causadas por fungos filamentosos não dermatófitos são infecções raras, exceto as onicomicoses, cuja prevalência vem crescendo nos últimos anos. Dentre esses agentes etiológicos destacam-se o *Scytalidium dimidiatum* e o *S. hyalinum*, fungos emergentes responsáveis por micoses em unhas e pele.
OBJETIVO - Investigar as características epidemiológicas das onicomicoses e micoses de outras localizações causadas pelos fungos do gênero *Scytalidium*, utilizando-se como parâmetros sexo, idade e localizações das lesões.
MÉTODOS – Avaliaram-se 81 amostras com cultura positiva para o gênero em estudo, oriundas de 74 pacientes encaminhados ao Laboratório de Investigação em Dermatologia (ID) situado na cidade do Rio de Janeiro (RJ), no período de 1997 a 2006. As amostras foram submetidas a confirmação diagnóstica por exame direto e cultura.
RESULTADOS - A prevalência de onicomicoses por *Scytalidium spp*. foi de 0,87%, entre as idades de 41 e 60 anos (48,64%). Em relação à localização das lesões, os pés foram mais acometidos (91,36%), com predomínio do hálux esquerdo. No exame direto, as estruturas mais encontradas foram hifas hialinas; na cultura, a espécie S. dimidiatum foi a mais frequente.
CONCLUSÃO - As onicomicoses por *Scytalidium spp*. são raras e o *S. dimidiatum* foi a espécie mais isolada neste laboratório no período em estudo.
Palavras-chave: Dermatomicoses; Epidemiologia; Fungos; Onicomicose

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INTRODUCTION

Over the last decades, the number of patients susceptible to the most varied types of fungal infections of any etiology has increased significantly. With regard to dermatomycosis, in particular onychomicosis, it has been observed that a great portion of the world population is affected, especially individuals aged between 40 and 60 years. Immunodepressed, diabetic and older patients are considered at risk. [1,2,3] The genus *Scytalidium* was described in 1933 by Natrass, in its pycnidial stage, *Hendersonula toruloidea,* as a phytopathogen. Only in 1970 the first cases of cutaneous and ungual infections in humans were described. [4] Since then, there have been several changes in its taxonomic nomenclature. In a review by Lacaz *et al.* (1999) it became established that *Nattrassia mangiferae* is an anamorphous form of the genus *Scytalidium* and synonym of *Hendersonula toruloidea; Scytalidium dimidiatum* is the sinanamorphous form and synonym of *S. Lignicola; S. Hyalinum* may be considered a separate species or a hyaline mutant of *S. Dimidiatum.* [5]

S. dimidiatum is found in the soil and vegetation, but the natural habitat of *S. hyalinum* is unknown. [5,6,7] They are both etiologic agents of plantar, palmar, interdigital and ungual dermatomycoses, with lesions that are clinically indistinguishable from dermatophytoses. [5,8,9,10] A few studies describe the involvement of *S. dimidiatum* in invasive and subcutaneous infections in immunodepressed patients. [5,7,11,12] The pathogenicity of *Scytalidium* spp. is based on the production of extracellular enzymes such as amylases, proteases (keratinases) and lipases, with emphasis to the proteolytic activity, important in the pathogenesis because it is responsible for the hydrolisis of the keratin present in the nails and in the stratum corneum of the skin. [13,14,15] These fungi do not grow in culture media with cycloheximide [6,16] and show high resistance to the antifungal drugs traditionally used in clinical practice. [11,12,17]

This work aimed at investigating the epidemiologic characteristics of onychomycosis and other mycoses caused by the non-dermatophyte filamentous fungus *Scytalidium* spp., from cutaneous and ungual samples, using sex, age and site of infection as parameters.

The study was approved by the Ethics Committee of the Fluminense Federal University (approval number 091/05).

MATERIAL AND METHODS

From November of 1997 to December of 2006, 25,631 mycological exams of nail and skin scrapings, hair and, occasionally nail and skin biopsies were performed at the Service of Mycology of the Laboratory of Investigation in Dermatology (ID), located in Rio de Janeiro, RJ, Brazil. Of this total, 13,738 (53.6%) exams were negative for fungi and 11,893 (46.40%) revealed positive direct examination and/or culture for dermatophytes, yeasts or non-dermatophyte filamentous fungi collected from different anatomical sites. Of the positive samples, 6,173 were nail scrapings positive for various etiologies.

The inclusion criteria were samples with positive or negative direct examination and growth of the same agent in five or more inoculation points in Sabouraud agar surface, producing pure positive colonies for filamentous fungi of the *Scytalidium* spp. genus (*S. dimidiatum* and *S. hyalinum*). A total of 81 samples was analyzed, including 54 ungual and 27 cutaneous samples. These samples – subungual scrapings of toes and fingers collected from 50 patients and skin scrapings of the plantar regions and intergidital spaces of 24 patients – totaled 74 patients of both sexes with ages varying from 2 to 74 years. In five of these patients, the fungus was diagnosed in more than one anatomical site and in other two patients the association between cutaneous and ungual lesion was observed.

Data for the research were gathered from the identification file of each patient referred to the laboratory during this period. All the samples were submitted to direct examination with NaOH 20% and culture in Sabouraud agar and Sabouraud agar with chloramphenicol and cycloheximide, with subsequent analysis of the colonial macro and micromorphology, a standard methodology employed in laboratory for mycological diagnosis. Confirmation of *Scytalidium* spp. as the etiologic agent of dermatomycosis was based on the result of direct examination and on the identification of the species according to the macro and micromorphological characteristics of the colonies.

The Shapiro-Wilk test was used for normality of the age values, at the level of 5%. The p-value found ($p<0.05$) indicated rejection of the hypothesis for data normality and, consequently, the use of parametric testing. Hence, in the verification of the statistical difference between the distributions of age by sex, the Kruskal-Wallis non-parametric test was employed, with a 5% significance level.

To verify the association between categorical variables (sex and site of infection, sex and species, and sex and direct exam), Fisher's exact test was employed. This is a commonly used test for squared tables (2 lines and 2 columns) or those with a low cell count. Fisher's exact test investigates the existence of independence between the categories of two variables, where $p<0.05$ signals the existence of a

dependence relation between the categories.

The software used for the statistical analysis was R 2.6.2.

RESULTS

In this period 54 cases of onychomicosis by *Scytalidium* spp. were found, an occurrence of 0.87%, CI 95% = (0.66% - 1.14%), (54/6173) among the cases studied.

The sample population was constituted by 74 patients, half male and half female, distributed across different age ranges, including patients with skin and nail lesions (Graph 1). Based on the Kruskal-Wallis test (p=0.8722) there were no significant statistical differences in the distribution of age by sex.

In direct examination with NaOH 20%, 90.54% of the results were positive. Brown septate hyphae were found in 6.76% and hyaline septate hyphae, in 83.78%; 9.46% of the exams were negative and all of them were positive for *Scytalidium* spp. culture (Graph 2). Significant associations between direct examination results and sex were not found (p=0.5306).

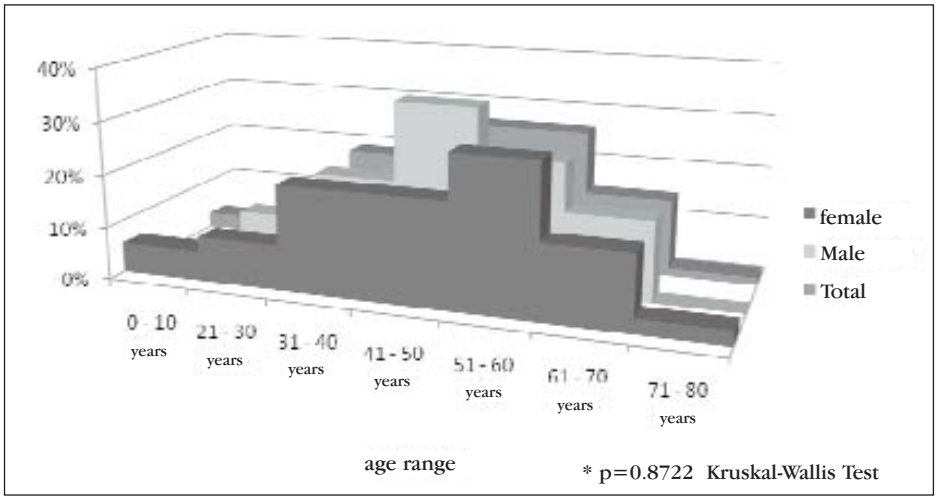
All the samples cultured in Sabouraud Agar showed growth typical to that of *Scytalidium* spp., distributed across the following species: black or gray colonies grew in 55 (74.32%) samples, diagnosed as macroscopically (Figure 1) and microscopically compatible with *S. dimidiatum*. Twenty-nine samples (78.38%) were collected from women and 26 (70.27%) from men; white colonies grew in 19 samples (25.68%), compatible macroscopically (Figure 2) and microscopically (Figure 3) with *S. dimidiatum*; of these 19 samples, 11 (29.73%) were collected from men and 8 (21.62%) from women. In this case, 74 samples are considered, since growth of *Scytalidium* spp. was compared in relation to sex (in 5 patients the species was diagnosed in more than one anatomical site and in other two patients there was an association between skin and nail lesion. All the samples showed the same growth. For ease of calculation, only one sample was considered per patient) (Graph 3).

With regard to the colonial micromorphology of *S. dimidiatum*, hyaline and/or brown hyphae and cylindrical or round arthroconidia, unicellular and bicellular of brownish coloration, were seen. In the micromorphology of *S. hyalinum*, hyaline septate hyphae and unicellular and bicellular hyaline arthroconydia were observed. In the comparison of the results of species by sex, no preferences in the choice of the host can be confirmed due to lack of association (p=1.000).

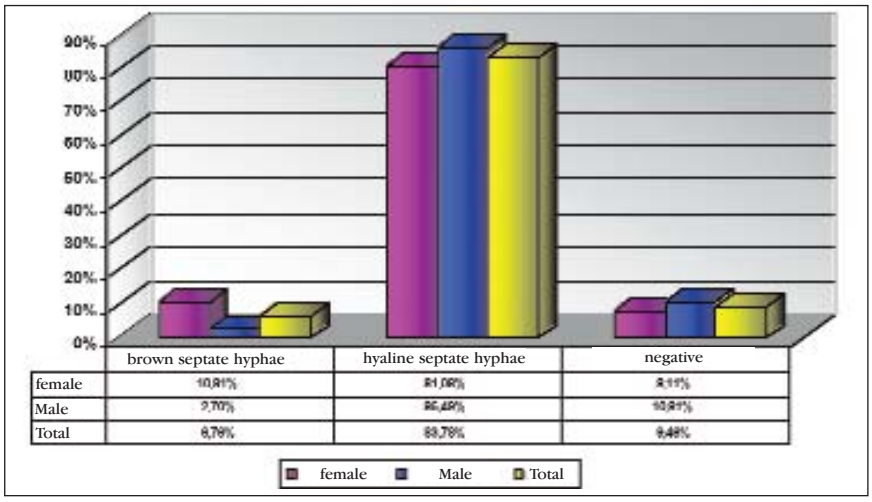
The feet were the most affected anatomical site (91.36%), whereas the hands were affected in 8.64% of the cases, only in women. The association between site of the lesion (hand and foot) and sex was statistically significant (p=0.0122). While all the men were affected in the feet, only 83.3% of the women had lesions in this area of the body. Of the 54 cases of onychomycosis, 47 (87.03%) were found in toenails; most of them were on the left toe (62.96%) and all of them in the distal and lateral subungual form. Of the 27 skin lesions, 48.15% were found in the plantar region, 40.74% in the interdigital spaces of the feet, and 11.11% in the toes. There was one case of dermatomycosis in the plantar region in vesicular clinical form.

DISCUSSION

In our country, studies that classify the fungi of the genus *Scytalidium* as primary pathogens are, so far, rare. Most publications on the subject are limited to the presentation of clinical cases in humans and, with rare exceptions, there is work mentioning the isolation of this fungus in prevalence studies of fungal infections of any etiology. [18,19,20,21,22.23] It is known that



Graph 1: Distribution of patients across different age ranges by sex* in mycological studies analyzed between 1997 and 2006 in Rio de Janeiro



*p=0.5306 Fisher's exact test

GRAPH 2: Results of direct examination of nail and skin scrapings of different sites in relation to sex of mycological studies analyzed between 1997 and 2006 in Rio de Janeiro

species of *Scytalidium* spp. were first recognized as etiologic agents of dermatomycosis in 1970 by Gentles & Evans and, since then, have often been isolated in various tropical countries such as Nigeria, Tobago, Gabo, Thailand, Jamaica and Australia, considered endemic regions, where prevalence may range from 9% to 24% of the population, reaching almost 47% in different epidemiological studies. In recent years, there has been an increase in the number of cases of dermatomycosis, especially in Europe, both in immunocompetent and immunocompromised patients, as observed in studies in England and France, which reported a prevalence of 11% and 34% respectively. [4,8,18,24] According to some authors, this higher frequency most often observed in temperate countries is due to the constant migration of individuals originating from endemic regions and individuals with a history of travel to these places, although there are exceptions. [16]

The low frequency of onychomycosis caused by *Scytalidium* spp. observed in this study - 0.87% - was also reported by Midgley *et al*. (1994) and Araújo *et al*. (2003b), differing from Escobar & Carmona-Fonseca (2003) and Lacroix *et al.* (2003), who found prevalence of 3.8% and 3.6%, respectively. [16,24,25,26] Coincidentally, there was an equal number of males and females in this study. Other studies reveal predominance of men, such as those by Lacroix *et al.* in

FIGURE 1: Macromorphology of the front and back of a Scytalidium dimidiatum colony in Sabouraud Agar after 15 days of growth

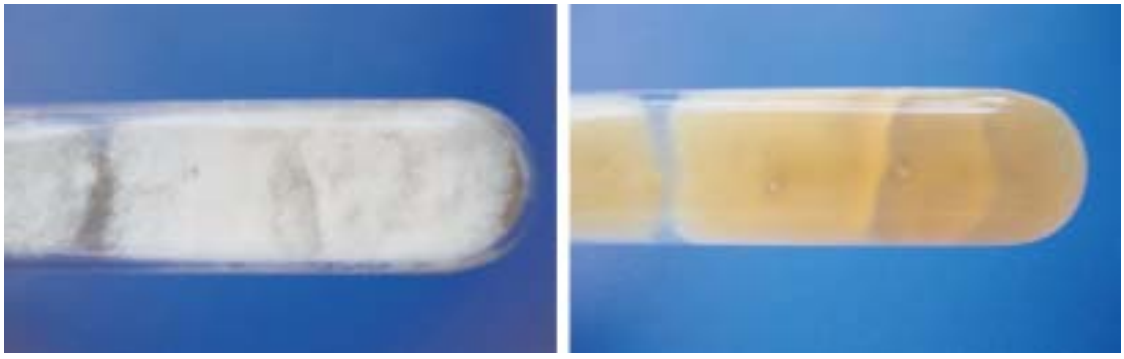
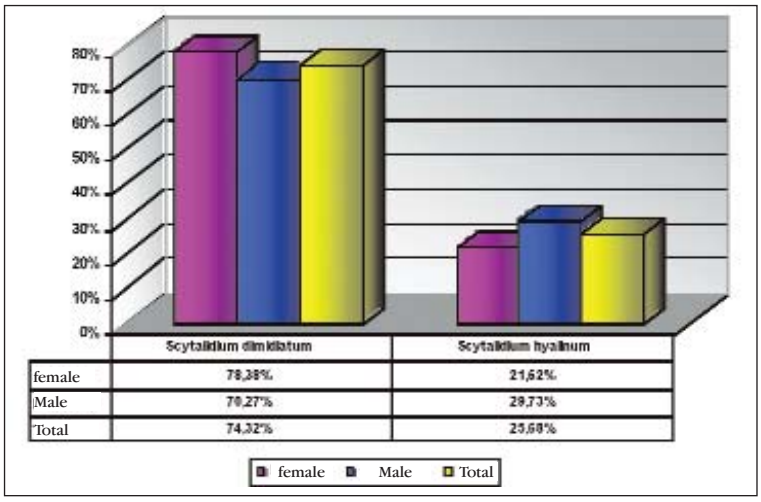


FIGURE 2: Macromorphology of the front and back of a Scytalidium hyalinum colony in Sabouraud Agar after 15 days of growth



*p=1.000 Fisher's exact test

GRAPH 3: Distribution of Scytalidium spp. by sex, based on the isolates of Scytalidium spp. analyzed between 1997 and 2006 in Rio de Janeiro

2003 (67.5% men to 32.5% women) and Frankell & Rippon (1989) in a review of clinical cases (75% men to 25% women). [9,24] The age distribution was similar to that reported by Lacroix *et al.* (2003), but different from that mentioned in the work of Escobar & Carmona-Fonseca (2003), between 21 and 50 years [24,26]. The fungal structures seen more frequently in direct examination were hyaline septate hyphae (83.78%). Escobar & Carmona (2000, 2003) reported finding the remains of spawn more frequently, saying they had not seen typical fungal structures. [26,27] *S. dimidiatum* (74.32%) was the most frequent species; similar prevalence was observed in European studies. In the study by Lacroix *et al.* (2003) *S. hyalinum* was isolated most frequently. The preferred site of infection was the feet (91.36%), which had been mentioned by other authors, and the most frequent onychomycoses were found in the nail of the hallux (52.70%). [24]

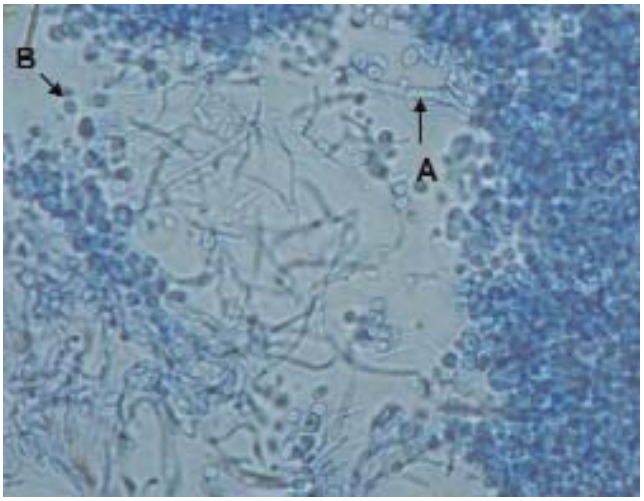


FIGURE 3: Micromorphology of positive culture for Scytalidium hyalinum, presence of hyaline septate hyphae (A) and unicellular and bicellular arthroconydia (B) (400X)

So far, dermatomycoses do not require mandatory notification, so there is no real knowledge of the extent of this problem in the population, despite studies that show that the incidence of these disorders has increased significantly. In Brazil, very few studies report the isolation of the emerging filamentous fungus *Scytalidium* spp. This shows the need for the implementation and dissemination of epidemiological studies on new species of emerging filamentous fungi as a measure of prevention and control of these difficult-to-treat dermatomycoses. Proper mycological diagnosis is extremely important, as these diseases may serve as fungi reservoirs for other more severe pathologies and, above all, lead to harmful aesthetic, psychosocial and occupational consequences in undiagnosed and untreated patients.

CONCLUSION

Based on this study, we concluded that onychomycoses caused by *Scytalidium* spp. had a low prevalence; the age range most frequently affected was between 41-60 years; the fungal structures more frequently seen in direct examination were hyaline septate hyphae; *S. dimidiatum* was the most frequent species; the feet were the most affected anatomical site, onychomycoses were more frequent among women and skin lesions were predominant among male patients. ❑

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