Onycomychosis due to *Scytalidium spp.*: A clinical and epidemiologic study at a University Hospital in Rio de Janeiro, Brazil *

Onicomicose por *Scytalidium spp.*: estudo clínico-epidemiológico em um hospital universitário do Rio de Janeiro, Brasil

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Abstract: BACKGROUND: *Scytalidium sp*. is a filamentous (thread-like), saprobic fungus which affects soil and plants. It is currently considered a primary pathogen of the nail. The prevalence of nail infections caused by this fungus has been increasing in recent decades, although few published studies have been done on its epidemiology.
OBJECTIVE: To study clinico-epidemiological data referring to patients with onychomycosis caused by *Scytalidium spp*. at a University Hospital in Rio de Janeiro.
METHODS: We evaluated the clinical and epidemiological data of 30 patients with onychomycosis by Scytalidium sp. through an observational study of 1295 patients who underwent mycological nail tests over a period of 16 months.
RESULTS: The majority of the patients were female (66.6%), with an average age of 56.7 years. 63.3% of them were nonwhite. 53.3% of the patients had attended elementary school and 36.6% referred a family income of 3 to 5 minimum wages. In 90% of cases, the toenails were affected, primarily with onycholysis (18 patients), and in 66% of the cases melanonychia was observed. In 43.3% of cases the disease had progressed for more than 5 years. 19 patients (63.3%) had undergone some medical treatment for their current condition.
CONCLUSIONS: Our data show that nail infection by S*cytalidium sp*. is chronic, affecting adults, particularly females (2:1). Clinically the disease resembles dermatophytosis. Prevalence of the disease in our sample was 4.86%, accounting for 26.92% of the positive tests.
Keywords: Epidemiology; Fungi; Mycoses; Onychomycosis

Resumo: FUNDAMENTOS: O *Scytalidium spp*. é fungo filamentoso, saprobio do solo e plantas, considerado, atualmente, patógeno primário das unhas. A prevalência das infecções ungueais causadas por este fungo vem aumentando nas últimas décadas, embora ainda sejam poucos os trabalhos publicados sobre sua epidemiologia.
OBJETIVO: Estudo clínico-epidemiológico dos pacientes portadores de onicomicose por *Scytalidium spp*. em um hospital universitário do Rio de Janeiro.
MÉTODOS: Foram avaliados os dados clínico-epidemiológicos de 30 pacientes com onicomicose por *Scytalidium spp*. por meio do estudo observacional de 1.295 pacientes que se submeteram a exame micológico ungueal no período de 16 meses.
RESULTADOS: A maioria dos pacientes era do sexo feminino (66,6%), a média de idade foi de 56,7 anos e 63,3% eram não-brancos. O nível de escolaridade em 53,3% dos pacientes era o ensino fundamental e a renda familiar predominante foi de 3 a 5 salários mínimos em 36,6% dos entrevistados. Em 90% dos casos, as unhas dos pododáctilos foram acometidas, sendo a alteração clínica mais comum a onicólise (18 pacientes) e em 66,6% dos casos observou-se melanoníquia. O tempo de evolução da doença foi maior do que cinco anos em 43,3% dos casos. Dezenove pacientes (63,3%) já haviam realizado tratamento medicamentoso para o quadro atual.
CONCLUSÕES: Os dados mostram que a infecção ungueal pelo *Scytalidium spp*. é crônica, mais comum no sexo feminino (2:1) e atinge indivíduos adultos. Clinicamente, é semelhante às dermatofitoses. A prevalência na amostra estudada foi de 4,86% e correspondeu a 26,92% dos exames positivos.
Palavras-chave: Epidemiologia; Fungos; Micoses; Onicomicose

Received on 15.09.2010.
Approved by the Advisory Board and accepted for publication on 05.10.10.
* Research conducted at: Mycology Laboratory of the Department of Dermatology, Pedro Ernesto University Hospital, State University of Rio de Janeiro (HUPE-UERJ), Rio de Janeiro (RJ), Brazil.
Conflict of interest: None / *Conflito de interesse: Nenhum*
Financial funding: None / *Suporte financeiro: Nenhum*

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INTRODUCTION

Non-dermatophyte filamentous fungi (FFND) are commonly found in nature in saprobial soil and plant debris and plant pathogens. A growing number of published papers over recent years consider these fungi as primary skin pathogens affecting nails in males. In tropical and subtropical countries the fungi appear to be endemic, with the result that primary pathogens are more frequently encountered in these countries. The prevalence of nail invasion by FFND varies from 1.45 to 17.6% depending on geographic distribution and the mycological or diagnostic methods used. They are more common in people over 60 years of age. [1,2]

The main FFND considered to be the primary pathogens of onychomycosis are as follows: *Scopulariopsis*, *Scytalidium*, *Fusarium*, *Aspergillus* and *Onychocola canadensis*. [3,4,5] The *Scytalidium* species are found in soil and plants. The *Dimidiatum* species belongs to the *Neoscytalidium* genus. Based on a genotyping study it was recently proposed that the *hyalinum* species can be considered to be simply a variant of *Neoscytalidium dimidiatum.* [6] Infection appears to be acquired by direct contact, especially by individuals not using protective clothing or footwear. It is not uncommon to find infections consisting of a mixture of dermatophytes and *Scytalidium spp.* [7] Clinically, nail and skin lesions caused by *Scytalidium spp.* are no different from those caused by dermatophytes. In around 97% of cases the legs are the most affected.

The frequency of *Scytalidium spp.* as a cause of onychomycosis varies significantly. The fungi were found in 2.3% of patients in a study conducted in France and in 1.25% in a study done in the city of Rio de Janeiro (Brazil). [8,9] Meanwhile, in Martinique, *Scytalidium spp.* was discovered as the cause of 56% cases of onychomycosis, with dermatophytes responsible for only 13% of the latter. [10] In some places this infection may be more predominant than dermatophytes.

Few studies exist describing the epidemiology of patients with onychomycosis caused by *Scytalidium spp.*

MATERIALS AND METHODS

An observational study, approved by the Research Ethics Committee (No.1510), was conducted at the Mycology Laboratory of a Rio de Janeiro University Hospital.

From 1st August 2006 to 3rd December 2007 all mycological nail examinations were evaluated in an effort to detect the presence of hyphae (hyaline or dematiaceous, septate, branched, with or without arthroconidia) whose culture would lead to identifying *Scytalidium* species.

Epidemiological data were noted such as sex, age, race, education, family income, leisure and social circumstances. Data also covered clinical nail manifestations, time of duration of the disease and concomitant skin changes, as well as information about previous treatments of all the patients who attended the clinic, and were willing to complete the questionnaire and submit to examination. All signed an informed consent form.

RESULTS

1295 patients were submitted to mycological examination of the nails over a period of 16 months. Of these, 471 (36.7%) underwent examination of the fingers and 824 (63.62%) of the toes. Tests on 1061 (81.93%) patients during this period displayed negative, or with contaminants such as bacteria and polysaprobia.

Of the 1295 patients, 80 (6.17%) were positive for dermatophytes and 154 (11.89%) for non-dermatophyte filamentous fungi. Of the 154 patients found with FFND, 63 were positive for *Scytalidium spp.* Of the total sample of patients undergoing nail examination, *Scytalidium sp.* was present in 4.86%. Among the 234 patients who tested positive, 34.18% (80) patients had dermatophytes and 26.92% (63) carried *Scytalidium spp.* Of the 154 patients positive for FFND, 40.9% (63) were patients with *Scytalidium* in the nails.

30 of the 63 patients tested positive for *Scytalidium sp.* agreed to attend the clinic and answer the questionnaire: 20 (66.6%) females and 10 (33.3%) males. 19 of the total (63.3%) stated that they were non-white and 11 (36,6%) as white. The average age of the sample was 56.7 years, with the majority aged between 40 and 60 years (19 patients).

16 patients (53.3%) had completed primary school education, 9 (30%) were high school graduates and 4 (13.3%) had been to university or equivalent. Only one patient (3.3%) admitted to being illiterate.

Only 6 (20%) patients said they normally walked barefoot. Family income ranged predominantly from 3 to 5 minimum wages in 11 (36.6%) of the patients in the sample. Progression of the disease was between 1 and 5 years in 14 patients (46.6%) and over 5 years in 13 (43.3%).

Toenails were affected in 90% of the cases. The most prevalent clinical abnormalities were onycholysis in 18 patients (60%), subungual hyperkeratosis in 17 (56.6%) and increased thickness of the nail plate in 6 (20%). (See Figure 1).

Color changes of the nail plate were also

assessed. Melanonychia was the main change detected in 20 patients (66.6%). When patients were separated according to race, it was observed that of 19 non-white patients 17 (89.4%) presented color changes, while among the 11 white patients color changes affected only 3 (27.2%). Yellowing was observed in 12 patients (40%) and leukonychia in 7 (23.3%).

As for skin changes, the plantar area was the most affected together with the toenails, affecting 22 (73.3%) patients. The interdigital areas presented changes in 18 (60%) cases, and only 4 (13.3%) patients were observed with changes in the palmar skin area. Scaling was the main change noted: 13.3% in the palmar area, 70% in the plantar region and 53.3% in the spaces between the toes.

19 patients (63.3%) had undergone topical or systemic medication for their current condition.

DISCUSSION

Interest in the study of onychomycosis caused by FFNDs, including by *Scytalidium spp.,* has increased in recent decades. Despite a growing number of articles on the subject, more wide-ranging studies on the epidemiological data of the affected population, as well as therapeutic modalities, are needed. [1,2,3,11]

Our study in Brazil, aimed at establishing the frequency of FFNDs, found that *Scytalidium spp.* accounted for 1.25% of the total of onychomycoses and 27.7% of the onychomycoses caused by FFNDs. The study showed that, given that this is not a rare disease, it should enter into the differential diagnosis of fungal onychopathies. [9] The prevalence of onychomycosis caused by *Scytalidium spp.* was found in 4.68% of the sample. These different results may be caused by geographical diversity i.e. dependent on where patients participating in the studies live. Comparing prevalence among the patients found positive during the study period we observed that *tinea unguium* is losing ground to FFND, given that 34.18% were found to be dermatophytes and 26.92% were *Scytalidium spp,* in addition to other fungi which are also etiological agents of onychomycosis caused by FFND. This situation is of some concern given that the majority of patients do not heal and have to keep returning to the hospital with their problem.

Figure 1: Clinical changes in onychomycosis caused by Scytalidium. Main clinical changes: onycholysis, subungual hyperkeratosis and yellowish discoloration of the nail plate

The results of both the Brazilian and French studies showed that the disease affected more women than men (2:1). [8] A further point: most published studies were conducted in Europe where the white population predominates, while other studies provided no information on the race of the participants. The fact that most of the patients in our sample were non-whites (63.3%) could simply indicate that most patients attended at public hospitals in Brazil come from the lower income strata. It is thus possible that no relationship exists between this mycosis and specific demographic characteristics. We were unable in our study to establish, for example, a relationship between the disease and low income or education.

63.3% of patients were aged between 40 and 60 years (i.e.adults but not elderly). The scientific literature reveals that the 'elderly' population is more likely to have onychomycosis of the feet caused by FFND. [8] Older people are also more at risk of dermatophytic onychomycosis. According to the literature the causes are: poor peripheral circulation, diabetes, repeated nail trauma, longer exposure to the fungal pathogen, physical inability to cut toenails, and slower nail growth. In our study 20% of patients had diabetes mellitus and 56.66% suffered some type of circulatory disorder. Unlike with dermatophytic onychomycosis, FFND-related nail infections did not appear to be associated with local or systemic predisposing factors. We did observe however that immunocompromised individuals ran an increased risk of subcutaneous or systemic spread of the disease. [10]

As with dermatophytosis, lesions involved the toenails more than the fingers. In 90% of cases the lesion was located in the big toe nail. While walking barefoot is considered to be a predisposing factor for geophilic transmission of onychomycosis caused by *Scytalidium spp.,* this custom was admitted by only 20% of patients at interview. [8.10] However, given the chronic infections in many patients, we assumed that there was a real possibility of contact with the fungus some years prior to the disease presenting. A case was

reported of an agricultural worker in Venezuela with mycetoma caused by *S. dimidiatum (N. dimidiatum)* where it was suspected that the source of the infection was a type of mango tree (*Mangifera indica)*. [6] Since mango trees are common in Brazil it would be interesting to research and genotype this fungus in areas where they grow and to discover whether they grow near the homes or workplaces of patients infected with *Scytalidium sp.*

The clinical description of *Scytalidium sp.* skin infections in the medical literature is similar to that described for dermatophytes. It is therefore important to identify the etiologic agent by mycological examination. [1,10] A further factor to be considered is the need to diagnose the disease correctly. The mycological examination depends not only on the skill and training of those doing the tests, but also on clinical correlation - which depends substantially on the ability of highly trained specialists to understand the whole diagnostic picture i.e. dermatologists. Moreover, the sensitivity of the test can vary considerably, depending on factors such as accurate collection of the material, careful analysis under the microscope and correct identification of the fungus (Figure 2).

Nail infections caused by *Scytalidium spp.* often present clinically as a lateral/distal subungual lesion or paronychia, accompanied by nail dystrophy. [7] In our study we observed that most patients had concomitant distal and lateral involvement. Some patients also had complete nail plate dystrophy, possibly reflecting the long development time of the disease and the lack of effective treatment.

Melanonychia is brown or black coloring of the nail plate, which can be caused by deposits of melanin or of pigmentation produced by non-melanocytic lesions such as onychomycosis. The disorder has a varied etiology. Melanonychia of racial origin is a major cause of the nail being blackish - the most frequent manifestation (66.6% of cases). In a study conducted in France, melanonychia was observed more often in black-skinned people and appeared to be due more to skin color than to pigmentation caused by *S. dimidiatum.* [8] Most patients in our study were non-white (63.3%), with melanonychia present in 89.4%. The discoloration was present in only 27.2% of white patients, which suggests that the disorder could perhaps be due to the racial origin of the patient rather than to the fungus. The existence of melanonychia in the other nails of these same patients strongly suggests a racial component. [12]

Figura 2: Micromorphology of *Scytalidium (Neoscytalidium)* dimidiatum showing brown, septate hyphae forming arthroconidia. Lactophenol, 40

43% of the patients had had the infection for over 5 years, and 46.6% between 1 and 5 years, which gives an idea of its chronic nature. As for type and length of treatment, 63.3% of the patients reported that they had used topical or systemic medication in an attempt to cure the infection. The long timescale and the various attempts at treatment also suggest that therapy is difficult in terms of low affordability and equally low patient adherence. The lack of resolutive outcomes inevitably increases the associated public health costs.

Our data show that the epidemiology of onychomycoses, at least in our environment, is changing with regard to etiological agents. This suggests that a need exists for new observations from other regions and areas to ascertain whether the changes are merely regional or of wider scope. *Scytalidium* species must be considered in the differential diagnosis of the different etiological agents of onychomycoses where dermatophytes previously prevailed.

Encouragement should be given for studies leading to controlling or curing these infections.

CONCLUSIONS

In our sample the prevalence of the *Scytalidium* species as an onychomycosis agent was 4.86%. The species was isolated in 26.92% of the patients who tested positive on the nails. Our study revealed that onychomycosis caused by *Scytalidium spp.* was indeed a chronic infection, mainly affecting adults aged between 40 and 60, with a bias towards females by a ratio of 2:1. The infection normally presents as onycholysis, with subungual keratosis and yellow coloring of the distal and lateral parts of the nails. We were unable to correlate the disease with patients' previous medical history but we discovered, for example, that 20% were diabetic and around 60% suffered from circulatory diseases – both possible risk factors for infection. ❑

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How to cite this article / *Como citar este artigo*: Cursi IB, Freitas LBCR, Neves MLP, Silva IC, Orofino-Costa R. Onycomychosis due to Scytalidium spp.: A clinical and epidemiologic study at a University Hospital in Rio de Janeiro. An Bras Dermatol. 2011;86(4):689-93.