

An observational and descriptive study of the epidemiology of and therapeutic approach to onychomycosis in dermatology offices in Brazil*

Estudo observacional descritivo da epidemiologia e abordagem terapêutica da onicomicose nos consultórios dermatológicos no Brasil

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Resumo: **BACKGROUND:** Onychomycosis is a type of fungal infection that accounts for over 50% of all onychopathies. Some authors consider superficial mycosis the most difficult to be treated. Very few studies have been carried out in order to assess the epidemiology of onychomycosis in Brazil.

OBJECTIVE: To describe the epidemiological profile of onychomycosis in Brazilian dermatology offices and to assess the etiology of the disease, how often mycosis exams are requested, and the treatment adopted.

METHODS: A descriptive, observational study was carried out between May and July, 2010. Thirty-eight dermatologists from different Brazilian regions participated in the study, and 7,852 patients with any skin diseases who had all of their nails examined were included in the study.

RESULTS: Of the 7,852 patients, 28.3% were clinically diagnosed as having onychomycosis. Women over 45 years old who practiced exercises or with a personal history of the disease showed greater likelihood of having onychomycosis. The disease was most seen in the feet, and the majority of cases involved the hallux. On the hands, the index finger was the most affected. Mycosis exams were not requested for all clinically suspected cases. When exams were done, results showed that the most common fungus was *Trichophyton rubrum*. The most common clinical lesion was distal-lateral. The most prescribed topical treatments were amorolfine and ciclopirox olamine, while systemic treatments included fluconazole and terbinafine.

CONCLUSION: This study was important to describe the epidemiological behavior of onychomycosis in Brazilian dermatology offices and to determine important risk factors, such as gender, age, practice of exercises, personal history of the disease, and comorbidities.

Palavras-chave: Brazil; Epidemiology; Onychomycosis

Abstract: **BACKGROUND:** Fundamentos: As onicomicoses são infecções fúngicas que representam mais de 50% de todas onicopatias e são consideradas por alguns autores a micose superficial de mais difícil tratamento. Poucos estudos foram feitos para investigar a epidemiologia da onicomicose no Brasil. **Objetivo:** Descrever perfil epidemiológico da onicomicose nos consultórios brasileiros de dermatologia. Também observar a etiologia, a frequência da solicitação do exame micológico e a terapia empregada. **Métodos:** Foi realizado um estudo descritivo e observacional no período de Maio a Julho de 2010. Participaram 38 dermatologistas de diferentes regiões do Brasil e foram incluídos 7852 pacientes. **Resultados:** Dos 7852 pacientes, 28.3% apresentaram diagnóstico de onicomicose. Mulheres, maiores de 45 anos, praticantes de esportes, ou com histórico pessoal da doença, apresentaram chance maior de adquirir onicomicose. A doença foi mais frequente nos pés, sendo o hálux, o dedo mais acometido. Nas mãos, o primeiro dedo foi o mais atingido. Exame micológico não foi solicitado para todos os casos. Quando realizado, o fungo mais frequente foi o *Trichophyton rubrum*. A lesão clínica mais comum foi a distal-lateral. Os tratamentos tópicos mais prescritos foram amorolfina e ciclopirox olamina, enquanto os sistêmicos foram o fluconazol e a terbinafina. **Conclusão:** Este estudo foi de fundamental importância para descrever o comportamento epidemiológico da onicomicose nos consultórios dermatológicos brasileiros e determinar fatores de risco, como gênero, idade, prática de esportes, antecedente pessoal de onicomicose e comorbidades. Esperamos contribuir na melhora da abordagem terapêutica e prevenção desta doença.

Palavras-chave: Brasil; Epidemiologia; Onicomicose

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INTRODUCTION

Onychomycosis is a frequent fungal infection of the nails, accounting for 15% to 40% of all onychopathies.^{1,2} It is more frequent in toenails.³ The prevalence of onychomycosis in the general population has been estimated to be between 2% and 9%.^{4,5,6} These numbers have increased considerably in the past decades and are related to diabetes, peripheral arterial disease, psoriasis, immunodepression, and aging.^{6,7} Adults are 30 times more likely to have onychomycosis than children.^{6,7,8} Onychomycosis is found in over 90% of the elderly population. In advanced stages, onychomycosis can cause pain, discomfort, physical and occupational limitations, and it may interfere with quality of life.^{9,10}

Three groups of fungi can cause onychomycosis: (1) dermatophytes; (2) yeasts, and (3) non-dermatophyte filamentous fungi.¹¹ Dermatophytes (including the species *Epidermophyton*, *Microsporium*, and *Trichophyton*) account for 80-90% of cases; the most common are *Trichophyton rubrum* (71%) and *Trichophyton mentagrophytes* (20%). Yeasts cause 7% of all onychomycosis cases, and *Candida albicans* is the most common agent. Non-dermatophyte filamentous fungi only account for 2% of all cases.^{11,12} The different types of onychomycosis have been described as distal-lateral subungual, white superficial onychomycosis, and proximal subungual onychomycosis, at the estimated ratio of 360:59:1, respectively.¹³ Individuals can also show a combination of different types. Total dystrophic onychomycosis is the most severe type of onychomycosis.¹²

Analysis of the preliminary results of the EUROO (European Onychomycosis Observatory) study showed that most doctors do not conduct studies on mycosis. For this reason, the causative agent is often not identified, which negatively affects the choice of an appropriate treatment.¹⁴ Some authors also see this infection (superficial onychomycosis) as the most difficult to be treated. Even when the etiological agent is identified and treatment is appropriate, cure is not always obtained and relapses are frequent.¹⁴ The dissemination of onychomycosis is encouraged by the presence of environmental and social factors.¹⁵

It is important to highlight that onychomycosis is very often exclusively seen as an aesthetical issue, relatively not as important as those seen as functional. The real impact this disease has is unaccounted for. It affects the life quality of patients, mainly those who work with food or as receptionists and secretaries.

In spite of that, to date, very few studies have been carried out to assess the epidemiology of onychomycosis in Brazil.^{16,17} The main purpose of this paper was to describe the epidemiological behavior of

onychomycosis in Brazilian dermatology offices. The etiology of the disease, how often mycosis exams are requested, and the therapy adopted in primary or recurring cases were also assessed. Knowledge on the subject appears to improve preventive and therapeutic approaches by identifying risk factors.

MATERIAL AND METHODS

A descriptive, observational study was conducted for three months (May to July, 2010). Thirty-eight dermatologists from different Brazilian regions, experienced in the treatment of onychopathies, were included as researchers. Patients with skin diseases who spontaneously visited dermatology offices during that period and who agreed to take part in the study were included. The researcher physician filled in the technical file of the Brazilian National Observatory of Onychomycosis with information on the variables analyzed. All patients had all their nails examined.

Research subjects signed a free and informed consent form, which followed the guidelines of the Declaration of Helsinki and was approved by the Research Ethics Committee of Hospital Irmão Penteadó - Irmandade de Misericórdia de Campinas. Inclusion criteria were individuals seeking medical care due to any skin disease, not necessarily one involving the nails. The main exclusion criterion was not signing or not agreeing with the information detailed in the free and informed consent form.

The technical file used in this study for data collection was that of the Brazilian National Observatory of Onychomycosis, which explored the following variables: gender, age, comorbidities (concomitant existence of other diseases such as diabetes, psoriasis, peripheral arterial disease, immunodeficiency, among others), practice of exercises, personal history of onychomycosis, clinical assessment, mycosis examination, and prescribed treatment. Diagnosis of onychomycosis was clinical in all cases. We also investigated how often mycosis exams were requested and the results of these exams.

All patients had their fingernails and toenails clinically examined. Investigators were given 13 pictures of typical cases of onychomycosis in the hands and 13 pictures of onychomycosis in the feet to compare them with the findings in our study. In addition, the researchers filled in a questionnaire showing the location of onychomycosis and they measured the total height of the most invaded nail and the height of the non-invaded area with an onychomycosis meter. The purpose of this assessment was to determine the clinical type of the lesion, as well as the invaded area.

Statistical Analysis

A descriptive analysis of demographical data

(age, gender) was conducted. The association between two binary variables was tested by Fisher's exact test. The association between two category variables with more than 2 categories was tested by the Chi-squared test. Binary logistic regression was adopted to assess the influence of some variables if the patient had onychomycosis. The significance level was defined as $p \leq 0.05$. All analyses were done using MINITAB 14.0 and XLSTAT 2010 Software.

RESULTS

Prevalence

A total of 7,852 patients were included in the study. Onychomycosis was clinically observed in 2,221 (28.3%) patients. The relationship between prevalence and the other variables is shown below.

Prevalence of onychomycosis by gender

Of the 7,852 recruited patients, gender was correctly filled in the questionnaires answered by 7,849 patients. Of those, 2,219 patients were diagnosed as having onychomycosis. There was a total of 5,369 women, and 1,562 (29.1%) had onychomycosis; 2,480 male patients were recruited, and onychomycosis was found in 657 (26.5%) (Graph 1). Considering only the patients diagnosed with onychomycosis, 1,562 (70.4%) were women (Table 1). Even accounting for the difference in sample size for men and women, the frequency of onychomycosis was proportionally higher in women, and a statistically significant association was found ($p = 0.018\%$, Fisher's exact test).

The odds ratios are used to calculate the odds of a group having onychomycosis in relation to another group, considering the effect of the other variables on the model. This calculation showed that female patients are 30% more likely to have onychomycosis as compared to male patients.

Prevalence of onychomycosis by age

Of the 7,852 questionnaires, information about age was correctly given by 7,687 patients. Of these, 2,157 had onychomycosis. Of the 718 patients aged between 0-17 years, 36 (5%) had onychomycosis; of the 1,109 patients aged between 18-25, 186 (16.8%) had onychomycosis; of the 1,544 patients aged between 26-35, 307 (19.9%) had the disease; of the 1,355 patients aged between 36-45, 417 (30.8%) were positively diagnosed; of the 1,749 patients aged between 46-59, 647 (37%) presented with the disease, and of the 1,212 patients older than 60, 564 (46.5%) had onychomycosis. Based on this data, we concluded that prevalence of onychomycosis increases as patients become older (Graph 2). Most onychomycosis cases were observed in older patients, mainly those aged 46-59 and older than 60 ($p < 0.001$), a trend confirmed by the Chi-squared test.

Prevalence of onychomycosis by practice of exercises

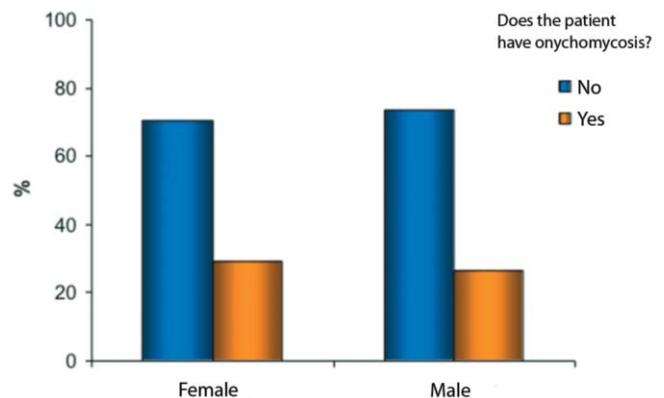
Eight hundred and fifty-two (852) questionnaires lacked information about the practice of exercises. According to information found in the 7,000 questionnaires answered, 5,035 (71.9%) patients did not practice exercises on a regular basis. Among these patients, 1,452 (28.8%) had onychomycosis. Considering the 1,965 patients who regularly practiced exercises, we noticed that 660 (33.6%) were diagnosed with onychomycosis. A significant association between the practice of exercises and onychomycosis was found ($p < 0.001$; Fisher's exact test). People who regularly practice exercises are 3 times more likely to have onychomycosis than sedentary people.

Prevalence of onychomycosis by personal history

This information was found in only 6,669 questionnaires. Data showed that among the 5,074 patients with no personal history of onychomycosis, 949 (18.7%) were diagnosed with the disease. On the other hand, of the 1,595 patients who had had this infection in the past, 1,072 (67.2%) were positively diagnosed (Graph 3). The association between onychomycosis and personal history is statistically significant ($p < 0.001$, Fisher's exact test). Having a personal history of onychomycosis increases the likelihood of a new infection by almost 20 times.

Mycosis Examination

Of the 2,221 patients clinically diagnosed with onychomycosis, mycosis examinations were requested of only 1,262 (56.8%) patients. However, only 508 direct exams were considered in the analysis. Of these, 403 (79.3%) showed positive results and 86 (16.9%) were negative. There was no information in the other questionnaires. Of the 403 positive results, hyaline hyphae compatible with dermatophyte filaments were seen in 357 (88.6%), and 46 (11.4%) were



GRAPH 1: Prevalence of onychomycosis by gender

TABLE 1: Prevalence of onychomycosis by gender

Gender	Does the patient have onychomycosis?						Total	
	NO		YES		n	%		
	N	%	N	%				
Female	3807	67.6	1562	70.4	5369	68.4		
Male	1823	32.4	657	29.6	2480	31.6		
Total	5630	100.0	2219	100.0	7849	100.0		

diagnosed as yeasts.

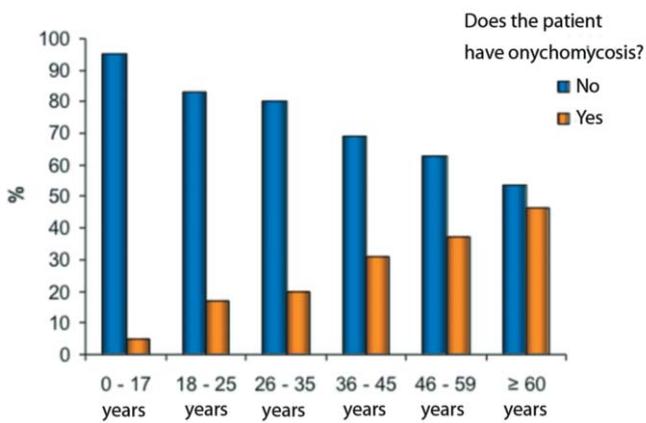
A total of 419 cultures were performed and *Trichophyton rubrum* was the most isolated fungus, identified in 57.8% of cultures. (Graph 4)

Treatment

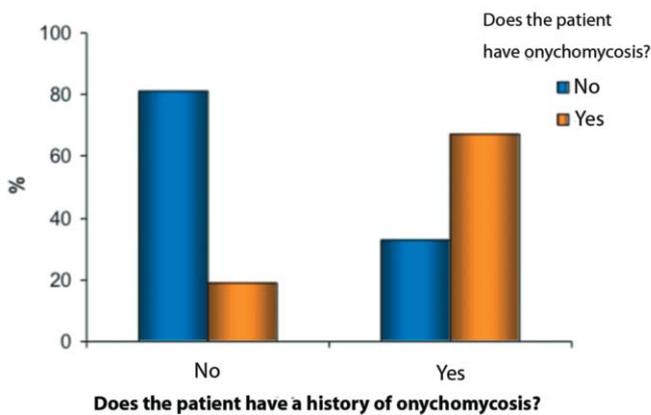
Some form of treatment for onychomycosis was prescribed to 1,622 patients. Exclusive topical treatment was prescribed to 588 (36.3%), systemic medication to 157 (97%), a combination of topic and systemic treatment to 623 (38.4%), surgery to 21 (1.3%), surgery associated with another therapy to 199 (12.3%). Table 2 shows these different treatments and associations. It is important to emphasize that of all the patients to whom some kind of treatment was prescribed (1,622), direct examination was only requested of 784 (48.3%).

Of the 1,622 patients treated, 1,448 (91.7%) received some kind of topical treatment. The most common was almorofine nail lacquer, prescribed to 606 (37.3%) patients, followed by ciclopirox olamine nail lacquer, used by 454 (27.9%), and ciclopirox lotion prescribed to 145 (8.9%) patients (Graph 5). These three treatments accounted for 75% of all treatments adopted.

Exclusive or combined systemic treatment was prescribed to 896 patients. The most common medication was fluconazole, used by 415 patients (46.3%),



GRAPH 2: Prevalence of onychomycosis by age range



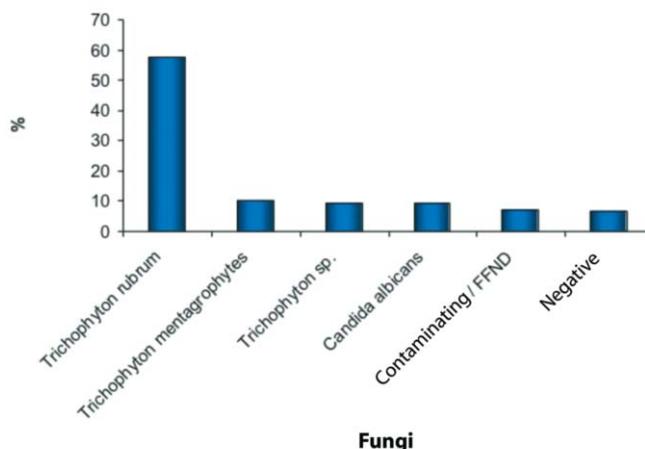
GRAPH 3: Prevalence of onychomycosis by personal history

followed by terbinafine, prescribed to 359 (40.1%). These two drugs corresponded to 86.4% of all systemic treatments used (Graph 6).

As for surgical treatment, the unguinal lamina was removed in 215 patients. The most common technique was abrasion, performed in 170 patients (79.1%), followed by chemical avulsion, which was done in 40 (18.6%) patients.

Location and percentage of affected area

Information concerning location was given by 2,108 patients. Of these, 1,666 had onychomycosis



GRAPH 4: percentage of identified fungi

TABLE 2: Treatment

Monotherapy or Associations	n	%
Topical and Systemic	623	38.4
Topical	588	36.3
Systemic	157	9.7
Topical, Systemic and Ungual lamina removal	95	5.9
Topical and Ungual lamina removal	87	5.4
Topical/Topical	30	1.8
Ungual lamina removal	21	1.3
Systemic and Ungual lamina removal	17	1.0
Systemic/Systemic	4	0.2

exclusively in the feet, 202 in the hands, and 240 in at least one foot and one hand. Thus, 442 patients showed hand infection and 1,906, feet infection. Based on these data, we can conclude that onychomycosis is more commonly found in toenails than fingernails. Of the 442 patients with lesions in the hands, 138 (31.2%) had only their right hand compromised, 99 (22.4%) only the left hand, 205 (46.4%) both hands, totaling 343 patients with a lesion in the right hand and 304 patients with a lesion in the left hand. This shows that it is more common for both hands to be affected rather than only one. There was a significant statistical difference in relation to the side affected, with the right side being more frequently affected than the left side (Z-test for two proportions, $p = 0.003$).

Data show the first finger (left $n=125$ and right $n=149$) was the most commonly affected. In a little more than 40% of patients who had the disease in the left hand, onychomycosis only affected the first finger. The same percentage is observed for the right hand. The frequency of patients with onychomycosis in all fingers was similar in both hands (around 10%). The most common lesion in the hands was distal-lateral subungual ($n=225$, 59%) followed by total dystrophic ($n=66$, 17%), white superficial ($n=55$, 15%) and proximal ($n=26$, 7%) (Table 3).

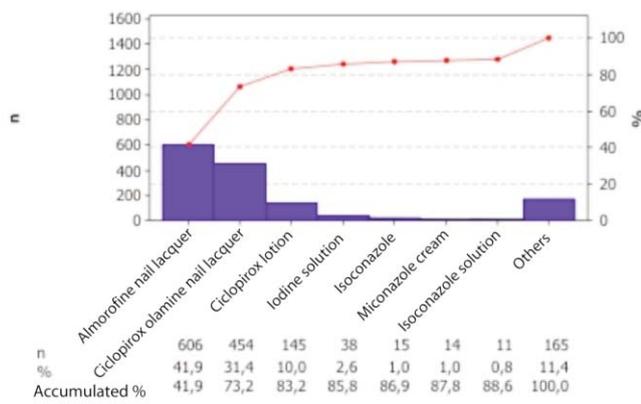
As for the feet, 1,906 patients had onychomycosis. Of these, 322 (16.89%) had the disease only in the right foot, 389 (20.41%) in the left, and 1,195 (62.7%) in both feet. Thus, 1,517 patients were diagnosed with onychomycosis in the right foot and 1,584, in the left foot. We noticed it is more common to find the infection in both feet rather than in only one. The left side is the most affected, with a significant statistical difference (Z-test for two proportions, $p=0.005$).

The infection was exclusively found in the right or left hallux in over 60% of patients. All fingers were affected in approximately 10% of patients. The most common lesion in the feet was distal lateral subungual ($n=979$, 60%), followed by total dystrophic ($n=420$, 26%), white superficial ($n=166$, 10%), and proximal ($n=27$, 1%) (Table 4).

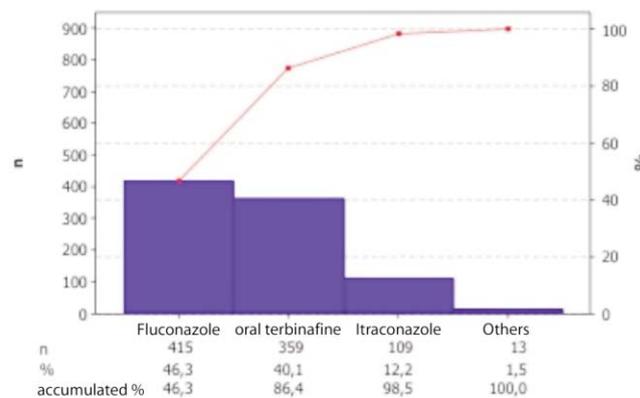
In 2,074 questionnaires (93.4% of clinical onychomycosis cases), there was information about the percentage of invaded area for the most affected nail. The average area of nail affected was 49.4%, with 31.3% standard deviation and variation between 5% and 100%.

Comorbidities

Among the 7,852 questionnaires evaluated, 2,135 (27.5%) patients with some disease other than



GRAPH 5: Topical treatments by prescription frequency



GRAPH 6: Systemic treatments by prescription frequency

TABLE 3: Type of lesion in the hands

Type of lesion	n	% (total of 377 patients)
Distal lateral subungual	225	59.7
Total dystrophic	66	17.5
White superficial	55	14.6
Proximal	26	6.9
Distal lateral subungual, Proximal	1	0.3
Total dystrophic, Distal lateral subungual	1	0.3
Total dystrophic, Proximal	1	0.3
White superficial, Distal lateral subungual	1	0.3
White superficial, Total dystrophic, Distal lateral subungual	1	0.3
Total	377	100.0

onychomycosis were found. Of the 2,221 patients clinically diagnosed with onychomycosis, 910 (41%) showed another comorbidity. More than 600 different comorbidities or combinations were recorded, which made it difficult to analyze the relationship between onychomycosis and other diseases. Therefore, we analyzed the most frequent comorbidities found in our sample.

Among patients with peripheral arterial disease (PAD), 59.3% were diagnosed with onychomycosis; among those with diabetes, 52.8% were diagnosed with onychomycosis. Concerning patients with high blood pressure, the percentage of onychomycosis was 39.9%. For those with diabetes combined with PAD, the percentage of onychomycosis increased to 78.7%. For the combination of high blood pressure and diabetes, we noticed a frequency of 65.3%. When high blood pressure and peripheral arterial disease coexisted, the frequency of onychomycosis was 67.9%.

DISCUSSION

Onychomycosis is the most common disease of the nails. It has been more frequently diagnosed all

over the world and is, therefore, a significant clinical infection.^{1,2,7,8,10} This increase is probably due to changes in lifestyle, the frequent use of closed in tight shoes, and the increased number of individuals with immunodeficiency (HIV).¹⁸

This is the first epidemiological study on onychomycosis of broad coverage in Brazil. To date, very few studies have investigated the prevalence, etiology and treatment of onychomycosis simultaneously in different Brazilian states.^{16,17} In this study, onychomycosis was found in 28.3% of participants. The Achilles project, carried out in Europe, showed a 26.9% prevalence of onychomycosis, considered greater than expected.¹⁹ Other studies report an estimated prevalence between 3% and 22% in Finland, England and the United States.^{7,8,10} In Canada, it is around 6% and in Spain, levels are between 1.7% and 2.6%.^{1,20} In HIV-positive individuals and people with diabetes, this number increases to 19% and 26%, respectively.^{21,22,23}

Our study has also shown greater prevalence of onychomycosis in women (29.1%). These results are in accordance with epidemiological findings on ony-

TABLE 4: Type of lesion in the feet

Type of lesion	n	% (total of 1,624 patients)
Distal lateral subungual	979	60.3
Total dystrophic	420	25.9
White superficial	166	10.2
Proximal	27	1.7
Total dystrophic, Distal lateral subungual	14	0.9
White superficial, Distal lateral subungual	10	0.6
White superficial, Total dystrophic	8	0.5
Total	1,624	100.0

chomycosis from studies developed in Rio de Janeiro and São José do Rio Preto.^{16,17} However, these data differ from those of other studies, which reported greater prevalence in male individuals.^{12,15,24} Gupta et al. stated that men are three times more likely to be affected by onychomycosis than women.¹⁵ Similarly, Vender et al. documented that men are 2.4 times more likely to have the disease.¹²

The age group most affected by onychomycosis was that of patients aged 60 years, followed by the range between 46 and 59 years. If we analyze the incidence percentages for the different age ranges studied, we can conclude that onychomycosis prevalence is ascending, from the lowest age ranges to the highest. These data are similar to those of the European Onychomycosis Observatory (EUROO), a study conducted in several countries of Europe, north of Africa and Russia.¹⁸

When we compare patients who regularly practiced exercises to those who did not practice exercises on a regular basis, we notice a higher prevalence in the first group, confirmed by statistical tests.

Another important datum was personal history of the disease. In the group of patients with a previous history of onychomycosis, the frequency of the infection was 67.2%, while only 18.7% of the researched participants with no personal history of onychomycosis had the infection.

Considering the joint analysis of gender, age, practice of exercises, and history of onychomycosis, we noticed that all of these variables significantly influence the likelihood of one being affected by onychomycosis. Considering the main variables, we noticed that female individuals are 30% more likely to have onychomycosis than male patients; an increase of a category in the age range leads to a 52% increase in the likelihood of being affected by onychomycosis; the risk for patients over 60 years old is 8 times higher than for patients aged between 0 and 17; patients who regularly practice exercises are three times more likely to have onychomycosis than sedentary individuals; prior personal history of the disease increases the likelihood of recurrence by almost 20 times.

As for location, the feet were more affected than the hands. The nails of the first fingers were most affected in the hands. As for toenails, halluxes were most affected. The most common clinical type both in the hands and feet was distal-lateral subungual, followed by total dystrophic, white superficial and proximal subungual, respectively. These data are in accordance with the EUROO study. However, we noticed that in Brazil, total dystrophic was more frequent than in the European study. This type represents the most advanced stage of onychomycosis, suggesting that the individual waited too long to seek medical help.

Direct exam was requested of 56.8% patients with onychomycosis. However, the result was only known for 22.9% of these individuals. Culture for fungi was requested in 18.9% of cases. This datum, in spite of representing a weakness in the diagnosis of onychomycosis, is common in Brazil and other countries. In the EUROO study, only 39.6% of patients with onychomycosis seen by dermatologists were submitted to these tests. Knowledge about the presence of fungi is important, as well as the determination of type and species. This prevents misdiagnosis and helps determine the best therapeutic strategy.¹⁸

Dermatophytes were the most common fungi and *Trichophyton rubrum* was the most isolated fungus in cultures. These data are in accordance with those found in the world literature.

We also noticed that 41% of patients diagnosed with onychomycosis were also affected by some other comorbidity. Diabetes, high blood pressure and peripheral arterial disease were the most common. These are expected data, in accordance with the world literature, as these diseases are most frequent in older patients. For these patients, treatment choice depends on medication already used to avoid eventual drug interactions.

As for treatment, we observed that a combination of systemic and topical medication, followed by topical monotherapy, was the most common (38.4% and 36.3%, respectively).

The choice of topical monotherapy (amorolfine - 41.9% and ciclopirox - 31.4%, both as nail lacquers) can be explained by lack of involvement of the unguinal matrix or by the possibility of drug interactions, since many patients in the age range in which onychomycosis is most prevalent are also given drugs to control associated diseases.¹⁸

The combination of systemic drugs (fluconazole, terbinafine and itraconazole, in 98% of cases) with topical medication is preferred when the unguinal matrix is involved. Fluconazole and terbinafine were most often prescribed. These two agents have been widely prescribed because they offer the possibility of a shorter treatment, with higher chances of cure and fewer relapses.²⁵ These drugs share characteristics that increase their efficacy, such as fast penetration into the unguinal bed and permanence in the nails months after the treatment has been interrupted.^{26,27,28}

Nail debridement, considered as adjuvant in the treatment of onychomycosis, was done in 13.6% of cases, combined with other therapeutic treatments. Abrasion of the unguinal nail plate is a mechanical procedure that reduces critical fungi mass and also allows greater penetration of the topical medication and greater bioavailability of the drug.^{29,30}

Some limitations of this study were a significant

number of unanswered questions and a small sample of male patients. Future research studies should collect data in different locations (such as universities and hospitals), with the same amount of individuals of both genders. This approach can provide us with more accurate information on the different aspects of onychomycosis in the Brazilian population, as well as help us associate the type of fungus with the area of the nail affected and the type of lesion.

CONCLUSION

This study was significantly relevant to establish the prevalence of onychomycosis in Brazilian offices and the relationship between variables such as gender, age, practice of exercises, prior personal history of onychomycosis and comorbidities. A few important risk factors for this infection found in our study were female gender, older age and the practice of exercises, association with other diseases, and the profile of therapeutic choice by dermatologists in Brazil. □

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