Fingernail Onychomycosis Caused by Molds: Epidemiological, Clinical, and Laboratory Characteristics

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Background: *Fingernail onychomycosis caused by molds is uncommon. The majority of previous studies reported fingernails onychomycosis caused by yeast among women due to wet work.*

Objective: *To study prevalence, clinical, and laboratory characteristics from patients with fingernail onychomycosis caused by molds and compared findings with toenail onychomycosis.*

Material and Method: *The present study was retrospectively conducted in outpatient dermatology clinic of a university hospital between January 2012 and December 2014.*

Results: *One thousand four hundred ninety six nails from 1,102 patients presented with onychomycosis were included in the study. Among these nails, 221 (14.8%) were fingernails. Of patients with fingernail onychomycosis, 61.5% were male and the mean age (SD) was 53.1 (21.4) years. Thumbs were the most common site of onychomycosis infection (31.7%). Dermatophytes (DMPs) were the leading causative organism in fingernail onychomycosis (76.9%), including Trichophyton rubrum (53.4%), Trichophyton mentagrophytes (22.6%), and Trichophyton tonsurans (0.9%). Of patients who had non-dermatophyte molds (NDMs) fingernail onychomycosis (21.3%), the causative organisms were Fusarium spp. (14.5%), Aspergillus spp. (3.6%), and Neoscytalidium dimidiatum (2.7%). Four patients (1.8%) had mixed DMPs and NDMs infection. Comparing the fingernail and toenail groups, patients with fingernail onychomycosis were significantly younger (mean age 53.1 vs. 61.5, respectively, p-value <0.001). DMPs were more commonly found to be the cause of onychomycosis in fingernails than in toenails (76.9% vs. 68.4%, respectively, p-value <0.001).*

Conclusion: *Prevalence of fingernail onychomycosis was 14.8%. Thumbs were the most common site of fingernail onychomycosis. T. rubrum was the leading responsible organism. Patients with fingernail involvement were significantly younger, with DMPs being the most common causative organism than those with toenail involvement.*

Keywords: *Fingernail onychomycosis, Toenail onychomycosis, Molds, Dermatophytes, Non-dermatophytes*

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Onychomycosis is fungal infection of nail and primarily caused by yeasts and molds, which consist of dermatophytes (DMPs) and non-dermatophyte molds (NDMs). This condition is found worldwide and affects both fingernails and toenails[1,2]. Organisms that cause onychomycosis vary geographically. In Western countries, the majority cases were caused by DMPs[3,4]. In contrast to tropical countries, NDMs were found to be more frequently responsible for toenail infections[5,6].

Predisposing factors for onychomycosis include walking barefoot and close contact with soil surface. Given the proximity of the feet to these transmission sources, toenail has been the common site of involvement[6-9]. Fingernail onychomycosis exclusively caused by molds has been infrequently reported in the literature. The majority of previous studies reported high prevalence of yeasts in fingernails, and most notably among women due to wet work[1,2]. Reports about causative molds in finger onychomycosis was limited and may vary according to different countries. The aim of this study was to analyze prevalence, demographic data, clinical manifestations, and laboratory investigations from patients with fingernail onychomycosis caused by molds and compare findings with toenail onychomycosis. This study will provide information to use in diagnosis and treatment for physician.

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Material and Method

This retrospective medical chart review was conducted in outpatients who attended the Department of Dermatology, tertiary care teaching hospital in Bangkok, Thailand and were diagnosed with molds onychomycosis between January 2012 and December

2014. The present study was approved by the Siriraj Institutional Review Board (SIRB). Onychomycosis patients aged 15 years or older were enrolled in the study. Children were excluded due to distinct nail exposure e.g., occupation or work. Demographic data, clinical presentations, and laboratory investigations were recorded and analyzed. Patients with underlying nail diseases, such as psoriasis and lichen planus, were excluded.

Nails to be tested were sterilized with 75% alcohol. A nail sample was collected for mycological examination from a location that depended on the clinical presentation of onychomycosis. In cases of distal and lateral subungual onychomycosis, the hyperkeratotic nail bed was scraped with sterile scalpel. In proximal subungual onychomycosis, the nail was punctured with the tip of a scalpel blade and subungual material was scraped. In white superficial onychomycosis, the affected surface was scraped to obtain sample material. For total dystrophic onychomycosis, samples were collected by combining the techniques described above. Nail sample material was placed on a slide and microscopically studied in 20% potassium hydroxide. For fungal culture, each sample was inoculated into Sabouraud dextrose agar, with and without cyclohexamine. Cultures were incubated at 27°C and examined every four days for four weeks. Identification of microorganisms was based on observation and description of macroscopic and microscopic characteristics of the colonies. Diagnostic criteria, as described in a review by Gupta et al[3], were used for NDMs onychomycosis diagnosis. NDMs diagnosis required at least three of the following: positive microscopic examination, positive mycological culture, at least two consecutive isolations from repeated sampling and histology[3]. Mixed infection was defined as infection by DMPs and NDMs, for at least two consecutive isolations.

Statistical analysis

Descriptive statistics (means and percentages) were used to describe demographic data, clinical characteristics, and laboratory investigations. Comparisons among categorical variables were analyzed by Chi-square test or Fisher's exact test. Continuous variables with and without normal distribution were analyzed by Student's t-test and Mann-Whitney U test, respectively. A p-value ≤ 0.05 was considered statistically significant. All statistical data analyses were performed using PASW Statistics for Windows version 18.0 (SPSS Inc., Chicago, IL, USA).

Results

Patients' characteristics

One thousand four hundred ninety six nails from 1,102 patients presented with onychomycosis were included. Two hundred twenty-one of the included nails were fingernails (14.8%). Among patients with fingernail onychomycosis, 61.5% were male and the mean age (SD) was 53.1±21.4 years.

Clinical manifestations

Thumbs were the most common site of onychomycosis infection (31.7%), following by fourth fingers (25.3%), third fingers (16.7%), second fingers (13.1%), and fifth fingers (13.1%). Fingers from right hand (50.2%) and left hand (49.8%) were similarly affected. For right hand involvement, thumbs were the most common site (40.5%), following by fourth fingers (18.9%), third fingers (16.2%), second fingers (12.6%), and fifth fingers (11.7%). For the left hand, fourth fingers were most commonly affected (31.9%), followed by thumbs (22.7%), third fingers (17.3%), fifth fingers (14.5%), and second fingers (13.6%). A majority of patients (83.2%) had involvement in only one fingernail. For patients with more than single nail involvement, 12.3% of patients had two nails involvement, 3.4% had three nails, and 0.6% had four affected nails. Only one patient (0.6%) had six nails simultaneous involvement. In patients with more than one infected nail, 50% of patients had infection of the same hand.

Comparing the fingernail and toenail involvement groups, patients with fingernail onychomycosis were significantly younger (mean age 53.1 vs. 61.5, respectively, p-value <0.001) (Table 1).

Laboratory investigation

Regarding causative organisms in fingernail onychomycosis, DMPs (76.9%) were the leading agents, these were *Trichophyton rubrum* (53.4%), *T. mentagrophytes* (22.6%), and *T. tonsurans* (0.9%). In patients who had NDMs fingernail onychomycosis (21.3%), 14.5% had *Fusarium* spp., 3.6% had *Aspergillus* spp. and 2.7% had *Neoscytalidium dimidiatum*. Four patients (1.8%) had mixed DMPs and NDMs infection that included *T. mentagrophytes* with *Aspergillus* spp. (0.9%), *T. rubrum* with *Aspergillus* spp. (0.45%), and *T. mentagrophytes* with *N. dimidiatum* (0.45%).

Comparing the fingernail and toenail involvement groups, DMPs were more commonly found to be the cause of onychomycosis in fingernails than in toenails (76.9% vs. 68.4%, respectively, p-value

Table 1. Demographic data, clinical manifestations and laboratory investigation of patients with fingernail onychomycosis, comparing with toenail onychomycosis

Factors	Patients with fingernail onychomycosis (n = 221)	Patients with toenail onychomycosis (n = 1,275)	*p*-value
Mean age (year), (SD)	53.1 (21.4)	61.5 (14.6)	0.001
Sex			0.101
Male	136 (61.5%)	709 (55.6%)	
Female	85 (38.5%)	566 (44.4%)	
Causative organisms			
Dermatophytes	170 (76.9%)	872 (68.4%)	0.011
Nondermatophytes	47 (21.3%)	309 (24.2%)	0.339
Mixed dermatophytes and non-dermatophytes	4 (1.8%)	94 (7.4%)	0.002

0.011). Moreover, mixed DMPs and NDMs infection was found less common in patients with fingernail onychomycosis (Table 1).

Discussion

Fingernail onychomycosis caused by molds is an uncommon condition. Toenails were found to be four to 25 times more frequently affected than fingernails due to causative molds locating primarily in soil, water, and decaying vegetation[2,4,5]. Fingernail onychomycosis creates both clinical and cosmetic complications for the patient. In addition to cosmetic and functionality quality of life burdens, onychomycosis infection can also spread to both other parts of the patient's body and to other persons[1,2]. Prevalence of fingernail onychomycosis was reported as being 4 to 26.5% of all patients diagnosed with onychomycosis[4,6]. Similarly, the prevalence of fingernail onychomycosis in the present study was 14.8%.

Prevalence of fingernail onychomycosis may vary by gender, depending on the causative organisms. Most previous reports included the investigation of both molds and yeasts. In cases where onychomycosis was caused by yeasts, infection rates in females tended to be higher than in males. Specifically, traumatic injuries and hands submerged in water were predisposing factors for yeast infections in fingernail onychomycosis commonly found in females. Regarding mold-related infections, previous studies had reported both male predominance and both genders equally affected[1,2]. Similar to one of those reports, the present study found males to be slightly more predisposed to develop mold-related fingernail onychomycosis.

Previous studies revealed that fingernail onychomycosis by yeasts and molds was a disease mostly affected middle-aged patients, with mean ages ranging from 29.4 to 41.4 years[1,2]. The mean age of patients in the present study was slightly higher. Generally, mold-related onychomycosis was a common nail disorder in the elderly, with incidence increasing commensurately with age. Repeated trauma, circulatory problems, and difficulty maintaining nail hygiene have been reported as reasons that the elderly have higher susceptibility to onychomycosis[1,2,5,7]. In the present study, patients with fingernail onychomycosis were significantly younger than patients with toenail onychomycosis.

Regarding fingers affected by onychomycosis, previous study found that thumbs were most commonly affected; similar to our study. Regarding side of affected hands, the fact that previous study found right hand to be more frequently affected than the left hand, may be due to trauma-related injuries to the dominant hand[4]. However, the present study demonstrated both sides being affected equally, but right-hand thumbs were more frequent affected than the left. In contrast, the fourth finger was the most affected finger on the left hand in the present study, a finding that discounts the proposed trauma hypothesis.

The organisms that cause onychomycosis vary geographically. The majority of onychomycosis cases, especially in Western countries, were caused by DMPs, with *T. rubrum* and *T. mentagrophytes* to be the most common organisms[8,9]. Prevalence of NDMs toenail onychomycosis is increasing and its distribution is varied. *Neoscytalidium* spp. was mainly found in West Indies, South America, West Africa, and Asia[10,11]. The most commonly observed causative organism in fingernail onychomycosis worldwide was DMPs. Previous studies in fingernail onychomycosis reported *T. rubrum* as the principle pathogen, followed by *T. mentagrophytes*[1,2,12]. Consistent with previous reports, the majority of fingernail onychomycosis cases in the present study were caused by *T. rubrum* and *T. mentagrophytes*. Knowing the common causative organisms will be useful to choose appropriate

management for patients because onychomycosis caused by *Neoscytalidium* spp., is considered to be recalcitrant to treatment with traditional oral antifungal agents[13].

Concerning NDMs infection, NDMs are usually found in soil and plants, so infection may be acquired by direct contact via occupational exposure and/or lifestyle habits. Accordingly, toenail is the main site of NDMs onychomycosis. Prevalence of NDMs infection ranged from 5.9 to 18.2% in patients with fingernail onychomycosis caused by yeasts and molds[1,2,7,14]. The present study found 21.3% of cases infected by NDMs. However, NDMs-related fingernail onychomycosis was less than DMPs-related fingernail onychomycosis. Among NDMs infection, *Aspergillus* spp. and *Fusarium* spp. were reported to be common organisms responsible for fingernail onychomycosis, especially in immunocompromised patients[2,12-15]. In the present study, 14.5% of cases were infected by *Fusarium* spp. and 3.6% by *Aspergillus* spp. Only 2.7% of cases were caused by *N. dimidiatum*, which is endemic in Thailand and tropical countries. Consistent with previous studies, *Neoscytalidium* spp. of the fingernail was rare due to the causative organism being commonly transmitted from the ground[7,14]. In addition, the present study found that 1.8% of cases had mixed-infection fingernail onychomycosis (DMPs and NDMs). Further study regarding mixed infection in fingernail onychomycosis should be conducted.

Limitations of the present study include the retrospective medical chart review design, which could have resulted in bias if medical records yielded incomplete data. Another limitation involves potential selection bias, given that our hospital is Thailand's largest tertiary care referral center. As such, we have a high proportion of complicated and severe cases.

Conclusion

Prevalence of fingernail onychomycosis was 14.8%. Thumbs were the most common site of onychomycosis infection. *T. rubrum* was the leading responsible organism. Patients with fingernail involvement were significantly younger, with DMPs being the most common causative organism. DMPs were more common in the fingernail than in the toenail.

What is already known on this topic?

Fingernail onychomycosis caused by molds is uncommon. The majority of previous studies reported fingernails onychomycosis caused by yeast among women due to wet work.

What this study adds?

Prevalence of fingernail onychomycosis caused by molds was 14.8% of total patients presented with onychomycosis.

Dermatophytes, particularly *T. rubrum* and *T. mentagrophytes* were the leading causative organism in fingernail onychomycosis. Knowing the common causative organisms will be useful to choose appropriate management for patients.

Patients with fingernail involvement were significantly younger, with DMPs being the most common causative organism than those with toenail involvement.

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Potential conflicts of interest

None.

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โรคเชื้อราที่เล็บนิ้วมือโดยมีสาเหตุจากราสาย: ระบาดวิทยา ลักษณะทางคลินิก และทางห้องตรวจปฏิบัติการ

จรัสศรี พียาพรรณ, สุมนัส บุณยะรัตเวช, สุธาสินี ไพฑูรย์วัฒนกิจ, ลลิตา มัฏฐาพันธ์

ภูมิหลัง: *โรคเชื้อราที่เล็บนิ้วมือเป็นภาวะที่พบไม่บ่อย การศึกษาส่วนมากในอดีตรายงานโรคเชื้อราที่เล็บมือโดยมีสาเหตุจากเชื้อยีสต์ในกลุ่มผู้หญิงที่ทำงานสัมพันธ์กับน้ำ*

วัตถุประสงค์: *เพื่อศึกษาถึงความชุก ลักษณะทางคลินิก และทางห้องปฏิบัติการ ของผู้ป่วยโรคเชื้อราที่เล็บนิ้วมือที่มีสาเหตุจากราสายและเปรียบเทียบลักษณะดังกล่าวกับผู้ป่วยโรคเชื้อราที่เล็บนิ้วเท้า*

วัสดุและวิธีการ: *การศึกษาแบบย้อนหลัง ทำในคลินิกผู้ป่วยนอก แผนกโรคผิวหนังของโรงพยาบาลมหาวิทยาลัย ระหว่างเดือนมกราคม พ.ศ. 2555 ถึง ธันวาคม พ.ศ. 2557*

ผลการศึกษา: *เล็บทั้งหมด 1,496 เล็บ จากผู้ป่วย 1,102 ราย ที่มาด้วยโรคเชื้อราที่เล็บได้เข้าร่วมในการศึกษา จากเล็บทั้งหมดพบว่า 221 (14.8%) เป็นเล็บนิ้วมือ ในผู้ป่วยโรคเชื้อราที่เล็บมือพบว่า 61.5% เป็นเพศชาย อายุเฉลี่ย 53.1 ปี เล็บหัวแม่มือเป็นตำแหน่งของการติดเชื้อบ่อยที่สุด (31.7%) กลากแท้เป็นเชื้อก่อโรคที่พบมากที่สุดในโรคเชื้อราที่เล็บนิ้วมือ (76.9%) โดยเป็นเชื้อ Trichophyton rubrum (53.4%), Trichophyton mentagrophytes (22.6%) และ Trichophyton tonsurans (0.9%) ในกลุ่มผู้ป่วยโรคเชื้อราที่เล็บมือโดยมีสาเหตุจากเชื้อกลากเทียม (21.3%) เชื้อที่เป็นสาเหตุที่สำคัญ ได้แก่ Fusarium spp. (14.5%), Aspergillus spp. (3.6%) และ Neoscytalidium dimidiatum (2.7%) มีผู้ป่วย 4 ราย (1.8%) มีสาเหตุการติดเชื้อร่วมกันระหว่างกลากแท้และกลากเทียม เมื่อเปรียบเทียบระหว่างเล็บนิ้วมือและเล็บนิ้วเท้า พบว่า ผู้ป่วยโรคเชื้อราที่เล็บนิ้วมือมีอายุน้อยกว่าอย่างมีนัยสำคัญ (อายุเฉลี่ย 53.1 และ 61.5 ตามลำดับ, p-value <0.001) กลากแท้พบเป็นสาเหตุของโรคเชื้อราที่เล็บนิ้วมือบ่อยกว่าเล็บนิ้วเท้า (76.9% และ 68.4% ตามลำดับ, p-value <0.001)*

สรุป: *ความชุกของโรคเชื้อราที่เล็บนิ้วมือเท่ากับ 14.8% เล็บหัวแม่มือเป็นตำแหน่งของการติดเชื้อบ่อยที่สุด T. rubrum เป็นเชื้อสาเหตุที่พบมากที่สุด ผู้ป่วยโรคเชื้อราที่เล็บมือมีอายุที่น้อยกว่าอย่างมีนัยสำคัญและกลากแท้พบเป็นสาเหตุบ่อยกว่า เมื่อเปรียบเทียบกับผู้ป่วยโรคเชื้อราที่เล็บเท้า*