SURVEY AND COMPARISON OF CLINICAL AND LABORATORY FINDINGS AMONG SUBJECTS WITH FINGERNAIL AND TOENAIL ONYCHOMYCOSIS

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Abstract. There are few studies of the clinical and laboratory findings in onychomycosis patients. In this study, we aimed to determine the clinical and laboratory findings among onychomycosis patients and compare them between patients with fingernails and toenail onychomycosis in order to determine if there are differences between these factors. We retrospectively reviewed the charts of patients diagnosed with having onychomycosis at the Department of Dermatology, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok, Thailand. A total of 1,109 patients were included in the study, composed of 1491 infected nails: 129 (8.7%) were fingernails and 1362 (91.3%) were toenails. The mean age of subjects with fingernail onychomycosis was 52.5 years and of toenail subjects was 62.4 ($p<0.001$). Sixty-five point nine percent of subjects with fingernail onychomycosis were males and 55.7% of subjects with toenail onychomycosis were male ($p=0.025$). The male to female ratio among subjects with fingernail onychomycosis was significantly higher than among subjects with toenail onychomycosis ($p=0.025$). The causative organisms isolated among fingernail onychomycosis subjects were *Trichophyton rubrum* (58.1%) and *T. mentagrophytes* (20.9%) and among toenail onychomycosis were *Neoscytalidium dimidiatum* (32.5%) and mixed infection (12.5%). Fingernail onychomycosis was significantly associated with the presence of tinea faciei ($p<0.001$), tinea corporis ($p<0.001$), tinea manuum ($p<0.001$) and tinea capitis ($p=0.040$). Toenail onychomycosis was significantly associated with tinea pedis ($p<0.001$). Fingernail onychomycosis was significantly associated with younger subjects, males, the causative organism *T. rubrum* and the presence of tinea faciei, tinea corporis, tinea manuum and tinea capitis. Toenail onychomycosis was significantly associated with older subjects, females, the causative organisms *N. dimidiatum* or mixed infection and the presence of tinea pedis. In conclusion, onychomycosis could spread fungal infection to the adjacent skin. Distinct causative organisms between fingernail and toenail infection may lead to different management.

Keywords: fingernail onychomycosis, fungal skin infection, onychomycosis, toenail onychomycosis.

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INTRODUCTION

Onychomycosis can involve either the toenails, the fingernails or both. There are few studies of fingernail onychomycosis (Di Chiacchio *et al*, 2013; Elewski and Charif, 1997; Heikkila and Stubb, 1995; Nkondjo Minkoumou *et al*, 2012; Segal *et al*, 2015; Soltani *et al*, 2015). Previous studies have reported fingernail onychomycosis to be more common in middle-aged patients and occur equally in both genders (Bramono and Budimulja, 2005; Das *et al*, 2008; Gelotar *et al*, 2013; Jesudanam *et al*, 2002; Neupane *et al*, 2009; Veer *et al*, 2007). Since fingernails can transmit infectious organisms to other parts of the body, fingernail onychomycosis can be associated with infection in other parts of the body (Das *et al*, 2008; Gelotar *et al*, 2013).

The aims of this study were to determine the clinical and laboratory findings among onychomycosis and compare them between patients with fingernail onychomycosis and toenail onychomycosis in order to determine if there are differences between these factors.

MATERIALS AND METHODS

We conducted this study retrospectively by reviewing the records of outpatients aged ≥15 years diagnosed with exclusively fingernail or exclusively toenail onychomycosis presenting to the outpatient clinic, Department of Dermatology, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok, Thailand during 2012 to 2015. Patients with a combination of fingernail and toenail onychomycosis or with other nail diseases, such as psoriasis or lichen planus, or with *Candida* infections, were excluded from the study. We recorded demographic data, clinical presentation, and laboratory results for each study subject.

According to the Department of Dermatology's protocol, a microscopic examination and fungal culture were conducted on each subject. Nails were disinfected with 75% isopropyl alcohol before sample collection. All nail samples were collected and examined with 20% potassium hydroxide (KOH) solution. For fungal culture, nail sample was placed in Sabouraud dextrose agar with and without cycloheximide, then incubated at 27°C and examined every 4 days for 4 weeks. The cultured fungi were identified based on colony characteristics and growth morphology.

Histology and Periodic Acid Schiff staining were performed on all samples from patients with an atypical presentation of onychomycosis and in those with discordant results between the KOH microscopy and fungal cultures.

The diagnostic criteria for onychomycosis were: clinical findings consistent with onychomycosis (subungual hyperkeratosis, onycholysis, and yellow-brown discoloration) and a positive laboratory investigation for a fungus (microscopic examination, positive mycological culture or positive histology). A positive diagnosis of nondermatophyte mold (NDM) onychomycosis required at least 3 of the following: a microscopic examination showing fungi, a mycological culture growing out at least two positive findings on repeat sampling, dermatophyte (DMP) exclusion and a histological confirmation. Infections with both DMPs and NDMs were classified as mixed infections. Coexisting fungal skin infections were diagnosed by a positive microscopic skin examination during the 6 months prior to or after diagnosis of onychomycosis.

Demographic data, clinical characteristics, and laboratory results were described using descriptive statistics and presented as means ± standard deviations (SD) for continuous data and numbers and percentages (%) for categorical data. Categorical data were analysed using the chi-square (χ^2) or Fisher's exact test. Continuous variables with and without normal distribution were analyzed using the Student's t-test and Mann-Whitney U test, respectively. A p-value ≤0.05 was considered statistically significant. All statistical analyses were performed using the Statistical Package for Social Sciences (SPSS) for Microsoft Windows, version 18.0 (SPSS Inc, Chicago, IL).

This study was approved by the Institutional Review Board, Siriraj Hospital (Si 579/2017).

RESULTS

A total of 1109 subjects were included in the study; 53.7% males. The mean age of study subjects was 60.7 years. A total of 1491 infected nails were found in the 1109 patients: 129 (8.7%) with fingernail onychomycosis and 1362 (91.3%) with toenail onychomycosis. The demographic, clinical and laboratory data of study subjects are shown in Table 1.

The mean (± SD) age of fingernail onychomycosis patients was 52.5 (±21.9) years and of toenail subjects was 62.4 (±14.1) years (p<0.001). Of subjects with fingernail onychomycosis, 65.9% were males, while 55.7% of subjects with toenail onychomycosis were male (p=0.025).

The most common fungal group causing fingernail onychomycosis was DMPs. *T. rubrum* caused significantly more cases of fingernail onychomycosis than toenail onychomycosis (58.1% *vs.* 19.2%; p<0.001). *N. dimidiatum* and mixed fungal infections caused significantly more cases of toenail onychomycosis than fingernail onychomycosis (32.5% *vs.* 4.7%; p<0.001 and 12.5% *vs.* 3.9%; p=0.004, respectively).

The most common coexisting fungal skin infections among study subjects were tinea pedis (43.1%), tinea corporis (4.4%), tinea cruris (4.1%), tinea manuum (2.6%), tinea faciei (1.6%), and tinea capitis (0.4%). Fingernail onychomycosis was significantly associated with tinea faciei (p<0.001), tinea corporis (p<0.001), tinea manuum (p<0.001), and tinea capitis (p=0.040) and toenail onychomycosis was significantly associated with tinea pedis (p<0.001).

DISCUSSION

The proportion of fingernail onychomycosis cases in our study (8.7%) is similar to previously studies (4% - 26.5%) (Bonifaz *et al*, 2007; Di Chiacchio *et al*, 2013; Papini *et al*, 2015; Segal *et al*, 2015). The lower proportion of fingernail to toenail onychomycosis cases may be due to: fingers are less likely to have recurrent nail trauma than toes, fingers are a farther distance from pathogenic fungi, fingernails are easier to cut, fingernails are easier to maintain good hygiene and fingernails grow faster.

An important factor associated with developing onychomycosis is older age (Gupta, 2000). Fingernail onychomycosis has been reported to occur more commonly in middle-aged patients (Das *et al*, 2008; Gelotar *et al*, 2013) but in our study they occurred in those of older age. Fingernail onychomycosis may be more common in younger subjects than toenail onychomycosis due to fingernail trauma is more likely to occur at work among those who are still working while toenail

Table 1
Demographic, clinical, and laboratory findings among study subjects.

Characteristics	Fingernails (*n*=129)	Toenails (*n*=1362)	*p*-value
Demographic data			
Mean±SD age in years	52.5±21.9	62.4±14.1	<0.001*
Gender, *n* (%)			
Male	85 (65.9%)	758 (55.7%)	0.025*
Female	44 (34.1%)	604 (44.3%)	
Mycological culture results, *n* (%)			
Trichophyton rubrum	75 (58.1%)	261 (19.2%)	<0.001*
Trichophyton mentagrophytes	27 (20.9%)	335 (24.6%)	0.353
Other dermatophytes	2 (1.6%)	15 (1.1%)	0.653
Neoscytalidium dimidiatum	6 (4.7%)	443 (32.5%)	<0.001*
Other nondermatophytes	14 (10.9%)	138 (10.1%)	0.796
Mixed infection	5 (3.9%)	170 (12.5%)	0.004*
Site of fungal coinfection, *n* (%)			
Tinea faciei	10 (7.8%)	12 (0.9%)	<0.001*
Tinea corporis	5 (11.6%)	55 (4.0%)	<0.001*
Tinea manuum	18 (14.0%)	17 (1.2%)	<0.001*
Tinea cruris	9 (7.0%)	56 (4.1%)	0.128
Tinea pedis	15 (11.6%)	668 (49.0%)	<0.001*
Tinea capitis	2 (1.6%)	2 (0.1%)	0.040*

*p-value<0.05 indicates statistical significance, SD: standard deviation.

trauma is more likely to occur at home among those who have already retired, have poor peripheral blood circulation and have difficulty in maintaining good toenail and foot hygiene.

Previous studies reported females are more likely to have fingernail onychomycosis than males, probably because their hands are immersed in water more often than men (Bramono and Budimulja, 2005; Gelotar *et al*, 2013; Neupane *et al*, 2009; Nkondjo Minkoumou *et al*, 2012; Segal *et al*, 2015). Female fingernail onychomycosis patients have been reported to be more likely to have their infection caused by *Candida* spp while male fingernail onychomycosis patients have been reported to be more likely to have their infections caused by DMP (Segal *et al*, 2015). In the present study, males accounted for almost 70% of all fingernail onychomycosis patients. A reason for the higher proportion of men in this study may be that this study included patients with DMP and NMD onychomycosis but we did not include *Candida* onychomycosis cases in the study.

Fingernail onychomycosis has been

reported to be caused more by DMPs than NDMs (Elewski, 1998). In our study, *T. rubrum* and *T. mentagrophytes* were the first and second most commonly isolated organisms causing fingernail onychomycosis, consistent with the findings of several previous studies (Das *et al*, 2008; Foster *et al*, 2004; Gelotar *et al*, 2013). NDM infections have been increasing worldwide (Grover and Roy, 2003; Hazarika *et al*, 2019; Salakshna *et al*, 2018). Treating NDM onychomycosis has been reported to be more difficult due to problems associated with drug resistance (Bunyaratavej *et al*, 2015). *N. dimidiatum*, commonly found in dirt, can easily infect body parts that are in close proximity to the ground, such as toenails (Bunyaratavej *et al*, 2015; Das *et al*, 2008; Foster *et al*, 2004; Gelotar *et al*, 2013). *T. rubrum* has been reported to be the most commonly isolated cause of tinea faceii, tinea corporis, tinea manuum, and tinea cruris (Craddock and Schieke, 2019). This finding suggests co-existing fungal skin infections are often caused by the same fungus that caused the onychomycosis. NDMs, such as *N. dimidiatum*, have been frequently reported to be associated with tinea pedis (Bunyaratavej *et al*, 2015; Grover and Roy, 2003; Hazarika *et al*, 2019), as was seen in our study.

Comparing the site of coexisting skin infections between fingernail and toenail onychomycosis, we found fingernail onychomycosis to be significantly associated with fungal skin infections in other parts of the body (particularly the upper body), including the scalp, face, trunk, and hands. This can be explained by the fingernail's ability to carry and easily transmit a pathogen to these areas. Once fingernail onychomycosis is diagnosed, a careful search for coexisting fungal skin infections should be made, such as tinea capitis, tinea faciei, tinea corporis, and tinea manuum. In toenail onychomycosis patients, the examiner should also search for coexisting tinea pedis.

Due to the retrospective nature of our study design, incomplete data and bias could not be completely avoided in this study. Some confounding data such as occupation, history of manicure or pedicure and family history of dermatophytosis were not completely assessed. Furthermore, subclinical onychomycosis was not excluded in this study. A previous study reported the prevalence of subclinical onychomycosis to be 14.3% (Leeyaphan *et al*, 2018). A prospective study to elucidate the cause and effect of fingernail onychomycosis, toenail onychomycosis, subclinical onychomycosis and concurrent fungal infections is required.

In conclusion, younger age, male gender, presence of *T. rubrum*, tinea faciei, tinea corporis, tinea manuum and tinea capitis were significantly associated with fingernail onychomycosis. Toenail onychomycosis was significantly associated with older age, female gender, the causative organism *N. dimidiatum* or mixed infection, and coinfection with tinea pedis. Onychomycosis can spread fungal infection to the adjacent skin. Distinct causative organisms differ between fingernail and toenail infection and may require different management. This is the largest epidemiological study of fingernail and toenail onychomycosis in Thailand.

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REFERENCES

Bonifaz A, Cruz-Aguilar P, Ponce RM. Onychomycosis by molds. Report of 78 cases. *Eur J Dermatol* 2007; 17: 70-2.

Bramono K, Budimulja U. Epidemiology of onychomycosis in Indonesia: data obtained from three individual studies. *Nihon Ishinkin Gakkai Zasshi* 2005; 46: 171-6.

Bunyaratavej S, Prasertworonun N, Leeyaphan C, Chaiwanon O, Muanprasat C, Matthapan L. Distinct characteristics of *Scytalidium dimidiatum* and non-dermatophyte onychomycosis as compared with dermatophyte onychomycosis. *J Dermatol* 2015; 42: 258-62.

Craddock L, Schieke S. Fungal Diseases. In: Kang S, Amagai M, Bruckner A, et al, editors. Fitzpatrick's Dermatology. 9th ed. New York: McGraw Hill Education; 2019. p. 2925-51.

Das NK, Ghosh P, Das S, Bhattacharya S, Dutta RN, Sengupta SR. A study on the etiological agent and clinico-mycological correlation of fingernail onychomycosis in eastern India. *Indian J Dermatol* 2008; 53: 75-9.

Di Chiacchio N, Suarez MV, Madeira CL, Loureiro WR. An observational and descriptive study of the epidemiology of and therapeutic approach to onychomycosis in dermatology offices in Brazil. *An Bras Dermatol* 2013; 88 (Suppl 1): 3-11.

Elewski BE. Onychomycosis: pathogenesis, diagnosis, and management. *Clin Microbiol Rev* 1998; 11: 415-29.

Elewski BE, Charif MA. Prevalence of onychomycosis in patients attending a dermatology clinic in northeastern Ohio for other conditions. *Arch Dermatol* 1997; 133: 1172-3.

Foster KW, Ghannoum MA, Elewski BE. Epidemiologic surveillance of cutaneous fungal infection in the United States from 1999 to 2002. *J Am Acad Dermatol* 2004; 50: 748-52.

Gelotar P, Vachhani S, Patel B, Makwana N. The prevalence of fungi in fingernail onychomycosis. *J Clin Diagn Res* 2013; 7: 250-2.

Grover S, Roy P. Clinico-mycological profile of superficial mycosis in a hospital in North-East India. *Med J Armed Forces India* 2003; 59: 114-6.

Gupta AK. Onychomycosis in the elderly. *Drugs Aging* 2000; 16: 397-407.

Hazarika D, Jahan N, Sharma A. Changing trend of superficial mycoses with increasing nondermatophyte mold infection: a clinicomycological study at a tertiary referral center in Assam. *Indian J Dermatol* 2019; 64: 261-5.

Heikkila H, Stubb S. The prevalence of onychomycosis in Finland. *Br J Dermatol* 1995; 133: 699-703.

Jesudanam TM, Rao GR, Lakshmi DJ, Kumari GR. Onychomycosis: a significant medical problem. *Indian J Dermatol Venereol Leprol* 2002; 68: 326-9.

Leeyaphan C, Bunyaratavej S, Chadchavalpanichaya N, Rujitharanawong C, Phaitoonwattanakij S, Matthapan L. Clinical and laboratory findings in trauma-induced nail dystrophy versus onychomycosis. *Siriraj Med J* 2018; 70: 490-5.

Neupane S, Pokhrel DB, Pokhrel BM. Onychomycosis: a clinico-epidemiological study. *Nepal Med Coll J* 2009; 11: 92-5.

Nkondjo Minkoumou S, Fabrizi V, Papini M. Onychomycosis in Cameroon: a clinical and epidemiological study among dermatological patients. *Int J Dermatol* 2012; 51: 1474-7.

Papini M, Piraccini BM, Difonzo E, Brunoro A. Epidemiology of onychomycosis in Italy: prevalence data and risk factor identification. *Mycoses* 2015; 58: 659-64.

Salakshna N, Bunyaratavej S, Matthapan L, Lertrujiwanit K, Leeyaphan C. A cohort study of risk factors, clinical presentations, and outcomes for dermatophyte,

nondermatophyte, and mixed toenail infections. *J Am Acad Dermatol* 2018; 79: 1145-6.

Segal R, Shemer A, Hochberg M, *et al*. Onychomycosis in Israel: epidemiological aspects. *Mycoses* 2015; 58: 133-9.

Soltani M, Khosravi AR, Shokri H, Sharifzadeh A, Balal A. A study of onychomycosis in patients attending a dermatology center in Tehran, Iran. *J Mycol Med* 2015; 25: e81-7.

Veer P, Patwardhan NS, Damle AS. Study of onychomycosis: prevailing fungi and pattern of infection. *Indian J Med Microbiol* 2007; 25: 53-6.