

## Coexistence of Fungal Infections in Psoriatic Nails and their Correlation with Severity of Nail Psoriasis

### Abstract

**Background:** Nail involvement in psoriasis is often complicated by concomitant fungal infections. The aim of this study was to investigate the prevalence of fungal infections in nail psoriasis and correlate it with the severity of nail psoriasis. **Materials and Methods:** This retrospective study included patients with nail psoriasis aged  $\geq 18$  years with at least one fingernail and one toenail involvement who were treated at Siriraj Hospital from September 2012 to January 2014. Severity of nail psoriasis was assessed by Nail Psoriasis Area Severity Index (NAPSI) score. The nail clippings from the the least and most severely involved psoriatic fingernails and toenails were cultured to determine the presence of coexisting fungal infections and isolate the fungal species. **Results:** Sixty-two patients (33 males, 29 females) fulfilling the inclusion criteria were included in the study. The mean age at the time of presentation was 51.3 years mention SD. The most common nail change consistent with psoriasis was onycholysis, followed by subungual hyperkeratosis. The most commonly isolated fungi in the most severely affected fingernails were *Candida* spp. (41.9%) manifesting as paronychia in 5 patients (19.2%). The most commonly isolated fungi in the most severely affected toenails were nondermatophytes (NDMs) other than candida (32.3%). Dermatophytes were not detected from any of the psoriatic nails. The fungal species isolated from the most severely affected fingernails were significantly different than the isolated fungal species in the most severely affected toenails ( $P = 0.026$ ). Fungal organisms were identified in 32.3% of the most severely affected fingernails and in 27.4% of the most severely affected toenails. The overall rate of isolation of fungus was significantly significantly higher in severely affected nails than in the least affected nails ( $P < 0.005$ ). **Conclusion:** A high rate of concomitant fungal infections, especially yeasts and NDMs, was found in psoriatic nail patients. The rate of isolation of fungal species was higher in severely involved psoriatic nails than mildly involved ones. The spectrum of fungal species isolated from the the severely involved toenails and fingernails were also different from each other. These organisms may be true pathogens that cause onychomycosis or their presence may reflect colonization, contamination, or concurrent infection.

**Keywords:** *Fingernails, fungal infection, nail psoriasis, prevalence, severity, Thailand, toenails*

### Introduction

Psoriasis is one of the most common chronic inflammatory skin disease. Nail involvement can be found in approximately 20–78% of patients with psoriasis.<sup>[1,2]</sup> Moreover, psoriatic patients with nail involvement may have nail changes that are similar to the manifestations of onychomycosis. Treatment options in psoriatic nail patients include topical corticosteroid, intralesional corticosteroid, and/or immunosuppressive drugs, whereas patients with onychomycosis require systemic and topical antifungal agents. A subset of patients with nail psoriasis may have concomitant fungal infections.

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This study was aimed to investigate the prevalence of fungal infections in nail psoriasis and correlate it with the severity of nail psoriasis.

### Materials and Methods

#### Patients

This retrospective study included patients with nail psoriasis aged 18 years or older with at least one fingernail and one toenail involvement who were treated at the Department of Dermatology, Siriraj Hospital from September 2012 to January 2014. Siriraj Hospital is Thailand's largest university-based national tertiary referral center. Patients who received treatment

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with systemic or topical antifungal agents within a period of 6 months prior to the enrollment were excluded. The protocol for this study was approved by the Siriraj Institutional Review Board (SIRB), Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok, Thailand. Written informed consent was obtained from all the study participants.

### Clinical examination

Demographic data, including age, gender, occupation, underlying diseases, types of psoriasis, disease duration, and treatments, were recorded. Severity of the skin involvement was evaluated by the Psoriasis Area Severity Index (PASI). Severity of the nail involvement was assessed by Nail Psoriasis Area Severity Index (NAPSI).<sup>[3]</sup>

### Mycological examinations

The least and the most affected toenails and fingernails based on the minimum and maximum NAPSI score, respectively, were selected. Culture was used as a definite criterion to determine the presence of dermatophytes or nondermatophytes (NDMs) and to isolate the fungal species. According to the study by Gupta *et al.*, a diagnosis of NDM onychomycosis required a consistent organism from culture in repeated isolations.<sup>[4]</sup>

### Statistical analysis

All data analyses were performed using SPSS Statistics version 18 (SPSS, Inc., Chicago, IL, USA). Comparison of rate of positive fungal culture results among the most severely affected fingernail and the most severely affected toenail was analyzed using McNemar–Bowker test. Chi-square test was employed to compare pathogens between fingernails and toenails. Data are presented as number or number and percentage. A *P*-value less than 0.05 was regarded as being statistically significant.

### Results

Sixty-two patients (33 males, 29 females) with a mean age of 51.3 years at the time of presentation (range: 18–80) were enrolled. Mean PASI score was 13.0 (range: 0.2–55.8). The distribution of patients with nail psoriasis based on the morphological variant of cutaneous psoriasis has been presented in Table 1.

The most common psoriatic nail change was onycholysis (83.9%), followed by subungual hyperkeratosis (51.6%). The mean duration of nail changes at the time of presentation was 7.3 years (range: 1 month to 40 years). The median NAPSI score of the most and least severely affected fingernails was 6 (range: 1–8) and 4 (range: 0–8), respectively. Median NAPSI score of the most and least severely affected toenails was 6 (range: 1–8) and 2 (range: 0–8), respectively. The most commonly isolated fungal species in the most severely affected fingernail belonged to *Candida* spp. (41.9%) manifesting

**Table 1: Distribution of patients with nail involvement by the morphological type of cutaneous psoriasis (n=62)**

| Type of psoriasis             | Nail involvement, n (%) |
|-------------------------------|-------------------------|
| Chronic plaque type psoriasis | 52 (72.2%)              |
| Guttate psoriasis             | 6 (8.3%)                |
| Pustular psoriasis            | 1 (1.4%)                |
| Erythrodermic psoriasis       | 1 (1.4%)                |
| Others                        | 2 (2.8%)                |

as paronychia in 5 patients (19.2%). The most commonly isolated fungal species in the most severely affected toenails were NDMs other than candida (32.3%). Dermatophytes were not detected from any of the psoriatic nails [Table 2]. The causative fungal species in the most severely affected fingernails were significantly different than those in the most severely affected toenails ( $P = 0.026$ ).

Fungal organisms were identified in 32.3% of the most severely affected fingernails and in 27.4% of the most severely affected toenails. The rate of isolation of fungus was significantly higher in severely affected fingernails and toenails than in the least affected fingers and toenails (both  $P < 0.005$ ).

### Discussion

The association of onychomycosis and nail psoriasis remains unclear and sometimes contradictory, as observed from studies outlined in Table 3. The clinical differentiation of psoriatic nails with onychomycosis can be challenging sometimes.

Few of the previous studies reported that the prevalence of onychomycosis in patients with nail psoriasis did not differ significantly from the rate observed in the control group, whereas some other studies showed higher prevalence in the study group.<sup>[5-10]</sup> These sometimes disparate differences in findings may be due to variations in study methodology and diagnostic criteria.

In the present study, NDMs were frequently discovered in more severely involved psoriatic toenails. These finding may be suggestive of contamination rather than true pathogens given the fact that the NDM species are widely distributed in the environment. Yeasts were likely to be found more often in more severely involved psoriatic fingernails than in toenails probably owing to the fact that fingernails are more often exposed to water than toenails.

Bunyaratavej *et al.* reported *Neoscytalidium dimidiatum* to be a common cause of onychomycosis among general population in Thailand.<sup>[11]</sup> In contrast, *N. dimidiatum* infection was isolated in only one toenail in the present study. Even though dermatophytes are a common cause of onychomycosis worldwide, this study did not find any dermatophyte-related onychomycosis. Rapid growth of psoriatic nails may decrease the probability of fungal invasion of the nail plate.<sup>[7,11,12]</sup> Moreover, the presence

**Table 2: The results of fungal cultures compared by severity between fingernails and toenails in psoriatic nail patients**

| Type of fungus                       | Fingernails, n (%) |              | Toenails, n (%) |              |
|--------------------------------------|--------------------|--------------|-----------------|--------------|
|                                      | Most severe        | Least severe | Most severe     | Least severe |
| <i>Candida</i> spp.                  | 26 (41.9%)         | 19 (30.6%)   | 14 (22.6%)      | 11 (17.8%)   |
| Non-dermatophytes other than candida | 12 (19.4%)         | 10 (16.1%)   | 20 (32.3%)*     | 14 (22.6%)   |
| Mixed organisms                      | 2 (3.2%)           | 1 (1.6%)     | 1 (1.6%)        | 1 (1.6%)     |
| No growth                            | 22 (35.5%)         | 31 (50.0%)   | 27 (43.5%)      | 36 (58.1%)   |

Non-dermatophytes included *Aspergillus niger*, *Penicillium* spp., *Fusarium solani*, *Cladosporium* spp., *Neoscytalidium dimidiatum*, and *Curvularia* spp. \**Neoscytalidium dimidiatum* was isolated in only 1 toenail (most severely affected toenail group)

**Table 3: Literature review of onychomycosis in psoriatic nail patients**

| Author                          | Prevalence of onychomycosis in psoriatic nails | Comments  |
|---------------------------------|--|---|
| Gupta et al. <sup>[4]</sup>     | 27.0%  | Dermatophytes (8.0%), yeast (0.5%), mold (0.8%) (toenails only)             |
| Larsen et al. <sup>[5]</sup>    | 21.5%  | Dermatophytes (9.8%), yeast (12.7%), mold (5.1%) (fingernails and toenails) |
| Staberg et al. <sup>[8]</sup>   | 0.0%   | Dermatophytes (13.0%), yeast (15.0%) (fingernails and toenails)             |
| Salomon et al. <sup>[7]</sup>   | 18.0%  | Dermatophytes (7.2%), yeast (6.0%), mold (6.0%) (fingernails and toenails)  |
| Shemer et al. <sup>[1]</sup>    | 23.0%  | Dermatophytes (22.0%), yeast (7.0%), mold (8.9%) (fingernails and toenails) |
| Natarajan et al. <sup>[6]</sup> | 47.9%  | Yeast (18.75%), mold (18.75%) (fingernails and toenails)                    |
| The present study               | 32.3%  | Fingernails: non-dermatophytes (20.3%), <i>Candida</i> spp. (42.4%)         |
|                                 | 27.4%  | Toenails: non-dermatophytes (32.2%), <i>Candida</i> spp. (22.0%)            |

of antimicrobial peptides, such as  $\beta$ -defensin-2 and cathelicidin, in the skin and nail units in psoriatic patients strengthens the immune defense against pathogens. Increased expression of cytokine interleukin-17 (IL-17A) may also play a significant role in defense mechanisms against extracellular bacterial and fungal infections, especially in psoriasis.<sup>[12-14]</sup> However, the exact mechanisms remain unknown.

There are a few limitations of this study. First, this was not a case-control study as no healthy controls were recruited. Second, dermoscopic examinations for supportive evidence of clinical findings to distinguish onychomycosis from nail psoriasis were not performed. Third, this study also enrolled older cases of nail psoriasis who were previously treated with systemic immunosuppressive therapy, which may have increased the risk of overgrowth of organisms, especially yeasts.

## Conclusion

A high rate of concomitant fungal infection, especially yeasts and NDMs, was found in patients with psoriatic nails. The rate of isolation of fungal species was higher in severely involved psoriatic nails than mildly involved ones. The spectrum of fungal species isolated from the the severely involved toenails and fingernails were also different from each other. These organisms may be true pathogens that cause onychomycosis or their presence may reflect colonization, contamination, or concurrent infection in patients with nail psoriasis. Interestingly, although *N. dimidiatum* is the most common cause of NDM onychomycosis in Thailand, this pathogen was isolated in only one toenail, which was in the most severely affected

toenail group. Further prospective controlled studies are encouraged to confirm these findings and further elucidate the relationship between nail psoriasis and fungal infection.

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## Conflicts of interest

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