Research Article

Overall Prevalence and Prevalence Compared among Psoriasis Treatments of Onychomycosis in Patients with Nail Psoriasis and Fungal Involvement

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Background. Whether nail psoriasis can increase the risk of onychomycosis is still being debated, and data relating to the prevalence of onychomycosis among psoriasis patients receiving different treatments is limited. Objectives. To investigate the overall prevalence and prevalence compared among psoriasis treatments of onychomycosis in patients with nail psoriasis and fungal involvement. Methods. A prospective study of three groups of nail psoriasis being treated with only topical medication, methotrexate, or biologics (25 patients per group, 150 nails) was conducted at Siriraj Hospital (Bangkok, Thailand) during November 2018 to September 2020. Demographic data, psoriasis severity, and nail psoriasis severity were recorded. The nail most severely affected with psoriasis on each hand was selected for mycological testing. Potassium hydroxide, periodic acid-Schiff stain, and fungal culture were performed.

Results. The prevalence of onychomycosis in nail psoriasis was 35.3%. Among the treatment groups, the prevalence of onychomycosis was significantly higher in the methotrexate group than in the topical treatment and biologic treatment groups (p = 0.014). Candida spp. was the main causative organism, followed by Trichophyton rubrum. Thumb was most commonly affected (59.3%). The most common abnormality of the nail matrix and the nail bed was pitted nail (71.3%) and onycholysis (91.3%), respectively. Multivariate analysis revealed diabetes, wet-work exposure, and methotrexate treatment to be predictors of onychomycosis. Conclusions. Several factors, including psoriasis treatment, were shown to increase the risk of onychomycosis in nail psoriasis. Further research is needed to determine whether biologic agents, especially interleukin-17 inhibitors, can increase risk of onychomycosis and Candida infection/colonization of the nails.

1. Introduction

Psoriasis is a multifactorial chronic disorder that has an etiopathogenesis that derives from the alteration of signaling pathways, which leads to a defect in the functional and structural properties of the skin [1]. It can cause nail pathology on both the hands and feet. The reported prevalence of nail involvement in patients with psoriasis varied considerably from 15% to 86% [2, 3]. The presence of nail involvement was reported to be a predictor of psoriatic arthritis, and it was also found that nail involvement may occur a few years before the development of joint disease [4]. Psoriasis can affect the nail matrix and nail bed resulting in several clinical presentations, including pitting, crumbling, onycholysis, and subungual hyperkeratosis [5].

Onychomycosis is a fungal nail infection that is caused by dermatophytes, yeasts, and filamentous fungi. It is a common nail disease that accounts for 50% of nail disorders. Its prevalence in the general population and in patients with psoriasis can reach up to 30% and 56%, respectively [5, 6]. Clinical features of nail psoriasis and onychomycosis may overlap, and pathologies of both diseases may occur in the same patient. Several factors, including nail pathologies, patient behavior, immune status, and treatments for psoriasis, may contribute to the development of onychomycosis in nail psoriasis.
Topical treatments, such as steroids, vitamin D3 analogs, tazarotene, trifarotene, topical calcineurin inhibitors, and 5-fluourouracil, can be used to treat nail psoriasis [7–9]. For patients with severe skin involvement and nail psoriasis, conventional systemic treatments (ciclosporin, methotrexate, and acitretin), small molecule drugs, and biologics are recommended. Due to their immunosuppressive properties, ciclosporin, methotrexate, and biologics may aggravate onychomycosis in nail psoriasis [3]. On the other hand, there is evidence that vitamin A and its active metabolite, all-transretinoic acid, exert host-protective effects in infections and direct fungistatic effect against Candida albicans [9–11]. Recently, small molecule drugs, such as apremilast and tofacitinib, have been shown to be effective for treating nail psoriasis [3, 12].

Although several studies have investigated the prevalence of onychomycosis in patients with nail psoriasis, few studies have addressed its prevalence among patients receiving different treatments for psoriasis. Among those studies, a cross-sectional study reported a prevalence of onychomycosis of 34.8% (8/23) among patients not being treated with immunosuppressive agents, and yeasts, and filamentous fungi were the predominant pathogens [13]. Other studies reported that factors affecting the immune status, including diabetes, administration of topical corticosteroids, and systemic treatments for psoriasis, were risk factors for onychomycosis in patients with psoriasis [6, 14]. A randomized prospective open-label study reported that the risk of onychomycosis in psoriasis patients receiving treatment with an antitumor necrosis factor (anti-TNF) was 20.3% compared to 13.9% in patients that did not receive any biological agents [15]. Moreover and importantly, published data relating to the prevalence of onychomycosis among patients receiving anti-interleukin (IL-) 17, in which mucocutaneous candidiasis is a side effect of concern, is comparatively scarce [16].

Thus, the aim of this study was to investigate the overall prevalence and prevalence of onychomycosis among different treatments for psoriasis, including topical medication, methotrexate, or biologic therapy in patients with nail psoriasis. Our secondary objective was to identify significant risk factors for developing onychomycosis in this patient population.

## 2. Materials and Methods

This prospective study was conducted at the Department of Dermatology, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok, Thailand during November 2018 to September 2020. The inclusion criteria were psoriasis patients with fingernail pathologies aged 18 years or older who attended the outpatient dermatology clinic at our center and who were being treated with only topical treatment, methotrexate, or biologic agents for at least four weeks. The exclusion criteria were (i) patients with a history of receiving any topical or systemic antifungal agents during the 12-week period prior to the start of this study, (ii) patients taking other immunosuppressant drugs, (iii) pregnant or lactating patients, and/or (iv) patients with other nail diseases. All patients who voluntarily agreed to participate in

| Characteristics (N = 75) | Values |
|-------------------------|--------|
| Gender, n (%)           |        |
| Female                  | 38 (50.7%) |
| Male                    | 37 (49.3%) |
| Age (years), mean ± SD  | 46.8 ± 15.3 |
| Body mass index (kg/m²), mean ± SD | 25.0 ± 5.0 |
| Duration of psoriasis (years), median (IQR) | 11.0 (7.0, 20.0) |
| Psoriasis types, n (%)  |        |
| Plaque                  | 64 (85.3%) |
| Guttate                 | 7 (9.3%) |
| Erythrodermic           | 3 (4.0%) |
| Pustular                | 1 (1.3%) |
| Psoriatic arthritis, n (%) | 13 (17.3%) |
| Occupation, n (%)       |        |
| No increased risk of hand exposure to water†  | 40 (53.3%) |
| Increased risk of hand exposure to water†    | 35 (46.7%) |
| Patient right-handed, n (%)         | 68 (90.7%) |
| Patient left-handed, n (%)           | 7 (9.3%) |
| Handwashing frequency (times/day), median (IQR) | 6.0 (4.0, 10.0) |
| Current psoriasis severity |        |
| Psoriasis Area and Severity Index score, median (IQR) | 5.0 (3.2, 10.2) |

| Nail severity            | Values |
|--------------------------|--------|
| Nail Psoriasis Severity Index score (0-8), median (IQR) | 4.0 (2.0, 4.0) |
| Nijmegen-Nail Psoriasis Activity Index tool (0-15), median (IQR) | 4.0 (3.0, 5.0) |

| Most severely affected fingernail, n (%) |        |
|----------------------------------------|--------|
| Thumb                                  | 89 (59.3%) |
| Index finger                           | 22 (14.7%) |
| Middle finger                          | 16 (10.7%) |
| Ring finger                            | 13 (8.7%) |
| Little finger                          | 10 (6.7%) |

| Nail matrix pathology, n (%)           |        |
|---------------------------------------|--------|
| Pitting                               | 107 (71.3%) |
| Leukonychia                            | 69 (46.0%) |
| Crumbling                             | 55 (36.7%) |
| Red spots lunula                      | 2 (1.3%) |

| Nail bed pathology, n (%)              |        |
|---------------------------------------|--------|
| Onycholysis                            | 137 (91.3%) |
| Subungal hyperkeratosis                | 53 (35.3%) |
| Oil drop                              | 30 (20.0%) |
| Splinter hemorrhage                    | 29 (19.3%) |
| Beau lines, n (%)                      | 19 (12.7%) |
| Paronychial involvement, n (%)         | 73 (48.7%) |

†Driver, lawyer, merchant, collegian, teacher, or retired. §Housekeeper, farmer, fisherman, mechanic, builder, or barber. Abbreviations: SD: standard deviation; IQR: interquartile range.
Table 2: Results of potassium hydroxide (KOH), periodic acid-Schiff (PAS) stain, and culture techniques.

| Specimens collected from distal part of fingernails (N = 150) | KOH testing | PAS stain† | Culture | Interpretation | n(%) | Pathogen |
|---------------------------------------------------------------|-------------|------------|---------|----------------|------|----------|
| Direct microscopy                                             |             |            |         |                |      |          |
| KOH testing                                                   | PAS stain   | Culture    | Interpretation | n(%) | Pathogen |
| —                                                             | —           | No growth | No pathogen | 62 (41.3%) |     | (i) Candida spp. (n = 24) |
| +                                                             | —           | No growth | Discordant results | 1 (0.7%) |     | (ii) C. albicans (n = 5) |
| —                                                             | —           | Candida    | Colonization | 34 (22.7%) |     | (iii) C. krusei (n = 5) |
| —                                                             | +           | No growth | Pathologic fungi | 7 (4.7%) |     | Candida spp. (n = 25) |
| +                                                             | —           | Candida    | Onychomycosis | 46 (30.7%) |     | C. albicans (n = 15) |
| +                                                             | +           | Candida    | Candida infection at the nail fold | 13 (17.8%) |     | C. dubliniensis (n = 2) |

| Specimens collected from proximal part of fingernails that had at least grade 1 of paronychial involvement (N = 73) | KOH testing | Culture | Interpretation | n(%) | Pathogen |
|----------------------------------------------------------------------------------------------------------------|-------------|---------|----------------|------|----------|
| Direct microscopy                                             |             |         |                |      |          |
| Specimens collected from the distal part of the most severely affected psoriatic nail from each hand were tested for onychomycosis using potassium hydroxide (KOH), nail clipping for periodic acid-Schiff stain (PAS) technique, and fungal culture on Sabouraud dextrose agar and chloramphenicol media with and without cycloheximide (HiMedia Laboratories, Mumbai, India). Specimen collection and interpretation of KOH examination, PAS stain, and fungal cultures were performed by experienced technicians and one dermatopathologist. Cultures were incubated at 30°C and examined weekly up to 4 weeks. Chromogenic Candida Agar (Oxoid, Basingstoke, UK) was used to identify C. tropicalis, C. krusei, C. albicans, and C. dubliniensis on the basis of the morphology and color of the colonies [19]. Blue and brown/pink colonies indicate C. tropicalis and C. krusei, respectively. Green colonies indicate C. albicans or C. dubliniensis. The ability to grow at 42°C differentiates C. albicans (growth) from C. dubliniensis (no growth) [20]. Other Candida species that developed natural, mauve, or rose colors would be referred to Candida spp. in this study.

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Specimens were collected from the nail bed as proximally to the cuticle as possible using a scalpel blade. Onychomycosis was diagnosed if (i) culture was positive for pathologic fungi whether direct microscopy (KOH and PAS) was positive or negative or if (ii) culture was negative, but PAS stain revealed pathological forms of fungal infection whether direct KOH examination was positive or negative. Fungal colonization of the nail was diagnosed if culture was positive for Candida species, but direct microscopy was negative. If the results were negative for all three...
Figure 1: Representative pictures of clinical findings of psoriatic nail with fungal infection. Culture and microscopic identification from specimens collected from the distal part of psoriatic nail were also demonstrated. The fungi were inoculated onto the Chromogenic Candida Agar (a–d) and the Sabouraud dextrose agar with chloramphenicol (e) and inoculated at 30°C for 4 weeks. (a) Candida spp., (b) C. albicans, (c) C. krusei, (d) C. dubliniensis, and (e) Trichophyton rubrum.
2.1. Sample Size Calculation and Statistical Analysis. The sample size for each group was calculated using \( \lambda \). Previous studies reported the prevalence of onychomycosis in psoriasis patients treated with topical medication, methotrexate, and biologic agents to be 20%, 50%, and 13%, respectively [14, 15, 21]. Using a 2-sided type I error of 0.05 and 80% power, a sample of 25 patients per group was required (75 patients in total).

Descriptive statistics were used to summarize patient demographic and clinical characteristics. Data are described as mean plus/minus standard deviation (SD) for continuous data with normal distribution and as median and interquartile range (IQR) for nonnormally distributed continuous data. Categorical data are described as number and percentage. The results of univariate analysis and multivariate analysis are shown as odds ratio and adjusted odds ratio with their 95% confidence intervals, respectively. Statistical Package for the Social Sciences 18.0 (SPSS, Inc., Chicago, IL, USA) was used for data analysis, and a \( p \) value less than 0.05 was considered to be statistically significant.

### 3. Results

Among the 75 enrolled patients, the gender distribution was almost equal, and the mean age was 46.8 ± 15.3 years. The most common underlying disease was dyslipidemia (24.0%), followed by hypertension (22.7%), diabetes mellitus (18.7%), metabolic syndrome (13.3%), and obesity (12.0%). Table 1 shows the demographic and clinical characteristics of the included patients. Most patients had psoriasis without psoriatic arthritis (82.7%). Forty patients (53.3%) had an occupation that did not expose the patient to an increased risk of hand exposure to water. The median handwashing frequency of patients was 6 times/day, with a minimum of 2 times/day and a maximum of 20 times/day. Patterns of nail involvement and nail pathology were similar between the right hand and the left hand. Thirteen patients (17.3%) had oral candidiasis. We also found significant correlation between oral candidiasis and *Candida* infection of the nails (\( p = 0.015 \), data not shown).

Of 150 fingernails (1 from each hand of each of 75 patients), the thumb was the most severely affected fingernail on both hands. Pitted nail and onycholysis were the most common abnormalities of the nail matrix and nail bed, respectively. Seventy-three fingernails had paronychial involvement with 71.2%, 26.0%, and 2.7% of grades 1, 2, and 3 paronychial involvement, respectively. Fifty-three fingernails (35.3%) had *Candida* infection in the oral cavity.

### Table 3: Analysis for risk factors independently associated with onychomycosis in patients with nail psoriasis.

| Variable                                      | Univariate analysis | Multivariate analysis |
|-----------------------------------------------|---------------------|-----------------------|
|                                               | Crude odds ratio (95% confidence interval) | \( p \) value | Adjusted odds ratio (95% confidence interval) | \( p \) value |
| Male gender                                   | 0.68 (0.27-1.70)    | 0.411                 |                                                    |        |
| Concomitant diabetes mellitus                 | 6.06 (1.53-24.02)   | \textbf{0.010}       | 7.04 (1.44-34.50)                                 | \textbf{0.016} |
| Duration of psoriasis ≥10 years               | 0.99 (0.37-2.70)    | 0.989                 |                                                    |        |
| Handwashing frequency ≥6 times/day            | 1.83 (0.73-4.58)    | 0.200                 |                                                    |        |
| Occupation that increased the risk of hand exposure to water | 5.05 (1.89-13.52)  | \textbf{0.001}       | 4.12 (1.36-12.51)                                 | \textbf{0.012} |
| Nail Psoriasis Severity Index score ≥4        | 1.30 (0.52-3.24)    | 0.570                 |                                                    |        |
| Nijmegen – Nail Psoriasis Activity Index score ≥4 | 1.70 (0.65-4.46)  | 0.281                 |                                                    |        |
| Topical treatment: methotrexate               | 3.19 (1.00-10.17)   | \textbf{0.050}       | 2.12 (0.55-8.16)                                 | 0.275  |
| Biologic\( ^* \)                              | 0.58 (0.18-1.91)    | 0.372                 | 0.46 (0.12-1.86)                                 | 0.277  |
| Biologic treatment\( ^* \): topical          | 1.71 (0.53-5.60)    | 0.372                 | 2.16 (0.54-8.65)                                 | 0.277  |
| Methotrexate                                  | 5.46 (1.63-18.36)   | \textbf{0.006}       | 4.57 (1.11-18.93)                                 | \textbf{0.036} |
| Pitted nails                                  | 1.51 (0.54-4.23)    | 0.434                 |                                                    |        |
| Leukonychia                                   | 1.14 (0.46-2.83)    | 0.785                 |                                                    |        |
| Crumbling                                     | 1.69 (0.65-4.41)    | 0.282                 |                                                    |        |
| Onycholysis                                   | 0.46 (0.10-2.07)    | 0.311                 |                                                    |        |
| Subungual hyperkeratosis                      | 1.09 (0.43-2.77)    | 0.850                 |                                                    |        |
| Paronychial involvement                       | 0.90 (0.36-2.25)    | 0.817                 |                                                    |        |
| *Candida* infection in the oral cavity        | 3.33 (0.92-12.01)   | 0.066                 | 2.82 (0.59-13.39)                                 | 0.192  |

Variables with a \( p \) value < 0.20 in univariate analysis were included in multivariate analysis. A \( p \) value < 0.05 in multivariate analysis was considered statistically significant. *Interleukin- (IL-) 17 inhibitors, antitumor necrosis factor, and anti-IL 12/23 were used in 20, 4, and 1 patient, respectively.
The risk of onychomycosis was highest in the methotrexate group than in the other two groups. Patients with diabetes and wet-work exposure was higher and 28% in biologic treatment). However, the number of onychomycosis was highest in the methotrexate group ($p = 0.007$). Table 4 shows that the prevalence of onychomycosis in univariate analysis ($p = 0.002$, $p = 0.028$), and wet-work exposure remained as the only risk factor independently associated with onychomycosis in multivariate analysis ($p = 0.007$). The risk of Candida colonization of the nail did not increase significantly in the biologic treatment group even though the main biologics used were interleukin-17 inhibitors.

4. Discussion

A systematic review in 2014 showed an increased prevalence of onychomycosis in psoriatic patients (18%) compared to the prevalence in the general population (9.1%); however, the high heterogeneity among the 10 included studies limits the reliability of their findings [22]. We reviewed the literature in the PubMed database using the keywords “prevalence,” “onychomycosis,” “psoriasis,” and “treatment.” Thirty studies were included and summarized, as shown in Table 5 [2, 6, 13–15, 21, 23–46]. It was shown that the prevalence of onychomycosis in psoriatic nails in Asian countries ranged from 20.3% (Kuwait) to 47.9% (India) compared to the prevalence of 18.0% (Belgium, Poland) to 62.0% (Bulgaria) in European countries [2, 6, 13–15, 23, 25, 27–33, 35, 37, 40, 41, 44–46]. The prevalence of onychomycosis in controls with clinical abnormality in Asian countries ranged from 4% (Pakistan) to 40.6% (Turkey) compared to the prevalence of 22.4% (Poland) to 51.3% (Italy) in European countries [2, 14, 15, 32, 33, 35, 37, 44–46]. The first study of the prevalence of onychomycosis in psoriatic nails at our center was published in 2018, and that study found a prevalence of 32.3% [23]. The
| Authors (year, country)                                      | Patients : Controls | Fungal tests | Overall  | Prevalence of onychomycosis (%) | Prevalence of onychomycosis among different treatments of psoriasis (%) | Organisms from psoriatic nails (%) |
|------------------------------------------------------------|---------------------|--------------|----------|-------------------------------|---------------------------------------------------------------------|----------------------------------|
|                                                            |                     |              |          | Psoriasis patients | Controls | Topical | Systemic | Biologics | (i) DMPs | (ii) Moulds | (iii) Yeasts | (iv) Other |
| Toenails                                                   |                     |              |          | No clinical   | Clinically abnormal | No clinical | Clinically abnormal |                   |          |            |            |                |
| 1. Gupta et al. (1997, Canada and USA)                     | 561 : 922           | KOH+C/S      | 15.3     | 12.7 (38/298) | 27 (71/263) | 6.9 (54/776) | 43.8 (64/146) |                  | (i) DMPs | 84.9        | (ii) Moulds | 9.4          |                  | (iii) Yeasts | 5.7          |
| 2. Hamnerius et al. (2004, Sweden)                         | 239 : 245           | KOH+C/S      | 3.5      | 4.6 (11/239)  | —          | 2.4 (6/245)  | —                  | (i) DMPs | 54.3        | (ii) Yeasts | 37.1         | (iii) Moulds | 8.6          |                  |
| 3. Zawirska et al. (2006, Poland)                          | 70 : 60             | KOH+C/S      | 9        | 11.4 (8/70)   | —          | 3.3 (2/60)   | —                  | (i) DMPs | —           | (ii) Yeasts | 11.1         | (iii) Moulds | 11.1         |                  |
| 4. Piérard-Franchimont et al. (2006, Belgium)              | 233 : 0             | C/S+PAS      | 18.0     | —             | 18.0 (42/233) | —          | —                  | (i) DMPs | 100         | (ii) Yeasts | —           | (iii) Moulds | —            |                  |
| 5. Leibovici et al. (2008, Israel)                         | 113 : 102           | KOH+C/S      | 38.6     | —             | 47.6 (54/113) | 28.4 (29/102) | —                  | (i) DMPs | 77.8        | (ii) Yeasts | 11.1         | (iii) Moulds | 11.1         |                  |
| 6. Altunay et al. (2009, Turkey)                           | 60 : 60             | KOH+C/S      | 8.3      | 8.3 (5/60)    | 8.3 (5/60)  | —          | —                  | (i) DMPs | 100         | (ii) Yeasts | —           | (iii) Moulds | 100          |                  |
| 7. Vender et al. (2016, Canada)                            | 12 : 0              | KOH+C/S      | 25       | —             | 25 (3/12)   | —          | —                  | (i) DMPs | 33.3        | (ii) Yeasts | 66.7         |                | (iv) No growth | —            |
| Toenails and fingernails                                  |                     |              |          |                |            |            |                    |                  | (i) DMPs | 47.6        | (ii) Yeasts | 47.6         | (iii) Moulds | 4.8          |                  |
| 8. Staberg et al. (1983, Denmark)                          | 78 : 41             | KOH+C/S      | 25.2     | 26.9 (10/39)  | 30.8 (12/39) | 19.5 (8/41) | —                  | (i) DMPs | 50.0        | (ii) Yeasts | 50.0         | (iii) Moulds | 4.8          |                  |
| 9. Szepes (1986, Hungary)                                  | 137 : 341           | C/S          | 64.4     | 63.1 (83/137) | 66.0 (225/341)| —          | —                  | (i) DMPs | 12.9        | (ii) Yeasts | 28.9         | (iii) Moulds | 31.3         |                  |
| 10. Stander et al. (2001, Germany)                         | 250 : 102           | KOH+C/S      | 27.3     | 30.4 (76/250) | 19.6 (20/102)| —          | —                  | (i) DMPs | 36.2        | (ii) Yeasts | 36.2         | (iii) Moulds | 28.9         |                  |
| 11. Salomon et al. (2003, Poland)                          | 106 : 0             | KOH+C/S      | 13.8     | Not tested (n = 23) | 18 (15/83)  | —          | —                  | (i) Moulds | 37.5        | (ii) DMPs | 31.3         | (iii) Yeasts | 37.5         |                  |
| 12. Larsen et al. (2003, Denmark)                          | 79 : 142            | KOH+C/S      | 15.8     | Not tested (n = 14) | 26.2 (17/65) | Not tested (n = 89) | 34.0 (18/53) | (i) DMPs | 45.5        | (ii) DMPs | 45.5         | (iii) Yeasts | 45.5         | (iv) No growth |
| 13. Kacar et al. (2006, Turkey)                            | 168 : 164           | KOH+C/S      | 10.5     | Not tested (n = 91) | 28.6 (22/77) | Not tested (n = 132) | 40.6 (13/32) | (i) DMPs | 36.4        | (ii) Yeasts | 36.4         | (iii) Moulds | 9.1          | (iv) No growth  |
### Table 5: Continued.

| Authors (year, country) | Patients : Controls | Fungal tests | Overall | Prevalence of onychomycosis (%) | Prevalence of onychomycosis among different treatments of psoriasis (%) | Organisms from psoriatic nails (%) |
|-------------------------|--------------------|--------------|---------|-------------------------------|---------------------------------------------------------------|----------------------------------|
|                         |                    |              | No clinical | Clinically abnormal | No clinical | Clinically abnormal | Topical | Systemic | Biologics |
| 14. Pawlaczyk et al. (2007, Poland) | 481 : 3,986 | KOH+C/S 36.3 | 6.0 (20/327) | 18.8 (29/154) | — | 39.6 (1579/3986) | — | — | — | (i) DMPs 65.5 | (ii) Yeasts 27.6 | (iii) Moulds 6.9 |
| 15. Sánchez-Regaña et al. (2007, Spain) | 20 : 0 | KOH+C/S 30 | — | 30 (6/20) | — | — | — | — | — | (i) Yeasts 66.7 | (ii) Moulds 33.3 |
| 16. Shemer et al. (2009, Israel) | 312 : 0 | KOH+C/S 34.3 | — | 34.3 (23/67) | — | — | — | — | — | (i) DMPs 74.0 | (ii) Moulds 39.1 | (iii) Yeasts 30.4 |
| 17. Natarajan et al. (2010, India) | 72 : 0 | KOH+C/S +PAS 31.9 | Not tested (n = 24) | 47.9 (23/48) | — | — | — | — | — | (i) Moulds 50 | (ii) Yeasts 50 |
| 18. Kavaliauskiene et al. (2010, Lithuania) | 30 : 529 | KOH+C/S 23.6 | — | 23.3 (7/30) | 23.6 (125/529) | — | — | — | — | (i) DMPs 71.4 | (ii) Yeasts 28.6 |
| 19. Zisova et al. (2011, Bulgaria) | 228 : 0 | KOH+C/S 62 | — | 62 (141/228) | — | — | — | — | — | (i) Yeasts 69.2 | (ii) DMPs 30.8 |
| 20. Rizzo et al. (2013, Italy) | 31 : 274 | C/S+PAS 37.7 | — | 41.9 (13/31) | — | 37.2 (102/274) | — | — | — | Anti-TNF 20.3 | (i) IFX 33.0 | (ii) ETA 15.5 | (iii) ADA 13.3 |
| 21. Al-Mutairi N et al. (2013, Kuwait) | 315 : 180 | KOH+C/S 18.0 | — | 20.3 (64/315) | — | 13.9 (25/180) | — | — | — | (i) DMPs 65.6 | (ii) Yeasts 28.1 | (iii) Moulds 6.3 |
| 22. Mendez-Tovar et al. (2015, Mexico) | 150 : 0 | KOH+C/S 28 | Not tested (n = 67) | 50.6 (42/83) | — | — | 21.4 | MTX, CsA 31 | Anti-TNF 11.9 | (i) Yeasts 50 | (ii) DMPs 32 | (iii) Moulds 18 |
| 23. Tsentemeidou et al. (2017, Greece) | 23 : 0 | KOH+C/S 34.8 | — | 34.8 (8/23) | — | — | 34.8 | — | — | (i) Yeasts 37.5 | (ii) Moulds 37.5 | (iii) DMPs 12.5 |
| 24. Zander et al. (2017, Germany) | 2781 : 136,137 | Not specified | 6.4 | 7.8 (219/2781) | 6.4 (8678/136,137) | — | — | — | — | (i) Yeasts 50.0 | (ii) DMPs 29.2 | (iii) Moulds 20.8 |
| 25. Romaszkiewicz et al. (2018, Poland) | 102 : 2335 | KOH+C/S 22.4 | — | 23.5 (24/102) | 5 (5/100) | 22.4 (520/2325) | 25 | MTX 20.8 | CsA 12.5 | Anti-TNF 37.5 | (i) Yeasts 50 | (ii) DMPs 29.2 | (iii) Moulds 20.8 |
| Authors (year, country)          | Patients: Controls | Fungal tests | Prevalence of onychomycosis (%) | Prevalence of onychomycosis among different treatments of psoriasis (%) | Organisms from psoriatic nails (%) |
|---------------------------------|--------------------|--------------|----------------------------------|-----------------------------------------------------------------------|-----------------------------------|
|                                 |                    | Overall      | Psoriasis patients               | Controls                                                              | Topical | Systemic | Biologics |
|                                 |                    |              | No clinical | Clinically abnormal             | No clinical | Clinically abnormal |
| 26. Chaowattanapanit et al.     | 62:0               | C/S          | 32.3       | —                             | 32.3 (20/62) | —                 | —         | —         | —         | (i) Yeasts 41.9 |
| (2018, Thailand)                |                    |              |            |                               |             |                   |           |           |           | (ii) Moulds 19.4 |
|                                 |                    |              |            |                               |             |                   |           |           |           | (iii) No growth 35.5 |
| 27. Tabassum et al.             | 159:318            | KOH+C/S      | 14         | —                             | 34 (54/159) | —                 | 4 (13/318) | 34        | —         | (i) Yeasts 37.0 |
| (2019, Pakistan)                |                    |              |            |                               |             |                   |           |           |           | (ii) Moulds 35.2 |
|                                 |                    |              |            |                               |             |                   |           |           |           | (iii) DMPs 7.4 |
| 28. Jendoubi et al.             | 163:0              | KOH+C/S      | 33.7       | Not tested (n = 47)           | 47.4 (55/116)| —                 | —         | —         | —         | Fingernails: Yeasts 100 |
| (2019, Tunisia)                 |                    |              |            |                               |             |                   |           |           |           | Toenal: DMPs 100 |
|                                 |                    |              |            |                               |             |                   |           |           |           | (i) Yeasts 43.6 |
|                                 |                    |              |            |                               |             |                   |           |           |           | (ii) DMPs 43.3 |
|                                 |                    |              |            |                               |             |                   |           |           |           | (iii) Moulds 13.2 |
| 29. Gallo et al.                | 711:8670           | KOH+C/S      | 51.1       | —                             | 49.1 (349/711)| —                 | 51.3 (4397/8570)| —         | —         | —         | Anti-TNF 92.8 |
| (2019, Italy)                   |                    |              |            |                               |             |                   |           |           |           | Anti-IL17 33.3 |
|                                 |                    |              |            |                               |             |                   |           |           |           | Anti-IL23 0 |
| 30. Abes et al.                 | 38:0               | KOH+C/S +PAS | 57.9       | —                             | 57.9 (22/38) | —                 | —         | 33.0      | Anti-TNF 50 |
| (2020, Brazil)                  |                    |              |            |                               |             |                   |           |           |           | Anti-IL17 0 |
|                                 |                    |              |            |                               |             |                   |           |           |           | Anti-IL23 0 |
| 31. The present study           | 75:0 (150 nails)   | KOH+C/S +PAS | 36         | —                             | 36 (54/150) | —                 | —         | 44.0      | Anti-TNF 50 |
|                                 |                    |              |            |                               |             |                   |           |           |           | Anti-IL17 25 |
|                                 |                    |              |            |                               |             |                   |           |           |           | Anti-IL12/23 0 |
|                                 |                    |              |            |                               |             |                   |           |           |           | Anti-TNF 83.3 |
|                                 |                    |              |            |                               |             |                   |           |           |           | Anti-IL17 1.9 |
|                                 |                    |              |            |                               |             |                   |           |           |           | Anti-IL12/23 0 |
|                                 |                    |              |            |                               |             |                   |           |           |           | Anti-TNF 83.3 |
|                                 |                    |              |            |                               |             |                   |           |           |           | Anti-IL17 1.9 |
|                                 |                    |              |            |                               |             |                   |           |           |           | Anti-IL12/23 0 |

**Abbreviations:** KOH: potassium hydroxide examination; C/S: culture; PAS: Periodic-Schiff stain; MTX: methotrexate; ACT: acitretin; CsA: ciclosporin; anti-TNF: antitumor necrosis factor; IFX: infliximab; ETA: etanercept; ADA: adalimumab; IL: interleukin; DMPs: dermatophytes.
prevalence in this study was 35.3% (53/150), which is close to, but higher than that from the previous study. It seemed that the prevalence of onychomycosis in psoriatic patients in the present study was in a range of the reported prevalence of onychomycosis in controls with clinical nail abnormality in Asian countries [15, 35, 45]. Yeasts (Candida spp.) were more commonly identified in the present study, which is similar to several previous studies [2, 1314, 23, 24]. Chadeganipour et al. used molecular technique to identify Candida species in clinical samples of patients with psoriasis [47]. Molecular technique can provide 95% sensitivity and 100% specificity [48]. In that study, C. parapsilosis was the most prevalent species among Candida species of fingernail infection and none of Candida species were albicans. A lower number of clinical samples and different technique to identify Candida species in Chadeganipour’s study may explain the results different from our study [47].

Our study showed diabetes, methotrexate treatment, and wet-work exposure to be significant risk factors associated with onychomycosis. Methotrexate was at greater risk of developing onychomycosis compared to biologic treatment. The pathogenesis of nail psoriasis may increase or decrease the risk of onychomycosis. Generally, rapid nail growth, increase in antimicrobial peptides, and compact orthokeratotic nail plate will decrease the risk of onychomycosis in nail psoriasis [5]. However, other factors that increase the risk of onychomycosis also play an important role. Methotrexate can increase the risk of onychomycosis by immunosuppressive effect and slow the rate of nail growth [6].

Studies reporting the prevalence of onychomycosis in psoriasis patients who were on biologic treatment mainly included patients receiving anti-TNF treatment [14, 15, 21, 24]. Three out of four studies, including a randomized prospective study, showed a higher prevalence of onychomycosis in psoriatic patients treated with anti-TNF than in patients that received other types of treatments [14, 15, 21, 24]. There are some possible explanations why biologics did not increase the risk of onychomycosis in our study. First, the faster nail growth rate in psoriasis [49–51] acts as a protective factor against onychomycosis. Second, biologic treatment is more effective for treating nail psoriasis than methotrexate [52] because it reduces nail pathology and the opportunity of the fungi to invade the nail keratin. Third and last, the biologics most often used in our study were interleukin-17 inhibitors, which may have less immunosuppressive effect than anti-TNF.

4.1. Limitations. This study has some mentionable limitations. Even though we enrolled a sufficient number of patients to satisfy the minimum described by our sample size calculation, 75 patients represent a relatively small number of patients. Besides, only 20 patients were treated with interleukin-17 inhibitors, which could limit the generalizability of our results. Secondly, toenails were not included in this study since several other factors influence the risk of developing onychomycosis of the toenails compared to the fingernails. Thirdly, in cases of diagnostic discordance among the 3 diagnostic methods, a retest was not performed. Our rationale for this is that all three diagnostic methods were performed by experienced technicians and one expert dermatopathologist. Finally, molecular biology testing, which provides high sensitivity, high specificity, and accurate identification of fungal species, could not be performed in this study due to its relatively high cost. Alternatively, our laboratory used a culture-based method to identify fungal species. Only C. albicans, C. dubliniensis, C. tropicalis, and C. krusei could be identified. This is why we reported the other groups of Candida as Candida spp.

5. Conclusions

The prevalence of onychomycosis in nail psoriasis in this study was 35.3%. Among the three different psoriasis treatment groups, the prevalence of onychomycosis was significantly higher in the methotrexate treatment group than in the topical treatment and biologic treatment groups. Several factors can affect the risk of onychomycosis, including occupation, psoriasis treatment, host status, and nail growth rate. Molecular identification would be the best method to elucidate the etiology and establish an epidemiological inference with previous findings in the literature.

Data Availability

The data used to support the findings of this study are included within the article.

Conflicts of Interest

All authors declare no conflicts of interest.

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