Evaluation of Frequency of Onychomycosis in Nail Psoriasis by Polymerase Chain Reaction Before and After Methotrexate Therapy in Patients Attending Benha University Hospital

The Department of Dermatology and Andrology, Faculty of Medicine, Benha University

Abstract

Background and Objectives: In patients with Ps, nail changes morphologically resemble ONM. In these cases, diagnostic procedures are essential to exclude the presence of concomitant fungal infection. Both Ps and ONM are common diseases in the general population. It is possible that in some patients the two diseases co-exist.

Study Design: Clinical trial study

Patients and methods: All patients were subjected to:

- Detailed history taking. Initial screening. PASI score &NAPSI scores evaluation
- Examination of nail material in patients and control groups by:
  - Microscopic examination (KOH)
  - Culture on Sabouraud agar
  - Detection of Fungal DNA by PCR
- Patients will receive MTX once a week. The total course will be 21 weeks. After the course of the treatment, another nail samples will be collected for KOH, culture and PCR assay.

Limitations: Small number of patients.

Results: The frequency of ONM in patients with nail Ps was high, PCR positive results 7%, this figure is slightly higher than that reported in many other studies. Psoriatic nails ONM were equal in both males and females (50% vs 50%). The frequency of ONM in psoriatic nails after MTX therapy using PCR was also high as patients with PCR positive results after treatment 7%.

Conclusion: The need for obligatory mycological testing of all nail Ps patients before and after therapy as large number of patients with nail Ps were diagnosed to have ONM. PCR was more sensitive and specific in fungus detection.

Key words: Psoriasis is (Ps), Onychomycosis (ONM), KOH, culture, PCR.
Introduction

Psoriasis is (Ps) one of the most common causes of abnormal nail morphology and for the development of nail dystrophy (1).

Onychomycosis (ONM) is a common nail problem, treatment of ONM usually requires systemic antifungal agents, which may have significant side-effects, and it is thus essential to identify the causative organisms before starting systemic treatment. The current methods for diagnosing ONM include potassium hydroxide (KOH) microscopy, fungal culture, nail plate biopsy and microscopy, each of which has its own merits and drawbacks. Recently, polymerase chain reaction (PCR) has been used to detect the causative organisms in ONM with varying success (2).

In many patients with Ps, nail changes morphologically resemble ONM. In these cases, additional diagnostic procedures are essential to exclude the presence of concomitant fungal infection (3). Both Ps and ONM are common diseases in the general population. It is possible that in some patients the two diseases co-exist (4).

Methotrexate (MTX) is used as a cost-effective treatment for moderate to severe Ps (5). In treating both skin and nail Ps, the experts agreed that systemic therapies will most likely be required besides topical therapy; their choice for first-line systemic therapy would be MTX (6).

Patients and methods

This is a clinical trial study conducted on patients of nail Ps who selected from those attending the Dermatology and Andrology clinic, Benha University Hospital in the period from October 2014 to 2015. Psoriasis was diagnosed clinically and patients were selected from different age and sex groups. This study was approved by the Research Ethics Committee at Faculty of Medicine, Benha University. The study will include 20 patients of nail psoriasis attending to Benha University Hospital out-patient clinic. Ten apparently normal volunteers with matched age and sex with patients group will be selected as a control group. There was acceptance from subjects who participated in this study. All participants will sign an informed written consent.

Any patient with any of the following conditions will be excluded from the study

-
• Age below 18 years
• Pregnant and lactating women
• History of tuberculosis or any active infectious disease
• Systemic disease
• Previous treatment with any systemic antipsoriatic therapy or phototherapy within one month or application of topical antipsoriatic therapy within 7 weeks prior to the study initiation.

All patients were subjected to
• Detailed history taking
• Initial screening
• PASI score evaluation

Plaques were graded based on three criteria: redness (R), thickness (T), and scaliness (S). Severity was rated for each index on a 0-5 scale (0 for no involvement; 5 for severe involvement). The body was divided into 7 regions: head (h), upper extremities (u), trunk (t), and lower extremities (l). In each of these areas, the total surface area (A) affected was graded on a 0 to 7 scale (0, no involvement; up to 70% involvement) ($\alpha$).

Table 1: PASI score evaluation

<table>
<thead>
<tr>
<th>Score</th>
<th>0</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>7</th>
</tr>
</thead>
<tbody>
<tr>
<td>Erythema(E) None</td>
<td>Slight</td>
<td>Moderate</td>
<td>Severe</td>
<td>Very severe</td>
<td>-</td>
<td>-</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Induration(I) None</td>
<td>Slight</td>
<td>Moderate</td>
<td>Severe</td>
<td>Very severe</td>
<td>-</td>
<td>-</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Desquamation(D) None</td>
<td>Slight</td>
<td>Moderate</td>
<td>Severe</td>
<td>Very severe</td>
<td>-</td>
<td>-</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Area(A) 0</td>
<td>1</td>
<td>2,3</td>
<td>4,5</td>
<td>6,7</td>
<td>8,9</td>
<td>10,11</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

The sum of values of erythema, induration and desquamation is multiplied by value of the area, then by $\cdot \lambda$ for head (h), $\cdot \gamma$ for trunk (t), $\cdot \alpha$ for upper limbs (u) and $\cdot \xi$ for lower limbs (l).

The composite PASI score can then be calculated: PASI = $\cdot \lambda (Rh + Th + Sh) Ah + \cdot \gamma (Ru + Tu + Su) Au + \cdot \alpha (Rt + Tt + St) At + \cdot \xi (Rl + Tl + Sl) Al$.

Interpretation of PASI score:
- If PASI score < 20: mild psoriasis
- If PASI score 20 - 10: moderate psoriasis
- If PASI score > 10: severe psoriasis

ξ-NAPSI score evaluation

**Table (\(\Upsilon\))**: Outline of NAPSI score evaluation

<table>
<thead>
<tr>
<th>Finger nails</th>
<th>ξ</th>
<th>R¹</th>
<th>R²</th>
<th>R³</th>
<th>R⁴</th>
<th>L¹</th>
<th>L²</th>
<th>L³</th>
<th>L⁴</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nail matrix psoriasis</td>
<td>ξ</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nail bed psoriasis</td>
<td>ξ</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Toe nails</td>
<td>ξ</td>
<td>R¹</td>
<td>R²</td>
<td>R³</td>
<td>R⁴</td>
<td>L¹</td>
<td>L²</td>
<td>L³</td>
<td>L⁴</td>
</tr>
<tr>
<td>Nail matrix psoriasis</td>
<td>ξ</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nail bed psoriasis</td>
<td>ξ</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

The nail is divided into ξ quadrants. Each quadrant is evaluated for presence of any features of nail bed psoriasis (\(\cdot\) - ξ) and nail matrix psoriasis (\(\cdot\) - ξ). Score is ξ if no sign of nail bed involvement is present in any quadrant. Score is ξ if signs of nail bed involvement are present in all ξ quadrants. Score for matrix is calculated in a similar way (\(\wedge\)).

σ-Examination of nail material in patients with nail psoriasis and control group by:
  - Direct microscopic examination: (\(\wedge\)σ KÖH wet mount)
  - Culture on Sabouraud agar
  - Detection of Fungal DNA by PCR

\(\wedge\)-Patients will receive treatment with MTX once a week. The total course of treatment will be \(\wedge\) weeks
After the course of the treatment, another nail samples will be collected from patients for direct microscopic examination with KOH, culture on Sabouraud agar and for PCR assay.

**Results**

The result of this study showed that there was statistically significant difference between PASI scores before and after MTX therapy (M ± SD: \(12.01\pm 2.0\) vs \(1.0\pm 0.1\), \(P<0.002\)). There was statistically significant difference between NAPSI scores before and after therapy (M ± S.D: \(31.05\pm 2.0\) vs \(21.20\pm 2.0\), \(P<0.002\)) (Chart 1). There was positive but insignificant correlation between degree of PASI score improvement and NAPSI score improvement on MTX therapy (\(r=0.215\), \(P=0.151\)). There was a negative but insignificant correlation between NAPSI before treatment and duration of Ps (\(r=-0.11\), \(P=0.21\)). NAPSI before treatment showed non significant difference as regards sex (\(P=0.66\)).

NAPSI score before treatment showed non significant difference between negative and positive patients by PCR (M ± S.D: \(31.0\pm 2.0\) vs \(32.1\pm 2.0\), \(P=0.9\)) (Chart 4). The frequency of ONM in patients with nail Ps was calculated, total number of patients with PCR positive results =\(57\%,\) total number of patients with PCR negative results before treatment =\(43\%.\) This figure is slightly higher than that reported in many other studies, and this could be because of the features of study population (Chart 5). Psoriatic nails ONM were equal in both males and females as \(50\%\) vs \(50\%).\) The frequency of ONM in psoriatic nails after MTX therapy using PCR was also high as total number of patients with PCR positive results after treatment =\(7\%,\) total number of patients with PCR negative results after treatment =\(93\%).\) KOH microscopy, culture and PCR respectively yielded positive rates before treatment and after treatment as \(11.57\%, 1.57\%\) and \(57\%\) vs \(4\%, 7\%\) and \(7\%)\) respectively. Thirteen patients out of \(13\) positive patients became more severe after treatment by PCR, however not detected by KOH or culture. The sensitivity and specificity for PCR and KOH was \(0.57\) and \(0.5\) respectively before treatment and was \(0.7\) and \(0.9\) respectively after treatment with MTX. PCR was more sensitive and specific in fungus detection before (area
under curve PCR=0.5%, KOH=0.51) and after therapy (area under curve PCR=0.5%, KOH=0.5) (Charts 4 & 5).

Chart 1: Comparison of PASI and NAPSI before and after treatment

Chart 2: Results of NAPSI scores before treatment as regards to PCR
Chart 3: Results of PCR before and after treatment

Chart 4: ROC curve for KOH and PCR before treatment
Chart 5: ROC curve for KOH and PCR after treatment
**Patient no. (12)**  
A: Fingers of the right hand before treatment.  
B: Fingers of the left hand before treatment.  
C: Thumbs before treatment.  
Discussion

The evaluation of nail Ps was done in a subjective way. The NAPSI was suggested as a standardized means of evaluating and following-up the nail disease. Its application on nail evaluation during treatment demonstrated that NAPSI can be considered a good tool for progression follow-up of patients (9 & 11). NAPSI does not take into consideration the number of lesions, but only their presence or absence (11).

The NAPSI was found an easy and quick procedure, and can bring information about changes in plate and matrix. The NAPSI does not quantify the lesions and may not have the sensitivity to detect small changes. However, this method proved to be capable of detecting

changes in nail lesions numerically, and it can be used for global assessment of the topical or systemic treatment (17).

Onychomycosis is a fungal infection of the nail plate caused by dermatophytes, yeast and moulds. ONM is the most common nail disease worldwide and constitutes about half of all onychopathies. Both Ps and ONM are common diseases in the general population (17).

Patients with nail Ps have increased risk for ONM. Studies have suggested that it is mainly due to structural changes of nail Ps. However, there are no studies of the genetic role that could present these patients. It was suggested that there is genetic susceptibility of ONM in nail Ps by HLA-DR^1 and HLA-DR^2, which increases susceptibility to fungal infection in nail Ps (17).

The aim of this study was to evaluate the frequency of ONM in patients with nail Ps by PCR, to compare the detection rates by PCR with those of microscopy with KOH and culture in nail specimens and to detect the rate of clinical and mycological cure of psoriatic nails after MTX therapy.

Methotrexate has been widely used as an effective systemic therapy for Ps for 46 years ago (15). In this study, PASI score were calculated before and after MTX therapy. There was statistically significant difference between PASI scores before and after therapy (M ± SD: 12.01 ± 2% vs 12% ± 0.1%, P < 0.002).

In the study by (61) comparing MTX and cyclosporine in patients with severe Ps, by mean dose of MTX 2767 mg weekly for 1 month showed a more rapid clinical response in MTX group, with a 6964: improvement in mean PASI (patient number 36). In a study by (17) treated patients by mean dose of MTX 15 mg weekly for 12-week, mean PASI change from
baseline was 58% (patient number 84). In a study by (19) used mean dose of MTX 25 mg weekly after 16 weeks achieved PASI 35% for MTX (patient number 110) and 18.9% for placebo.

In a study by (14) showed that MTX administered at a dosage of at least 15 mg weekly for 16 weeks effectively cleared Ps, with a 75% reduction in mean PASI relative to baseline. Overall, data suggested that patients with moderate to severe Ps achieve a 64–66% improvement in mean PASI during the first 4–6 months of MTX therapy.

Psoriasis often was controlled at a mean dosage of 15 mg/week; after 8 weeks of MTX therapy, approximately 75% of patients were achieved a 75% improvement on the PASI 75 (14).

In study by (21) showed that MTX administered by a flexible dose increase scheme, 12 or 16 weeks, 45.6% of patients achieve PASI75 (patient number 765) compared to a calculated PASI75 of 44.4 for placebo.

In the current study, NAPSI scores were calculated before and after MTX therapy. There was statistically significant difference between NAPSI scores before and after therapy (M ± S.D: 32.05 ± 17.08 vs 18.4 ± 15.68, P<0.001).
Both MTX and cyclosporine were effective in treatment of psoriatic nails. After 24 weeks of treatment (M ± SD: 1866 ± 1165 vs 2568 ± 1962, P = .6627). There was no significant difference in the reduction in the mean NAPSI score at the end of treatment between the two groups. The relative reduction in the scores from baseline to 24 weeks of treatment was non significant (4363 vs 3762, P = .6649). MTX was found to be more effective on nail matrix lesions, whereas cyclosporine was more effective in nail bed involvement (r1).

MTX may produce benefit to nail Ps in tandem with skin improvement. It does not thin the nail in the same manner as acitretin (r2). Acitretin may decrease the thickness of the nail resulting in nail atrophy and fragility. Therefore patients with thickened nails and severe subungual hyperkeratosis are better candidates for acitretin treatment (r3).

In study by (r4) treated 317 patients with MTX for 52 weeks and showed a 48% NAPSI improvement, (r5) reported a patient who had a complete resolution of all 36 nails affected by psoriasis within 9–13 months with 5 mg/week systemic MTX; he had no skin involvement and did not respond to topical therapies.

In study by (r6) studied the fingernail growth after MTX treatment and showed significantly slower growth (t=21.51, P < .002). The greatest suppression of nail growth has been found during MTX therapy. MTX has a marked suppressive effect on the epidermis in that it decreases epidermal cell division and DNA synthesis. In study by (r7) suggested that MTX treatment is not ideal as it significantly slows the growth of nails. In these cases, biological treatment is efficient, but this kind of treatment is usually given to patients suffering from severe forms of Ps.
Nail Ps was also improved with other treatment modalities. In an open-label study of moderate to severe isolated nail Ps treated with low dose acitretin 0.1–0.3 mg/kg/day, after 6 months there was a 17% mean reduction in their NAPSI score (patients number=31) (4,8). Infliximab produced a significant reduction in NAPSI scores by week 20, with continued improvement at week 50 that was sustained through week 100, the mean improvement in NAPSI score from baseline to week 50 was 47.1% (9,10). In a study of 82 patients with psoriatic arthritis and concurrent psoriatic nail dystrophy, adalimumab achieved a mean reduction of 60% in NAPSI score at week 21, with continued improvement to week 100 (11). An unblinded study was designed to evaluate the efficacy and safety of adalimumab in the treatment of nail Ps. Mean NAPSI at baseline and at 21 week in patients with cutaneous Ps M ± SD was (1.0 ± 2.1) vs 0.9 ± 0.8 for the fingernails and 1.5 ± 2.0 vs 1.3 ± 1.1 for toenails (12). NAPSI score was improved by 41% after 24 weeks of etanercept therapy (13). Alefacept, with three of six patients were achieving ≥30% or greater improvement in NAPSI after 21 weeks. Ustekinumab, with median improvement of 200 in NAPSI score at week 20.

In the current study, there was positive but insignificant correlation between degree of PASI score improvement and NAPSI score improvement on MTX therapy (r = 0.185, P=0.215). Simple linear correlation showed weak association between PASI improvement and NAPSI improvement (r=0.185, P=0.177) (14). In study by (15) did a comparative study to find out the correlation between the NAPSI score and N-NAIL score with the severity of the disease using PASI score. First group included patients with PASI score <7 (n=5) and a second group included patients with PASI score >7 (n=5), the two groups showed significant difference as regards PASI improvement (P=0.01) and sex (P=0.33) and showed insignificant difference as regards NAPSI improvement (P=0.35) and age (P=0.7).
In the current study, there was a negative but insignificant correlation between NAPSI before treatment and duration of Ps ($r=-0.11, P=0.21$).

Duration of psoriasis was significantly higher in patients with psoriatic nail change than psoriatic patients without nail change ($r^2$). The group of patients with nail disease had longer disease duration ($\gamma \cdot \gamma \cdot \gamma$ vs $\gamma \cdot \gamma \cdot \gamma \cdot \gamma$ years) ($r^\gamma$). The disease duration may also influence the severity of the nail lesions observed. Patients with nail involvement have usually had cutaneous manifestations of Ps for a longer time than those without nail involvement ($r^\gamma; \gamma^\gamma \& r^\gamma$). Nail Ps has been shown to be associated with longer duration of skin lesions. There is an association between the duration of Ps and the severity of nail involvement ($r^\gamma$). Nail Ps is also associated with higher disease severity ($r^\gamma$). Duration of psoriatic skin lesions was significantly longer in patients with nail changes (mean duration $\gamma \cdot \gamma \cdot \gamma \cdot \gamma$ years) than in those without nail changes (mean duration $\gamma \cdot \gamma \cdot \gamma \cdot \gamma$ years) ($P=\gamma \cdot \gamma \cdot \gamma \cdot \gamma$ ($r^\gamma$).

In this study, NAPSI before treatment showed non significant difference as regards sex ($P=\gamma \cdot \gamma \cdot \gamma \cdot \gamma$). In study by ($r^\gamma$) found non significant difference in the mean NAPSI score between males and females, by ($r^\gamma$) found no differences between male and female ($P=\gamma \cdot \gamma \cdot \gamma \cdot \gamma$). While ($r^\gamma$) found that the NAPSI score tended to be lower in women ($P=\gamma \cdot \gamma \cdot \gamma \cdot \gamma$).

In healthy nails, the compact orthokeratotic nail plate acts as a natural barrier preventing the development of fungal infections, which may be disturbed in abnormal nail plates in diseases such as nail Ps. Therefore, it is hypothesized that the prevalence of ONM in patients with nail Ps might be higher than in the general population ($r^\gamma \& r^\gamma$). In normal nails, the hyponychium provides protection against entry of organisms, in Ps involving the distal nail bed this defense may be lost resulting in distal ONM ($r^\gamma \& r^\gamma$). On the contrary ($r^\gamma$) suggested that the immune response against microbial skin infections appears to be remarkably strong in Ps, and the fast turnover of the nails in Ps patients may constitute an effective defence against dermatophytes. Therefore, a decreased prevalence of ONM might be possible as well.
In the current study, nail changes severity in patients with Ps were not a predisposing factor for the development of ONM. NAPSI score before treatment were calculated for patients according to PCR results. NAPSI score before treatment showed non significant difference between negative and positive patients by PCR (M ± S.D: 31.9 ± 21.2 vs 32.1 ± 20.3, P = 0.5).

In study by (41) could not find any significant difference in the NAPSI scores between these ONM group and non ONM group; hence suggest that the severity of nail infection cannot be used as a marker for ONM a finding which was also reported by (42).

On the other hand, (43) found that nail changes were more severe in patients with ONM, suggesting that the presence of fungal infection may intensify nail Ps through köebner effect. In study by (44) showed that psoriatic patients with concomitant ONM have higher NAPSI scores for fingernails (>9.0) than that without ONM (<8.0). In study by (45) suggested that a higher NAPSI score means a more distracted nail unit barrier and as a result, an easier penetration of the pathogenic microorganisms.

In the current study, the frequency of ONM in patients with nail Ps was calculated. Nail scrapings collected from patients before therapy were examined using PCR. Total number of patients with PCR positive results =57%, total number of patients with PCR negative results before treatment =53%. This figure is slightly higher than that reported in many other studies, and this could be because of the features of study population (majority of the patients were farmers, housewives and in other occupations involving manual work which may independently increase the risk of ONM).

In study by (46) found that the spread of pathogens in the psoriatic group is different from that in the general population, because of the relatively high rate of yeast colonization. Psoriatic nail were found to have higher incidence of ONM as reported by (47) (47); (48) (<4.2); (49) (4.7); (48) (4.8) and (48) (4.7). In study by (46) showed that 13 patients out of 21 patients with psoriatic nail change evidence of ONM were found (47). In study by (46) showed that 22 patients out of total of 111 psoriatic patients had concomitant ONM (47).
The presence of fungal nail infection in psoriatic nails and its significance is a matter of controversy. Many studies reported a prevalence rate of ONM to be less than 30% in patients with psoriatic nail disease (56; 57; 51; 3; 51; 46). Other reports believe that the rapid growth of the nails is a cause for the lack of difference in the incidence of ONM in patients with Ps and people without the disease and found that the incidence of ONM in patients with Ps is identical to that of the general population (45) (275; 115; 43; 115; 61; 4.65; 61; 115; 62; 115).

In this study, psoriatic nails ONM were equal in both males and females as \( \frac{50}{70} \text{ vs } \frac{50}{70} \). This result was in consistent with (2%) as fungal agent was isolated in \( \frac{70}{70} \) men and \( \frac{70}{70} \) women out of \( \frac{70}{70} \) psoriatic patients. On the other hand (\( \frac{70}{70} \)) found higher prevalence of ONM in psoriatic nails in males \( (P < \cdots \cdot \cdot \cdot \cdot ) \).

In general population results of various studies showed no sex predilection in the prevalence of ONM (\( \frac{70}{70} \; \frac{70}{70} \; \frac{70}{70} \) and \( \frac{70}{70} \)).

In a study by (\( \frac{70}{70} \& \; \frac{70}{70} \)) suggested that males were found to have twice or three times as likely ONM than females, which they attributed to the suggestion that men exercise more, increased trauma and longer use of occlusive footwear as perspiration of the feet when wearing socks and/or shoes can generate a warm moist environment. On the contrary (\( \frac{70}{70} \)) found that the male to female ratio was \( \frac{70}{70} : \frac{70}{70} \), with a predilection for females probably because females see the doctor more often or for cosmetic reasons. In study by (\( \frac{70}{70} \)) showed that Candidal ONM was more common in females; this has been attributed to greater burden of wet work with increased trauma facilitating easy entry to fungal pathogens.

In the current study, the frequency of ONM in psoriatic nails after MTX therapy using PCR was also high as total number of patients with PCR positive results after treatment = \( \frac{70}{70} \) (\( \frac{70}{70} \)), total number of patients with PCR negative results after treatment = \( \frac{70}{70} \) (\( \frac{70}{70} \)).
In study by \( (\xi \lambda) \) found that in \( \ll \) cases, the ONM had been present prior to the start of treatment and in four cases it appeared during treatment with MTX. \((\xi \lambda & \xi \lambda)\) suggested that some antipsoriatic therapies, such as MTX and cyclosporine, might alter the immune status, promoting ONM development. Faster outgrowth of psoriatic nails might delay the development of ONM, while the fungal infection might induce Köebnerization and delay or inhibit an antipsoriatic drug’s action. In study by \((\xi \lambda)\) found that additional risk factors for ONM were as included: intake of MTX (current or preceding) \((\%7)\); diabetes \((\%7)\); administration of topical corticosteroids \((\%7)\); the presence of mycoses in the family \((\%7)\). That required the inclusion of antifungal therapy to the other antipsoriatic therapy, regardless of the low success rate was warranted as the added fungal infection could lead to even greater worsening of the nail status of patients.

Differentiation between the two may be difficult. Furthermore, the continued use of oral terbinafine, which is the most frequently prescribed antifungal agent because it is highly effective and has little hepatotoxicity, may aggravate Ps; some have reported that terbinafine may induce the de novo development of psoriatic lesions or exacerbate preexisting Ps \((\bar{\gamma})\). Therefore, oral itraconazole or topical antifungal preparations should be used in patients with Ps and a concomitant fungal infection \((\gamma \cdot \gamma)\).

KOH procedure is only a screening test for the presence or absence of fungi and can't identify the type or the species \((\xi \bar{\eta})\). Fungal culture can identify specific pathogen but it takes a long incubation period. The false negative rate of fungal culture is approximately \(\gamma \cdot \%\) and the sensitivity was about \(\%7\) \((\gamma \gamma)\). PCR is an adequate tool for the diagnosis of dermatophytic ONM. It is much adapted to cases where culture is negative or contaminated by overgrowing moulds, which makes the identification of the causal agent problematic \((\gamma \gamma \bar{\eta})\).

In the current study, KOH microscopy, culture and PCR respectively yielded positive rates before treatment and after treatment as \((\gamma \gamma \cdot \%\), \(\gamma \gamma \cdot \%\) and \(\gamma \%\) vs \(\gamma \cdot \%\), \(\gamma \cdot \gamma\) and \(\gamma \gamma \cdot \%\)\) respectively. Thirteen patients out of \(\gamma \gamma\) positive patients became more severe after treatment by PCR, however not detected by KOH or culture.
In this study, mycological culture was chosen as the reference method to assess the performance of other tests. The sensitivity and specificity for PCR and KOH was \( \cdot.0^{\circ}\) and \( \cdot.0^{\circ}\) respectively before treatment and was \( \cdot.0\%\) and \( \cdot.0\%\) respectively after treatment with MTX.

In total, \( \cdot.0\) patients with clinically suspected ONM were using a topoisomerase II-based PCR, compared the detection rate of dermatophytes for the three methods KOH microscopy, culture and PCR respectively that yielded positive rates of (\( \cdot.0\%\), \( \cdot.0\%\) and \( \cdot.0\%\)), and negative rates of (\( \cdot.0\%\), \( \cdot.0\%\) and \( \cdot.0\%\)). Two culture-positive specimens were not detected by PCR, but PCR picked up \( \cdot.0\) specimens missed by culture. This study demonstrates that PCR has a higher positive and lower negative rate for detection of dermatophytes compared with KOH microscopy or culture. PCR should be used as a complementary method for confirmation of clinically suspected dermatophytic ONM (\( \cdot.0\)).

In the current study KOH and PCR results were compared by culture results as standard method for fungus detection in nail Ps in order to detect the most sensitive and specific method, PCR was more sensitive and specific in fungus detection before (area under curve PCR=\( \cdot.0\), KOH= \( \cdot.0\)) and after therapy (area under curve PCR=\( \cdot.0\), KOH= \( \cdot.0\)).

In study by (\( \cdot.0\)) concluded that the sensitivity of the PCR was \( \cdot.0\%\) and showed a significant increase in detection rate for dermatophytes in clinical samples compared to culture. Also, (\( \cdot.0\)) concluded that KOH had a sensitivity of \( \cdot.0\%\) whereas mycological culture was of \( \cdot.0\%\) sensitivity.

**Conclusion**

The need for obligatory mycological testing of all nail Ps patients before and after therapy as large number of patients with nail Ps were diagnosed to have ONM. PCR was more sensitive and specific in fungus detection before (area under curve PCR=\( \cdot.0\), KOH= \( \cdot.0\)) and after therapy (area under curve PCR=\( \cdot.0\), KOH= \( \cdot.0\)).
References

Diagnosis of nail psoriasis: importance of biopsy and histopathology.

Evaluation of PCR for the diagnosis of dermatophytes in nail specimens from patients with suspected onychomycosis. British Asso. of Dermatologists.

Prevalence and epidemiology of unsuspected onychomycosis in patients visiting dermatologists’ offices in Ontario, Canada: a multicenter survey of 1001 patients.

Do fungi play a role in psoriatic nail?
Mycoses; 50: 231-221.

Methotrexate and psoriasis in the era of new biologic agents.


(7) Naldi, L. (2011):

Fingernail psoriasis reconsidered: A case-control study.

Infliximab induction and maintenance therapy for moderate-to-severe psoriasis: a phase III, multicentre, double-blind trial.

Therapeutic effects of a 21-week course of alefacept on nail psoriasis.

Modification of the nail psoriasis severity index.

NAPSI utilization as an evaluation method of nail psoriasis in patients using acitretin.

Forty-eight-hour diagnosis of onychomycosis with subtyping of Trichophyton rubrum strains.

Role of HLA-DR Alleles to Increase Genetic Susceptibility to Onychomycosis in Nail Psoriasis.
Skin Appendage Disord.; 1:11-15.

Efficacy and safety results from the randomized controlled comparative study of adalimumab vs. methotrexate vs. placebo in patients with psoriasis (CHAMPION).

Efficacy and safety of cyclosporine versus methotrexate in severe psoriasis: a study from north India.

J. Dermatol.; 30: 251-

(*) Flytstrom, I.; Stenberg, B.; Svensson, A. and Bergbrant, I.M. (17):

Methotrexate vs cyclosporin in psoriasis: effectiveness, quality of life and safety. A randomized controlled trial.


(*) Heydendael, V.M.; Spuls, P.I.; Opmeer, B.C.; de Borgie, C.A.; Reitsma, J.B.; Goldschmidt, W.F.; Bossuyt, P.M.; Bos, J.D. and de Rie, M.A. (13):

Methotrexate versus cyclosporine in moderate-to-severe chronic plaque psoriasis.


Relationship between methotrexate dosing and clinical response in patients with moderate to severe psoriasis: Subanalysis of the CHAMPION study.


(*) West, J.; Simon, O. and John, F. (16):

Safety and Efficacy of Methotrexate in Psoriasis: A Meta-Analysis of Published Trials.

PLOS. ONE; 22(5): 22-22.

(*) Gümüşel, M.; Özdemir, M.; Mevlitoğlu, I. and Bodur, S. (11):

Evaluation of the efficacy of methotrexate and cyclosporine therapies on psoriatic nails: a one-blind, randomized study.


(*) Berker, D. (11):

Management of nail psoriasis.


(*) Tan, E.S.; Chong, W.S. and Tey, H.L. (12):

Nail psoriasis: a review.

A 51-week trial comparing briakinumab with methotrexate in patients with psoriasis.  

Lee, J.Y. (20\textbullet{}):  
Severe nail psoriasis successfully treated by low dose methotrexate.  
Dermatol. Online J.; \textbullet{} \textcopyright{} 2009; \textbullet{} Rapkin.  

Dawbek, R.P.R. (20\textbullet{}):  
The Effect of Methotrexate, Corticosteroids and Azathioprine on Fingernail Growth in Psoriasis.  
Br. J. Derm.; \textcopyright{} 2010; \textbullet{} Rapkin.  

Rigopoulos, D.; Gregoriou, S. and Lazaridou, E. (20\textbullet{}):  
Treatment of nail psoriasis with adalimumab: an open label unblended study.  
J. E. A. D. V.; \textbullet{} \textcopyright{} 2010; \textbullet{} Rapkin.  

Hussain, W.; Coulson, I. and Owen, C. (20\textbullet{}):  
Severe recalcitrant nail psoriasis responding dramatically to infliximab: report of two patients.  
Clin. and Exp. Dermatol.; \textbullet{} \textcopyright{} 2010; \textbullet{} Rapkin.  

Reich, K.; Ortonne, J. P.; Kerkmann, U.; Wang, Y.d.; Saurat, J.H.; Papp, K.F.; Langley, R.G. and Griffiths, C.E.M. (20\textbullet{}):  
Skin and nail responses after 1 year of infliximab therapy in patients with moderate-to-severe psoriasis: a retrospective analysis of the EXPRESS trial.  
Dermatol.; \textbullet{} \textcopyright{} 2010; \textbullet{} Rapkin.  

Effectiveness of adalimumab in treating patients with active psoriatic arthritis and predictors of good clinical responses for arthritis, skin and nail lesions.  
Ann. Rheum. Dis.; \textbullet{} \textcopyright{} 2010; \textbullet{} Rapkin.  

Luger, T.A.; Barker, J. and Lambert, J. (20\textbullet{}):  

Sustained improvement in joint pain and nail symptoms with etanercept therapy in patients with moderate-to-severe psoriasis.


Ustekinumab in nail psoriasis: an openlabel, uncontrolled, nonrandomized study.

(⁷⁶) Sharada, R.G. and Thomas, J. (⁷⁶):
A Study on Psoriasis of Nails-Severity Scoring System.

Frequency of nail changes in patients with psoriasis reporting to PNS, Shifa Naval Hospital, Karachi.

(⁷⁴) Armesto, S.; Esteve, A.B.A.; Coto-Segura, C.P.; Drake, C.M.; Galache, A.C.; Martínez-Borra, C.J. and Santos-Juanes, D. J. (⁷⁴):
Nail Psoriasis in Individuals with psoriasis vulgaris: A Study of Patients.

(⁷³) Augustin, M.; Reich, K.; Blome, C.; Schafer, I.; Laass, A. and Radtke, M.A. (⁷³):
Nail psoriasis in Germany: epidemiology and burden of disease.

(⁷²) Baran, R. (⁷²):
The burden of nail psoriasis: an introduction.
Dermatol.; 171: 0–5.

A significant association exists between the severity of nail and skin involvement in psoriasis.

Disease severity, quality of life and health care in plaque type psoriasis: a multicenter cross-sectional study in Germany.

Dermatol.; vol. 12%, no. 2%–3.

Coexistence of onychomycosis in psoriatic nails: a descriptive study.
Indian J. Dermatol. Venereol. Leprol.; 2%:2%–2%.

Nail psoriasis: a retrospective study on the effectiveness of systemic treatments (classical and biological therapy).

(4) Elewski, B.E. (4):
Onychomycosis: pathogenesis, diagnosis, and management.

Psoriatic nails: a prospective clinical study.
J. Cutan. Med. Surg.; 2%:2%–2%.

(4) Avner, Sh.; Nathansohn, N. and Trau, H. (4):
Prevalence of onychomycosis in deformed nails of psoriatic patients and response to itraconazole.
J. Am. Acad. Dermatol.; 2%:2%–2%.


The prevalence, aetiological agents and therapy of onychomycosis in patients with psoriasis: a prospective controlled trial.
Clin. Exp. Dermatol.; 2%:2%–2%.


(4)
Onychomycosis in patients with psoriasis – a multicentre study.


Onychomycosis in psoriatic patients – rationalization of systemic treatment.

Mycoses; 34: 34-34.

(5) Zaias, N. (1977):
Psoriasis of the nail: A clinical-pathological study.


Onychomycosis in patients with psoriasis.


Mycotic infections of psoriatic nails.

Mycoses; 9: 47-51.

Nail psoriasis: a combined treatment with cloetasol nail lacquer and tacalcitol ointment.


Dermatophyte infection in psoriasis.


Frequency of appearing the mycosis of toe nails in patients suffering from psoriasis.


(5) Pawlaczyk, M.; Rokowska, A.; Chmielewska, I.; Janicka, D. and Gutowska-Ryters, A.
(1992):
Does onychomycosis more frequently affect patients suffering from psoriasis?


Dermatophyte and non-dermatophyte onychomycosis in Singapore.

Australas J. Dermatol.; 119: 129-123.

Prevalence of dermatophyte onychomycosis in the United Kingdom: results of an omnibus survey.

(¶) Kiraz, M.; Yegenoglu, Y.; Erturan, Z. and Ang, O. (¶): The epidemiology of onychomycosis in Istanbul, Turkey.

(¶) Ching, C.C.; Wang, S.H. and Chou, M.C. (¶): The causative pathogens of onychomycosis in southern Taiwan.


(¶) Hwang, S.M.; Suh, M.K. and Ha, G.Y. (¶): Onychomycosis Due to Nondermatophytic Molds.

(¶) Jesudanam, T.M.; Rama-Rao, G.R. and Lakshmi, D.J. (¶): Onychomycosis is a significant medical problem.

(¶) Kim, J.Y.; Baek, G.H. and Gong, H.S. (¶): Nail Dystrophy in Psoriatic Arthritis Presenting as Nail Onychomycosis: A Case Report.
Hand Surgery, Vol. 1, No. 1, 139 - 144.

(¶) Reisberger, E.M.; Abels, C. and Landthaler, M. (¶): Histopathological diagnosis of onychomycosis by periodic acid Schiff-stained nail clippings.


(¶) Wisselink, G.J.; van Zanten, E. and Kooistra-Smid, A.M. (¶):
Trapped in keratin; a comparison of dermatophyte detection in nail, skin and hair samples directly from clinical samples using culture and real-time PCR.


(\textsuperscript{\textregistered}) Shenoy M.M.; Teerthanath S.; Karnaker V.K.; Girisha B.S.; Krishna Prasad M.S.; Pinto J. (\textsuperscript{\textregistered} \textbullet\textregistered): 

Comparison of potassium hydroxide mount and mycological culture with histopathologic examination using periodic acid-Schiff staining of the nail clippings in the diagnosis of onychomycosis.