## **INVESTIGATIVE REPORT**

# Increased Prevalence of Onychomycosis among Psoriatic Patients in Israel

Vera LEIBOVICI<sup>1</sup>, Klilah HERSHKO<sup>2</sup>, Arieh INGBER<sup>1</sup>, Maria WESTERMAN<sup>1</sup>, Nurit LEVIATAN-STRAUSS<sup>3</sup> and Malka HOCHBERG<sup>1</sup>

Departments of <sup>1</sup>Dermatology, <sup>2</sup>Pathology, and <sup>3</sup>Biostatistics Consultant, Hadassah University Hospital, Jerusalem, Israel.

Published data on the prevalence of onychomycosis in psoriasis patients compared with healthy controls are controversial, We therefore conducted a prospective study of toenail onychomycosis, among 113 psoriatic and 106 healthy non-psoriatic subjects, selected from the normal population in the Jerusalem area in the period 2003-05.

The results revealed a prevalence of 47.6% to enail onychomycosis among psoriatic patients, compared with 28.4% in normal controls (p=0.0054).

Both gender and age affected the prevalence of onychomycosis in both psoriatic and healthy controls, with a higher prevalence in male and elderly subjects. The type and duration of psoriasis were also found to have an impact on the prevalence of onychomycosis. However, the body area involved did not affect the prevalence of onychomycosis in psoriatic patients. Approximately the same percentages of dermatophytes and yeasts were found in psoriatic patients as in healthy controls. However, a higher percentage of moulds was found in psoriatic patients. *Key words: onychomycosis; psoriasis; prevalence.* 

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Vera Leibovici, Department of Dermatology, Hadassah University Hospital, PO Box 12018, IL-91120 Jerusalem, Israel. E-mail: doctor\_ima@yahoo.com

Onychomycosis is a fungal infection of the nails that is very common worldwide. Recent scale surveys of onychomycosis in the general population of the USA and Canada have shown an incidence of 14% (1) and 6.5% (2), respectively. By comparison, the 'Achilles' project, the largest survey of onychomycosis in 20 European countries, revealed an incidence of 29% (3). Onychomycosis has been reported as gender- and age-related, being more prevalent in males and increasing with age in both genders (4). Increased incidence of onychomycosis is associated with various conditions, such as peripheral arterial disease, diabetes mellitus, immunosuppression caused by HIV or immunosuppressive agents employed in various diseases, such as organ transplantation and malignant diseases (5).

Reports on the incidence of onychomycosis in psoriasis offer highly variable data on prevalence, ranging from 10% to 30%, and up to 56%. Psoriatic nail pathologies, such as pitting, subungual hyperkeratosis, oil spots and onycholysis, are difficult to distinguish clinically from onychomycosis, and diagnosis relies on mycological tests.

In the study of Hammerius et al. (6), involving 239 psoriatic patients, the prevalence of onychomycosis was identical with that in the normal population. Staberg et al. (7) and Larsen et al. (8) encountered a higher prevalence of onychomycosis in psoriatic patients compared with patients with other skin diseases. A more recent study by Gupta et al. (9) showed that psoriatic patients had a 56% higher odds of developing onychomycosis compared with non-psoriatic patients. In view of these controversial data, we decided to conduct a comparative, prospective study of toenail onychomycosis in psoriatic and non-psoriatic subjects in the Jerusalem population.

## MATERIALS AND METHODS

## Patients and clinical examination

During the period 2003 to 2005, data were collected from 113 psoriatic patients (53 women and 60 men from the Dermatology Department and out-patient clinic at the Hadassah University Hospital in Jerusalem, Israel) and 102 non-psoriatic healthy controls, from the normal population (58 women and 44 men) recruited from parents and grandparents of children attending the outpatient clinic. The normal subjects had no dermatological diseases and had never consulted a general practitioner or dermatologist for nail problems. The study was approved by the Helsinki committee for clinical trials of the Hadassah Medical Center, and informed consent was obtained from all patients. Epidemiological and clinical data, including gender, age, type and duration of psoriasis, and area of body were recorded. The control group included subjects aged 14-84 years (median 45 years). The age of psoriatic patients ranged from 16 to 79 years (median 44 years). Duration of the disease was between 17 months and 70 years, and the area of body involved was 5–90%. Types of psoriasis included 11 palmo-plantar psoriasis and 102 plaque-type psoriasis.

#### Mycological examination

Nail samples were collected from clinically-affected nails of patients and examined by direct microscopy and cultured. Nail samples were dissolved in 30% potassium hydroxide, then direct microscopic examination was carried out. In parallel, nail samples were plated out on two different types of Sabouraud glucose agar (SDA, Hy-lb, Rehovot, Israel): one with cyclohexamide to select for dermatophytes and *Candida albicans*, and one without

Table I. Distribution of fungi among psoriasis subjects vs. controls

	Controls	Psoriasis n (%)	
	<i>n</i> (%)		
Candida albicans	2 (2)	1 (0.8)	
Candida parapsilosis	0 (0)	4 (3.5)	
Candida species	0 (0)	1 (0.9)	
Total yeasts	2 (2)	6 (5.2)	
Trichophyton Rubrum	23 (22.5)	40 (35.4)	
Trichophyton Mentagrophytes	4 (3.9)	2 (1.8)	
Total dermatophytes	27 (26.4)	42 (37.2)	
Scapuloriopsis brevicaulis	0 (0)	6 (5.2)	
Total moulds	0 (0)	6 (5.2)	
Total fungi	29 (28.4)	54 (47.6)	

cyclohexamide to isolate other yeasts and moulds. Cultures were incubated at 28°C for 2–4 weeks until colonies developed. Colonies were examined macroscopically and microscopically for identification of fungi genera and strain. The data was included only if both direct microscopy and culture were positive.

#### Statistical examination

Descriptive statistics for fungi and fungi group are given for each subject group. Basic descriptive statistics are given for gender and age. The association between fungus and subjects group was tested: (*i*) by  $\chi^2$  test models to compare psoriasis vs. normal subjects, and psoriasis vs. onychomycosis; and (*ii*) by models of logistic regression with specific fungus or fungi group as the dependent variable, and subject group, age and gender, type of psoriasis, duration of disease and area of body involved, as explanatory variables. Subject group (normal subjects, psoriasis and onychomycosis) is used in the model as a categorical variable. Stepwise selection method is used with entry testing based on the significance of the score statistic, and removal testing based on the probability of the Wald statistic.

## RESULTS

The prevalence of toenail onychomycosis in psoriatic patients was 47.6% vs. 28.4% in control patients (p=0.0054) (Table I). Both gender and age affected the prevalence of onychomycosis, causing higher prevalence in males (p < 0.0001) and older subjects (p=0.001) (Table IIa). Type of psoriasis and duration of the diseases was also found to have an impact on the prevalence of onychomycosis. The prevalence of onychomycosis was higher in the plaque-type psoriasis compared with the palmo-plantar type. The longer the psoriasis was present, the more the onychomycosis prevailed. Regarding the area of the involved body, it was found not to affect the prevalence of onychomycosis in psoriatic patients (Table IIb).

Mycological characterization of fungal isolates showed the following distribution: 37.2% dermatophytes (*T. rubrum* 35.4%, *T. mentagrophytes* 1.8%) 5.2% yeasts, 5.2% moulds in psoriatic patients compared with 26.4% dermatophytes, 2.0 yeasts and no moulds in healthy controls (Table I).

## DISCUSSION

The dermatological literature on the relationship between psoriasis and onychomycosis is ambiguous. Certain authors found no difference in the incidence of onychomycosis between psoriatic patients and the normal population (6, 7), or between these patients and patients with other skin diseases (8). Based on these results, a hypothesis has been proposed claiming that the rapid growth of psoriatic nails decreases the opportunity of fungi to invade these nails, and thus limit the prevalence of onychomycosis. However, our findings are in line with those of Gupta et al. (9) indicating that psoriatic patients have significantly higher odds of developing onychomycosis compared with non-psoriatic patients.

Table II. (a) Variables in the logistic regression model for total fungi (Y/N) and (b) Association of onychomycosis events in psoriasis group with psoriasis duration, psoriasis type, patient's age and gender and area of body involved, tested using a model of logistic regression

	B S		SE Wald	df	p	Exp(B)=odds ratio	95% CI for Exp(B)	
		SE					Lower	Upper
a)								
Gender	1.515	0.334	20.638	1	0.000	4.551	2.367	8.750
Age	0.044	0.010	20.478	1	0.000	1.045	1.025	1.066
Group	1.005	0.354	8.501	1	0.004	2.731	1.390	5.367
Constant	-3.935	0.616	40.845	1	0.000	0.020		
b)								
Gender	1.089	0.425	6.578	1	0.010	2.972	1.293	6.833
Duration	0.054	0.020	7.325	1	0.007	1.056	1.015	1.098
Psoriasis type	1.847	0.758	5.936	1	0.015	6.343	1.435	28.036
Constant	-3.468	1.018	11.613	1	0.001	0.031		

a) Model for *total fungi* (each variable is a Y/N variable, yeasts, moulds or dermatophytes), demonstrating higher probability of fungi in the psoriasis group vs. normal, p=0.004. Both gender and age are significant (p < 0.001 for both), meaning a higher proportion of positive fungi in males vs. females and in the older subjects.

b) The dependent variable is *total fungi* Y/N (yeasts, moulds or dermatophytes), and psoriasis duration, psoriasis type, patient's age and patient's gender and area of body involved are the explanatory variables. Psoriasis duration, type and gender are significant in the model (p=0.007, 0.015 and 0.010, respectively). Age and the area of body involved are not significant within the psoriasis group.

B: estimated coefficient in the logistic regression; SE: standard error; CI: confidence interval.

A possible explanation is that the abnormal capillary unit in psoriatic nails impairs the defence normally supplied by the healthy hyponychium, predisposing the nail to fungal infection (9–13).

In both psoriatic patients and normal controls, a higher prevalence of onychomycosis in males and elderly subjects was noted. The type of psoriasis and duration of disease were also found to have an impact on the prevalence of psoriasis.

Our findings indicate that the profile of dermatophytes and yeast isolates was similar in psoriatic patients and normal subjects, as reported in previous publications, but that there was a higher percentage of moulds in psoriatic patients.

Because it is impossible to determine the presence of onychomycosis in psoriatic nails by clinical examination alone, we suggest that all patients with subungual hyperkeratosis or onycholysis should be tested directly for the presence of fungi, in particular before the application of topical corticosteroids. If the presence of fungal infection is confirmed, management by antifungal drugs may prevent Koebnerization of the nail and adjacent skin, and spare these patients from unnecessary complications.

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