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Pharmacological implications of psoriasis and superficial fungal infections: Analysis of risk factors and underlying mechanisms

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Abstract: Psoriasis (Ps) is a chronic inflammatory skin condition that is often accompanied by superficial fungal infections, which may exacerbate disease severity and impact treatment effectiveness. This study investigates the association between fungal infections and psoriasis severity in the Kashgar region and identifies risk factors relevant to pharmacological interventions. A cross-sectional analysis was conducted among 196 psoriasis patients, evaluating clinical characteristics, psoriasis area severity index (PASI) scores, and the presence of fungal infections through microscopy and culture. Logistic regression analysis was used to identify independent risk factors, providing insights for targeted pharmacological approaches. Patients with fungal infections exhibited significantly higher PASI scores and longer disease duration ($P < 0.05$). Key risk factors included head and nail involvement. These findings suggest that managing fungal infections may optimize psoriasis treatment outcomes. This study highlights the link between fungal infections and psoriasis severity, advocating for integrated therapeutic strategies. The findings provide a foundation for future pharmacological research aimed at improving patient outcomes.

Keywords: Psoriasis, fungal infections, risk factors, PASI Score, pharmacological interventions, treatment optimization

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INTRODUCTION

Psoriasis is a chronic, multifactorial inflammatory disease characterized by an intricate pathogenesis that includes genetic predisposition and environmental influences1 (Sweet and Smoller, 1997). Recent studies suggest that superficial fungal infections can aggravate psoriasis symptoms, thereby impacting both disease severity and patient quality of life (Dascălu *et al*., 2024). This interaction between fungal infections and psoriasis not only complicates the clinical picture but also presents new opportunities for targeted therapeutic intervention (Langan *et al*., 2018). A deeper understanding of the role of fungal infections in psoriasis progression could inform the development of integrated treatment approaches that combine antifungal therapies with immunomodulatory agents, potentially leading to improved patient outcomes and optimized management strategies.

Psoriasis is a common chronic inflammatory skin disease that affects millions of people worldwide. Recent studies have shown that the interaction between psoriasis and superficial fungal infections may play a significant role in disease progression and treatment outcomes. However, the underlying mechanisms and risk factors for this association remain poorly understood. This study aims to fill this gap by investigating the relationship between fungal infections and psoriasis severity in a specific region (Kashgar) and identifying potential risk factors that could guide targeted pharmacological interventions. Our findings may provide new insights into the pathogenesis of psoriasis and contribute to the development of more effective integrated therapeutic strategies.

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MATERIALS AND METHODS

This cross-sectional study included 196 psoriasis (Ps) patients who received outpatient or inpatient treatment at our hospital from April 2022 to April 2024.

Inclusion criteria: (1) Diagnosis of Ps according to the Chinese Psoriasis Diagnosis and Treatment Guidelines (2023); (2) Patients who provided informed consent and voluntarily participated in the study.

Exclusion criteria: (1) Systemic corticosteroids or immunosuppressants within the past three months, systemic antifungal medications within three months, or topical antifungal treatments within two weeks before enrollment; (2) Severe primary diseases such as significant heart, liver, or kidney dysfunction (i.e., ALT, AST levels exceeding twice the upper limit of normal, or Cr above the upper normal limit); (3) Positive urine test, pregnancy, planning to become pregnant, or lactation; (4) History of nail disease, nail trauma; (5) Tuberculosis or cancer. Ethical approval was obtained from the Ethics Committee of the First People's Hospital of Kashgar Region, Xinjiang (Ethics Approval No.: KDYY-EC-SOP-008-03.0).

Clinical data collection

Clinical data collected included disease duration, age at onset, severity of skin lesions, and sites affected by lesions. The severity of psoriasis was assessed using the Psoriasis Area and Severity Index (PASI), with additional assessments for the presence of fungal infections.

Laboratory testing and interpretation of results

Sample Collection: Areas for sample collection were first disinfected with 75% ethanol. Skin scales from lesion margins were gently scraped with a blunt sterilized scalpel, discolored or brittle nail scrapings were collected, and scalp lesion samples were obtained either from scales or by extracting hair using sterile tweezers. The collected nail scrapings, scales, and hair served as the analysis samples.

Microscopy for Fungal Detection: Samples were placed on a clean slide with a drop of fungal fluorescent solution (Nanjing Hanrui Biotechnology Co., Ltd., Batch No.: 23120701), thoroughly mixed, and observed under a fluorescent microscope at low magnification to detect hyphae or spores as indicators of positive results.

Fungal Cultures: All samples underwent fungal culture on potato agar medium at 27°C for 1-3 weeks; colonies were considered positive. If no growth occurred after three weeks, the result was deemed negative. Samples suspected of containing Candida species were transferred to Chromagar medium and incubated at 37°C for 48 hours, with colony color used for identification. Species Identification: Morphological identification was performed using lactophenol cotton blue staining to observe conidia morphology under a microscope, and colony color was used to distinguish fungal species.

STATISTICAL ANALYSIS

Statistical analysis was conducted using SPSS 29.0 software. For normally distributed data, means and standard deviations ($\bar{x} \pm s$) were reported; non-normally distributed data were expressed as median (M, interquartile range Q1, Q3) and analyzed using t-tests or Mann-Whitney U tests. Categorical data were analyzed with the χ^2 test. Logistic regression was used to identify independent risk factors for fungal infection in Ps patients, with Ps fungal infection status as the dependent variable and sex, age, BMI, PASI, and palmar-plantar involvement as independent variables. A p-value < 0.05 was considered statistically significant.

RESULTS

Comparison of clinical characteristics between psoriasis patients with and without fungal infections

Patients in the Psoriasis with Fungal Infection group showed significantly longer disease duration and higher PASI scores compared to those without fungal infections ($P < 0.05$). Additionally, the proportion of patients with head and nail involvement was significantly higher in the fungal infection group ($P<0.05$). No statistically significant differences were observed in other clinical characteristics ($P> 0.05$). Details are provided in table 1.

Multivariate logistic regression analysis of fungal infection risk factors in psoriasis patients

Logistic regression analysis was performed using fungal infection status as the dependent variable. Statistically significant clinical variables and PASI scores (age and PASI score as continuous variables) were included as independent variables. The results identified disease duration, PASI score, head involvement, and nail involvement as significant risk factors for fungal infection in psoriasis patients ($P < 0.05$), as shown in Table 2.

DISCUSSION

Psoriasis (Ps) is a common chronic inflammatory disease with lesions that may cover the entire body, affecting skin appendages and mucous membranes. It significantly impacts the mental and physical health and quality of life of patients, affecting over 125 million people worldwide. In China, the prevalence of Ps is approximately 0.47%. The complex pathogenesis of Ps is thought to be related to chronic inflammation caused by immune system imbalances and abnormal keratinocyte proliferation. Some studies suggest that immune dysregulation plays a more significant role. Researchers believe that microbial imbalance on the skin and mucosa leads to immune responses in genetically susceptible hosts, triggering a chronic inflammatory process associated with autoimmune dysfunction (Christophers, 2010, Zhou and Yao, 2022). Fungal infections may play a direct or indirect role in the onset and progression of Ps.

In this study, the Ps group with fungal infections showed significantly longer disease duration and higher PASI scores than the non-infection group ($P < 0.05$). Furthermore, the proportions of head and nail involvement were higher in the fungal infection group ($P < 0.05$). Malassezia species were the most frequently identified fungi, followed by Candida (Campione *et al*., 2024). Malassezia, a lipophilic yeast from the Basidiomycota phylum, is a dominant resident fungus found primarily in the scalp, face, and chest, where sebum production is high (Baroni *et al*., 2010, MéndezTovar *et al*., 2015). Research analyzing the skin microbiota of Ps lesions, unaffected Ps skin, and healthy control skin on the back and elbow has shown that Malassezia species are more abundant in Ps lesions, particularly on the back, with Malassezia restricta dominating in the back lesions and Malassezia globosa in elbow lesions (Theelen *et al*., 2018, Stehlikova *et al*., 2019). Significant associations have also been observed between Corynebacterium, Lactobacillus, and Streptococcus species in Ps elbow lesions, which were not present in healthy skin (Fang *et al*., 2022, Gao *et al*., 2010). Patients with high levels of Malassezia distribution exhibited elevated PASI scores, neutrophils, eosinophils, peripheral blood leukocyte counts, and IgG levels compared to those with lower distribution. Rudramurthy *et al*. found higher carriage rates of Malassezia in Ps lesions than in controls.

Table 1: Comparison of clinical characteristics between psoriasis patients with and without fungal infections

Clinical Feature	No Fungal Infection (N=115)	Fungal Infection (N=81)	OR (Univariate Analysis)	OR (Multivariate Analysis)	OR (Combined Analysis)	
Age (years)	Mean ± SD	39.8 ± 17.7	39.4 ± 15.0	1.00 (0.98-1.02, p=.881)	-	-
Gender [n (%)]	Male	77 (67%)	51 (63%)	-	-	-
	Female	38 (33%)	30 (37%)	1.19 (0.66-2.16, p=.563)	-	-
Hypertension [n (%)]	No	87 (75.7%)	64 (79%)	-	-	-
	Yes	28 (24.3%)	17 (21%)	0.83 (0.42-1.64, p=.582)	-	-
Diabetes [n (%)]	No	91 (79.1%)	67 (82.7%)	-	-	-
	Yes	24 (20.9%)	14 (17.3%)	0.79 (0.38-1.65, p=.532)	-	-
Coronary Heart Disease [n (%)]	No	88 (76.5%)	64 (79%)	-	-	-
	Yes	27 (23.5%)	17 (21%)	0.87 (0.44-1.72, p=.681)	-	-
Psoriasis Type [n (%)]	Guttate Psoriasis	4 (3.5%)	0 (0%)	-	-	-
	Psoriatic Arthritis	4 (3.5%)	4 (4.9%)	15651360.71 (0.00-Inf, p=.989)	-	-
	Erythrodermic Psoriasis	6 (5.2%)	0 (0%)	1.00 (0.00-Inf, p=1.000)	-	-
	Pustular Psoriasis	3 (2.6%)	4 (4.9%)	20868480.95 (0.00-Inf, p=.989)	-	-
	Plaque Psoriasis	95 (82.6%)	72 (88.9%)	11862083.91 (0.00-Inf, p=.989)	-	-
	Palmoplantar Pustulosis	3 (2.6%)	1 (1.2%)	5217120.24 (0.00-Inf, p=.990)	-	-
Disease Duration (years)	Mean ± SD	101.5 ± 109.0	148.0 ± 132.2	1.00 (1.00-1.01, p=.010)	1.00 (1.00-1.00, p=.210)	-
Occupation [n (%)]	Self-employed	13 (11.3%)	6 (7.4%)	-	-	-
	Farmer	18 (15.7%)	7 (8.6%)	0.84 (0.23-3.10, p=.797)	-	-
	Retired	15 (13%)	15 (18.5%)	2.17 (0.65-7.22, p=.208)	-	-
	Student	20 (17.4%)	14 (17.3%)	1.52 (0.46-4.96, p=.491)	-	-
	Employee	49 (42.6%)	39 (48.1%)	1.72 (0.60-4.95, p=.311)	-	-
PASI Score	Mean ± SD	12.5 ± 7.2	16.5 ± 6.8	1.08 (1.04-1.13, p<.001)	1.05 (1.00-1.10, p=.031)	1.06 (1.01-1.11, p=.012)
Foot Microscopy	Positive	0 (0%)	14 (17.3%)	-	-	-
	Negative	115 (100%)	67 (82.7%)	0.00 (0.00-Inf, p=.986)	-	-
Foot Culture	Positive	0 (0%)	10 (12.3%)	-	-	-
	Negative	115 (100%)	71 (87.7%)	0.00 (0.00-Inf, p=.982)	-	-
Foot Culture Type	Rhodotorula	0 (0%)	2 (2.5%)	-	-	-

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	Dermatophytes	0 (0%)	8 (9.9%)	1.00 (0.00-Inf, p=1.000)	-	-
	No Growth	2 (1.7%)	1 (1.2%)	0.00 (0.00-Inf, p=.992)	-	-
	None	113 (98.3%)	70 (86.4%)	0.00 (0.00-Inf, p=.992)	-	-
Nail Microscopy	Positive	0 (0%)	17 (21%)	-	-	-
	Negative	115 (100%)	64 (79%)	0.00 (0.00-Inf, p=.985)	-	-
Nail Culture	Positive	0 (0%)	9 (11.1%)	-	-	-
	Negative	115 (100%)	72 (88.9%)	0.00 (0.00-Inf, p=.983)	-	-
Nail Culture Type	Rhodotorula	0 (0%)	9 (11.1%)	-	-	-
	No Growth	2 (1.7%)	2 (2.5%)	0.00 (0.00-Inf, p=.984)	-	-
	None	113 (98.3%)	70 (86.4%)	0.00 (0.00-Inf, p=.983)	-	-
Limb Microscopy	Positive	0 (0%)	8 (9.9%)	-	-	-
	Negative	115 (100%)	73 (90.1%)	0.00 (0.00-Inf, p=.984)	-	-
Limb Culture	Positive	0 (0%)	4 (4.9%)	-	-	-
	Negative	115 (100%)	77 (95.1%)	0.00 (0.00-Inf, p=.983)	-	-
Limb Culture Type	Malassezia	0 (0%)	3 (3.7%)	-	-	-
	Candida	0 (0%)	1 (1.2%)	1.00 (0.00-Inf, p=1.000)	-	-
	No Growth	2 (1.7%)	0 (0%)	0.00 (0.00-Inf, p=.988)	-	-
	None	113 (98.3%)	77 (95.1%)	0.00 (0.00-Inf, p=.990)	-	-
Trunk Microscopy	Positive	0 (0%)	16 (19.8%)	-	-	-
	Negative	115 (100%)	65 (80.2%)	0.00 (0.00-Inf, p=.985)	-	-
Trunk Culture	Positive	0 (0%)	9 (11.1%)	-	-	-
	Negative	115 (100%)	72 (88.9%)	0.00 (0.00-Inf, p=.983)	-	-
Trunk Culture Type	Malassezia	0 (0%)	6 (7.4%)	-	-	-
	Candida	0 (0%)	2 (2.5%)	1.00 (0.00-Inf, p=1.000)	-	-
	Dermatophytes	0 (0%)	1 (1.2%)	1.00 (0.00-Inf, p=1.000)	-	-
	No Growth	1 (0.9%)	0 (0%)	0.00 (0.00-Inf, p=.990)	-	-
	None	114 (99.1%)	72 (88.9%)	0.00 (0.00-Inf, p=.986)	-	-
Scalp Microscopy	Positive	0 (0%)	56 (69.1%)	-	-	-
	Negative	115 (100%)	25 (30.9%)	0.00 (0.00-Inf, p=.988)	-	-
Scalp Culture	Positive	0 (0%)	48 (59.3%)	-	-	-

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Scalp Culture Type	Negative	115 (100%)	33 (40.7%)	0.00 (0.00-Inf, p=.983)	-	-
	Malassezia	0 (0%)	46 (56.8%)	-	-	-
	Candida	0 (0%)	1 (1.2%)	1.00 (0.00-Inf, p=1.000)	-	-
	Dermatophytes	0 (0%)	1 (1.2%)	1.00 (0.00-Inf, p=1.000)	-	-
	No Growth	2 (1.7%)	0 (0%)	0.00 (0.00-Inf, p=.994)	-	-
	None	113 (98.3%)	33 (40.7%)	0.00 (0.00-Inf, p=.984)	-	-
Scalp Involvement	No	70 (60.9%)	24 (29.6%)	-	3.84 (1.98-7.43, p<.001)	3.86 (2.00-7.45, p<.001)
	Yes	45 (39.1%)	57 (70.4%)	3.69 (2.01-6.77, p<.001)	-	-
Nail Involvement	No	93 (80.9%)	52 (64.2%)	-	2.41 (1.15-5.05, p=.020)	2.61 (1.26-5.42, p=.010)
	Yes	22 (19.1%)	29 (35.8%)	2.36 (1.23-4.52, p=.010)	-	-

Note: PASI, Psoriasis Area and Severity Index.

Table 2: Multivariate logistic regression analysis of independent risk factors for fungal infection in *Psoriasis vulgaris*

Risk Factor	Estimate (β)	Std. Error	Z-value	P-value
Disease duration	0.001772	0.001413	1.254	0.210
PASI score	0.050531	0.023442	2.156	0.031*
Scalp involvement	1.345190	0.336747	3.995	<0.001**
Nail involvement	0.878601	0.378455	2.322	0.020*

Notes: PASI: Psoriasis Area and Severity Index. Significance codes: ***p < 0.001, **p < 0.01, *p < 0.05.

Other studies have shown that Malassezia colonization is associated with lower Th2 cytokine levels in guttate Ps patients, potentially leading to immune dysregulation that could contribute to Ps development. Folliculitis caused by Malassezia has also been observed to transform into guttate Ps lesions, with cellular debris locally inducing Ps plaques. Candida, from the Ascomycota phylum, commonly resides in the oral cavity, gut, and vaginal areas of healthy individuals, with Candida albicans accounting for 75% of Candida infections (Rudramurthy *et al*., 2014, Wal *et al*., 2022). Candida can activate the immune system to produce antibodies that suppress keratinocyte function and is positively associated with PASI scores in Ps patients (Mba and Nweze, 2020). Studies on oral mucosa and fecal samples from Ps patients found Candida colonization in 76% of the oral samples and 72% of the fecal samples, mainly C. albicans (77% in saliva, 64% in feces) and Candida tropicalis (28% in both saliva and feces), with colonization associated with longer Ps duration.

Sarvtin *et al*. found a significant difference in Candida colonization between Ps patients and healthy controls, with Ps patients showing lower levels of anti-Candida albicans IgM, IgA, and IgG antibodies and reduced humoral immune response (De Aguiar Cordeiro *et al*., 2023). Large-scale, multicenter systematic reviews have confirmed that Candida colonization rates are significantly higher in Ps patients than in controls, especially in mucosal regions, and colony counts have been positively correlated with Ps severity (Waldman *et al*., 2010).

Multivariate logistic regression analysis in this study identified disease duration, PASI score, head involvement, and nail involvement as significant risk factors for fungal infection in Ps patients. Fungi, as opportunistic pathogens present on the skin and mucosal surfaces, can cause superficial skin infections. Various Candida species can infect the skin surface, mouth, and genital mucosa. In sebum-rich skin regions, lipophilic fungi like Malassezia are common causes of dandruff and seborrheic dermatitis (Picciani *et al*., 2013). When the barrier function of Ps patients' skin and mucosa is compromised, microbial dysbiosis can lead to opportunistic fungal infections. Common sites for superficial fungal infections include humid, poorly ventilated areas like the axilla, groin, elbows and feet, which are also typical sites for inverse Ps. In a study of 138,939 individuals, the prevalence of Ps was 2%, with onychomycosis as the most common fungal

comorbidity (7.8% prevalence) (Sarvtin *et al*., 2015, Aldona *et al*., 2018). Onychomycosis (3.4%) and tinea pedis (3.1%) had the highest treatment demands (Lesan *et al*., 2018). The study concluded that Ps patients have an increased risk of skin comorbidities, particularly fungal infections.

In the Kashgar region, with its wide temperature fluctuations and strong UV exposure, the prevalence of skin conditions is high, particularly those with impaired skin barrier function, such as Ps, seborrheic dermatitis, skin tumors, actinic dermatitis and acne. Additionally, due to socioeconomic and hygiene factors, the risk of microbial infections is higher than in other areas (Zander *et al*., 2017).

In conclusion, the chronic inflammatory state of Ps may predispose patients to fungal infections. Disease duration, PASI score, head involvement and nail involvement are independent risk factors for fungal infections in Ps patients, highlighting the need for early intervention and screening to prevent fungal comorbidities. These findings provide clinical guidance for screening and prevention of fungal infections in Ps patients. Due to the limited sample size in this study, no significant correlation was observed between PASI score and lipid metabolism disorders. As a cross-sectional study, further multicenter, large-sample studies are needed to clarify the temporal relationship between Ps and fungal infections and their impact on Ps severity.

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Conflict of interest

There is no conflict of interest.

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