



The role of candida albicans in the pathogenesis of psoriasis vulgaris: a systematic literature review

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ABSTRACT

Introduction: Psoriasis is a chronic, inflammatory skin disease that is related to many genetic, and environmental factors, as well as infectious pathogens. Findings suggest that the Candida species, particularly Candida albicans, may play a role in the pathogenesis of psoriasis vulgaris. In this study, we aimed to systematically review the possible association between C. albicans and the prevalence of psoriasis.

Methods: A systematic search of existing literature was performed in the PubMed, Scopus and Google Scholar databases and the Google search engine using the following search strategy ((Candida albicans OR C. albicans OR Candida)) AND (psoriasis vulgaris OR plaque psoriasis OR psoriasis) to find relevant articles that described a possible positive or negative association between C. albicans and the incidence or progression of psoriasis. The search was not limited to articles that were published within a specific time period; however, only those written in the English language were included in the review.

Result: Of the 499 articles in total that were identified during the initial database search, 491 were excluded from the review because they failed to meet the inclusion/exclusion criteria. The total number of people involved in the selected studies, including both patients and healthy controls, was 1260. The analysis of the results of the included documents showed that the colonization of C. albicans is more prevalent in biological specimens taken from psoriatic patients.

Conclusion: Studies show that C. albicans, opportunistic yeast, like diploid fungus, may be involved in the pathogenesis of psoriasis.

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Introduction

Psoriasis is a chronic, inflammatory and proliferative skin disease that is associated with a number of genetic and environmental factors (1). In addition, trauma, salts (especially lithium salts), beta-blockers, anti-malaria drugs, alcohol, and tobacco are widely recognized as being risk factors for psoriasis (1). Psoriasis is characterized by increased keratinocyte proliferation and infiltration of inflammatory cells, particularly T lymphocytes, monocytes,

and neutrophils in the dermis and epidermis. The severity of psoriasis lesions is measured using the psoriasis area and severity index (PASI) score (2). Based on epidemiological data, psoriasis affects 1.5 to 3 percent of the population worldwide, and its prevalence is similar in men and women (1). There are several forms of psoriasis. Of these, psoriasis vulgaris, which is also known as plaque psoriasis, is the most common type. This type of psoriasis is

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characterized by red plaque and silver sticky scales, and it typically affects the extensor limbs. Existing research findings have shown that the age of onset of psoriasis varies from 12 years to 60 years (1). Although men and women are equally affected by psoriasis vulgaris, the majority of existing research indicates that, within the younger age group, women are more likely to be affected than men (1).

Many infectious factors, including intestinal yeasts and endotoxins of gram-negative bacteria, may be involved in the pathogenesis and progression of psoriasis (3). Findings show that the *Candida* species, especially *Candida albicans*, may induce the pathogenic cycle of psoriasis by stimulating T cells (4). The yeast-like fungus *C. albicans* is not typically pathogenic and is a normal flora of the mucous membranes, skin, and gastrointestinal and vaginal mucosa (5,6). It may also exist in small quantities in the mouth of healthy adults (7). However, findings show that *C. albicans* is an opportunistic pathogen that can cause acute and chronic infection in skin, nails, vagina, bronchi, lungs, and the gastrointestinal tract (8,9).

It can also cause various infections under certain conditions such as pregnancy, diabetes, Addison's disease, hyperthyroidism, hyperparathyroidism, antibiotics and steroids usage, and immune deficiency (10). Thus, it is suggested that systemic antifungal therapy may reduce psoriasis lesions (3).

Due to the increasing prevalence of *C. albicans* in patients with psoriasis and the need to determine the possible role *C. albicans* plays in the aggravation and prevalence of psoriasis lesions, studying the association between psoriasis lesions and *C. albicans* can be of great importance. Therefore, in this study, we systematically reviewed the prevalence of *Candida* in patients with psoriasis.

Methods

Search methods

A systematic literature search was performed by searching PubMed and Scopus as two known databases for the following key terms "psoriasis" and "*Candida albicans*" in the titles, keywords, and abstracts of documents in which the relationship between *C. albicans* and incidence of psoriasis lesions had been investigated in a patient population. For this purpose, we used the following search strategy, ((*Candida albicans* OR *C. albicans* OR *Candida*)) AND (psoriasis vulgaris OR plaque psoriasis OR psoriasis), to identify all the relevant articles in PubMed. Similarly, to identify potentially eligible articles in the Scopus, we performed a customized search strategy in which "*Candida albicans*" was searched in the Scopus, and the results were then screened for instances of "psori-

asis vulgaris." Afterwards, the records obtained in both databases were limited to the articles published in the English language. The database search was performed on August 2015. To minimize the possibility of data loss, reference lists of previously included documents were also manually screened for potentially eligible articles.

After searching the abovementioned databases, the Google search engine and Google Scholar database were also searched for the previously described key terms. Two authors conducted the literature search independently.

Study selection

All papers that were identified via the customized search method that met the inclusion and exclusion criteria were examined in the study regardless of the date of publication prior to August 2015. However, to avoid any mistranslations or misinterpretations during the data extraction process, the search was limited to articles that were published in the English language. Furthermore, articles that were deemed to be irrelevant from a subject perspective were also excluded in the first step of the article selection process. In terms of study types, articles that involved all types of clinical design, including clinical trials, prospective cohorts, case-controls, and comparative and cross-sectional studies, were included; however, conference proceedings, review articles, meta-analysis, editorials, and abstracts were excluded from further assessment.

Moreover, duplicated documents or articles that reported similar data involving the same population were also excluded. In situations in which it was not possible to access the full text or the articles had relevant abstracts but were not yet published, these articles were also excluded from further data processing. Finally, we also omitted those trials that had been conducted on animals.

Eligibility criteria

All documents reporting the relationship between *C. albicans* and psoriasis vulgaris that were conducted on a human population were eligible for further evaluation. Due to the lack of adequate data in this subject area, exclusion criteria were only limited to study design types and papers that were written in the English language. Almost all relevant documents, irrespective of their publication date or the number of patients involved, were included in this study.

Data extraction

General information, including the name of the authors, publication date, total number of studied participants in each study, country of origin, and type of study design, were extracted. Other

available information, including the demographic data of the studied population, the assessment methods used in each article, and the main findings, were collected based on the main purpose of this review. All the extracted data were analyzed based on the results of articles that reported the possible association between *C. albicans* and psoriasis vulgaris. Similar to search method and selection of articles, all data processing, including data extraction and data analysis, were performed independently by two reviewers in accordance with the standard protocol recommended in the PRISMA checklist 2009 (11). To avoid possible misinterpretation, any discrepancies between the authors' findings during the processes of data synthesis were resolved before further analysis was performed and the conclusions developed.

Measured variables

Among the included studies, different methods have been used to identify *C. albicans* in the saliva and skin samples of patients with psoriasis. These methods include the total colony count of *C. albicans* from the skin and oral cavity, serum level of immunoglobulin M (IgM), IgA, and IgG antibodies against *C. albicans*, isolation of *C. albicans* 26S rRNA gene, and secretion of cytokine, chemokine, and prostaglandins in the peripheral blood mononuclear cells (PBMC) of participants.

Results

Literature search results

A total of 119 relevant articles were found in PubMed and 375 in the Scopus databases. Furthermore, two additional relevant articles were found and included following the reference list screening of the selected documents. Following the search in the Google search engine and Google Scholar, three papers were also included for further assessment. After a comprehensive review of the abstracts of the selected articles, 311 irrelevant articles were excluded from the next stage of the systematic review. Additionally, 67 documents were further excluded due to language irrelevancy or duplication. Seventy-two articles in which different types of *Candida* species other than *C. albicans* or any other microbial and fungal pathogens had been isolated from specimens were also excluded from further evaluation. In addition, 17 studies that had been performed on animal models were omitted from this study, as too were six further papers for which the full text was not available, and 18 review articles. Finally, after fully reviewing the selected articles, only eight relevant documents that fully met the inclusion/exclusion criteria were selected and used for data extraction and subsequent data

analysis. Figure 1 shows the step-by-step process by which the literature search and article selection was conducted.

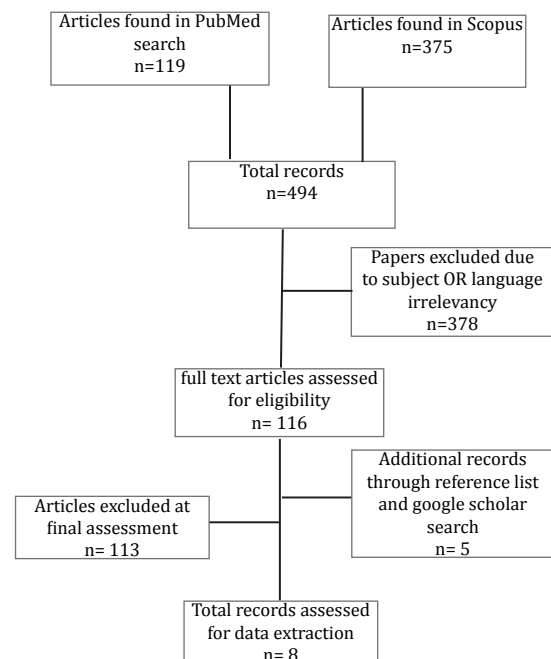


Figure 1. Flowchart of the literature search method and strategy for the selection of relevant document.

General characteristics of the included articles

The total number of people involved in the selected articles in which the absence or presence of *C. albicans* had been investigated in skin tissue and saliva samples were 1260. Of these, 655 were patients with psoriasis lesions, and 605 were healthy individuals who had represented control subjects. The number of studied patients enrolled in the selected articles varied from 30 to 280 among the reviewed literature. According to the extracted demographic data, patients of both genders had been studied in the selected documents as a means of evaluating the possible association between *C. albicans* and psoriasis. In one study, the gender ratio had not been reported; as such, we asked the authors to provide the demographic data of the studied population to analyze the extracted data based on gender and age. Therefore, among the selected literature, 331 patients were male, and 324 were female (in the patient group). The age of the patients that participated in the selected literature varied from 10-year-old children to 84-year-old adults. Among the selected documents for data extraction, five were case-control, two were observational, and one was a prospective cohort study. The most recent and oldest selected articles in this literature review had been published in 2015 and 2001 respectively. Table 1 provides an overview of the general characteristics of the included articles in chronological order of their publication date.

Table 1. General information of the included literatures.

NO	Author Year Reference	Coun-try	Study design *	Sex ratio	Age range	Participants number
1	Pezeshkpoor 2015 (12)	Iran	C-CS	Male: 47 Female: 53	12-62	100
2	Taheri Sarvtin 2014 (13)	Iran	C-CS	Male: 66 Female: 84	12-72	150
3	Picciani 2013 (14)	Brazil	C-CS	Male: 134 Female: 146	18-75	280
4	Bedair 2012 (15)	Jordan	C-CS	Male: 108 Female: 92	18-47	200
5	Darwazeh 2012 (16)	Jordan	C-CS	Male: 108 Female: 92	18-47	200
6	Leibovici 2008 (17)	Israel	PS	Male: 89 Female: 111	18-84	200
7	Kanda 2002 (4)	Japan	OS	Male: 16 Female: 14	30-43	30
8	Waldman 2001 (3)	Israel	OS	Male: 60 Female: 40	10-82	100

* PS: Prospective study; C-CS: Case-Control study; OS: Observational study.

Study results

The results of the data analysis that was conducted as part of this literature review showed that the colony count of *C. albicans* is higher in patients with psoriasis. Different methods were employed to identify *C. albicans* in saliva and skin samples, clearly highlighting the possible involvement of this fungus pathogen in psoriasis lesions. Table 2, provides an overview of the methods by which *C. albicans* in psoriasis lesions had been identified. According to the results reported in the included literature, *C. albicans* was identified in the skin and oral specimens of patients with psoriasis. Furthermore, reports showed that the serum level of IgM, IgA, and IgG antibodies against *C. albicans* were lower in patients with psoriasis than they were in the healthy control population. This indicates that there was a reduction in the immune responses of the humoral system in this patient population. Although the results were often contradictory, some studies reported that a high rate of *C. albicans* colonization may be

identified in the skin and oral specimens of patients with psoriasis. Furthermore, reports showed that the serum level of IgM, IgA, and IgG antibodies against *C. albicans* were lower in patients with psoriasis than they were in the healthy control population. This indicates that there was a reduction in the immune responses of the humoral system in this patient population. Although the results were often contradictory, some studies reported that a high rate of *C. albicans* colonization may be

Table 2. General information of the included literatures.

NO	Author Reference	Variables ®	Method of assessment *	Main findings
1	Pezeshkpoor (12)	Colony count	CI, SE	<i>C. albicans</i> was in 46% of patients and 18% of controls
2	Taheri Sarvtin (13)	Serum levels of IgM, IgA, and IgG against <i>C. albicans</i> , 26S rRNA gene for <i>Candida</i> and colony count	CT, PCR, AD	<i>Candida</i> colonies were high and serum IgM, IgA, and IgG levels against <i>C. albicans</i> were lower in patients than in controls
3	Picciani (14)	Colony detection	TE, CSE	Candidiasis is higher in psoriatic patients and it is associated with disease severity
4	Bedair (15)	Colony count	SE	<i>Candida</i> colonies were higher in the patients than controls
5	Darwazeh (16)	Colony detection	CI, SE	Mucosal lesions caused by <i>Candida</i> were strongly associated with psoriasis
6	Leibovici (17)	Colony detection	FT	<i>C. albicans</i> was high in patients than controls (32%) vs. (21%)
7	Kanda (4)	Cytokine, chemokine and PGE secretion	ELISA	<i>C. albicans</i> induce chemokine, and cytokine secretion in patients and controls
8	Waldman (3)	Colony count	CT	<i>Candida</i> was detected in 78% of patients and 50% of the controls

* CI: Colony identification; SE: Smear examination; CT: Clinical tests; PCR: Polymerase chain reaction; AD: Antibody detection; TE: Tissue examination; CSE: Cytopathological smear examination; FT: Fungal test; ELISA: Enzyme-linked immunosorbent assay. ® Ig: Immunoglobulin; PGE: Prostaglandin E.

associated with the severity of the disease.

One limitation of the current study was that a limited number of published articles examined the correlation between the colonization of *C. albicans* and the biological samples of psoriatic patients. The small sample size described in some of the studies also represented a limitation that may have affected the significance of the results of the current study.

Discussion

Many factors, including microbial and fungal pathogens, may be involved in the pathogenesis of psoriasis vulgaris and other inflammatory skin diseases. Studies show that there is an association between perianal streptococcal cellulitis and plaque-type psoriasis (12). The findings of existing research suggests that, because *C. albicans* is commonly observed in psoriasis lesions, it can be considered to represent a main pathogenic factor in the incidence or exacerbation of psoriasis. The results of existing research studies have also revealed that *C. albicans* may play a role in the pathogenesis of other skin diseases such as atopic dermatitis (13). Similar findings have demonstrated that the *Candida* species, especially *C. albicans*, are more frequent pathogens found in biological specimens of patients with plaque psoriasis (3). It is also commonly accepted that *Candida* induces chemokine, interleukin 4 (IL4), and interferon gamma (IFN- γ) secretion in both patients with psoriasis and healthy individuals (4). However, it is necessary to emphasize that *C. albicans* is not the only factor that can induce or aggravate the pathogenicity of psoriasis.

Many factors may lead to the involvement of *C. albicans* in the pathogenesis of diseases such as psoriasis. However, on the cellular level, studies have shown that antimicrobial peptides (AMPs) may play an important role in the regulation of *Candida* growth in skin and oral cavities (14,15). AMPs are biologically active components that are found in almost all living organisms. They are predominantly known for the role they play in killing pathogenic microorganisms including bacteria and fungus (16,17). Since AMPs may induce inflammatory responses in humans, decreases in the level of AMP secretion in biological environments, such as saliva, or the abnormal and excessive production of AMPs may be considered to represent a possible underlying cause of psoriasis pathogenicity (18,19). Therefore, antibiotics and anti-inflammatory agents may be useful for the treatment of psoriasis.

The results of this literature review showed that *Candida* species, especially *C. albicans*, may be involved in the pathogenesis of psoriasis;

therefore, treatment with antifungal agents can be considered to represent a potential therapeutic approach for the treatment of psoriasis lesions.

Conclusion

The results of this systematic literature review suggested that fungal pathogens, especially *C. albicans*, may play a role in the pathogenicity of psoriasis vulgaris. The data also suggested that due to the high rate of *Candida* colonization in biological specimens of psoriatic patients, antibacterial, antifungal and anti-inflammatory agents may represent a useful therapeutic approach for the management of psoriasis lesions.

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Conflict of Interest

The authors declare no conflict of interest.

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