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Molecular Detection of HWP1 and Assessment of Interleukin Levels in Cutaneous Candidiasis Caused by *Candida albicans*

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Abstract

Candida albicans is the leading cause of cutaneous candidiasis, a common superficial skin infection whose course depends on both fungal virulence determinants and the host immune response. This study aimed to determine the frequency of the hyphal wall protein 1 (HWP1) gene among *C. albicans* isolates recovered from patients with cutaneous candidiasis and to compare serum interleukin (IL)-1α, IL-17 and IL-22 levels between these patients and healthy controls.

This cross-sectional case–control study was conducted in Kirkuk City, Iraq, between November 2024 and April 2025; an ethics approval certificate was issued by the University of Anbar Scientific Ethical Approval Committee (approval no. EAC-2026-08-007, issued 3 August 2026) and with written informed consent from all participants (parental/guardian consent and participant assent for those aged 15–17 years). Skin swabs from 180 patients aged 15–65 years with clinically suspected cutaneous candidiasis, admitted to the surgical wards of three hospitals, were examined directly with 10% KOH and cultured on Sabouraud dextrose agar (SDA) at 37 °C for up to 7 days. C. albicans was identified by CHROMagar Candida and biochemical tests, and the HWP1 gene (572 bp) was detected by conventional PCR with positive and no-template controls. Serum IL-1α, IL-17 and IL-22 were measured by ELISA in the 47 culture-confirmed patients and in 47 healthy controls and compared with Welch's t-test.

Of the 180 samples, 47 (26.1%) were positive by both direct KOH examination and culture, and 133 (73.9%) were negative. Seventeen of the 47 isolates were identified as *C. albicans* and tested by PCR; HWP1 was detected in 13 of these 17 isolates (76.5%). Compared with healthy controls, patients had significantly higher serum IL-1α (51.84 ± 6.03 vs 8.14 ± 0.57 pg/ml), IL-17 (42.95 ± 2.14 vs 21.64 ± 1.33 pg/ml) and IL-22 (75.09 ± 8.21 vs 13.27 ± 0.54 pg/ml) (mean ± SE; $P < 0.001$ for each).

The HWP1 gene was carried by most *C. albicans* isolates from cutaneous candidiasis, and patients showed elevated serum IL-1α, IL-17 and IL-22, consistent with activation of innate and Th17-type immunity. Because

only the presence of the gene was assessed, these findings are descriptive and do not establish HWP1 expression, an association with disease severity, or causality.

Keywords: *Candida albicans*, HWP1, cutaneous candidiasis, IL-1α, IL-17, IL-22.

Introduction and literature review

1 Introduction

It is estimated that fungal diseases claim the lives of over 1.6 million people annually and it affects more than one billion people worldwide (Gupta et al., 2012; Bongomin et al., 2017). Fungal infections are thus an important but largely underdiagnosed global health issue especially in immunocompromised patients and in the low resource area where diagnosis and treatment of this condition might be delayed. Of these infections, candidiasis is the most common of all fungal infections with about 75-88 percent of all fungus diseases in the world. Even though the number of antifungal treatments and diagnostic methods has increased significantly, the prevalence of candidiasis is on the rise, with the morbidity and death rates thereof becoming alarming (Hani et al., 2015; Bouopda, 2020). This trend has been credited to the rising utilization of immunosuppressive regimens, the extent of hospitalization, invasive medical operations and the rising number of chronic disease patients.

Candidiasis has a wide clinical presentation which includes superficial mucocutaneous infection to life-threatening systemic diseases like candidemia and invasive candidiasis (Calderone & Clancy, 2012). Superficial infections are typical to the oral cavity, gastrointestinal tract, genitourinary tract, nails, and skin, and systemic infections are likely to affect various body organs and are linked with high mortality rates. In particular, cutaneous candidiasis is a widespread dermatological disease that can be experienced by people of any age and socioeconomic status. It presents its clinical significance of about 1 percent outpatient visits and up to 7 percent inpatient dermatological consultations (Taudorf et al., 2019).

Cutaneous candidiasis can be primary or secondary infection or a complication of underlying dermatological conditions like psoriasis, atopic dermatitis or underlying diaper dermatitis. Individuals are further predisposed to infection because of environmental factors such as heat, humidity and poor hygiene as well as host-related factors such as obesity, diabetes mellitus, immunosuppression and antibiotic use. *Candida* species may colonize a number of different anatomical locations, but typical locations of cutaneous candidiasis include intertrigo, angular cheilitis, diaper dermatitis, and interdigital infections. These disorders are usually defined in terms of erythema, maceration, itching and discomfort which greatly impacts on the quality of life of patients.

There are many species of the genus Candida that can lead to infection, though *Candida albicans* is the most commonly isolated and clinically relevant one (Taudorf et al., 2019; Nurdin et al., 2021). Its pathogenicity is associated with a number of virulence factors such as ability to adhere to host tissue, form biofilm, phenotypic variation, and generation of hydrolytic enzymes. These include adhesion molecules including the hyphal wall protein 1 (HWP1), which is important to mediate attachment to epithelial cells and tissue invasion. The presence of such virulence genes increases the colonizing capacity and survival of the organism in the host, which leads to disease progression, and resistance to antifungal treatment (Inci et al., 2013; Nas et al., 2008).

The host immune system employs some defense mechanisms to destroy fungus and they are the innate and adaptive immune system. One of the first lines of the immune system is known as innate immunity, in the course of which physical barriers (the skin, the mucous membrane) and cellular components (neutrophils, macrophages, dendritic cells, etc.) are engaged (Abood, 2014). The epithelial cells play a vital role in the detection of invading pathogens and activating of the immune system. They express a number of pattern recognition receptors (PRRs), such as Toll-like receptors (TLRs), C-type lectin receptors (CLRs), and mannose receptors

(MRs), that sense pathogen-associated molecular patterns (PAMPs) on Candida albicans (Kiyoura & Tamai, 2015).

When the fungal pathogens are recognized, these receptors initiate intracellular signaling pathways which result in the synthesis of pro-inflammatory cytokines, chemokines and antimicrobial peptides. At the initial phases of the infection, the keratinocytes react to the fungi settlement by secretion of cytokines responsible of causing inflammation and attracting immune cells to the area of infection. It leads to the buildup of leukocytes, especially neutrophils, which play a crucial role in the clearance of fungi using such methods as phagocytosis, degranulation, and the release of reactive oxygen species (Martinez-Rossi et al., 2017; Ali et al., 2001). Adaptive immunity also helps to improve the capacity of the host to get rid of fungal infections by stimulating particular T-helper (Th) cell reactions. Two of them are Th1 and Th17 cells whose contribution is pivotal in antifungal defence. Th1 cells enhance cell-mediated immunity by producing the cytokine such as interferon-gamma (IFN- 7) which activates the macrophages and enhances their microbicidal activities. Th17 cells on the other hand are quite important in mucocutaneous immunity against *Candida albicans*. They stimulate the synthesis of anti-microorganism peptides and chemotactic agents by the epithelial cells, which enhances the recruitment of neutrophils and strengthens of the epithelial wall (Hau et al., 2015; Heinen et al., 2017).

Neutrophils are recruited and activated by IL-17, and IL-22 helps to maintain epithelial integrity and repair. Their role in host defense has been highlighted as deficiency in these cytokines or their signal transduction pathways has been linked to predisposition to candidiasis (Jin and Dong, 2013; Conti et al., 2009; Zelante et al., 2012). Besides, cytokines IL-1 have been found to be important in the initiation of inflammatory conditions and the orchestration of antifungal reactions (Vonk et al., 2006). Although immune responses can be effective in the control of fungal infections, overactive or over-regulated immune responses may result in tissue damage and pathological inflammation. Oxidative stress is one of the most important processes in this process, as a result of the imbalance between the formation of reactive oxygen species (ROS) and the antioxidant defense system. The production of ROS during phagocytosis is a normal antimicrobial activity of neutrophils and monocytes, nevertheless, the overproduction of ROS may harm host tissues and interfere with cellular metabolism. This oxidative disequilibrium has been involved in the pathogenesis and the development of cutaneous candidiasis (AL-Dhwahery et al., 2019).

Over the years, molecules techniques have become popular in the diagnosis and characterization of fungal infections. The methods based on polymerase chain reaction allow the detection of particular fungal genes quickly and sensitively, allowing the correct identification of *Candida* species and their virulence factors (Ali, 2014). One of them, HWP1 gene has become an essential molecular marker of *Candida albicans*, as it correlates with the development of hyphae and their ability to stick to the tissues of the host. The fact that this gene was detected not only helps in identifying the species, but also gives information on the pathogenicity of the clinical isolates (Inci et al., 2013; Nas et al., 2008).

Cytokine levels of patients with cutaneous candidiasis could be used to offer useful information about the host immune response and severity of the disease. Interleukins (e.g. IL-17, IL-22, IL-1) can be measured and used to understand the immunopathogenesis of the disease and to find possible therapeutic targets. These immunological markers may also be used as a guide to treatment response and prognosis thus enhancing clinical management approaches. Since candidiasis is becoming more common, antifungal resistance is appearing, and the interactions between the host and pathogen are complex, there is an urgent requirement in in-depth research that is both molecular and immunological. To develop more effective diagnostic and treatment intervention, it is important to understand how virulence genes like HWP1 are expressed, as well as the host immune response. The aim of the present study was therefore to determine the frequency of the HWP1 gene among *C. albicans* isolates from patients with cutaneous candidiasis and to compare serum IL-1α, IL-17 and IL-22 levels between these

patients and healthy controls. This will help us understand better the pathogenic processes of Candida albicans and the host immune response and eventually lead to the diagnosis, treatment and prevention of this prevalent but clinically serious fungal infection.

1.1 Research Questions

(1) What is the frequency of the HWP1 gene among *Candida albicans* isolates recovered from patients with cutaneous candidiasis. (2) Do serum IL-1α, IL-17 and IL-22 levels differ between patients with cutaneous candidiasis and healthy controls.

Experimental Methods

Table 1 and 2 demonstrated the instruments, kits and solutions to be used in this investigation to identify fungal infections and its association with the levels of some interleukins.

Table 1 : The instruments

Name	Company	Country
Centrifuge	Biobase	China
Thermal cycler	Tryte-Technology	China
Oven	Memmet	Germany
Electrophoresis supply	Biobase	China
UV transilluminator	Biobase	China
Incubator	Memmet	Germany

Table 2: The kits, and solutions

Name	Company	Country
IL-1α	SunLong	China
IL-17	SunLong	China
IL-22	SunLong	China
Primers	Metagene	Australia
Master mix	Tinzyme	China
Nuclease free water	Tinzyme	China
Ladder	Tinzyme	China
SDA	HiMedia	India

2.1 Sample collection

This cross-sectional case–control study was conducted in Kirkuk City, Iraq, between November 2024 and April 2025. A total of 180 patients aged 15–65 years with clinically suspected cutaneous candidiasis (erythematous, macerated and/or pruritic skin lesions), admitted to the surgical wards of three hospitals in Kirkuk City, were enrolled; lesions were recorded according to whether they appeared before or after surgery. Patients who had received topical or systemic antifungal therapy during the preceding 2 weeks, pregnant women and patients with known primary immunodeficiency were excluded. The patient group comprised 98 males and 82 females. The control group consisted of 47 apparently healthy volunteers (25 males and 22 females) of comparable age, with no skin lesions and no history of fungal infection, recruited from hospital staff and

accompanying relatives at the same hospitals. Serum cytokines were measured in all 47 culture-confirmed patients and in all controls; the 133 culture-negative patients were not included in the immunological comparison.

Ethical approval. An ethics approval certificate was issued by the University of Anbar Scientific Ethical Approval Committee (approval no. EAC-2026-08-007, issued 3 August 2026) and was conducted in accordance with the Declaration of Helsinki. Written informed consent was obtained from all adult participants; for participants aged 15–17 years, written consent was obtained from a parent or legal guardian together with the participant's own assent. All laboratory testing was performed in private laboratories. The certificate issue date is later than the reported data-collection period; whether retrospective approval or a separate earlier approval applied must be verified before submission.

2.2 Identification

Each swab was first examined directly in a 10% potassium hydroxide (KOH) mount and was then inoculated into Sabouraud dextrose broth (Oxoid, England) and plated onto Sabouraud dextrose agar (Oxoid, England). Plates were incubated at 37 °C and examined daily for up to 7 days, and yeast colonies were subcultured by streaking to obtain pure cultures (Guthrie & Fink, 1991). Isolates were identified to species level by colony colour on CHROMagar Candida (green colonies indicating *C. albicans*) and by biochemical testing; only isolates confirmed as *C. albicans* were carried forward to the molecular analysis.

2.3 Genetic Study

2.3.1 DNA Extraction

The confirmed *C. albicans* isolates (n = 17) were subcultured on SDA at 37 °C for 48 h, and genomic DNA was extracted with the Fungi/Yeast Genomic DNA Isolation Kit (Norgen Biotek, Canada) according to the manufacturer's instructions.

2.3.2 Detection of HWP1gene

The HWP1 gene was amplified by conventional (single-target) PCR. Each 25 µl reaction contained 12.5 µl of 2X GoTaq Green Master Mix (Promega, USA), 1 µl of each forward and reverse primer, 3 µl of genomic DNA and 7.5 µl of nuclease-free water. Cycling conditions were: initial denaturation at 94 °C for 4 min; 35 cycles of 94 °C for 30 s, 52 °C for 1 min and 72 °C for 2 min; and a final extension at 72 °C for 5 min. The C. albicans reference strain ATCC 10231 was included as the positive control, and nuclease-free water in place of template DNA served as the negative (no-template) control in every run. A single band of 572 bp was scored as HWP1-positive. The primer sequences are listed in Table 3.

Table 3: The sequence forward and reverse primers of HWP1 gene

Primer	Primer sequence	Length (bp)	References
HWP1-F	5'-TCAGTTCCACTCATGCAACCA-3'	572 bp	**Inci et al., 2013**
HWP1-R	**5'-AGCACCGAAAGTCAATCTCATGT-3'**		

2.3.3 Agarose Gel Electrophoresis of DNA

Genomic DNA (to verify integrity) and PCR products were separated by electrophoresis on a 2% agarose gel, visualized under UV transillumination (Wealtec, Dolphin-View, USA), and fragment sizes were estimated against a DNA ladder run in parallel.

2.3.4 Blood samples

Five millilitres of venous blood were collected from each culture-confirmed patient (n = 47) and from each control participant. Serum was separated by centrifugation and assayed for the selected interleukins following the kit manufacturer's instructions.

2.4 Measurements

- **IL -1*α***: IL-1α was measured by using Human interleukin 1α (IL-1α) ELISA kit from Sun long company, China (Catalogue number: SL0981Hu).
- **IL -17**: The IL -17 was assayed employing Human interleukin 17 (IL -17) ELISA kit provided by Sun long company, China (Catalogue number: SL 0978Hu).
- **IL -22**: Human interleukin 22 (IL -22) ELISA kit (IL -22) of Sun long company, China (Catalogue number: SL0988Hu) was used to measure IL -22.

2.5 Statistical analysis

Data were analysed with SPSS (version 26; IBM Corp., USA). Continuous variables are presented as mean ± standard error of the mean (SE), and frequencies as n/N (%). Normality was checked with the Shapiro–Wilk test, and mean cytokine levels of patients and controls were compared with Welch's independent-samples t-test, which does not assume equal variances. Two-tailed $P < 0.05$ was considered significant, and P values below 0.001 are reported as $P < 0.001$.

Results and Discussions

3.1 Isolation of C. albicans

Skin swabs were collected from all 180 patients with suspected cutaneous candidiasis. Direct microscopy with 10% KOH and culture on SDA (37 °C, up to 7 days) were each positive in 47 samples (47/180; 26.1%) and negative in 133 (133/180; 73.9%) (Table 4, Figure 1). Of the 47 culture-positive samples, 17 yielded isolates confirmed as *C. albicans* by CHROMagar Candida and biochemical testing, and these 17 isolates constituted the denominator for the molecular analysis.

		Positive samples

Procedures	Samples	**No.**	%
Direct examined by 10% KOH	180	47	**26.1**
Culturing Procedure	**180**	**47**	**26.1**

Table 4 Distribution of positive cultured cases



Figure 1. Colonies of C. albicans on SDA.

The pathogenic agents of cutaneous candidiasis are yeasts which are usually colonized by the gastrointestinal tract, mucosal membranes, and superficial folds of the skin. Under normal physiological conditions, these organisms exist as commensals and do not cause disease. Nevertheless, some predisposing factors may interfere with the homeostasis between the host defenses and the microbial flora enabling these yeasts to become opportunistic pathogens (Heymann, 2004). Examples of such conditions are the use of immunosuppressive drugs, chronic metabolic disorders like diabetes mellitus, immunological deficiencies related to malignancies and long-term use of broad-spectrum antibiotics, which weaken the host immune response and favour fungal proliferation (Heymann, 2004). Moreover, poor hygiene, excessive moisture, and maceration of skin can also contribute to the development of cutaneous infections.

The overall prevalence rate as reported in the current study (26.1) is in line with the other regional and international studies. As an example, the prevalence rate of (27.6) was equally high in Babylon (Mahmmud, 2000) showing that there was a similar epidemiological pattern in the same environmental and demographic contexts. This prevalence however is rather high compared to other areas like Libya where a prevalence of 10% was recorded (Ellabid & Khalifa, 2001) and Italy where prevalence was identified at 17% (Di-Silverio et al., 1989). These differences in prevalence can be explained by the changes in climatic conditions, population specifics, diagnostic methods, access to healthcare, and awareness of fungal infections.

3.2 HWP1 gene detection

Following the extraction of genomic DNA of *Candida albicans*, using a standardized protocol with subsequent agarose gel electrophoresis to verify the integrity of the genomic DNA, the existence of the HWP1 gene was examined in the obtained isolates. The findings showed that HWP1 gene was present in 13 of the 17 *C. albicans* isolates tested (13/17; 76.5%) (Figure 2). This observation indicates the commonness of this virulence-

related gene in clinical isolates and the significance of the gene in the pathogenicity of *C. albicans*. The quality of the extracted DNA was well verified by the formation of clear distinct bands on the electrophoresis plate, which showed little degradation and allowed further analysis using molecular techniques.

The HWP1 (Hyphae Wall Protein 1) is an important gene in the process of *C. albicans* adhesion to host epithelial cells, one of the critical stages of infection establishment and development. This gene also contains an expression of a cell surface protein that is exclusively activated in the hyphal phase of the organism, enabling it to be bound to host tissues and participate in biofilm formation. It is regarded as a significant virulence factor because the conversion of yeast into hyphae promotes the invasion of tissues and avoidance of host immune. The detection of HWP1 in most isolates therefore suggests a potential for hyphal adhesion in these strains; however, because only the presence of the gene was determined, its expression and any effect on pathogenicity were not assessed in this study.

The 76.5% prevalence rate in this study is consistent with previous studies which have reported a high frequency of the HWP1 gene in *C. albicans* isolates of clinical samples. The fact that some of the isolates (4/17; 23.5%) lack the gene could either be the indication of genetic variability between strains or variation in virulence patterns. This variability may affect the severity and clinical picture of candidiasis since the strains that do not express important adhesion-related genes might have weaker colonization and invasion capabilities of the host tissues. There is also a possibility that different virulence factors might be able to substitute loss of HWP1 in these isolates, which may be indicative of the multifactorial nature of *C. albicans* pathogenicity. Molecular diagnostic techniques like polymerase chain reaction (PCR) to detect virulence genes are a faster and sensitive method of detecting and characterising fungal pathogens. Molecular assays are more specific than traditional diagnostic measures and have the ability to identify genetic determinants that are directly linked to pathogenic processes. This increases the accuracy of diagnosis and can lead to improved clinical management of infections. The frequent detection of the HWP1 gene in *C. albicans* isolates in this study supports its use as a molecular marker in descriptive studies of clinical isolates. The results also give a clue about the pathogenic properties of the isolates and the significance of integrating the molecular tools in studying fungal infections. To understand the connection between HWP1 carriage or expression, clinical severity, and treatment outcomes of patients with candidiasis, further studies are suggested.

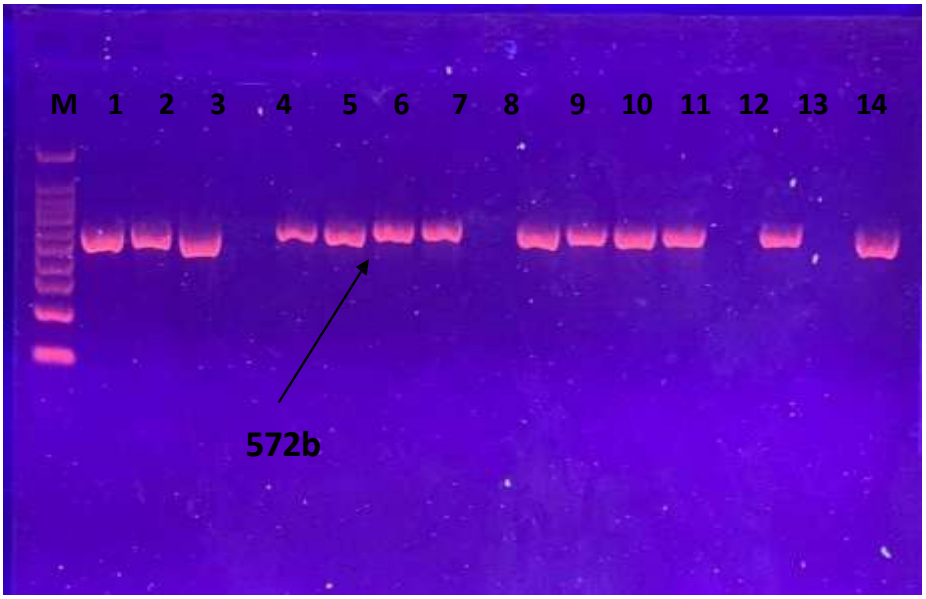


Figure 2. Agarose gel (2%) electrophoresis of HWP1 PCR products from representative C. albicans isolates. Lane M, DNA ladder; lanes 1–14, clinical isolates. HWP1-positive isolates show a single 572-bp band.

All 17 *C. albicans* isolates were screened for the HWP1 gene by PCR, and amplification produced a single band of 572 base pairs (bp) in 13 of them (Figure 2), indicating the presence of the gene in these isolates. PCR is a sensitive and specific tool that can detect virulence genes in small amounts of fungal DNA. The detection of HWP1 in most isolates is consistent with the recognized contribution of this adhesin to *C. albicans* pathogenicity. These results are similar to those of Monroy-Pérez et al. (2016), who detected ALS1 in 100% (39/39) and HWP1 in 89.7% (35/39) of *C. albicans* isolates from women with vulvovaginal candidiasis. The high frequencies in both studies underline the importance of adhesion-related genes in *C. albicans* colonization. By contrast, the present frequency is considerably higher than that reported in the Iraqi study by Ali (2014), in which 9 of 25 *C. albicans* isolates carried HWP1; this difference may reflect differences in sample size, origin of the isolates, or DNA extraction and amplification methods.

The present findings differ markedly from those of Inci et al. (2013), who detected HWP1 in only 5.3% (11/206) of *C. albicans* clinical isolates by multiplex PCR. Such variation may be due to geographical differences, genetic variation among strains, the clinical sources of the isolates, or the primers and PCR conditions used. Because HWP1 is closely related to hyphal formation, epithelial adhesion and biofilm formation, its frequent carriage in the present isolates may indicate a greater adhesive potential, although this was not tested directly. The present findings are closer to those of Nas et al. (2008), who detected HWP1 expression by reverse-transcriptase PCR in 62% of *C. albicans* strains from women with vaginitis. Together, these discrepancies highlight the variability in HWP1 carriage among *C. albicans* populations and support the inclusion of this gene, alongside other virulence determinants, in future molecular studies of pathogenic *C. albicans* strains.

3.3 Interleukins

Serum interleukin levels in patients (n = 47) and healthy controls (n = 47) are shown in Table 5 and Figures 3–5. Compared with controls, patients had significantly higher IL-1α (51.84 ± 6.03 vs 8.14 ± 0.57 pg/ml; Welch's $t = 7.21$), IL-17 (42.95 ± 2.14 vs 21.64 ± 1.33 pg/ml; $t = 8.46$) and IL-22 (75.09 ± 8.21 vs 13.27 ± 0.54 pg/ml; $t = 7.51$), with $P < 0.001$ for all three comparisons.

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Table 5: Serum interleukin levels in patients with cutaneous candidiasis and healthy controls (mean ± SE). *Significantly different from control (Welch's t-test, P < 0.001).

Groups / Parameter	Control (n = 47)	Patients (n = 47)	P-Value
IL-1α (pg/ml)	8.14± 0.57	51.84± 6.03*	**< 0.001**
IL-17 (pg/ml)	21.64 ± 1.33	42.95 ± 2.14*	**< 0.001**
IL-22 (pg/ml)	**13.27 ± 0.54**	**75.09 ± 8.21***	**< 0.001**

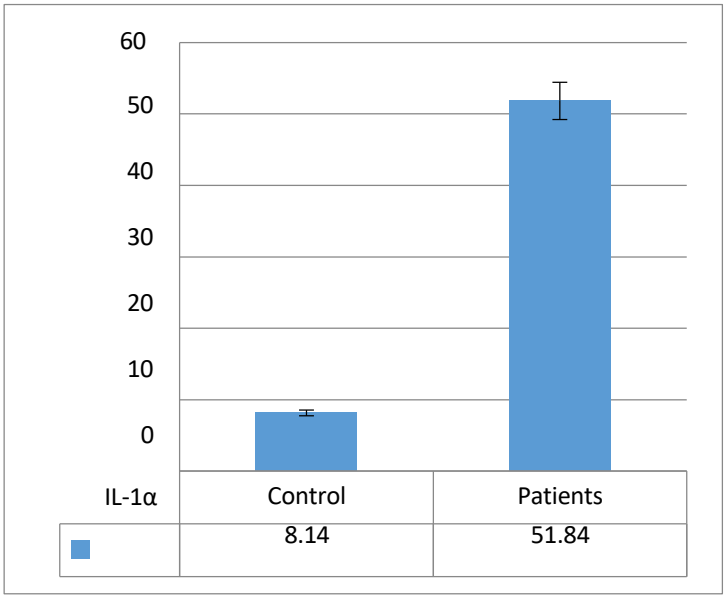


Figure 3: Serum IL-1α levels (pg/ml) in patients and controls (mean ± SE).

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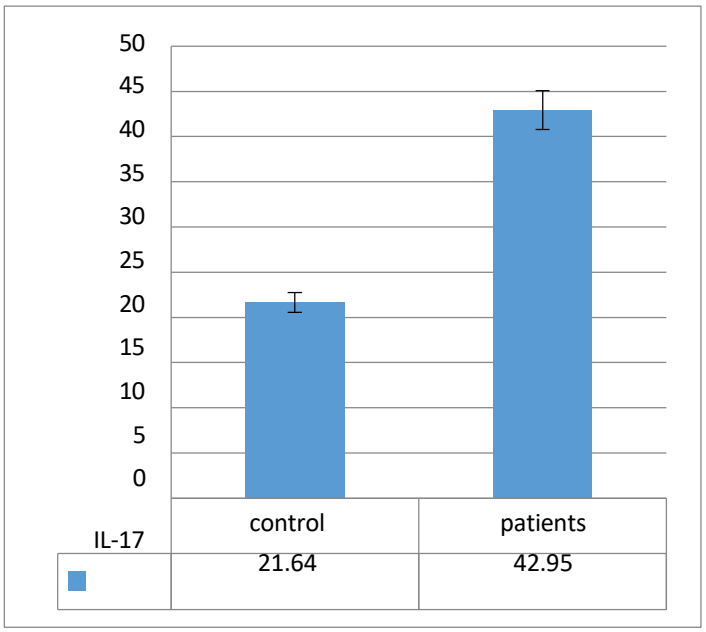


Figure 4. Serum IL-17 levels (pg/ml) in patients and controls (mean ± SE).

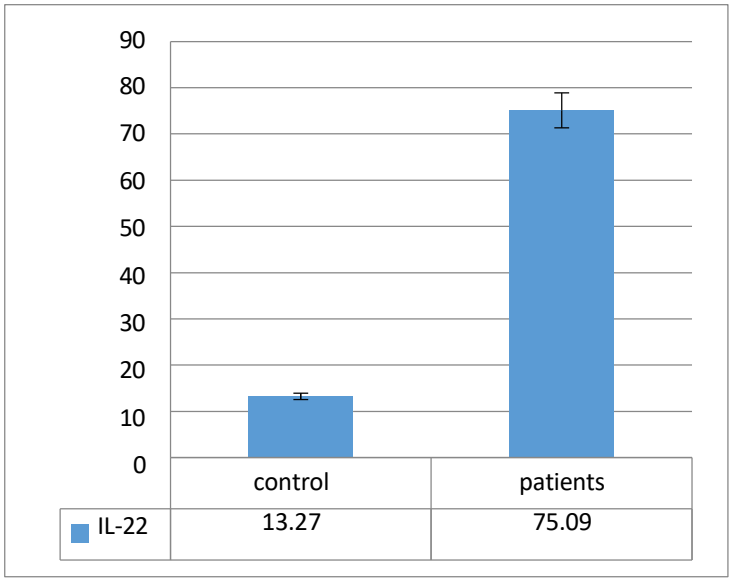


Figure 5. Serum IL-22 levels (pg/ml) in patients and controls (mean ± SE).

The levels of IL-17 and IL-1a are supposed to rise in case of fungal infections as a response of the host immune system to the invading pathogens. In the current research, there was increased presence of these cytokines in patients with cutaneous candidiasis, which indicates the stimulation of both innate and adaptive immune responses. This is consistent with Vonk et al. (2006), who showed in a murine model that endogenous IL-1α and IL-1β are essential for host defence against disseminated candidiasis (Vonk et al., 2006). The main pro-inflammatory cytokine is IL-1 that is crucial in triggering the inflammatory reaction, facilitating the immune cells recruitment, and strengthening the immune system against fungal infections. The IL-1a rise in the present case is thus in line with its activities of mediating early immune responses during *Candida* infections.

Moreover, the results of this research indicated that cutaneous candidiasis was associated with markedly higher serum levels of IL-17. The IL-17 is believed to be an important cytokine involved in antifungal immunity especially in mucocutaneous infections instigated by *Candida albicans*. The high level of IL-17 in this study

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indicates its significant contribution in the host defense against cutaneous candidiasis. This is in line with Huang et al. (2004), who showed in mice that IL-17 is a key component in the systemic host defense against infections by *Candida albicans* (Huang et al., 2004). Il-17 also helps in immune protection by enhancing the recruitment and activation of neutrophils which are the major effector cells in clearing of fungus.

IL-17 acts as a primary controller of antifungal response by initiating the expression of a particular group of genes, such as pro-inflammatory cytokines, chemokines as well as antimicrobial peptides. These intermediates increase the potential of epithelial cells and immune cells to react to fungal attack (Jin & Dong, 2013). The findings of the current research are consistent with those of Conti et al. (2009), who demonstrated in a murine model of oral candidiasis that Th17 cells and IL-17 receptor signalling are essential for mucosal host defence (Conti et al., 2009). They also discussed that *Candida* infection induces the production of IL-17 that subsequently controls the expression of pro-inflammatory cytokines, chemokines and antimicrobial proteins. All of them lead to neutrophil recruitment and candidacidal activity thus protecting against fungal infections.

IL-17 has also been noted to have a synergistic effect with other cytokines, including IL-6, to increase the efficacy of innate immunity. These cytokines are important in the activation of neutrophils and macrophages allowing them to effectively destroy fungal pathogens in the initial phases of infection (Mohammed et al., 2020). Such a coordinated immune response plays a crucial role in curbing the infection spread and disease progression. Another important cytokine, in addition to IL-1a and IL-17, is IL-22 that is also involved in the immune response to fungal infections. IL-22 has been shown in experimental models to regulate the balance between antifungal immunity and inflammatory pathology (Zelante et al., 2012). This is relevant to the host response to fungal infection because IL-22 is vital in preserving epithelial barrier integrity and tissue repair. These observations are in agreement with the findings of the current study that also showed increased levels of IL-22. The fact that the IL-1a, IL-17 and IL-22 levels were high in this study is consistent with the involvement of these three cytokines in the host response to cutaneous candidiasis, although their source and kinetics were not examined here. The cytokines play a role in the activation and coordination of immune responses necessary in the regulation of fungal infections and the homeostasis of tissues.

Conclusions

In this study, the HWP1 gene was detected in 13 of 17 (76.5%) *Candida albicans* isolates recovered from patients with cutaneous candidiasis, and serum IL-1α, IL-17 and IL-22 levels were significantly higher in patients than in healthy controls. These findings show that HWP1 is commonly carried by *C. albicans* isolates from cutaneous infections in this setting and that cutaneous candidiasis is accompanied by a systemic cytokine profile consistent with activation of IL-1-driven innate and Th17-type immunity. Because endpoint PCR detects only the presence of DNA, the results do not establish HWP1 expression, a relationship between HWP1 carriage and cytokine levels or disease severity, or any causal effect, and should therefore be regarded as descriptive.

Limitations and future directions. The number of *C. albicans* isolates analysed molecularly was small (n = 17); only one virulence gene was screened, whereas other determinants such as the ALS gene family and secreted aspartyl proteinases were not examined; HWP1 transcription was not measured, and HWP1 status was not correlated with cytokine levels, lesion severity or treatment outcome; and patients were recruited from surgical wards in a single city, which may limit generalizability. Future studies should include larger and more diverse cohorts, quantify HWP1 and other virulence-gene expression by RT-qPCR, confirm species identity by sequencing, and relate molecular and cytokine findings to clinical severity and treatment response. Such work may support molecular risk assessment and the development of strategies targeting fungal adhesion, biofilm formation or the host cytokine response in cutaneous candidiasis.

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NA

Supplementary Material

NA

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