

Article

Candida albicans-The Virulence Factors and Clinical Manifestations of Infection

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Citation: Al Nakeeb R. H., Hameed N. D., Jumah Y. H. Candida albicans-The Virulence Factors and Clinical Manifestations of Infection. American Journal of Biology and Natural Sciences 2026, 3(9), 232-238.

Received: 10th Jul 2026

Revised: 11th Jun 2026

Accepted: 20th Aug 2026

Published: 30th Sep 2026



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Abstract: The commensal fungus *Candida albicans* is a part of the typical flora of the microbiota that is frequently found on the skin and mucosal surface of healthy individuals along with the vaginal and gastrointestinal tracts. *Candida* can manifest in many ways and symptoms may range from mild mucocutaneous infections to severe life threatening invasive infections of multiple organs. *Candida albicans* is an opportunistic microorganism that could transition from typical flora (commensal state) to pathogenic state depends on a range of factors that might interfere with the balance of *Candida*. The gastrointestinal tract is the main site of *Candida albicans* infections, while the infection is caused by immune system abnormalities, mucosal damage of intestine and dysbiosis of microflora. The Candidemia and invasive infections of *Candida albicans* are connected to elevated blood counts of *Candida albicans*. This paper reviews the pathogenic features of *Candida albicans* and the symptoms of candidiasis.

Keywords: *Candida albicans*, oral cavity, virulence traits, gastroenterology, dermatovenerology.

Introduction

Candida albicans is normally found on the surface of the genitourinary tract, intestines, mouth, and vagina in 80% of healthy individuals. Any balance in the relationship between this opportunist pathogen and the host immunity results in mucosal infections, which could then disseminate via the blood system and infect different organs [1]. It is responsible for 40% of candidemia and 60% of mucosal infections. Infections by *Candida albicans* are reported to be caused by several virulent factors

including adhesion to host as well as abiotic medical surfaces [2]. It has also been documented that *Candida albicans* is resistant to conventional antifungal agents like azoles, especially when it occurs as biofilms [3]. Several factors involved in the pathogenicity of *Candida albicans*. The most virulent factors of *Candida albicans* are reviewed here to understand how candidiasis is developed and gain more understanding of the complex interactions between different species that might affect the outcome of the disease [4].

Methods

Fungal infection-causing pathogens, such as *Candida albicans*, affect not only the whole body but also the skin and mucous membrane surfaces. Up to 400,000 cases of systemic fungal infections exist in the various species of *Candida*. Among all the species, more than 70% of the world's fungal infections belong to *Candida albicans*. This article focuses on an overview of the pathogenicity properties and symptoms of *Candida albicans* in the skin, mouth, and invasive infections.

Candida albicans can exist in many forms such as hyphae, pseudohyphae, and blastospores (Figure 1). Additional cell matter is added to the outer surface of the blastospore during asexual reproduction. New cell matter, which grows from a small bud, creates a partition to form a separation between the parent and daughter cells.

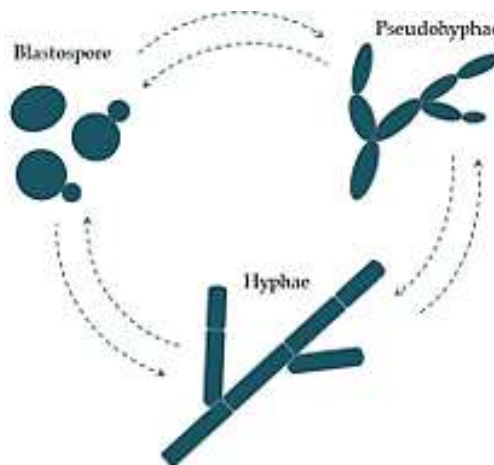


Figure 1. *Candida albicans*' morphological changes and transitions throughout the infection process

It is also possible to revert morphological changes from blastospore to hyphae and Pseudohyphae. Pseudohyphae comprises chains of elongated yeast cells, whereas hyphae comprise branching chains of tubular cells that do not constrict at septation points. High CO₂ levels, alkaline pH, serum, and temperatures exceeding 37 °C all contribute to filamentation. Lack of carbon and nitrogen is another factor that favors filamentation. Several pathways involving various transcription factors are activated when this change of morphology takes place. It is also facilitates adherence to host cell via adhesion proteins. The cell membrane enables communication between the cell and the environment.

Results

Candida possessed specific features as well. One group of virulence factors was played a role in colonization or the beginning of the infection, whereas another group helped with the spread of the virus [5]. Polymorphism implies that *Candida* will vary depending on the changes in the environment; therefore, *Candida albicans* can be transformed from the commensal into the pathogenic form. It is characterized by the morphological alteration in the blastospores [6, 7]. Nuclei of the hyphal forms separate outside the septum region, but inside the germ tube. After separation, one nucleus goes to the center of the germ tube, and the other one comes back to the mother cell [8]. Yeast, a kind of *Candida albicans*, can be found in the human microbiome. Transition to the pathogenic form takes place through yeast transformation into hyphal [9] (figure 2). While Active penetration, in contrast, is influenced by the behavior of the fungus and induces endocytosis [10]. Signaling pathways are

involved in hypha formation. Cyclic adenosine monophosphate-dependent protein kinase A is the most important [11]. It has been shown that candida lysin, which is a specific toxin produced by hyphae, is vital for the development of candidiasis [12]. Candida lysin is a cytotoxic α -helical amphipathic peptide with 31 amino acid residues [13]. It is an essential factor responsible for causing damage to host cells, and it is produced by the hyphae of *Candida albicans*. It is thought to be involved in systemic infections and death [14]. Candida lysin can harm the epithelial membrane directly through intercalation, permeabilization, and formation of pores [15, 16].

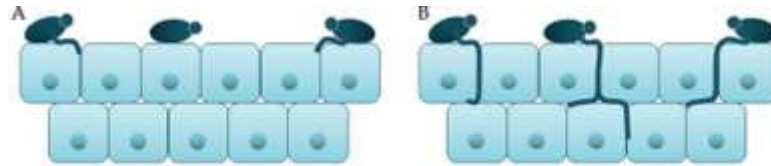


Figure 2. Diagrammatic representation of *Candida albicans* (A) adherence and colonization and (B) invasion and penetration.

The formation of biofilm

Biofilm of *Candida albicans* has a complicated structure and different morphological forms because this fungus has a morphological capability of transforming from yeast to hyphae [17]. There are several successive stages of biofilm development [18]. The lowest layer of the biofilm is formed at the initial stage, where individual cells of *Candida albicans* attach to the substrate. Cell proliferation occurs at the next stage, where the cells grow in elongated form, developing into filaments [19]. Hyphae formation shows that the process of biofilm formation has begun. The dispersal of non-attached cells at the final stage can result in the formation of new biofilms (Figure 3) [20]. Extracellular DNA and extracellular polymers constitute the extracellular polysaccharide matrix responsible for the structural integrity of the biofilm [21]. Besides, extracellular DNA is important in the attachment of the biofilm structure to the substrate [22]. In that they prevent the interaction between the fungus and target cells, the α -1,3-glucans, a major constituent of the extracellular matrix, significantly increase the resistance of the biofilm to antifungal drugs [23]. More α -1,3-glucans are produced in the extracellular matrix of biofilm forming *Candida albicans* than the planktonic ones [24]. Through facilitating nutrient, oxygen, and water circulation, the biofilm channels provide the cell with "multicellular" properties [25]. In relation to the behavior of the microbe and the production of signal molecules, intercellular communication, termed as quorum sensing, is a constituent of the biofilm [26]. "Autoinducers" are the molecules that employ signaling mechanisms in order to control population density. Suppression of target genes is triggered through the binding of signal molecules to a specific receptor and density [27]. This quorum sensing mechanism regulates virulent phenotypes and ensures that there is an optimal size of the biofilm fungal colony [28].

As the cells of biofilm occur deeper within, their genes get expressed more as the amino acids take part in the synthesis of antioxidants; this type of metabolism ensures that the cells become resistant to oxidative stress and starvation [29]. The biofilm cells generate a hypoxic condition along with increasing the activity of genes responsible for ergosterol, fatty acid, and glycolysis metabolisms [30].

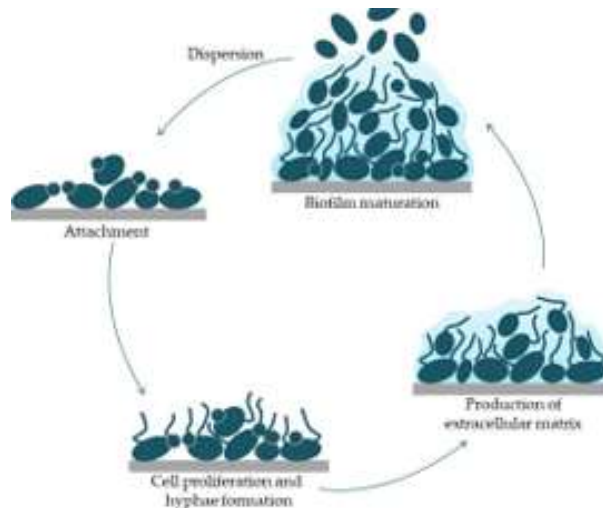


Figure 3. The stages of the production of *C. albicans* biofilms

Candida Albicans in the Oral Cavity

Among other fungi that attack the oral cavity, the most common one is *Candida* species causing candidiasis. *Candida* species are naturally found in all people [31]. *Candida albicans* is assumed to be a part of more than 80% of isolates from the oral cavity. It is also the most common type of *Candida* known as non-*albicans* *Candida* [32]. Oral homeostasis may be disrupted by a variety of factors such as systemic, local, genetic, and environmental [33]. Consequently, there occurs an opportunistic infection where the pathogen takes place of the native microbiota. These changes may lead either to overgrowth of *Candida* or to alteration of its virulence factors expression [34].

Discussion

GI system is one of the main sources within the body, and it is thought that humans are naturally carriers of *Candida albicans*, which is the most common one responsible for causing infections [35]. Disseminated candidiasis and the entry of *Candida albicans* into the bloodstream are usually the result of an invasive GI infection [36]. Immunocompromise, muco-intestinal barrier compromise, and dysbiosis of the normal flora are the main risk factors that make it possible for *Candida albicans* to turn from being a commensal/symbiotic into a pathogenic microorganism [37].

Candida albicans in Dermatovenereology

Although up to 80%-90% of all infections of candidiasis result from *Candida Albicans*, other *Candida* species have been known to act as pathogens for diseases [38]. This is because, although *Candida albicans* is a fungus that is normally commensal, when it acts as an invasive fungus in patients with weakened immunity, it causes systemic infections that usually turn out to be fatal [39].

Invasive Candida Infections

Candida Albicans infection may have a compromising effect on the immunity of the host [40]. Consequently, excessive or abnormal colonization coupled with lack of resistance to the disease by the host leads to invasion [41].

Conclusions

Comprehension of the exact causes and mechanisms of *Candida albicans* pathogenesis is important because of their wide scope of action, which involves biofilm formation, dimorphism, secretion of adhesion proteins, and extracellular hydrolytic enzymes. Diverse factors that play a major role in the development of candidiasis, such as age, immunosuppression, diabetes mellitus, neutropenia, and other related factors. In order to prevent the development of *Candida albicans* infections, chances of achieving the desired goal increase together with the knowledge about all these aspects.

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