
Review

***Candida* Infections: Epidemiology, Clinical Manifestations and Quality-of-Life Burden**

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Abstract

Candida infections represent a major global public health challenge and remain among the most common opportunistic fungal infections worldwide. Although *Candida albicans* remains the predominant pathogen, the incidence of infections caused by non-albicans species, particularly *Candidozyma auris*, has increased substantially in recent years. *Candida* infections range from superficial mucocutaneous disease to invasive life-threatening infections associated with high morbidity and mortality. In addition to clinical burden, growing evidence indicates a substantial negative impact on health-related quality of life, particularly among patients with recurrent vulvovaginal candidiasis and chronic fungal infections.

Keywords: *Candida* infections; *Candida albicans*; *Candidozyma auris*; candidiasis; epidemiology; antifungal resistance; invasive candidiasis; recurrent vulvovaginal candidiasis; health-related quality of life; disease burden

1. Literature Search Strategy

This narrative review was based on a literature search performed using the PubMed, Scopus, and Google Scholar databases. Articles published between 2020 and 2026 related to *Candida* infections, epidemiology, antifungal resistance, and quality of life were preferentially included. Additional relevant studies and official reports from the WHO, CDC, and ECDC were identified through manual screening of reference lists. The aim of the search was to provide a comprehensive overview of current knowledge regarding the clinical and public health burden of *Candida* infections.

2. Introduction

Candida infections are among the most common opportunistic fungal infections worldwide and represent an important public health challenge. Species of the genus *Candida* are part of the normal human microbiota and may colonize the oral cavity, gastrointestinal tract, genital tract, and skin without causing disease. Under conditions of impaired host immunity, microbiota disruption, or other predisposing factors, *Candida* species can cause a broad spectrum of clinical manifestations ranging from superficial mucocutaneous infections to life-threatening invasive disease [1–4]. Superficial forms primarily affect the oral cavity, skin, and genital mucosa, while invasive candidiasis includes

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candidemia and deep-seated organ involvement, predominantly occurring in hospitalized, critically ill, and immunocompromised patients [2,5,6].

Although *Candida albicans* remains the predominant causative agent of candidiasis, an increasing proportion of infections are caused by non-*albicans* *Candida* species, including *Candida glabrata*, *Candida parapsilosis*, *Candida tropicalis*, and the emerging multidrug-resistant pathogen *Candidoizyia auris*, with antifungal resistance posing a significant therapeutic challenge. Given its global distribution, multidrug resistance, high transmissibility, and significant mortality, *Candida auris* represents a serious and growing threat to public health worldwide [3,7,8].

Recent epidemiological trends indicate a growing global burden of candidiasis driven by population aging, increasing numbers of immunocompromised patients, widespread use of broad-spectrum antibiotics, invasive medical procedures, and emerging antifungal resistance [2,7,8]. Beyond their clinical consequences, *Candida* infections may significantly impair health-related quality of life, particularly in recurrent and chronic forms of disease, highlighting the need for improved prevention, early diagnosis, and effective treatment strategies [5,6,9]. The development of effective therapies for candidiasis depends on a comprehensive understanding of *Candida* pathogenic mechanisms and their impact on host immune responses [10].

2.1. Europe and Regional Epidemiology

According to the CDC Sexually Transmitted Infections Treatment Guidelines, uncomplicated vulvovaginal candidiasis is most commonly caused by *Candida albicans*, whereas recurrent and treatment-resistant infections are more often associated with non-*albicans* species [11]. The increasing occurrence of these infections, together with the emergence of antifungal resistance, has drawn attention to the growing burden of candidiasis. In recent years, a marked increase in infections caused by *Candidoizyia auris* has been observed in Europe. According to the European Centre for Disease Prevention and Control (ECDC), the first cases in the European Union and the European Economic Area were reported in 2014, followed by a steady rise in case numbers. In 2023, a total of 1,346 cases were reported from 18 European countries, although the true burden is likely higher because surveillance remains incomplete in many settings. The highest numbers of cases between 2013 and 2023 were reported in Spain, Greece, Italy, Romania, and Germany. Of particular concern is the fact that Greece, Italy and Spain have developed regional endemic transmission within a period of only five to seven years since the first documented case, indicating the extremely rapid potential for the spread of this pathogen through hospital networks [12–14]. Antifungal treatment can be difficult with invasive infection and with multi-drug-resistant strains being reported [14]. At the same time, many European countries still lack adequate surveillance systems, national guidelines and sufficiently developed capacities to control the spread of infection, which poses a significant challenge for the future control of candidiasis in Europe [13].

2.2. Serbia

In the Republic of Serbia, data on candidiasis are still limited due to the lack of systematic national surveillance of invasive fungal infections. According to Arsenijević and Denning's estimated burden, approximately 518 cases of candidemia, 187 cases of *Candida* peritonitis, 135,303 cases of recurrent vulvovaginal candidiasis and 208,489 cases of oral candidiasis are registered annually in Serbia, which indicates a significant burden on the health system with these infections [12]. Recent European data indicate the growing importance of infections caused by *Candidoizyia auris* in the region as well, with Serbia reporting eight cases of this infection in 2024, according to the ECDC report, indicating the need to strengthen national surveillance and laboratory diagnostics [13].

2.3. Clinical Manifestations

Oral candidiasis is one of the most common mucosal manifestations of *Candida* infection and may present as pseudomembranous, erythematous, hyperplastic candidiasis, or angular cheilitis. It occurs in association with local or systemic predisposing factors, including antibiotic use, denture wearing, diabetes mellitus, corticosteroid therapy, and immunosuppression [4,5,10].

Vulvovaginal candidiasis is another common mucosal infection and is predominantly caused by *Candida albicans*, which accounts for approximately 74–89% of cases, while non-*albicans* *Candida* species are increasingly recognized, particularly in recurrent and treatment-resistant infections [9,10,14].

Esophageal candidiasis is a more severe form of mucosal candidiasis that occurs mainly in patients with significant immunosuppression, including those with advanced HIV infection, hematological malignancies, organ transplantation, prolonged corticosteroid use, and other immunocompromising conditions [5,6]. The most common symptoms are dysphagia, odynophagia, retrosternal pain, and difficulty swallowing. Because esophageal candidiasis is often associated with impaired immune function, its diagnosis should prompt further evaluation of potential underlying conditions [5,15,16].

The role of *Candida* spp. in gastrointestinal disorders remains unclear. Although *Candida* species are common colonizers of the gastrointestinal tract, their detection in stool samples does not necessarily indicate infection or disease. At present, there is no consensus regarding the clinical significance of gastrointestinal *Candida* colonization in immunocompetent individuals, and current guidelines do not support the diagnosis of a separate “*Candida* overgrowth syndrome” [16–18]. For this reason, microbiological findings should always be interpreted together with clinical presentation and other diagnostic findings [5,6,16–18].

Some studies suggest that *Candida* species may contribute to intestinal inflammation through interactions with the host immune response and gut microbiota, particularly in patients with pre-existing gastrointestinal disorders [5,6,16–18]. In critically ill patients, gastrointestinal colonization has also been considered a possible risk factor for invasive candidiasis and candidemia, especially in the presence of mucosal barrier disruption, broad-spectrum antibiotic use, and severe underlying illness [5,6].

The ability of *Candida* species to form biofilms contributes to the persistence of infection and may reduce the effectiveness of antifungal treatment. Biofilm-associated cells are less susceptible to antifungal agents and host immune responses, which may partly explain the recurrent nature of some *Candida* infections [4]. Although biofilm formation is a well-recognized virulence factor of *Candida albicans*, several non-*albicans* *Candida* species, including *Candida glabrata*, *Candida parapsilosis*, and *Candida tropicalis*, also possess the ability to form biofilms, contributing to persistence, antifungal resistance, and treatment failure [4,11].

2.4. Quality of Life

Selected studies evaluating the impact of fungal infections on quality of life are summarized in Tables 1 and 2.

Table 1. Clinical spectrum, manifestations and major risk factors of *Candida* infections.

Category	Clinical Manifestations	Major Risk Factors
Superficial candidiasis	Oral candidiasis, vulvovaginal candidiasis, cutaneous candidiasis, <i>Candida</i> -associated nail infections	Antibiotic use, diabetes mellitus, pregnancy, denture wearing, corticosteroid therapy
Oral candidiasis	Pseudomembranous, erythematous, hyperplastic candidiasis, angular cheilitis	Denture use, antibiotic therapy, diabetes mellitus, immunosuppression
Vulvovaginal candidiasis	Vulvovaginal pruritus, burning, erythema, dyspareunia, vaginal discharge	Pregnancy, diabetes mellitus, antibiotic exposure, hormonal factors, vaginal microbiota disruption
Esophageal candidiasis	Dysphagia, odynophagia, retrosternal pain, difficulty swallowing	Advanced HIV infection, hematological malignancies, organ transplantation, prolonged corticosteroid therapy
Gastrointestinal candidiasis	Colonization, suspected invasive gastrointestinal candidiasis, gastrointestinal symptoms in selected patients	Critical illness, broad-spectrum antibiotics, disruption of mucosal barriers, immunosuppression
Invasive candidiasis	Candidemia, deep-seated organ infections, disseminated candidiasis	ICU stay, central venous catheters, major surgery, immunosuppression, prolonged hospitalization

Candida infections can substantially impair patients' quality of life due to recurrent symptoms, chronic disease course, treatment burden, psychosocial distress, and negative effects on daily functioning [9,19–22].

Recurrent vulvovaginal candidiasis significantly impairs the quality of life and sexual health of affected women. In a prospective multicenter study conducted in Austria, Poland and Slovakia, which included 360 women with chronic recurrent vulvovaginal candidiasis, the average duration of symptoms was 39.5 months, while 20% of patients had at least one relapsing episode during the follow-up period. After six months of treatment, an improvement in quality of life was registered in 65.2% of women according to the EQ-5D-5L score and in 75.4% of women according to the EQ-VAS score. At the same time, 9.5% of women showed a deterioration in quality of life, while 11.3% noted a deterioration in the subjective perception of health. The study also showed a significant negative impact of the disease on sexual health—pain during or after sexual intercourse was the most common problem, and after therapy, a reduction in the incidence of this symptom was reported in 66.3% of women. Fear of sexual intercourse due to pain was reduced in 59.9% of respondents, while in 37.6% of women, an improvement in partner relationships was noted. The authors conclude that recurrent candidiasis not only affects the physical symptoms of the disease but also significantly impairs the psychological well-being, sexual functioning, and overall quality of life of patients [19].

In addition, a recent study comparing women with acute vulvovaginal candidiasis and women with recurrent vulvovaginal candidiasis showed that recurrent forms of the disease have a significantly more pronounced negative impact on quality of life. The overall SF-36 quality of life score was significantly lower in women with recurrent candidiasis compared to women with acute infection (47.27 ± 18.31 vs. 71.17 ± 19.60 ; $p = 0.037$). The most pronounced differences were observed in the domains of physical functioning (54.28 ± 32.29 vs. 84.66 ± 25.90 ; $p = 0.021$), physical health limitations (36.90 ± 38.42 vs. 82.33 ± 35.53 ; $p = 0.029$), emotional functioning (45.00 ± 42.26 vs. 77.77 ± 38.49 ; $p = 0.037$) and perception of a change in health status (33.75 ± 23.33 vs. 51.33 ± 18.33 ; $p = 0.002$). Although there were no statistically significant differences in the levels of anxiety, depression and stress between the groups, the authors emphasize that recurrent candidiasis significantly

affects the daily functioning, physical health and emotional well-being of patients, further confirming that chronic and recurrent forms of the disease represent a significant burden on the quality of life of affected women [19].

Recent data suggest that the burden of vulvovaginal candidiasis goes beyond the physical symptoms of the disease alone and significantly affects health-related quality of life [19,20]. A recent narrative review that analyzed recurrent urogenital infections showed that women with recurrent vulvovaginal candidiasis consistently report reduced quality of life in the physical, psychological, social, and financial domains. Studies using validated instruments, such as the SF-36 questionnaire, showed significantly lower scores in all domains of quality of life compared to the general population [21]. Notably, the impact of recurrent vulvovaginal candidiasis on mental health was compared with the burden of patients with type 2 diabetes, while the overall impact on quality of life was similar to that of chronic respiratory diseases, such as asthma and chronic obstructive pulmonary disease. In addition to impaired physical functioning, recurrent infections have been associated with social withdrawal, feelings of shame, stigmatization, decreased work productivity, sexual dysfunction, and increased psychological distress [21,22]. Patients often reported feelings of frustration, helplessness, and loss of control, especially in cases of recurrent, misdiagnosed, or inadequately treated infections [22]. The authors emphasize that better patient education, more accurate diagnostics, social support, and adequate access to health care can significantly reduce the psychosocial burden associated with recurrent vulvovaginal candidiasis [21]. A recent qualitative study conducted in the United Kingdom further pointed to a significantly impaired quality of life in people with recurrent vulvovaginal candidiasis. The study included 32 participants aged 21 to 60 years, with 29 participants describing the disease as recurrent or cyclical, while three participants reported a persistent or chronic course of the disease. The duration of symptoms ranged from a few months to more than a decade. Respondents reported that recurrent vulvovaginal candidiasis significantly impairs daily functioning, emotional well-being, sexual health, and social relationships [22]. Intense itching, burning, pain, repeated vaginal secretions, sleep disturbances, and difficulty performing daily activities were often reported. Some respondents reported that they had to change their underwear several times a day, avoid sexual intercourse, adjust their clothing choices, and implement complex hygiene routines to prevent symptoms from recurring [21,22]. Many subjects described a state of constant hypervigilance, with continuous monitoring of symptoms and adjustments to daily behavior to prevent relapse.

In a multicenter study conducted in Canada [23] that included 307 adult patients with onychomycosis, the mean value of the Health Utilities Index Mark 3 (HUI3) was 0.73 (95% CI: 0.70–0.75), indicating a significant reduction in quality of life compared with the general population (utility = 0.86). Patients with concomitant diabetes had significantly lower utility scores than those without diabetes (0.70 vs. 0.76; $p = 0.02$). The lowest quality-of-life scores were observed among patients with severe onychomycosis and diabetes (utility = 0.69; 95% CI: 0.65–0.73), highlighting the additional burden of comorbid conditions on patient well-being. The authors concluded that diabetes had a greater impact on quality of life than the severity of fungal infection itself and emphasized the value of these utility estimates for future pharmacoeconomic analyses and reimbursement decisions [23].

Table 2. Impact of fungal infections on quality of life in selected studies.

Study	Population	QoL Instrument	Main Findings
Lietz et al. [19]	RVVC patients	EQ-5D/EQ-VAS	Sexual and psychosocial burden
Baghbani et al. [20]	Recurrent VVC	SF-36	Lower QoL in recurrent disease

Mickle AT et al. [23]	Onychomycosis patients	HUI3	Reduced utility scores
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In a certain number of patients, gastrointestinal symptoms such as flatulence, abdominal pain, diarrhea, constipation, sensation of incomplete bowel movements, intolerance to certain foods and chronic fatigue are often attributed to “chronic candidiasis” on their own initiative, although in most of these individuals there is no microbiological evidence of an invasive or mucosal infection caused by species of the genus *Candida*. The contemporary literature shows that such symptoms are significantly more often associated with disorders of gut–brain interaction and functional gastrointestinal disorders. A global Rome Foundation study conducted in 33 countries found that functional gastrointestinal disorders affect more than 40% of the adult population, with those affected having significantly lower physical and mental quality of life scores compared to the healthy population. Additionally, a review published in The Lancet states that patients with irritable bowel syndrome, functional dyspepsia, and other disorders of gut–brain interaction often have pronounced psychological distress, decreased work productivity, and impaired daily functioning, which can lead to the search for alternative explanations for the symptoms, including the incorrect belief of “*Candida* overgrowth” syndrome [16,17].

In patients with functional dyspepsia, long-term symptoms, diet-related anxiety, and a significant decrease in quality of life have been additionally described, especially in individuals with chronic and recurrent complaints [18].

2.5. Quality of Life and Treatment Efficacy

The efficacy of maintenance antifungal therapy in recurrent vulvovaginal candidiasis has been demonstrated in several studies. A recent network meta-analysis showed that weekly oral fluconazole or itraconazole significantly reduced the risk of early recurrence during active treatment [24].

In addition to reducing microbiological recurrence, successful management of recurrent vulvovaginal candidiasis has been consistently associated with improvements in health-related quality of life by alleviating symptoms, improving sexual functioning, and reducing the psychological burden associated with recurrent disease. While antifungal therapy remains the cornerstone of treatment, increasing attention has been directed toward interventions aimed at restoring the vaginal microbiota. A recent randomized double-blind placebo-controlled trial demonstrated that adjunctive oral supplementation with *Lactobacillus rhamnosus* CA15 improved vaginal health, clinical symptoms, and several domains of quality of life, supporting the potential role of microbiota-targeted interventions as complementary therapeutic strategies. Nevertheless, evidence regarding dietary interventions and probiotic supplementation remains limited, and further well-designed clinical trials are required before these approaches can be routinely recommended in clinical practice [19,21,22,25].

Long-term suppressive therapy with fluconazole has also been associated with prolonged remission and reduced recurrence rates in women with recurrent vulvovaginal candidiasis [26]. At the same time, increasing triazole resistance, particularly to fluconazole, represents an emerging therapeutic challenge in vulvovaginal candidiasis [27].

Recent therapeutic advances have expanded treatment options for recurrent vulvovaginal candidiasis. Ibrexafungerp, a first-in-class triterpenoid antifungal approved for vulvovaginal candidiasis, has demonstrated activity against both *Candida albicans* and several non-*albicans* *Candida* species, including isolates with reduced azole susceptibility [28,29]. Oteseconazole, a novel oral tetrazole antifungal, has shown high efficacy in reducing recurrence rates in women with recurrent vulvovaginal candidiasis and represents an

important option for long-term disease management [3]. For cutaneous candidiasis, topical and systemic antifungal therapies remain effective treatment options depending on disease severity and localization [28]. Invasive gastrointestinal candidiasis requires systemic antifungal treatment according to recommendations for invasive candidiasis [5,6].

Cutaneous candidiasis can negatively affect quality of life, especially in patients with recurrent or long-lasting disease. Symptoms such as erythema, maceration, pruritus, burning, and visible skin changes may cause discomfort and embarrassment, often leading to reduced self-confidence and social withdrawal. Infections involving intertriginous or genital areas are frequently associated with irritation, discomfort during daily activities, and emotional distress. In some patients, chronic or recurrent disease may also contribute to sleep problems, reduced work productivity, and psychological burden, particularly in the presence of underlying chronic illness or immunosuppression [28].

The role of *Candida* spp. in the development of gastrointestinal disorders remains incompletely understood and continues to be a subject of scientific debate. *Candida* spp. can be detected in the gastrointestinal tract of a substantial proportion of healthy individuals, where they usually behave as commensal microorganisms without causing disease [30–32]. Distinguishing colonization from true invasive infection represents a major diagnostic challenge, as the mere detection of *Candida* spp. in stool samples is insufficient to establish the diagnosis. Definitive differentiation requires endoscopic evaluation and histopathological verification demonstrating the presence of pseudohyphae and tissue invasion [31,32]. However, such procedures are rarely performed in routine clinical practice, and considerable diagnostic uncertainty remains.

Although no universal consensus or official clinical guidelines exist for the treatment of a distinct “*Candida* overgrowth syndrome,” certain clinical entities are more widely accepted. Evidence suggests a possible role for *Candida* spp. in the development of antibiotic-associated diarrhea [33]. On the other hand, emerging evidence from animal models and studies in patients with gastric ulcers indicates that the presence of *Candida* spp. on the gastric mucosa may contribute to enhanced inflammatory response, greater epithelial damage, and delayed ulcer healing [34,35]. These effects have been associated with reduced mucosal blood flow in the ulcer area and increased expression of proinflammatory cytokines [34].

2.6. Emerging Mechanisms of *Candida*–Host Interactions

Beyond the established clinical manifestations of candidiasis, growing evidence indicates that interactions between *Candida* species, the host, and the intestinal microenvironment influence whether these fungi remain harmless commensals or contribute to disease under favorable conditions [2,10,30,31]. Recent evidence indicates that the role of *Candida* species in the gastrointestinal tract extends beyond simple commensal colonization and involves complex interactions with the intestinal epithelium, host immunity, and resident microbiota. Under physiological conditions, *Candida* spp. coexist with the host without causing disease. However, disruption of intestinal homeostasis, alterations in the microbial community, or impaired immune function may facilitate fungal overgrowth and contribute to intestinal inflammation and disease susceptibility. Although the exact mechanisms are still being investigated, growing evidence suggests that *Candida* may influence epithelial barrier function, immune responses, and microbial ecology within the gastrointestinal tract [2,10,30,31].

Integrity of the intestinal epithelial barrier is essential for maintaining mucosal homeostasis. Experimental studies have shown that *Candida albicans* interacts closely with intestinal epithelial cells and may influence tight junction integrity and epithelial permeability during conditions favoring fungal overgrowth or invasion. Conversely, an intact epithelial barrier and balanced host–microbiota interactions help maintain *Candida* as a

harmless commensal organism. These findings emphasize that the transition from colonization to pathogenicity depends not only on fungal virulence factors but also on the integrity of the host epithelial barrier [2,10,30,31].

Host immune responses play a central role in controlling intestinal *Candida* colonization. Recognition of fungal cell wall components by pattern-recognition receptors initiates innate immune responses involving epithelial cells, macrophages, neutrophils, and dendritic cells. Subsequent activation of adaptive immunity, particularly Th17 lymphocytes and the IL-17/IL-22 signaling pathway, contributes to maintaining mucosal integrity and preventing excessive fungal proliferation [10]. Defects in these immune pathways have been associated with increased susceptibility to mucosal candidiasis, highlighting the importance of balanced immune regulation in host–fungal interactions [2,4,10,30].

Interactions between *Candida* species and bacterial members of the gut microbiota further influence fungal colonization and persistence. Commensal bacteria, particularly *Lactobacillus* species, contribute to colonization resistance by competing for nutrients, producing antimicrobial metabolites, and maintaining an acidic environment unfavorable for fungal overgrowth. Conversely, disruption of the bacterial microbiota following broad-spectrum antibiotic therapy may reduce colonization resistance and facilitate expansion of *Candida* populations. These bidirectional interactions illustrate the importance of considering the intestinal microbiome as an integrated bacterial–fungal ecosystem rather than separate microbial communities [2,4,30,31].

Fungal metabolism also contributes to host–microbe interactions within the gastrointestinal tract. *Candida* species produce a variety of metabolites capable of influencing microbial competition, biofilm formation, and host immune responses. In parallel, bacterial metabolites, including short-chain fatty acids and bile acid derivatives, may suppress fungal virulence, regulate morphogenesis, and contribute to maintenance of intestinal homeostasis. Although the clinical significance of these metabolic interactions is still being elucidated, they represent an important component of the complex ecological network within the gut microbiome [2,30,31].

Emerging evidence also suggests that fungal dysbiosis may influence gut–brain communication through interactions with the intestinal microbiota, immune mediators, and microbial metabolites. While current evidence is derived predominantly from experimental studies, alterations in the gut mycobiome have been proposed as potential contributors to systemic immune activation and disturbances in gut–brain signaling. Nevertheless, the precise clinical significance of these observations remains incompletely understood and warrants further investigation [2,5,16,17].

3. Conclusions

From a primary care perspective, the biggest challenge is not the treatment itself, but rather the lack of awareness among both patients and physicians about the psychosocial burden of recurrent infections. In addition to significant morbidity and mortality, recurrent and chronic forms of candidiasis may substantially impair health-related quality of life, particularly among women with recurrent vulvovaginal candidiasis. Recent epidemiological trends, including the emergence of multidrug-resistant species such as *Candida auris*, further emphasize the need for improved surveillance, early diagnosis and timely antifungal treatment. Greater awareness of the psychosocial burden associated with *Candida* infections may contribute to more comprehensive and patient-centered care.

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