iJRASET
International Journal For Research in Applied Science and Engineering Technology



INTERNATIONAL JOURNAL FOR RESEARCH

IN APPLIED SCIENCE & ENGINEERING TECHNOLOGY

Volume: 14 **Issue:** I **Month of publication:** January 2026

DOI: https://doi.org/10.22214/ijraset.2026.77025

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International Journal for Research in Applied Science & Engineering Technology (IJRASET)
ISSN: 2321-9653; IC Value: 45.98; SJ Impact Factor: 7.538
Volume 14 Issue I Jan 2026- Available at www.ijraset.com

Candida Species as Opportunistic Pathogens: Epidemiology, Virulence, Laboratory Diagnosis, and Antifungal Resistance

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Abstract: ***Candida species are among the most common opportunistic fungal pathogens affecting humans, particularly immunocompromised individuals. While* Candida albicans *has historically been the predominant etiological agent of candidiasis, recent epidemiological trends indicate a significant rise in infections caused by non-albicans Candida species, many of which exhibit intrinsic or acquired resistance to commonly used antifungal agents. These yeasts, which normally exist as commensals within the human microbiota, can transition to pathogenic forms under favourable host or environmental conditions. This review provides a comprehensive overview of the clinical and epidemiological features of Candida infections, with emphasis on laboratory diagnosis, virulence mechanisms, and antifungal resistance. Conventional and advanced diagnostic methods, including culture-based techniques, phenotypic tests, and molecular assays, are critically discussed. The growing challenge of antifungal resistance, biofilm-associated infections, and emerging multidrug-resistant species such as* Candida auris *is also addressed. Understanding these evolving dynamics is essential for improving patient outcomes, guiding antifungal therapy, and informing public health interventions.***

Keywords: Candida, candidiasis, antifungal resistance, laboratory diagnosis, non-albicans Candida

I. INTRODUCTION

Candida species are ubiquitous yeasts that form part of the normal human microbiota, colonising the skin, gastrointestinal tract, and mucosal surfaces of most healthy individuals. Under physiological conditions, host immune mechanisms and microbial competition prevent uncontrolled fungal proliferation. However, disruption of host immunity or microbiota balance can allow Candida to shift from a commensal to a pathogenic state, resulting in infections ranging from superficial mucocutaneous candidiasis to invasive and life-threatening systemic disease [1,2]. Globally, candidiasis represents a major burden on healthcare systems, particularly among immunocompromised populations such as patients with HIV/AIDS, malignancies, organ transplants, and those receiving intensive care [7,40,48]. In recent years, the epidemiology of candidiasis has evolved, characterised by increasing isolation of non-albicans Candida (NAC) species and the emergence of multidrug-resistant strains [5,7,51]. These changes have significant implications for diagnosis, treatment, and infection control practices. This review aims to synthesise current knowledge on Candida infections, focusing on epidemiology, virulence factors, laboratory diagnosis, antifungal susceptibility, and resistance, with the ultimate goal of enhancing clinical decision-making and patient outcomes.

II. TAXONOMY AND BIOLOGICAL CHARACTERISTICS OF CANDIDA

Candida belongs to the Kingdom Fungi, Phylum Ascomycota, Class Saccharomycetes, Order Saccharomycetales, and Family Saccharomycetaceae. Approximately 200 Candida species have been described, although only a limited number are commonly implicated in human disease [26].

Importantly, the genus Candida is polyphyletic, meaning that its members do not share a single common evolutionary ancestor. Molecular phylogenetic analyses have demonstrated that species such as *C. glabrata*, *C. guilliermondii*, and *C. lusitaniae* are more closely related to other genera than to *C. albicans*, necessitating ongoing taxonomic reclassification [27,28]. Despite their evolutionary divergence, these species share a pathogenic lifestyle, likely resulting from convergent evolution that enables colonisation and invasion of similar ecological niches within the human host.

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III. EPIDEMIOLOGY AND GLOBAL DISTRIBUTION

Candida infections are among the most common invasive fungal diseases worldwide, with candidemia being a leading cause of fungal bloodstream infections in hospitalised patients [7,40]. Surveillance studies from different geographical regions reveal marked variation in species distribution, influenced by healthcare practices, antifungal use, and patient demographics [39,45].

While *C. albicans* remains a major pathogen, a growing proportion of infections are attributed to NAC species such as *C. glabrata*, *C. parapsilosis*, *C. tropicalis*, *C. krusei*, and *C. auris* [41,42,44]. These species are frequently associated with antifungal resistance and poorer clinical outcomes. The emergence of *C. auris* as a global public health threat is particularly concerning due to its multidrug resistance, environmental persistence, and ability to cause hospital outbreaks [17,24,35].

IV. RISK FACTORS FOR CANDIDIASIS

Multiple host-related and healthcare-associated factors predispose individuals to Candida infections:

1) Immunosuppression and Neutropenia: Neutrophils play a critical role in fungal clearance; their depletion markedly increases susceptibility to invasive candidiasis [1,25].
2) HIV/AIDS: Oral and oesophageal candidiasis are common opportunistic infections in advanced HIV disease [2].
3) Cancer and Chemotherapy: Mucosal damage and immune suppression facilitate fungal translocation into the bloodstream [7].
4) Organ and Hematopoietic Stem Cell Transplantation: Long-term immunosuppressive therapy increases infection risk [1].
5) Broad-Spectrum Antibiotic Use: Disruption of bacterial flora promotes Candida overgrowth [50].
6) Indwelling Medical Devices: Catheters and prosthetic devices provide surfaces for biofilm formation [55].
7) Diabetes Mellitus: Hyperglycaemia enhances fungal growth and impairs immune responses [52].
8) Extremes of Age: Neonates and elderly individuals are particularly vulnerable due to immature or declining immunity [48].

V. VIRULENCE FACTORS OF CANDIDA SPECIES

Candida pathogenicity is mediated by a complex array of virulence determinants:

1) Morphological Plasticity: *Candida albicans* exhibits remarkable morphological flexibility, transitioning between yeast, pseudohyphal, and hyphal forms. Hyphae are particularly invasive and are associated with tissue penetration and immune evasion [25,27].
2) Adhesins and Invasins: Surface proteins facilitate adhesion to host tissues and abiotic surfaces, promoting colonisation and invasion [28].
3) Biofilm Formation: Biofilm formation on medical devices is a critical virulence trait, conferring protection against host immunity and antifungal agents. Biofilm-embedded cells can exhibit up to 1,000-fold increased resistance compared to planktonic cells [55].
4) Secreted Hydrolytic Enzymes: Candida secretes aspartyl proteases, phospholipases, lipases, and hemolysins that degrade host tissues and facilitate invasion [2,54].
5) Candidalysin: Candidalysin, a cytolytic peptide toxin produced by *C. albicans* hyphae, plays a key role in epithelial damage and immune activation during infection [25].

VI. LABORATORY DIAGNOSIS OF CANDIDA INFECTIONS

1) Culture-Based Methods: Sabouraud Dextrose Agar (SDA) remains the cornerstone for fungal isolation, supporting the growth of most Candida species [12–15]. Colonies typically appear smooth, creamy, and white to cream-coloured [8–11].
2) Chromogenic Media: CHROMagar Candida enables rapid presumptive identification based on species-specific colony pigmentation and is particularly useful for detecting mixed infections [18–23].
3) Microscopy and Phenotypic Tests: Gram staining reveals Gram-positive budding yeast cells with pseudohyphae or hyphae [29,30]. The germ tube test and chlamydospore formation are traditional methods for presumptive identification of *C. albicans*, though limitations exist due to overlap with other species [31–34].
4) Molecular Diagnostics: PCR-based assays, real-time PCR, and sequencing provide rapid, sensitive, and specific species identification, including detection of *C. auris* and resistant strains [35–37].

VII. ANTIFUNGAL SUSCEPTIBILITY AND RESISTANCE

Antifungal resistance has emerged as a major challenge in the management of candidiasis. Resistance mechanisms include target enzyme mutations, efflux pump overexpression, biofilm-associated resistance, and stress response adaptations [3,5,51].

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Species such as *C. glabrata*, *C. krusei*, *C. parapsilosis*, and *C. auris* frequently exhibit reduced susceptibility to azoles and, in some cases, echinocandins [38,42,44]. Antifungal susceptibility testing using broth microdilution methods is essential to guide therapy and monitor resistance trends [56,57].

VIII. TREATMENT AND PREVENTION STRATEGIES

Treatment selection depends on species identification, infection severity, and patient factors. Echinocandins are often first-line therapy for invasive candidiasis, while azoles remain important for mucosal infections [54]. Combination therapy, antifungal stewardship, infection control measures, and novel approaches targeting biofilms or host immunity are increasingly being explored [1,55,59].

Preventive strategies include catheter management, antibiotic stewardship, surveillance programs, and patient education, particularly in high-risk populations [40,49].

IX. DISCUSSION

The increasing burden of Candida infections, driven by changing epidemiology and antifungal resistance, represents a significant challenge to modern healthcare. Advances in diagnostic technologies have improved detection and species identification, yet timely diagnosis remains difficult in many settings. The rise of multidrug-resistant species underscores the importance of integrated diagnostic, therapeutic, and preventive strategies. Continued research into Candida virulence, host-pathogen interactions, and novel antifungal agents is essential for improving patient outcomes.

X. CONCLUSION

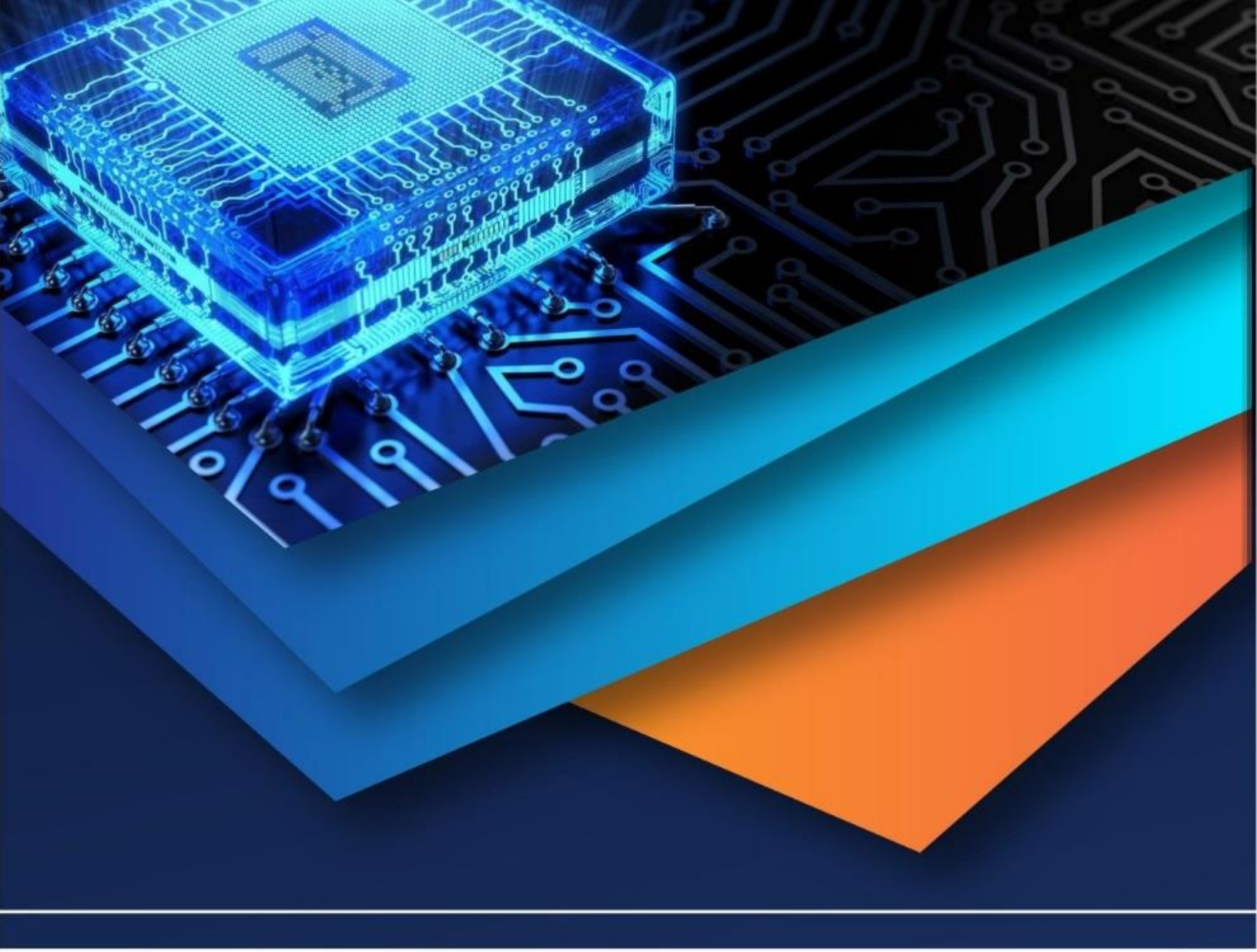
Candida species remain among the most important opportunistic fungal pathogens worldwide. The shift towards non-albicans species, increasing antifungal resistance, and emergence of highly resistant pathogens such as *Candida auris* demand heightened vigilance and ongoing research. Accurate diagnosis, species-level identification, and antifungal susceptibility testing are central to effective management. Future advances in diagnostics, therapeutics, and prevention will be critical in addressing the evolving challenges posed by Candida infections.

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