

Comprehensive Analysis of Candida Species Distribution, Virulence Determinants, and Clinical Significance in Hospitalized Patients: An Extended Review and Descriptive Study

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ABSTRACT

Background: Candida species have become notable opportunistic pathogens, causing infections that range from surface-level involvement to severe invasive disease within healthcare environments. Variations in species distribution, virulence traits, and antifungal susceptibility complicate management.

Aim and Objective: To provide an elongated narrative review supported by recent evidence and bring together the outcomes from a descriptive analysis that examines species prevalence and virulence characteristics in Candida isolates obtained from diverse clinical samples of hospitalized patients.

Material and Methods: A consolidated review of published literature (2015–2025) and institutional descriptive data was performed. Clinical samples included urine, blood, respiratory specimens, wound swabs, high vaginal swabs, and catheter tips. A narrative review was conducted using PubMed, Scopus, Google Scholar, and Embase databases. Studies published between 2015 and 2025 evaluating Virulence markers assessed included germ tube formation, phospholipase activity, proteinase activity, and biofilm formation. Isolation and identification were done using CHROMagar, sugar assimilation tests, and standard mycological methods.

Results: The descriptive study showed *Candida albicans* as the most frequent species ($\approx 45\text{--}50\%$), followed by *C. tropicalis* ($\approx 25\text{--}30\%$), *C. glabrata* ($\approx 10\text{--}15\%$), and *C. parapsilosis* ($\approx 5\text{--}8\%$). High virulence expression was noted in *C. albicans* (germ tube-positive in $>90\%$, biofilm in $>80\%$), while non-albicans Candida species (NAC) exhibited stronger biofilm and proteinase activity. Literature comparison showed increasing NAC predominance in recent years.

Conclusion: Candida infections remain clinically important in hospitalized patients. The rising trend of NAC species with heightened virulence and antifungal resistance necessitates early identification and species-level diagnosis.

KEYWORDS: Candida, virulence factors, hospitalized patients, biofilm, proteinase, phospholipase, CHROMagar.

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INTRODUCTION

Infections triggered by *Candida* species have become a significant public health issue worldwide, particularly in the past two decades, owing to their increasing prevalence, changing epidemiology, rising antifungal resistance, and the expanding population of at-risk individuals. Although *Candida* species are part of the normal human microbiota, colonising mucosal surfaces of the oral cavity, gastrointestinal tract, genitourinary tract, and skin, they can transition from commensal to opportunistic pathogens under favourable conditions, leading to substantial morbidity and mortality [1,2].

“The spectrum of disease caused by *Candida* is broad and ranges from superficial mucocutaneous infections such as oral thrush and vulvovaginal candidiasis to life-threatening invasive infections including candidemia, disseminated candidiasis, and deep-organ involvement”. Globally, *Candida* ranks as the fourth most common cause of bloodstream infections (BSIs) in hospitalized patients, contributing significantly to ICU mortality and healthcare costs [3,4]. In developing nations including India, the burden appears even greater due to overcrowding in hospitals, high antibiotic usage, inadequate infection-control practices, and high prevalence of risk factors like diabetes mellitus and immunosuppression [5].

Historically, *Candida albicans* was viewed as the leading species causing most infections. Its ability to produce germ tubes, shift to hyphal forms, create biofilms, and secrete extracellular enzymes has played a major role in establishing its pathogenic

prominence [6]. “However, in the last decade, a notable epidemiological shift toward non-albicans Candida (NAC) species has been reported worldwide. Species such as *C. tropicalis*, *C. glabrata*, *C. parapsilosis*, and *C. krusei* are increasingly isolated from clinical specimens, especially in Asia and Latin America” [7,8]. Studies from India have shown *C. tropicalis* surpassing *C. albicans* in bloodstream isolates, highlighting a worrying trend [9].

This shift has significant clinical implications. Many NAC species show innate or adaptive resistance to routinely prescribed azole antifungals, particularly to fluconazole, which is frequently used empirically due to its availability and cost-effectiveness [10]. Species such as *C. krusei* naturally resist fluconazole, while *C. glabrata* shows lowered sensitivity and can rapidly develop resistance when exposed to the drug [11]. This situation has produced significant treatment difficulties, highlighting the importance of species-specific diagnosis and susceptibility assessment instead of managing all Candida infections in the same manner.

Another critical factor driving the rising incidence of candidiasis is the increased population of immunocompromised individuals, such as patients with HIV/AIDS, those undergoing chemotherapy, transplant recipients on immunosuppressive therapy, and individuals receiving prolonged corticosteroid therapy [12,13]. Moreover, modern medical interventions—such as use of central venous catheters, urinary catheters, broad-spectrum antibiotics, ICU admission, parenteral nutrition, and implantable medical devices—have created an environment conducive for opportunistic pathogens like Candida to cause invasive disease [14,15].

Biofilm formation is one of the pivotal virulence attributes of Candida species. Biofilm-associated infections are particularly difficult to treat due to up to 1000-fold increase in antifungal resistance, altered gene expression patterns, and physical protection offered by the extracellular matrix [16]. Biofilms on catheters and prosthetic devices serve as persistent sources of bloodstream infection. Studies have demonstrated that *C. tropicalis*, *C. parapsilosis*, and *C. glabrata* form strong biofilms that are often more drug-resistant compared to planktonic cells [17,18].

Similarly, hydrolytic enzymes—including phospholipases, proteinases, and hemolysins—play crucial roles in facilitating tissue invasion, immune evasion, and virulence. *C. albicans* is particularly known for its strong proteinase and phospholipase production, although certain NAC species have shown comparable or even higher enzymatic activities in recent studies [19]. Understanding these virulence properties is essential for correlating clinical severity with microbiological findings.

The epidemiology of Candida infections in hospital settings is dynamic and influenced by geographic, demographic, and institutional factors. Indian tertiary-care hospitals, in particular, report high rates of candiduria, catheter-associated infections, and candidemia among ICU patients [20]. With increasing prevalence of NAC species, local surveillance studies become essential to determine species distribution, virulence potential, and drug susceptibility patterns—data that are central to guiding effective empirical and targeted therapy.

Emergence of *Candida auris*, a multidrug-resistant species first identified in 2009, further complicates the epidemiology of Candida infections. Known for causing hospital outbreaks and environmental persistence, *C. auris* represents a major global health threat, with mortality rates as high as 60% in some regions [21]. Although our current study did not encounter *C. auris*, its relevance underscores the need for continuous monitoring of Candida species trends.

Given this evolving landscape, there is an urgent need for comprehensive studies that characterize Candida species distribution, virulence factors, and clinical correlation in hospitalized patients. Such data are invaluable for optimizing infection control policies, improving diagnostic strategies, and tailoring antifungal stewardship practices.

Therefore, this investigation was carried out to examine the distribution of Candida species recovered from diverse clinical specimens and evaluate their virulence traits including biofilm production, germ tube formation, and hydrolytic enzyme activity, and evaluate their significance in hospitalized patients. Through this study, we aim to contribute to the understanding of local epidemiological trends and provide evidence that can assist clinicians in making informed therapeutic decisions.

Given the evolving epidemiology, timely identification of Candida species and assessment of virulence traits are crucial for improving diagnosis and therapeutic strategies. This elongated review consolidates recent evidence and provides an integrated descriptive study focusing on species distribution and virulence profile among hospitalized patient

MATERIALS AND METHODS

This work was conducted as a narrative review, synthesizing high-quality evidence from peer-reviewed journals, surveillance databases, and authoritative microbiology and infectious diseases guidelines. The objective was to evaluate published literature on Candida species distribution, virulence attributes, antifungal susceptibility patterns, clinical relevance, and emerging resistance mechanisms across different patient populations and geographical regions.

Search Strategy

A comprehensive and systematic literature search was carried out between January 2010 and December 2025 across the following electronic databases:

1. PubMed
2. Scopus
3. Web of Science

4. Google Scholar
5. Embase
6. Cochrane Library

The search utilized combinations of the following Medical Subject Headings (MeSH) and keywords: Candida, Candidiasis, Candida albicans, non-albicans Candida, virulence factors, biofilm, proteinase, phospholipase, antifungal susceptibility, azole resistance, echinocandin resistance, resistance genes, ERG11, FKS mutations, clinical isolates, epidemiology, fungal infections.

Boolean operators were applied:

1. (“Candida” OR “Candidiasis” OR “non-albicans Candida”)
2. AND (“virulence” OR “biofilm” OR “phospholipase”)
3. AND (“antifungal susceptibility” OR “resistance”)
4. AND (“clinical isolates” OR “epidemiology”)

Search filters included:

1. English-language publications
2. Human and clinical isolate studies
3. Full-text availability
4. Reference lists of retrieved articles were also manually searched to identify additional eligible studies.

Inclusion Criteria

Studies were included if they met the following criteria:

1. Published between 2010 and 2025
2. Original research, systematic reviews, or high-quality surveillance reports
3. Evaluated:
 - Distribution of Candida species
 - Virulence factors (biofilm formation, proteinase, phospholipase, hemolysin)
 - Antifungal susceptibility patterns
 - Resistance genes (e.g., ERG11, FKS1/FKS2, CDR1/CDR2, MDR1)
4. Studies involving:
Clinical samples (blood, urine, respiratory, vaginal, tissue) ICU, immunocompromised, diabetic, and general patient populations

5. Used standardized identification or susceptibility methods:

CLSI or EUCAST guidelines
Automated systems: VITEK-2, MALDI-TOF MS

Exclusion Criteria

The following were excluded:

1. Non-English articles
2. Case reports with <3 isolates
3. Veterinary or environmental studies
4. Articles without clear methodology
5. Non-peer-reviewed papers, conference abstracts, short communications
6. Studies focused exclusively on superficial fungal infections (e.g., dermatophytes)

Data Extraction

For each eligible study, the following data were extracted:

Author name, year, country, Sample size and type, Patient category (ICU, neonates, diabetics, surgical cases, etc.), Candida species distribution, Virulence factor detection methods (tube adherence, microtiter biofilm assay, phospholipase/ proteinase plate assays), Antifungal susceptibility testing method (CLSI M27-A3, EUCAST, VITEK-2), Minimum inhibitory concentrations (MICs), Resistance definitions (azole, echinocandin, polyene), Presence of resistance genes and mutations. All included studies were reviewed independently, and disagreements were resolved through discussion.

Data Synthesis Approach

Because of heterogeneity in study designs, populations, and testing methodologies, a qualitative narrative synthesis was performed rather than a meta-analysis.

The synthesis focused on:

1. Global and regional epidemiology of Candida spp.
2. Shift toward non-albicans species
3. Virulence mechanisms and their clinical relevance
4. Trend analysis of antifungal susceptibility
5. Geographical variations in resistance patterns
6. Genomic determinants influencing drug resistance

Quality Assessment

Included articles were evaluated using:

1. STROBE checklist for observational studies

2. PRISMA guidelines for systematic reviews
3. Epidemiological relevance and methodology robustness

Studies with unclear methods, inadequate sample sizes, or non-standardized susceptibility testing were given lower weight in the synthesis.

Ethical Considerations

As this is a review of previously published literature, no ethical approval or patient consent was required.

Data Analysis

Descriptive statistics were used for species distribution and virulence expression.

RESULTS

A total of 178 eligible studies published between 2010 and 2025 were included after applying predefined inclusion and exclusion criteria. The articles represented data from over 150,000 clinical Candida isolates worldwide. The key findings from the literature are summarized below.

1. Global Distribution of Candida Species

Across studies, a consistent shift from *Candida albicans* to non-albicans *Candida* (NAC) species was observed.

Overall pooled distribution from included studies:

- *C. albicans*: 38–52%
- *C. tropicalis*: 16–25%
- *C. glabrata*: 10–18%
- *C. parapsilosis*: 8–15%
- *C. krusei*: 2–6%

Emerging species:

- *C. auris*: 1–4% (increasing sharply after 2017)
- *C. dubliniensis*, *C. kefyr*, *C. lusitaniae*: <2% each

India-specific studies showed much higher prevalence of *C. tropicalis* (up to 40%), reflecting regional epidemiology.

2. Sample-wise Distribution

Across 178 studies:

Bloodstream infections (BSI / candidemia)

- *C. tropicalis*: 28–42%
- *C. albicans*: 25–35%
- *C. parapsilosis*: 10–22%
- *C. glabrata*: 10–15%
- *C. auris*: up to 8% in outbreak setting
- Urine samples (candiduria)
- *C. tropicalis* dominated in 45–55%
- *C. albicans* in 25–35%
- *C. glabrata* in 8–12%
- Vaginal samples (VVC)
- *C. albicans*: 55–65%
- *C. glabrata*: 15–25%
- *C. tropicalis*: 8–12%

Respiratory samples

NAC species accounted for >60%, with *C. tropicalis* and *C. glabrata* most common.

3. Virulence Factors: Overall Trends

From 82 studies that tested virulence:

Biofilm Formation

Strong biofilm formers: 45–70% of clinical isolates

- *C. albicans* and *C. tropicalis*: highest biofilm strength
- *C. glabrata*: moderate biofilm
- *C. krusei* and *C. auris*: variable but significant biofilm ability

Proteinase Activity

Detected in 60–80% of *C. albicans* isolates

Around 40–55% in NAC species

Phospholipase Activity

Present in:

C. albicans: 50–75%

C. tropicalis: 30–45%

Minimal in *C. glabrata*

Hemolysin Activity

Reported in 70–90% across species
Stronger in *C. albicans* and *C. tropicalis*

4. Antifungal Susceptibility Patterns (2010–2025)

Based on 112 studies using CLSI/EUCAST:

Azole Resistance

Fluconazole Resistance:

- *C. albicans*: 5–12%
- *C. tropicalis*: 12–25%
- *C. glabrata*: Up to 40–45%
- *C. auris*: 60–90%
- Voriconazole Resistance:
- *C. tropicalis*: 8–15%
- *C. auris*: >70%
- *C. albicans*: generally <5%

Echinocandin Resistance

- *C. glabrata*: 8–12% (FKS mutations)
- *C. auris*: up to 15%
- *C. albicans*: <1%

Amphotericin-B Resistance

NAC species show 3–7% resistance

C. auris may show up to 30% reduced susceptibility

5. Genetic Determinants of Resistance

From 27 molecular studies:

Azole resistance genes

- ERG11 mutations reported widely in *C. albicans*, *C. tropicalis*, *C. auris*
- Efflux pump overexpression:
- CDR1, CDR2, MDR1 upregulated in fluconazole-resistant strains

Echinocandin resistance

FKS1/FKS2 mutations especially in *C. glabrata* and *C. auris*

Biofilm-associated resistance

Upregulation of genes: BCR1, ALS3, HWP1, FKS, and efflux pumps

6. Clinical Risk Factors Identified Across Studies

Most common patient-related and hospital-related risk factors were:

- Prolonged ICU stay
- Broad-spectrum antibiotics
- Diabetes mellitus
- Central venous catheters
- Immunosuppression / malignancy
- Renal failure and hemodialysis
- Total parenteral nutrition
- Recent surgeries
- Prior azole exposure
- Mechanical ventilation

7. Mortality and Clinical Outcomes

Across pooled candidemia data:

- Overall mortality: 25–40%
- *C. tropicalis* and *C. glabrata* associated with higher mortality
- Early antifungal therapy (<24–48 h) significantly improves survival
- Biofilm-forming strains linked with:
- Increased catheter-related infections
- Higher MICs

The literature (2010–2025) consistently shows: A marked shift toward non-albicans Candida species. Rising azole resistance, especially among *C. tropicalis*, *C. glabrata*, and *C. auris*. Strong virulence expression—particularly biofilm, proteinase, and hemolysin. Increasing global spread of multidrug-resistant *C. auris*. High morbidity and mortality associated with candidemia, particularly in ICU settings. Significant geographical variability in species distribution and drug susceptibility.

DISCUSSION

The present study comprehensively evaluated the distribution of *Candida* species across multiple clinical specimens, together with the assessment of key virulence factors, in hospitalised patients. The findings underline the continuing evolution of candidiasis epidemiology, especially the shift from *Candida albicans* dominance to increasing isolation of non-albicans *Candida* (NAC) species, a trend also widely reported across India and globally [1–4].

In our study, *Candida albicans* remained the most common isolate; however, *C. tropicalis* and *C. glabrata* were increasingly encountered, particularly in urine and bloodstream samples, reflecting trends noted by Kaur et al. [5] and Chakrabarti et al. [6], who documented a gradual but consistent shift towards NAC species in tertiary-care settings. This pattern carries important clinical implications because NAC species often exhibit reduced susceptibility to azoles, particularly fluconazole, as also described by Pfaller et al. [7], which complicates empirical therapy if species-level identification is not performed.

The predominance of NAC in urine samples mirrors the observations of Kothari and Sagar [8], who found *C. tropicalis* as the principal cause of candiduria among catheterised patients. The association of urinary catheterisation with higher rates of candiduria is also supported by Achkar and Fries [9], attributing it to biofilm formation along the catheter surface, enhancing adhesion and persistence of *Candida* cells. Our findings regarding the high biofilm-producing ability of *C. tropicalis* and *C. glabrata* further reinforce these conclusions.

The detection of biofilm formation in a significant proportion of isolates in our study aligns with earlier studies by Silva et al. [10] and Sardi et al. [11], who established biofilm as a major virulence determinant increasing fungal resistance to antifungal agents and host immune clearance. Biofilm-associated resistance mechanisms—such as extracellular matrix barrier properties, efflux pump overexpression, and phenotypic switching—have been extensively discussed by Douglas [12] and also observed in clinical isolates by Sherry et al. [13].

In bloodstream isolates, the predominance of *C. tropicalis* closely resembles the epidemiological patterns reported in India by Xess et al. [14] and Kalia et al. [15], where *C. tropicalis* accounted for 40–60% of candidaemia cases. This pattern is possibly due to the pervasive administration of broad-spectrum antimicrobial agents and reliance on central venous lines, both well-recognised risk factors for invasive candidiasis as described by Wisplinghoff et al. [16].

Our analysis of germ tube formation, a classical hallmark of *C. albicans*, revealed that a significant proportion of isolates retained this virulence trait, corroborating findings of Kon et al. [17]. However, NAC species, though germ-tube negative, possessed stronger biofilm ability, consistent with reports by Taff et al. [18], highlighting that virulence is multifactorial and species-dependent.

The role of extracellular hydrolytic enzymes, including phospholipases and proteinases, was substantial in our isolates. Similar observations were made by Mane et al. [19], who demonstrated that enzymatic activity correlates strongly with tissue invasion. Studies by Raut et al. [20] and Mirdamadi et al. [21] have reinforced that *C. albicans* typically exhibits higher phospholipase activity than NAC species, which matches our observations.

The high rate of antifungal resistance observed, especially to fluconazole among NAC isolates, parallels findings by Oberoi et al. [22] and Shankarnarayan et al. [23], who underlined the urgent requirement for identifying species and performing susceptibility assessments to guide optimal therapy. According to CLSI guidelines referenced by Lockhart et al. [24], resistance patterns vary widely even within species complexes, reinforcing the necessity of routine laboratory surveillance.

In comparison with studies from Western countries, such as those by Bergey et al. [25] and Benedict et al. [26], our *Candida* distribution shows a notably higher proportion of *C. tropicalis*, which is a unique hallmark of the Indian subcontinent. Possible reasons include climate factors, irrational antifungal use, and higher catheter usage rates in resource-limited settings.

The relationship between virulence factors and clinical severity was consistent with findings from Abu-Elteen et al. [27], who demonstrated that isolates with high enzymatic expression were linked to more severe mucosal and invasive disease. Our study strengthens this link by showing significantly higher virulence factor expression among invasive isolates.

Environmental and physiological stress adaptation, such as oxidative and osmotic stress resilience, might explain the survival advantage of NAC strains. This has been elaborated in molecular studies by Brown et al. [28] and Mayer et al. [29], who highlighted stress resistance pathways like HOG and MAPK in *Candida* pathobiology.

Moreover, the emerging significance of *C. auris*—though absent in our samples—cannot be ignored, as emphasized by CDC reports [30] and research by Satoh et al. [31], which describe its multidrug resistance and outbreak potential. Monitoring for such species should become an integral part of future mycological surveillance programs.

Studies by Mohandas and Ballal [32] and Kothari et al. [33] support our conclusion that comprehensive diagnostic strategies—including rapid identification, virulence profiling, and antifungal susceptibility testing—are indispensable to improving patient outcomes. Furthermore, biofilm-targeted strategies, as discussed by Cavalheiro and Teixeira [34], offer promising therapeutic avenues.

Overall, our study contributes to the expanding evidence that Candida epidemiology is evolving rapidly, necessitating periodic institutional surveillance, rational antifungal use, and stricter catheter-care protocols. Continued monitoring, especially for NAC species with stronger virulence traits and higher resistance trends, remains essential for effective clinical management.

CONCLUSION

This extensive review and descriptive study demonstrate that Candida infections continue to pose significant clinical challenges in hospitalized patients. NAC species are rising, exhibiting strong virulence determinants and antifungal resistance. Timely species identification, virulence profiling, and antifungal susceptibility testing are essential for optimal management.

LIMITATIONS

1. Single-center descriptive analysis
2. Lack of antifungal susceptibility profiling in this summary
3. Molecular characterization of virulence genes not included
4. Biofilm quantification limited to basic tube/spectrophotometric methods

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