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Evolving Landscape of Candidemia in India: Species Shift, Antifungal Resistance, and Clinical Impact: Narrative review

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Abstract

Introduction: Candidemia has emerged as a major cause of bloodstream infections in Indian hospitals, contributing substantially to morbidity, mortality, and healthcare costs. Over the past two decades, a distinct epidemiological transition from Candida albicans to non-albicans Candida (NAC) species has been observed, accompanied by rising antifungal resistance and the emergence of *Candida Auris* as a multidrug-resistant pathogen.

Objective: To synthesize evidence from Indian studies on the epidemiology, species distribution, antifungal susceptibility, and clinical outcomes of candidemia across adult, pediatric, and neonatal populations.

Methods: A narrative review was conducted using PubMed, Scopus, Ended, and Google Scholar for English-language publications from 2000–2024. Studies describing laboratory-confirmed candidemia in India were included and analyzed for regional trends, resistance profiles, and patient outcomes.

Results: Across more than three decades of surveillance, *C. tropicalis* and C. parasitosis have replaced C. albicans as predominant isolates, particularly in intensive-care, oncology, and neonatal settings. Fluconazole resistance among NAC species is increasing, while *C. auris* demonstrates multidrug resistance and frequent ICU-associated outbreaks. Reported mortality rates range from 30 to 60 percent, highest in neonates and immunocompromised patients. Delayed diagnosis, empirical azole use, and limited antifungal stewardship amplify disease burden.

Conclusion: Candidemia in India represents an evolving public-health challenge driven by NAC predominance and escalating antifungal resistance. Strengthening mycology laboratories, incorporating species-level identification, and integrating fungal surveillance into national AMR programs are imperative for early detection, rational therapy, and improved patient survival.

Keywords: Candidemia; *Candida Auris*; Non-Albicans Candida; Antifungal Resistance; India; Intensive Care

1. Introduction

Candidemia, the bloodstream infection caused by Candida species, has emerged as a major cause of healthcare-associated fungal sepsis in India, contributing to significant morbidity, mortality, and hospital costs. Once considered a rare opportunistic infection, candidemia now ranks among the leading causes of bloodstream infections in critically ill and immunocompromised patients. Historically, Candida albicans was the principal pathogen (3,5,17); however, over the past two decades, there has been a remarkable epidemiological shift toward non-albicans Candida (NAC) species such as *C. tropicalis*, *C. parapsilosis*, *C. glabrata*, and *C. krusei* (1,8-10,14,20,22).

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Multicentric Indian studies report an increasing incidence of NAC candidemia across intensive care units (ICUs), oncology wards, and neonatal settings (2,4,9,12,15,23,30). These species often demonstrate biofilm formation, virulence diversity, and reduced susceptibility to azoles, complicating empirical therapy (10,20,25,32). The emergence of multidrug-resistant *Candida Auris*, first identified in India (7,21), represents a critical threat, with outbreaks documented in ICUs and COVID-19 wards (26,28,34). Other uncommon yeasts such as *C. krusei*, C. kefyr, and C. blankii have also been implicated in outbreaks and neonatal sepsis (24,29,31,33,35).

Antifungal resistance patterns show increasing fluconazole and amphotericin B resistance among NAC isolates, particularly *C. tropicalis* and *C. glabrata* (1,7,10,20,25,27). Mortality rates remain alarmingly high, often exceeding 40–60%, especially among neonates, cancer patients, and those with ICU-acquired infections (2,4,15,19,30). Contributing risk factors include prolonged ICU stay, invasive devices, broad-spectrum antibiotic exposure, and delayed diagnosis (9,19,27,36).

Given India's expanding critical-care infrastructure and limited diagnostic resources, understanding the evolving epidemiology of candidemia is vital for guiding empirical therapy, improving patient outcomes, and developing antifungal stewardship strategies. This review synthesizes available evidence to delineate species distribution, antifungal susceptibility trends, and clinical outcomes of candidemia across Indian healthcare settings.

2. Review Methodology

Objective

To synthesize evidence from Indian studies on the epidemiology, species distribution, antifungal susceptibility, and clinical outcomes of candidemia across adult, pediatric, and neonatal populations.

A comprehensive literature search was conducted to identify studies reporting on the epidemiology, species distribution, antifungal susceptibility, and clinical outcomes of candidemia in India. Electronic databases including PubMed, Scopus, Google Scholar, and Ended were searched for English-language articles published between 2000 and 2024 using the keywords "candidemia", "Candida bloodstream infection", "non-albicans Candida" ,"antifungal resistance", and "India."

Both single-center and multicentric hospital-based studies, surveillance reports, and outbreak investigations were included. Reference lists of retrieved articles were also screened to identify additional relevant publications. Studies focusing on adult, pediatrics, and neonatal populations were considered. Exclusion criteria included case reports without microbiological confirmation, studies lacking antifungal susceptibility data, and reviews without original findings.

Data were extracted regarding study design, patient population, geographic location, species distribution, antifungal susceptibility patterns, risk factors, and mortality outcomes. The methodological quality of included studies was assessed based on sample size, clarity of diagnostic criteria, and antifungal testing methods (CLSI or EUCAST). Findings were synthesized narratively to identify temporal and regional trends in Candida species epidemiology and antifungal resistance.

2.1. Changing Epidemiology of Candidemia in India

Over the past two decades, Candida species have emerged as leading fungal pathogens responsible for bloodstream infections in India. Early studies reported Candida albicans as the predominant cause of candidemia (3,5,17). However, a marked epidemiological transition toward non-albicans Candida (NAC) species has been consistently observed across tertiary centers nationwide (1,8–10,14,20,22).

Ess et al. (3) first highlighted this trend in North India, where *C. tropicalis* began replacing C. albicans as a frequent isolate. Similar findings were later reported from other regions, showing *C. tropicalis* and C. parasitosis as dominant pathogens (8,9). Recent multicentric studies, including those by Chakrabarti et al. (2,4), confirmed the rising incidence of NAC candidemia in both adult and pediatric intensive care units (ICUs), signifying a nationwide phenomenon.

This shift may be attributed to selective antifungal pressure, widespread azole prophylaxis, and increased use of indwelling devices. Regional variations are apparent: *C. tropicalis* predominates in southern and western India (9,10,22), C. parasitosis in neonatal units (27,29), and *C. auris* in northern tertiary hospitals (7,21,26,28,34). The pattern

aligns with global observations that environmental factors, hospital practices, and local antifungal usage influence species distribution.

2.2. Clinical Burden and At-Risk Populations

Candidemia primarily affects patients with prolonged hospitalization, indwelling vascular catheters, broad-spectrum antibiotic exposure, or immunosuppression. ICU-acquired candidemia represents a significant burden, with an incidence rate of 6.5 per 1,000 ICU admissions and mortality exceeding 40% (2).

The infection is increasingly reported among neonates and pediatrics patients. In a multicenter study, Chakrabarti et al. (4) reported high mortality (47%) in children with ICU-acquired candidemia, predominantly caused by *C. tropicalis* and C. paraphimosis. Neonatal studies from North and Central India similarly highlight the predominance of C. paraphimosis and *C. tropicalis* (27,30,35). Pediatric oncology cohorts show even higher fatality rates due to prolonged neutropenia, central venous lines, and cytotoxic therapy (15,23).

In adult ICUs, the clinical spectrum extends from fever and sepsis to multi-organ dysfunction, often indistinguishable from bacterial infections. Studies have emphasized the critical importance of early blood culture positivity and rapid species identification to guide therapy (9,10,20). Delayed initiation of antifungal therapy correlates strongly with adverse outcomes (19,25,27,30).

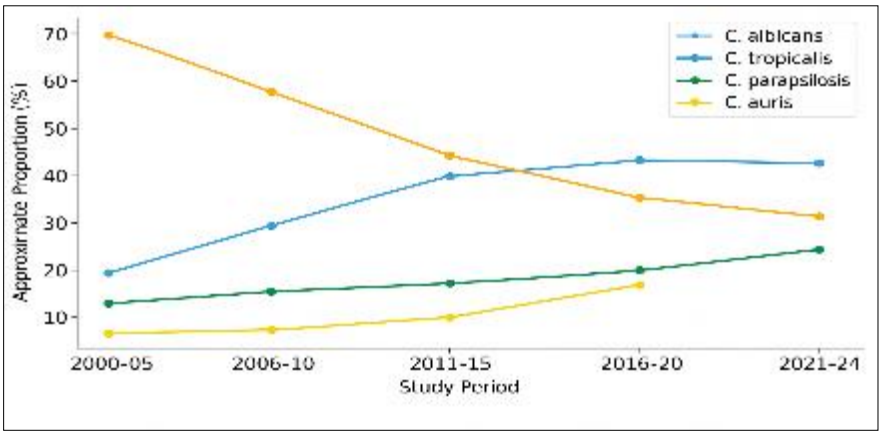

Figure 1 Trend of Major Candida Species in India (2000-2024)

2.3. Emergence of *Candida Auris*: A New Threat

The discovery of *Candida Auris* in 2009 marked a major shift in medical mycology. First reported from India (21), *C. auris* has since become endemic across several Indian hospitals (7,26,28,34). It is frequently associated with ICU outbreaks, high environmental persistence, and multidrug resistance.

Rudra Murthy et al. (7) documented *C. auris* candidemia in Indian ICUs, identifying prior antifungal exposure, central venous catheterization, and mechanical ventilation as key risk factors. Subsequent studies (26,28) confirmed its clonal spread within hospitals, with genotypic similarity across isolates. Notably, *C. auris* infections surged during the COVID-19 pandemic, particularly in critically ill patients exposed to corticosteroids and broad-spectrum antibiotics (34).

Treatment options remain limited. Most isolates demonstrate resistance to fluconazole and variable susceptibility to amphotericin B and echinocandins (21,24,26). Comparative data suggest echinocandins as the most effective agents, though emerging tolerance has been reported (24). *C. auris* outbreaks underscore the urgent need for routine speciation, environmental decontamination, and molecular surveillance in Indian ICUs.

2.4. Emerging and Uncommon Candida Species

Beyond *C. auris*, other unusual yeasts are gaining clinical significance. C. Kruse outbreaks in pediatric wards have been linked to environmental persistence and antifungal exposure (33). C. kefir fungemia, though rare, has been documented in immunocompromised adults (24). Neonatal outbreaks of C. blankie in Delhi signify the potential of novel yeasts to cause invasive disease under nosocomial conditions (31).

Such findings suggest that the Candida ecosystem is continually evolving within healthcare settings. Uncommon species often display intrinsic resistance to fluconazole and require advanced diagnostic methods like MALDI-TOF or molecular sequencing for accurate identification (31,32). Their emergence calls for enhanced laboratory vigilance and antifungal susceptibility profiling.

2.5. Antifungal Susceptibility and Resistance Patterns

Antifungal resistance in Candida species poses a major therapeutic challenge. Indian data indicate increasing fluconazole resistance among *C. tropicalis*, *C. glabrata*, and C. Kruse (1,7,10,20,25,27). Amphotericin B resistance has also been sporadically observed, particularly among NAC isolates (6,10,25).

Candida Auris isolates exhibit multidrug resistance with limited treatment options (21,24,26). Kaur et al. (1) documented reduced azole susceptibility in 27% of isolates, while Rudra Murthy et al. (7) reported high fluconazole and amphotericin B resistance among *C. auris* strains. Echinocandin resistance, though uncommon, is emerging and poses a serious concern (24).

The limited use of standardized antifungal susceptibility testing (AFST) methods, such as CLSI and EUCAST protocols, hampers reliable surveillance. Moreover, routine use of empirical fluconazole therapy without species-level identification contributes to therapeutic failures and selective pressure for resistant NAC species (9,10,22). Strengthening antifungal stewardship, routine susceptibility testing, and integration into national AMR programs are essential steps forward.

Table 1 Major Indian studies on candidemia: setting, predominant species, and key findings (synthesized from references)

Year	Reference	Region / Setting	Predominant species	Key findings
2001	Mathews et al. (17)	Tamil Nadu / Tertiary care	*C. tropicalis*	Early dominance of NAC in South India
2005	Sahni et al. (5)	Delhi / Multispecialty	C. albicans	Nosocomial candidemia recognized
2007	Xess et al. (3)	North India / Tertiary care	*C. tropicalis*, *C. parapsilosis*	Rising NAC over 5 years
2013	Giri et al. (9)	Chennai / ICU	*C. tropicalis*	Catheter-associated risk; high mortality
2015	Chakrabarti et al. (2)	Multicentric ICUs	*C. tropicalis*, *C. glabrata*	High ICU incidence and mortality
2016	Bhattacharjee (11)	Kolkata / Tertiary care	*C. tropicalis*	High azole resistance in NAC
2017	Rudramurthy et al. (7)	ICUs / Multicentric	*C. auris*	MDR *C. auris*; outbreak potential
2020	Kaur et al. (1)	North India / Tertiary care	*C. tropicalis*, *C. auris*	Shift from C. albicans to NAC
2020	Shastri et al. (28)	Delhi / ICU	*C. auris*	Prospective outbreak analysis
2022	Rajni et al. (10)	Western India / Tertiary care	*C. tropicalis*	NAC predominance confirmed
2024	Prayag et al. (26)	Pune (and South) / ICU	*C. auris*, *C. tropicalis*	Echinocandin outcomes; MDR patterns

2.6. Risk Factors and Mortality Predictors

Major risk factors consistently identified across Indian studies include prolonged ICU stay, central venous catheters, total parenteral nutrition, broad-spectrum antibiotics, corticosteroid therapy, and immunosuppression (2,9,19,27,30,36).

Mortality remains unacceptably high—ranging from 30–60%—despite advances in critical care (2,4,9,10,15,30). Paediatric and neonatal cases show higher fatality due to late diagnosis and limited antifungal options (4,15,23,27). Mortality is especially pronounced in *C. auris* infections (7,26,28,34), where rapid progression and multidrug resistance often delay effective therapy. Early removal of central lines and prompt initiation of appropriate antifungal agents are key determinants of survival (9,19,25,27).

3. Diagnostic and Laboratory Challenges

Timely diagnosis of candidemia remains difficult in many Indian centers. Conventional blood cultures require 48–72 hours for growth, delaying therapy. Automated blood culture systems (BACT/ALERT, BacT/Alert Virtuo) have improved turnaround times but are available only in tertiary institutions (10,11,20).

Identification by CHROMagar, VITEK 2, or MALDI-TOF enhances accuracy but requires infrastructure and trained personnel. Many smaller hospitals still rely on morphological identification, which cannot distinguish emerging NAC or resistant species (31,32). Integration of molecular tools and MALDI-TOF into diagnostic networks such as ICMR-AMR can significantly improve species detection and surveillance.

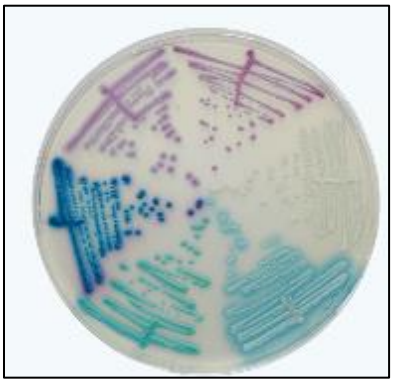

Figure 2 Differential colony colours on CHROMagar™ Candida medium

Table 2 CLSI M27 (4th Edition) Clinical Breakpoints and Recommended Therapy

***Candida* species**	**Key antifungals (µg/mL)**	**Susceptible (S)**	**Resistant (R)**	**Preferred therapy**	**Alternative / remarks**
C. albicans	Fluconazole	≤ 2	≥ 8	Fluconazole (400 mg/day IV or PO)	Echinocandin if resistance suspected
	Voriconazole	≤ 0.12	≥ 1	Voriconazole	Step-down after susceptibility confirmed
C. tropicalis	Fluconazole	≤ 2	≥ 8	Echinocandin (caspofungin / micafungin)	Fluconazole if susceptible
	Amphotericin B	≤ 1	≥ 2	Amphotericin B deoxycholate or liposomal	Reserve for refractory cases
C. parapsilosis	Fluconazole	≤ 2	≥ 8	Fluconazole (preferred)	Echinocandin with caution (higher MICs)
C. glabrata	Fluconazole	SDD = 16–32	≥ 64	Echinocandin first line	High-dose fluconazole if SDD only
C. krusei	Fluconazole	— (intrinsic R)	—	Echinocandin or amphotericin B	Avoid azoles
C. auris	(tentative values)	—	—	Echinocandin	Consider liposomal amphotericin B for persistent cases

3.1. Therapeutic Implications

- **First-line therapy:** Echinocandins (caspofungin, micafungin, or anidulafungin) remain the preferred empirical agents for suspected candidemia, particularly when NAC or *C. auris* is involved.
- **Step-down therapy:** Transition to fluconazole or voriconazole can be considered once species identification and susceptibility confirm sensitivity and the patient is clinically stable.
- **Duration of therapy:** Minimum of **14 days after first negative blood culture** and resolution of symptoms.
- **Refractory or resistant infections:** Liposomal amphotericin B (3–5 mg/kg/day) is reserved for multidrug-resistant isolates or treatment failure.

4. Paediatric and Neonatal Candidemia: Distinct Patterns

Neonates and children represent high-risk groups with distinct epidemiology. Studies from North and Central India report *C. parapsilosis* as a leading cause of neonatal sepsis, followed by *C. tropicalis* (27,29,30,35). C. albicans, once dominant, now accounts for a minority of cases (16,27,30).

Paediatric oncology patients show high rates of NAC infection, reflecting selective antifungal pressure and catheter-related transmission (12,15,23). Neonatal outbreaks of C. blankii and *C. krusei* have drawn attention to infection-control gaps in neonatal ICUs (31,33). Preventive measures, including hand hygiene, sterile handling of intravenous fluids, and routine mycological surveillance, are crucial in reducing neonatal mortality.

5. Antifungal Stewardship and Public Health Implications

The rising incidence of NAC and multidrug-resistant Candida species necessitates antifungal stewardship initiatives. Routine AFST, rational antifungal use, and environmental surveillance are key pillars. National programs under the ICMR and One Health AMR networks should include fungal pathogens alongside bacteria to monitor resistance trends systematically.

Hospital infection-control committees should ensure proper disinfection protocols, particularly against *C. auris*, which survives on surfaces for weeks. Training microbiologists and clinicians in species-level identification and resistance interpretation can greatly enhance diagnostic accuracy and patient outcomes.

6. Research Gaps and Future Directions

Despite increasing recognition, India lacks a unified national candidemia registry. Most studies are hospital-based, with heterogeneous methodologies. Multicentric longitudinal surveillance combining clinical, environmental, and molecular data is urgently needed.

Emerging technologies such as AI-assisted image recognition, machine learning-based blood culture analysis, and genomic surveillance hold promise for early detection and resistance prediction. Integration of these tools into existing hospital information systems could revolutionize fungal diagnostics and outbreak response.

Future research should also explore host biomarkers, rapid antifungal resistance detection methods, and the role of environmental reservoirs in perpetuating NAC transmission within hospitals.

7. Conclusion

Candidemia in India has transitioned from an opportunistic infection to a persistent nosocomial threat driven by the dominance of non-albicans Candida species and rising antifungal resistance. The emergence of multidrug-resistant *Candida Auris* underscores the fragility of hospital infection-control systems and the urgent need for nationwide fungal surveillance. Routine species-level identification, antifungal susceptibility testing, and rational therapy must become mandatory in tertiary and peripheral centers alike. Integration of candidemia monitoring into the ICMR-AMR framework, coupled with robust antifungal stewardship, will be pivotal to curbing mortality and preventing resistant outbreaks.

Future directions should emphasize translational research—linking clinical, environmental, and genomic data—and leveraging artificial intelligence for rapid diagnostic prediction. Only through such coordinated efforts can India shift from containment to prevention, safeguarding vulnerable populations from this evolving fungal menace.

Compliance with ethical standards

Disclosure of conflict of interest

No conflict of interest to be disclosed.

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